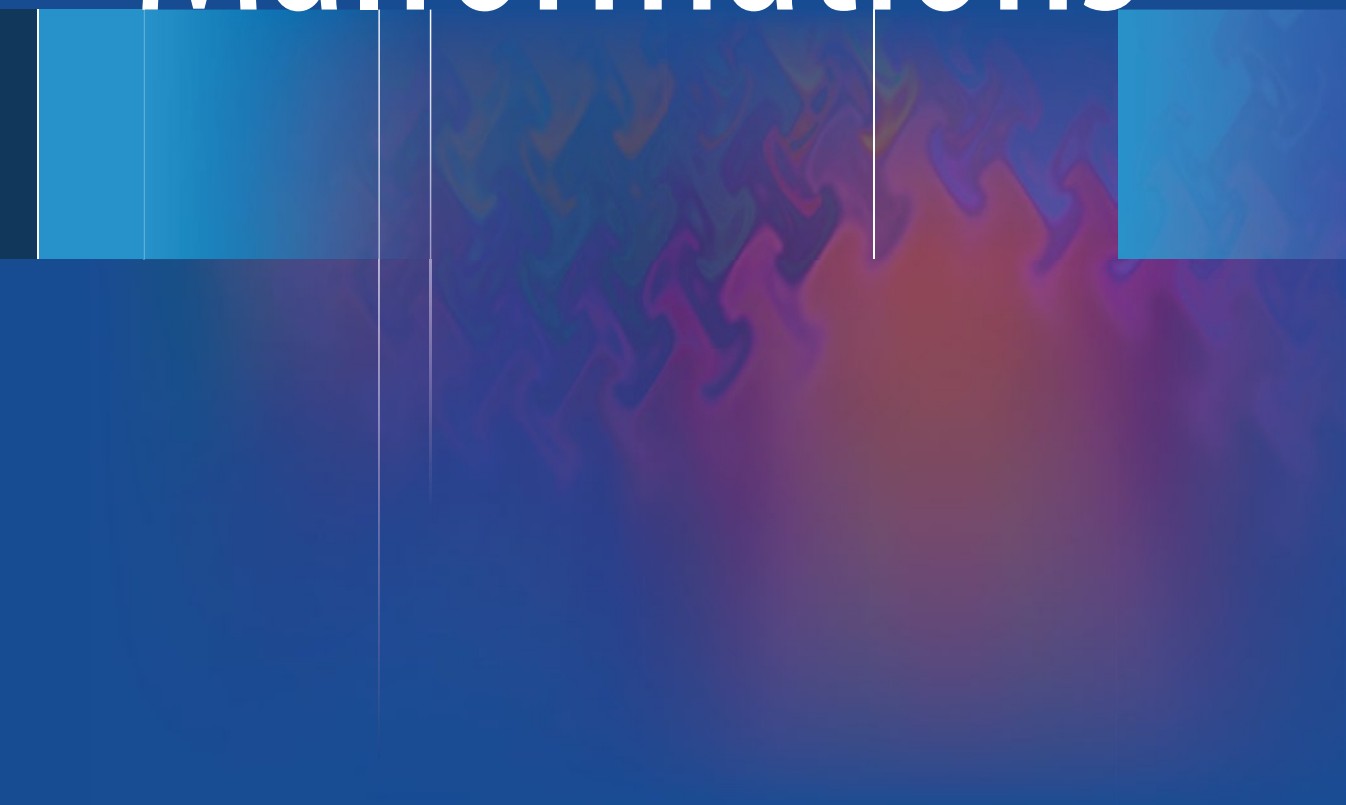
R. Shane Tubbs
W. Jerry Oakes
Editors

The Chiari Malformations



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We would like to dedicate this book to the patients who have collectively given us knowledge on the spectrum of Chiari malformation. Additionally, this book is written in the memory of Dr. Cornelis Joachimus van Houweninge Graftdijk who pioneered decompression for hindbrain herniation and his son Mr. Willem Aris van Houweninge Graftdijk and granddaughter Ms. Evelien van Houweninge Graftdijk who helped remind us of his story.

We thank our wives and children for their patience and support of our academia.

R. Shane Tubbs
W. Jerry Oakes

Foreword

The history of the Chiari malformation is long and interesting with the interest growing in each succeeding year. Thought to be rare when first described by Chiari in 1890, the increasing recognition can be partly attributed to the advent of magnetic resonance imaging. But instead of clarification, the visualization and accurate description made possible by this diagnostic tool has only brought forth new manifestations of the process and new controversies over management. The titles of the 34 chapters in this volume exemplify and are meant to clarify these controversies. Who to treat, when to treat, and how to treat are the primary problems, but the numerous variations of the theme such as syringomyelia, scoliosis, and associated bony abnormality are of great importance.

All these issues are presented and discussed and various solutions are brought forward. The authors are the world's experts.

John A. Jane, Sr., MD, PhD, FRCS(C)

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Introduction and Classification of the Chiari Malformations

1

R. Shane Tubbs and W. Jerry Oakes

Abstract

Once an uncommon clinical finding, the Chiari malformations are now frequently seen with the advent of more sophisticated imaging modalities. With over 100 years of experience with these entities, we currently have a much better understanding of their embryology and pathophysiology. However, many gaps still exist in our knowledge of the Chiari malformations. Long-term outcome studies are becoming more prevalent and patients are commonly operated on with generally favorable results. Since their original classification, the Chiari malformations have grown to include smaller subsets. Herein, we focus on the two most common forms of hindbrain herniation, the Chiari I and II malformations. As with any rapidly changing field, knowledge of the natural history of the untreated condition is essential before recommending intervention.

Since the original description and classification of hindbrain hernias more than 120 years ago, the Chiari malformations have revealed much of their pathophysiology and have become easily diagnosed radiologically. Patients are commonly operated on with generally favorable results. We once thought their clinical presentation was easily understood, but as time has shown the edges of the clinical issue, the indications for surgical intervention in some patient groups have become somewhat clouded and blurred. The natural history of a patient with 5 mm hindbrain hernia and a non-Valsalva-induced frontal headache is unlikely to improve with a Chiari decompression. With the availability of MRI, more and more patients are being labeled with the diagnosis but without symptoms or appropriate symptoms. Because so much progress has been made with our understanding of these conditions, their radiologic definition, details of operative intervention, and prediction of outcome, we feel justified in presenting this text devoted to this fascinating group of conditions.

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Toward the end of the nineteenth century, Professor Hans Chiari developed a classification system that is still used today. He described four types of patients based on postmortem dissection studies. This text will focus on the first two types and their variants. *Type I Chiari malformations* (*CIM*) are patients without neural tube defects who have the cerebellar tonsils move through the foramen magnum. Radiologically, significant caudal displacement is considered to be more than 5 mm. The brain stem remains within the posterior fossa and there may or may not be the development of a syrinx. *Type II Chiari malformations* (*CIIM*) are seen exclusively in patients who have a neural tube defect and have caudal displacement of the cerebellar vermis and lower brain stem. This movement is thought to occur in utero prior to the full development of the cerebellar tonsils. There are many other associated central nervous system anomalies seen with the CIIM. The vast majority of these patients have raised intracranial pressure and hydrocephalus. The relationship of the hindbrain hernia and hydrocephalus in itself is complex. *Type III Chiari malformations* are a rare and extreme form of hindbrain hernia where a portion of the cerebellum and brain stem migrate out of the craniocervical junction through a defect in the dura, skull, and soft tissue layers to present as a mass or sac on the back of the neck. The infants may be viable, and the surgeon will need to amputate nonfunctional nervous tissue without damage to vital medullary function. These lesions will not be discussed in any further detail because of their rarity and limited potential for the surgeon to improve the situation other than the closure of the skin to prevent infection and minimize trauma and drying of vital brain structures. *Type IV Chiari malformations* were originally thought to be part of the hindbrain spectrum where the cerebellum was hypoplastic or absent. This group of patients is also uncommon, usually has no therapeutic options available, and is not appropriate to be considered with the hindbrains hernias. They too will not be considered further.

More recently, two other subtypes of patients have been described. *Chiari 0 malformations* are individuals without a hindbrain hernia or one that is minimal (less than 5 mm) but have a "crowded" appearance of the craniocervical junction and have a syrinx that develops as a consequence of the lack of free and easy CSF movement across this area. Posterior fossa decompression with duraplasty may totally resolve the syrinx and associated symptoms if CSF egress from the fourth ventricle can be reestablished. *Chiari 1.5 malformations* are a hybrid of some aspects of the CIM and some of the CIIM. They are not associated with neural tube defects, but have significant caudal movement of the cerebellar tonsils and brain stem. Their symptoms and outcomes are more challenging than patients without caudal brain stem displacement.

One of the most impressive aspects of these entities has been the evolution of our understanding of the mechanism of their development. As recently as 1979, major neurology texts [1] have grouped the Chiari malformations and syringomyelia into the degenerative section and mentioned possible treatment with radiation therapy. Since that time, a pressure differential theory has been introduced and surgical decompression become commonplace.

We have elected to include a chapter on non-hindbrain hernia related syrinx development. This decision was made to help the reader appreciate the differential diagnosis of any patient with a syrinx and to underscore the large number of other causes, which must be excluded before assuming the syrinx is due to a minimal hindbrain hernia.

As with any rapidly changing field, knowledge of the natural history of the untreated condition is essential before recommending intervention. With the advent of readily available MRI, more and more asymptomatic patients present concerned and worried they have a potentially crippling and debilitating problem. The radiologist confronted with images "on the edge" of normal may report on images and mention an early problem and refer to "borderline changes." Clinicians faced with patients with an encyclopedic array of symptoms, many of which may be seen with the CIM, yield to referral pressure. Sorting through these issues has received significant medical and lay attention [2]. We hope that the experts we

have assembled here will provide light and understanding to these difficult issues. With the advent of MRI, the clinical pendulum has swung from the uncommon CIM patient diagnosed with major neurological problems to many "normal" people with unremarkable neurological examinations who are concerned with their survival.

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The Chiari Malformations: A Historical Context

2

R. Shane Tubbs and W. Jerry Oakes

Abstract

It was not until the late nineteenth century when reports of hindbrain herniation (Chiari malformations) began to be published. However, even earlier reports can be found in the extant literature. These include a report of hindbrain herniation in association with myelomeningocele by Tulp (1593–1674) in 1641. Cleland and Arnold would also report cases of hindbrain herniation found in patients with myelomeningoceles. Probably the first description of hindbrain herniation in the absence of myelodysplasia was made by Langhans in 1881. However, it was Chiari, 10 years later, who would classify and further our knowledge of these embryologic derailments. Penfield, Gardner, and Van Houweninge Graftdijk would each further our understanding of these malformations via surgical intervention. The evolution of surgery for hindbrain herniation is indebted to pioneers such as those described herein. Our current understanding and treatment of these embryological derailments are based on years of observation and surgical trial and error.

Early Descriptions of Hindbrain Herniation

Although a thorough study of hindbrain herniations associated with spina bifida aperta would not take place until the late nineteenth century, rare reports are found in earlier literature. For example, in *Observationes Medicae*, published in 1641, the famous Dutch physician and anatomist Nicolaes Tulp (1593–1674) described a myelodysplastic individual and may have referred to hindbrain herniation [2, 7]. In 1829, Jean Cruveilhier (1791–1874) of Paris also described a patient born with myelomeningocele in whom "… the considerably dilated cervical region

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contained both the medulla oblongata and the corresponding part of the cerebellum, which was elongated and covered the fourth ventricle, itself enlarged and elongated [7]."

Probably the first description of hindbrain herniation in the absence of myelodysplasia and what would become known as Chiari I malformation was described by Theodor Langhans as "pyramidal tumors." Langhans was born September 28, 1839, in Usingen (Nassau) Germany, and studied under Henle in Göttingen and von Recklinghausen in Berlin (see Fig. 2.1) [20]. He was also a student under such names as Virchow, Trauber, and Frerichs [6]. He served as assistant to von Recklinghausen until 1867 [24]. He was later made professor ordinarius in Giessen and then moved to Switzerland in 1872 where he was appointed professor and chair of Pathological Anatomy in Bern succeeding Klebs [23]. Langhans with the physician Sahli and the surgeon Kocher formed a triumvirate, which made the medical school at Bern famous [6, 30, 36].

In his 1881 publication *Über Höhlenbildung im Rückenmark in Folge Blutstauung* (regarding cavity creation in the spinal cord as a consequence of obstruction to blood flow), Langhans made many observations and hypotheses that were far ahead of his time [3]. For example, he speculated that pathology at the foramen magnum resulted in syrinx formation [25]. The following is a translation of excerpts of Langhan's publication *Über Höhlenbildung im Rückenmark in Folge Blutstauung* [3]:

> In the case, which first brought to my attention the necessity to look for cavity formation in the spinal cord following a change in the cerebellar cavity, I could not find a cause for the increase in pressure; but great pressure on the pons and medulla oblongata from above was indeed apparent. Upon dissection of the cerebellum, nothing was of note except for an obvious/significant development of both tonsils, which protruded down in the form of two symmetrical pyramidal tumors and pushed the medulla oblongata in a frontal direction at almost a right angle.
>
> The formation of the cavities, according to my observations, was connected to other changes in the central nervous system, more specifically to changes in the cerebellar cavity, which must have impeded the circulation to a great extent. The increase in pressure in the cerebellar cavity will hinder or greatly impede the outflow of blood and cerebral spinal fluid." "In all cases, the ventral part of the spinal cord is affected and if at all, only a small portion of the dorsal part. The cavities do not start in the medulla oblongata at the calamus scriptorius or in the upper 1–2 cm of the spinal cord." "The direction in which the central canal extends is constant – to the side and posteriorly. In my opinion, the decisive factor for this is the consistency of the white matter. The cavity creation starts there where the increased pressure, which exists in the cerebellar cavity stops and, therefore, a diverticulum can only occur toward the area of less pressure." "According to my theory, a diverticulum is more likely to occur than a widening of the central canal, because the development of the diverticulum in the dorsal part meets less resistance than a central expansion [3].

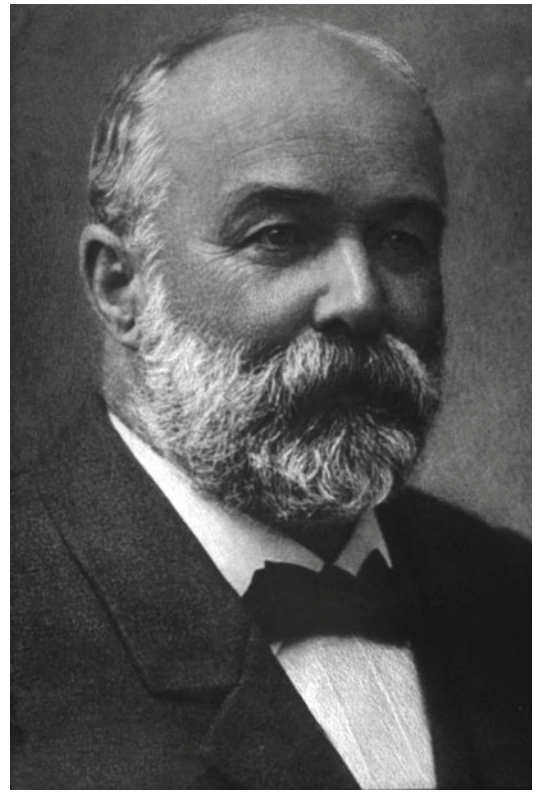

Fig. 2.1 Theodor Langhans

These descriptions are striking for several reasons including Langhans first describing pathologic tonsillar ectopia and hypothesizing that this obstruction at the foramen magnum results in development of syringomyelia. Additionally, the fact that syringomyelia normally does not include

the first segment of the cervical cord was clearly recognized by Langhans [22]. Lastly, Langhans realized that fluid accumulation within the spinal cord could occur via dilation of the central canal or outside of this region.

Hans Chiari will most be remembered for his 1891 paper *Ueber Veränderungen des Kleinhirns infolge von Hydrocephalie des Grosshirns* (concerning changes in the cerebellum due to hydrocephalus of the cerebrum) that described what is now regarded as the Chiari malformations [31–33]. Chiari (see Fig. 2.2) was born on November 4, 1851, in Vienna. Chiari came from a family of physicians and his father, Johann Baptist Chiari (1817–1854), is credited with describing prolactinomas [1]. Chiari studied medicine in Vienna, assisting one of the most revered pathologists at the time, Karl Rokitansky (1804–1878), at the Vienna Institute of Pathology [1]. Chiari was hired as a prosector [3] at the Vienna Institute, which was renowned for its knowledge and research under the control of Rokitansky. In 1875, Chiari completed medical school and Rokitansky retired. Richard Ladislaus Heschl (1824–1881) succeeded Rokitansky as head of Pathological Anatomy in Vienna [1], and Chiari assisted him until Heschl's death in 1881 [1]. In 1878, Chiari habilitated in pathological anatomy in Vienna, and 4 years later, he became extraordinarius at the German University in Prague. One year later, he was appointed ordinarius and superintendent of the pathological-anatomical museum in Prague [3].

Most of Chiari's accomplishments occurred while he was in Prague. For example, in 1877, Chiari was noted as the first to describe the features of a choriocarcinoma [1]. In 1899 and in conjunction with British internist George Budd (1808–1882), Chiari provided a clinical and pathological explanation of hepatic vein thrombosis the so-called Budd-Chiari syndrome [1]. Prior to Chiari, such a syndrome had been described but never explained to any extent. Among his other accomplishments, Chiari studied the relationship between carotid artery plaques and thrombosis. Chiari's name is also attached to the symptoms associated with aortoesophageal fistula after foreign body ingestion or gunshot wound. In 1883, Chiari probably described the first and only

Fig. 2.2 Hans Chiari

authentic case of traumatic pneumocephaly prior to roentgenography. He demonstrated a fistulous connection between a pneumatocele in the frontal lobes and the ethmoid sinuses in a patient who died of meningitis following rhinorrhea and thus first indicated a mechanism to explain meningitis in this context. Interestingly, Chiari implicated sneezing as a precipitating factor for this pathogenesis. Chiari also made significant contributions with his observations of pituitary adenomas and, in 1912, developed a novel transnasal approach to lesions of the pituitary gland [4]. Of note, Schloffer, who first performed a transsphenoidal pituitary operation in Innsbruck, Austria, examined pituitary adenomas from specimens that he obtained from Chiari in Prague.

In 1888, Chiari observed that syringes usually communicate with the central canal of the spinal cord. It was in 1891 in the journal *Deutsche Medizinische Wochenscriff* and later in 1896 that Chiari first published his works regarding hindbrain malformations. Chiari's type I malformation was first described by him in a 17-year-old woman who died of typhoid fever and suffered

from hydrocephalus but had "no symptoms referable to the cerebellum or medulla." Her malformation was described as a "peg-like elongation of tonsils and medial divisions of the inferior lobes of the cerebellum into cone shaped projections, which accompany the medulla oblongata into the spinal canal" while sparing the medulla [5].

In 1894, Julius Arnold (1835–1915) described a single myelodysplastic infant without hydrocephalus whereby the fourth ventricle and cerebellum herniated through the foramen magnum while sparing the medulla [6]. Arnold studied under Rudolf Virchow (1821–1902) and Nikolaus Friedreich (1825–1882) in Heidelberg, later becoming professor of anatomy [1]. Chiari's type II malformation was similar to Arnold's case and was described as a "displacement of parts of the cerebellum and elongated fourth ventricle, which reach into the cervical canal" [7]. Chiari later refined his description of type II malformations to include greater hindbrain involvement, as a "displacement of part of the lower vermis, displacement of the pons and displacement of the medulla oblongata into the cervical canal and elongation of the fourth ventricle into the cervical canal" [7]. In 1907, the Chiari type II malformation was renamed the Arnold-Chiari malformation by Schwalbe and Gredig while working in Arnold's laboratory [21]. Although little attention was given to the posterior fossa abnormalities in this report, Arnold's students seized this opportunity to immortalize their professor by affixing the moniker "Arnold-Chiari malformation" to this condition [2, 34]. In the end, however, it was the significant contributions of Chiari that shed the most light on these forms of hindbrain herniation; thus, now referring to them as Chiari malformations is appropriate.

Chiari type II malformation was described earlier by the Scottish physician John Cleland in 1883 [8] who called it the "basilar impression syndrome." Cleland noticed the malformation from autopsies and described it as the "inferior vermiform process, which extends up so far that what appears to be the pyramid touches the corpora quadrigemina, while the uvula looks backward and the laminated tubercle hang down from an exaggerated velum posticum, as an appendix three fourths of an inch in length, lying in the fourth ventricle" [8, 28]. Cleland argued that the malformation resulted from primary dysgenesis of the brainstem and that "hydrocephalus was obviously of much later origin, when the different parts of the brains were already formed" [8, 35]. Though it preceded Chiari's, Cleland's work had little impact on the scientific community's attempt at better understanding these malformations of the hindbrain [7, 26]. Chiari believed these malformations were due to hydrocephalus [7]. Chiari described one example of the most severe malformation of the hindbrain seen observed by him, type III; cervical spina bifida, whereby there is a partially absent tentorium cerebelli with prolapse of the fourth ventricle and cerebellum into the cervical canal, associated with a hydromyelic cavity communicating with the fourth ventricle [6]. Chiari's type IV malformation had no degree of hindbrain herniation and consisted of cerebellar hypoplasia, which Chiari also attributed to hydrocephalus [9]. In 1896, Chiari described an additional 63 cases of congenital hydrocephalus with an associated type I malformation in 14/63 and a type II malformation in 7/63 [10].

In 1906 and as a result of tensions within the Hapsburg Empire, Chiari left Prague (as head of the university and professor extraordinarius and superintendent of the Prague pathological-anatomical museum) to travel to the University in Strasbourg, France, where he was appointed ordinarius of pathological anatomy [3, 10]. On May 6, 1916, after an accomplished career, Hans Chiari passed away due to a throat infection [1, 9]. This prolific writer published approximately 180 papers between the years 1876 and 1916 and was always very careful to give credit to the discoveries of others [27].

Many years later, in 1935, Russell and Donald [12], at the London Hospital, described ten additional pathological specimens of hindbrain herniation.

Surgical History of the Chiari Malformations

Although many have attributed the first successful patient series to Gardner in the 1950s, earlier attempts at surgical decompression were attempted [15]. In the late 1930s, Wilder Penfield

in Montreal commented "the anomaly [Chiari malformation] may present itself as an unexpected clinical problem to be dealt with by the neurosurgeon." In 1938, Penfield and Coburn [11] reported a 29-year-old woman with loss of hearing and weakness on the right side of the face. Her history included removal of a thoracic "spina bifida" in infancy. On physical examination, she was noted to have nystagmus, absence of the right corneal reflex, truncal ataxia, and decreased peripheral reflexes. The patient underwent posterior cranial fossa exploration with the authors not considering hindbrain herniation in their differential. Later, they stated:

> In retrospect, it seems that we should have suspected the Arnold-Chiari malformation. Instead, a suboccipital craniotomy was carried out, with a tentative diagnosis of a tumor of the acoustic nerve bilaterally [11].

Unfortunately, the patient of Penfield and Coburn never regained consciousness and died 2 months later. At autopsy, the authors identified a Chiari II malformation and hydrocephalus. These authors suggested that in the future, the cerebellar tonsils be left intact and the posterior margin of the foramen magnum be removed with the posterior elements of C1 and C2 [11].

Not known to many is that 8 years prior to the publication of Penfield and Coburn, the Dutchman Cornelis Joachimus Van Houweninge Graftdijk (1888–1956) (see Fig. 2.3) operated a patient, in 1930, with myelomeningocele and ventriculogram-proven hindbrain herniation who had rapid head growth [29]. This contribution was published in his thesis for a Doctorate of Medicine entitled *Over Hydrocephalus* (About Hydrocephalus) [16]. With surgery, he attempted to relieve CSF obstruction at the craniocervical junction by redundant cerebellar tissue. Although his patient died, this report marks the first known attempt at surgical correction of a hindbrain herniation. Van Houweninge Graftdijk said:

> I decided to try widening the space through which the brain had herniated in order to allow for better flow of CSF. [16]

The idea that displacement of the foramina of the fourth ventricle into the upper end of the spinal canal might precipitate hydrocephalus, and

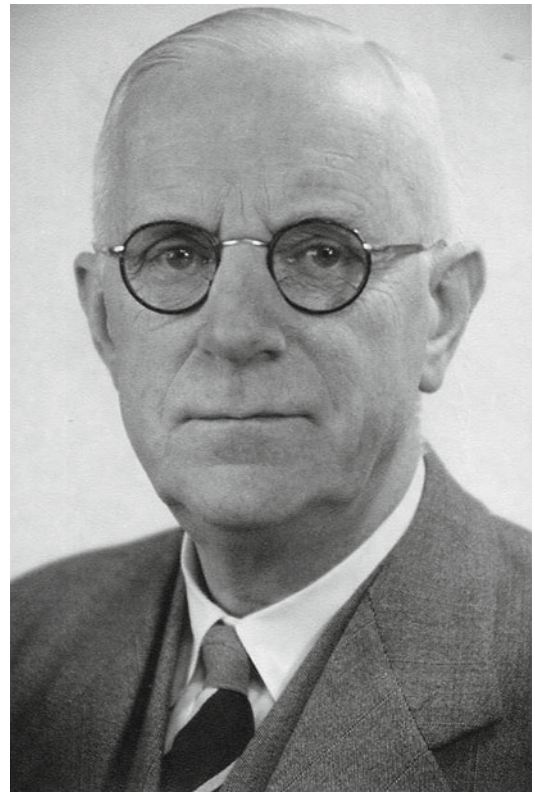

Fig. 2.3 Cornelis Joachimus Van Houweninge Graftdijk

that the whole of the anomaly might act as a valve, was first expressed by Van Houweninge Graftdijk in 1932 [16]. For this case, part of the occipital bone and posterior elements of the first two vertebrae were removed. Unfortunately, the patient developed fever on postoperative day 2 and 84 days after the operation; the bladder was perforated so that on day 98 postoperative, the patient died.

Van Houweninge Graftdijk also presented evidence that fluid could flow more readily from the spine to the head than vice versa [18]. It was in children with spina bifida that he concluded that the pressure within the meningocele was lower than the pressure within the cranium [19]. Conversely, Russell and Donald [12] commented on Van Houweninge Graftdijk's theory but hypothesized that hindbrain hernias did not cause hydrocephalus in these patients. Interestingly, in 1935, these authors stated:

> If hydrocephalus, either congenital or postoperative, were due to such a malformation, then

> air injected by the lumbar route would collect in the ventricles and not in the sulci upon the cerebral convexities. Such a result would be not only of academic interest but of clinical importance. It would point to the desirability of decompressing the spinal cord at the foramen magnum to facilitate the circulation of fluid in the leptomeningeal spaces. Such an operation has not yet been carried out. [12]

However, these authors, in a footnote, stated that while their above-mentioned paper was in press, their attention was drawn to the writings of Van Houweninge Graftdijk. Van Houweninge Graftdijk also surmised that cerebrospinal fluid can readily escape in an upward direction from the vertebral canal into the ventricles or cerebral meningeal spaces but has difficulty in passing from the ventricles down into the vertebral canal. To address such issues surgically, he excised redundant cerebellar tissue and/or bone over the posterior surface of the malformation as previously mentioned [12, 16]. Van Houweninge Graftdijk also postulated that caudal traction theory by the myelomeningocele is responsible for "pulling" the hindbrain caudally thus resulting in a Chiari II malformation [19].

Cornelis Joachimus Van Houweninge Graftdijk was born in Giessendam, Holland. His father was a family doctor in Giessendam, and his brother died young as the result of hydrocephalus. Although his brother and sisters were given the family surname "Graftdijk," Cornelis was given the name "Van Houweninge Graftdijk" as his parents did not want this surname to die out. Cornelis graduated from the University of Leiden, became a physician in 1913, and, following the advice of his teacher Professor Korteweg, became a ship doctor so that he could gain some "practical knowledge." In 1914, he studied surgery with Prof. Zaaijer for 5 years then began his own practice in Leiden at the hospital Diaconessenhuis. He maintained his affiliation with Prof. Zaaijer at the University Hospital in Leiden and, in addition to practicing general surgery, treated pediatric patients with hydrocephalus. This interest probably arose from his concern over his older brother who had hydrocephalus. Van Houweninge Graftdijk trained doctors in surgery and, for many years, was "chef de clinique" of the Department of Surgery at University Hospital.

In the early 1930s, Van Houweninge Graftdijk wrote his dissertation [16] on hydrocephalus and on June 21, 1932, he obtained his doctor's degree cum laude. Soon after, Prof. Zaaijer left the university and was replaced by Prof. Suermondt who had no interest in hydrocephalus. It is not clear why Van Houweninge Graftdijk did not succeed Prof. Zaaijer but as a result of this, he left University Hospital and was not able to continue working on hydrocephalus. He continued to practice at the hospital Diaconnessenhuis. He became chairman of the Dutch Association of Surgery, and in 1940, he wrote a book *Heelkunde voor Den Medicus Practicus* [17], a textbook of surgery for family doctors.

In 1938, McConnell and Parker [8] published their results of posterior fossa decompression for Chiari I malformation in five patients. Two of these patients had successful outcomes. In 1945, Bucy and Lichtenstein [2] reported successful decompression for a Chiari I malformation of a 40-year-old woman without hydrocephalus, and in 1948, Chorobski and Stepien [3] operated a woman with life-altering Valsalva-induced headache and Chiari I malformation that had full resolution of her symptoms. Most remembered for his direct approach to the hindbrain was Gardner. In 1957, he and Goodall [6] reported their efforts at surgically addressing syringomyelia by decompressing the hindbrain and sealing off the hypothetical communication between the syrinx and fourth ventricle in 17 patients. They reported improvement in 13, decline in 3, and death in 1. In their series, some patients had improvement of preoperative symptoms. The publication of Gardner and Goodall appears to have resulted in the widespread adoption of posterior fossa decompression for hindbrain herniation with larger reports following over the next few decades [1, 5, 7, 9, 10, 13]. Finally, it was Gardner in the 1950s that showed in a large series of patients that decompression of the hindbrain herniation in patients with syringomyelia often improved symptoms in patients. This report led to widespread adoption of this method of treatment. In fact, a PubMed search of the terms Chiari malformation and surgery yielded roughly 1,500 publications between 1950 and 2011 [14].

The evolution of surgery for hindbrain herniation is indebted to pioneers such as those described herein. Our current understanding and treatment of these embryological derailments are based on years of observation and surgical trial and error.

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Embryology of the Craniocervical Junction and Posterior Cranial Fossa

3

Mohammadali M. Shoja, R. Shane Tubbs, and W. Jerry Oakes

Abstract

The development of the craniocervical junction is a complex sequence that requires perfect arrangement between cranial and cervical components. The neural crest cells of the upper somites and the notochord are both important in the development of this region. Of particular significance is the proatlas. Recent molecular studies have increased our knowledge of the processes involved in the formation of the base of the skull and upper cervical spine. The orchestration of the developing rhombencephalon and craniocervical junction is critical in the proper adult neuro-osseous relationships. Derailment of these processes may result in hindbrain herniation.

In the embryo, the notochordal development precedes the formation of the neural tube and axial skeleton. The notochord plays a key role in the induction of neural tube formation, sclerotogenesis, and patterning of the paraxial mesoderm [1–4]. Sensenig [5] temporally divided the development of the vertebrae, including those in the occipital region, which fuse early to form the basiocciput and exocciput, into three overlapping stages. The first stage (fourth week of embryonic period) is characterized by the maturation of the notochord. The details on the development of the notochord during early embryonic life are beyond the scope of this chapter, and for this purpose, the readers are referred to Frazer [6] and Sensenig [5]. For convenience, the general aspects of notochordal development are schematized in Fig. 3.1. The second stage (the fifth and sixth weeks of the embryonic period) is characterized by the intense proliferation and migration of sclerotomic cells toward the notochord, formation of mesenchymal perinotochordal sclerotomes, expansion and patterning of the neural crest, and formation of the spinal nerves. Chondrification and ossification occur in the third stage beginning from the middle of the sixth week.

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Sclerotogenesis and Development of the Vertebrae

By the end of the fourth week of the embryonic period, the notochord induces ventromedial migration of the mesenchymal cells from the

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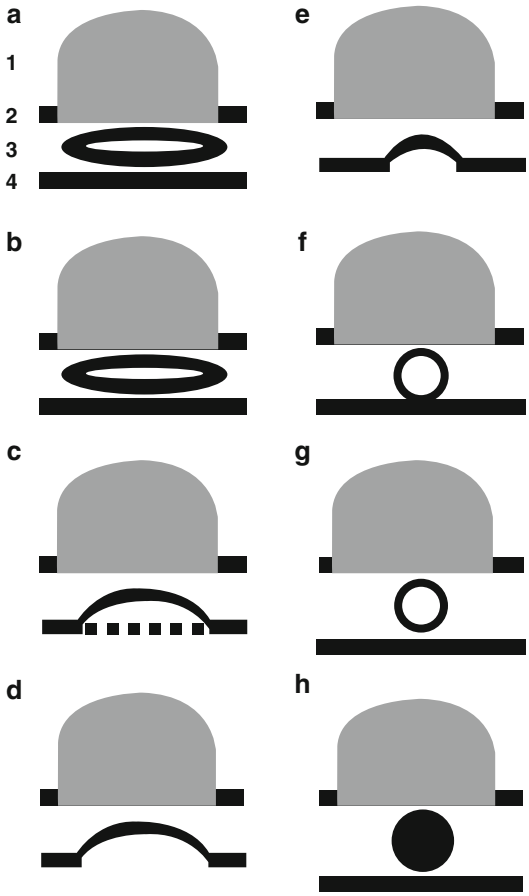

Fig. 3.1 A schematized drawing of the transverse section through the midportion of the embryonic plate showing notochordal development and maturation. With the formation of the primitive streak from the ectoderm on the dorsal midline of the embryonic plate, the mesodermal precursor cells originating from the primitive streak migrate between the ectoderm and endoderm (not shown here). The longitudinal midline condensation of the mesodermal cells forms the head process or notochordal plate in front of the primitive streak. (**a**) The notochordal plate (*3*) has a lumen, a floor next to the endoderm (*4*), and a roof next to the neural plate (*1*) of the ectoderm (*2*). (**b**) The floor of notochordal plate fuses with the endoderm. (**c**, **d**) The floor then disappears, leaving the roof of the notochordal plate (known as the notochordal groove at this stage) attached to endoderm on either side. (**e**, **f**) The notochordal groove deepens and its margins approximate each other by the growth of the endoderm. (**g**) Following the fusion of the margin of the notochordal groove, the notochordal tube is formed and is liberated from the endoderm. (**h**) The lumen of the notochordal tube disappears and the tube solidifies to form the mature notochord. This description is based on Frazer [6]

condensed paraxial mesoderm of somites. The migrated somital cells surround the notochord to form the primary sclerotomes. The primary sclerotomes are grossly segmented and the pattern of segmentation follows that in the respective somites. With the rearrangement (or re-segmentation) of the primary sclerotomes, sclerotomal cells from different somital origins combine together to form secondary sclerotomes with a segmentation pattern, which follows that in the final vertebrae [5]. The somitogenesis and formation of primary sclerotomes occurs in a craniocaudal direction. Similarly, the rearrangement of primary sclerotomes also occurs in a craniocaudal direction; thus, the vertebral differentiation in the occipital and cervical regions precedes the development in the caudal region [5]. Along with the process of sclerotomal rearrangement, a subpopulation of sclerotomes (derived from its densely packed cellular region) migrate dorsolaterally around the neural tube and between spinal nerves and ganglia to establish the mesenchymal primordia of the vertebral arch [5]. The subsequent chondrification of the mesenchymal primordium of each vertebra establishes the basic structure of the early vertebra composed of a cartilaginous centrum (vertebral body) and a neural arch around the neural tube [5, 7]. A point of utmost importance here is that the primary sclerotomes above and below the definite C2 vertebra adopt different patterns of rearrangement in order to fulfill the anatomical and functional requirements of the craniovertebral junction (composed of the occipital bone and C1–2 vertebrae) above and the rest of vertebral column below.

Development of Vertebrae Below C2

The *basic* concepts in the development of the vertebrae (below the definite C2 vertebra) were appreciated more than a century ago (cf. 7) and culminated in the seminal work of Sensenig [5]. By the end of the first month of gestation, the notochord and neural tube are surrounded by

the skeletogenic mesodermal tissue (of primary sclerotomes) derived from the ventromedial part of somites located on either side of the neural tube. An interesting review has been provided by Dockter [8]. The distribution of cells in each primary sclerotome is heterogeneous in a way that craniocaudal and mediolateral gradients exist; the density of cells is higher in the caudal and lateral portions than in the cranial and medial portions of the sclerotomes. Initial segmentation of primary sclerotomes follows the somital pattern; however, re-segmentation occurs shortly thereafter. The so-called fissure of von Ebner separates the two halves of the primary sclerotomes especially at their lateral sides where the spinal nerves and blood vessels emerge. The loosely cellular cranial half of each primary sclerotome combines with the densely cellular caudal half of the sclerotome above to form the secondary sclerotome corresponding to the future vertebrae (Fig. 3.2). Following dorsolateral migration of a subpopulation of sclerotomal cells, a dense lateral mass and a central mass (with dense upper and loose lower regions) are discernible in each secondary sclerotome (Fig. 3.2). The dense lateral mass gives rise to the vertebral arch (i.e., pedicle, articular facets, and lamina). Within the region of the central mass, the loose lower part is larger and gives rise to the centrum (body) of the vertebra. The narrow band of densely cellular sclerotomal tissue retained between the centra of the secondary sclerotomes has variably been referred to

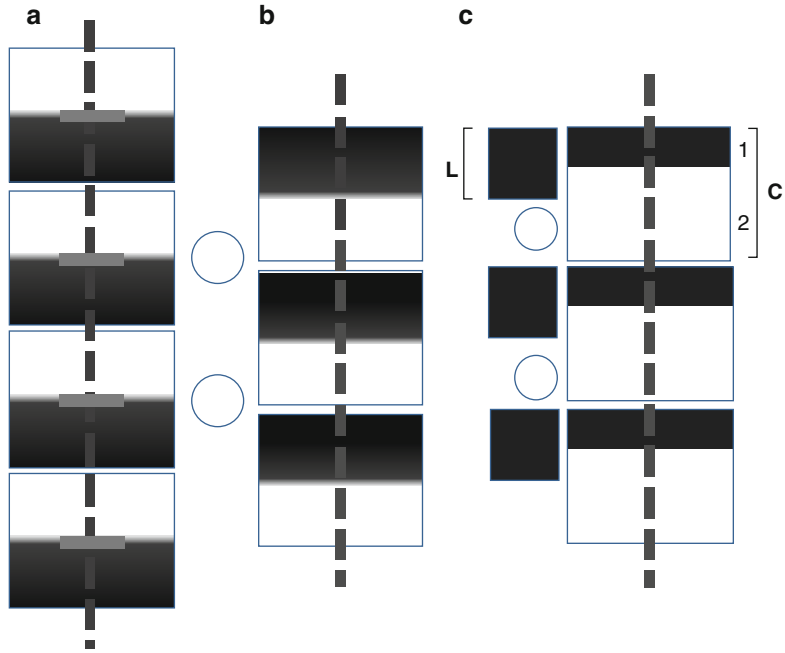

Fig. 3.2 A simplified model of the rearrangement of primary sclerotomes and development of vertebrae below C2. (**a**) Shows primary sclerotomes with loose upper (*white*) and dense lower (*dark*) regions partially separated by the fissures of von Ebner (*gray horizontal bars*). The longitudinal *dashed line* represents the notochord. (**b**) Shows the secondary sclerotomes following rearrangement. The *circles* represent the spinal root ganglia, nerves, and blood vessels emerging at the level of loosely cellular regions. (**c**) Shows the sclerotomic primordia of vertebrae following dorsolateral migration of a subpopulation of cells from the dense region between the spinal root ganglia and nerves. At this stage, the central (*C*) and lateral (*L*) masses are discernible. The central mass is composed of the hypochordal bow (*1*) and centrum (*2*)

as the hypochordal bow [7, 9], perichordal disc [5], hypocentrum [10], or intercentrum [11]. In this chapter, the term "hypochordal bow" is preferentially used. It has been advocated that hypochordal bows degenerate into the fibrous part of the intervertebral disc [7].

The Development of the Craniocervical Junction

Much of our current understanding of the ontogeny of the craniovertebral junction is indebted to the elegant studies of Ludwig [12], O'Rahilly and Müller [9], and Müller and O'Rahilly [13, 14]. The upper four somites are occipital somites 1–4. The ventromedial migration of sclerotomal cells from somites 1–4 toward the cephalic notochord yields the primary occipital sclerotomes 1–4 (O1–4). The hypoglossal nerve rootlets travel laterally between the hypochordal bows of the occipital sclerotomes and the first cervical spinal nerve between the hypochordal bows of O4 and sclerotome 5 (S5 or the first cervical sclerotome). Initially, the occipital sclerotomes 1–3 fuse to form the major portion of the mesenchymal basiocciput [9]. In an embryo of 9 mm CRL (the fifth week of the embryonic period), the hypochordal bows of O4 and S5, also, respectively, known as the hypochordal bows of the proatlas and atlas, are well distinguishable in the craniovertebral junction [12]. The notochord travels dorsal to the hypochordal bows [12]. The rostral O1–3 hybrid and O4 fuse together in the embryo of 9–11 mm CRL (the sixth week of the embryonic period) to form a mesenchymal O1–O4 hybrid surrounding the cephalic end of notochord [9]. This mesenchymal hybrid is called chordal cartilage once chondrification takes place later in the embryonic period. The hypochordal bow of O2 is small and soon disappears medially and fuses with the hypochordal bow of O3 laterally. The dorsolateral extensions of the hypochordal bows of O2–O4 give rise to the lateral masses or bars. Further dorsal extension of these masses contributes to the formation of exocciput, homologous to the neural arch of a typical vertebra. The portion of exocciput rostral to the hypoglossal nerve and canal is mainly derived from O3 and the caudal portion is derived from the O4. Ultimately, the lateral bars of S3 and S4 fuse to form a single exocciput ventral and dorsal to the hypoglossal canal. The mass of loosely packed sclerotomal cells between the hypochordal bows of proatlas and atlas, corresponding to the centrum of the primary sclerotome 5, contribute to the occipital condyles laterally and tip of the odontoid process of the axis medially [9, 13].

A simplified model of craniovertebral junction development is presented in Fig. 3.3. The hypochordal bow of O3 regresses except for its lateral extensions, which are intensified by fusing with the hypochordal bow of O2 and contribute to the exocciput. In a five-week-old embryo, the hypochordal bow of O3 is observed laterally above and anterior to the hypochordal bow of O4 [9]. The medial remnant of the hypochordal bow of O3 occasionally gives rise to an osseous partition within the hypoglossal canal [14]. The median portion of the hypochordal bow of O4 is retained as a continuous bar across the midline and starts fusing with the rest of the basiocciput rostrally in the mesenchymal stage [9]. Following chondrification, its fusion is completed and, in this way, it forms the basion. The hypochordal bow of S5 forms the anterior arch of the atlas and disappears from between the loosely packed regions of the S5 and S6 sclerotomes [14]. The lateral bar of S5 (C1) encircles the odontoid process and forms the neural arch of C1 (posterior arch of the atlas) [13, 14]. The lateral bar of S6 forms the neural arch of the C2 vertebra.

Development of the Occipital Condyle

The occipital condyles, located on the anterolateral corner of the foramen magnum, are two semilunar prominences with the concavity inward and convexity outward [10]. The medial part of the occipital condyle is larger than its lateral part. The occipital condyles are composed of a cartilaginous articular facet and an osseous portion. The articular facet is convex ventrodorsally and mediolaterally. Embryologically, the sclerotomic primordia of the occipital condyles are derived from the hypochordal bow of S4 and the loosely

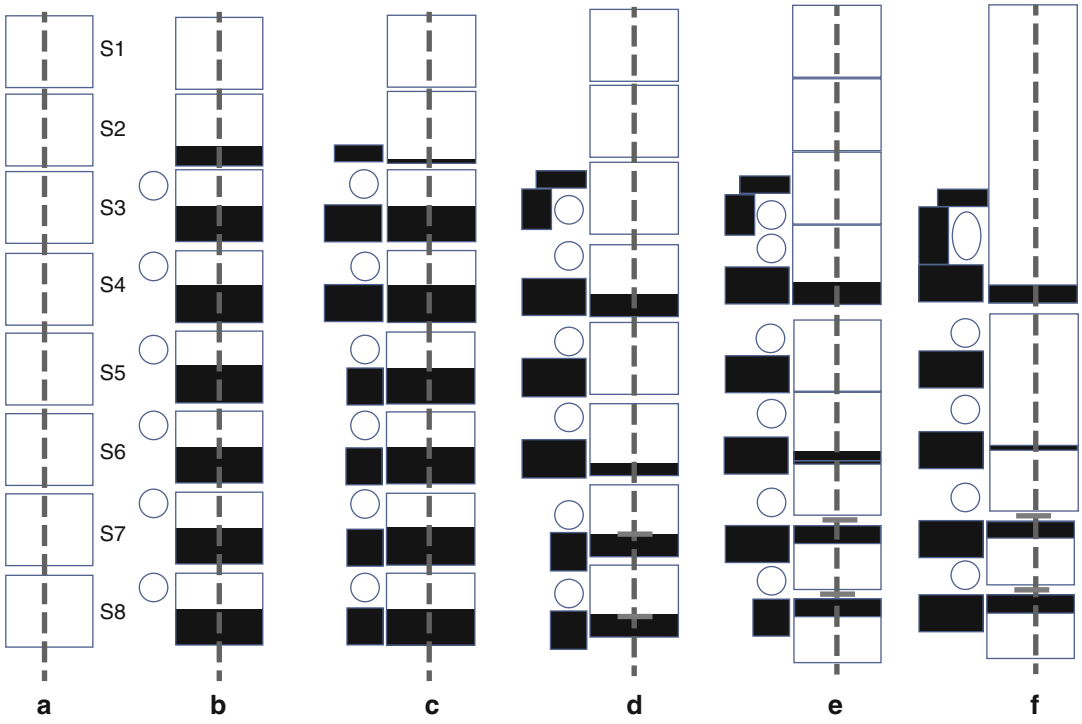

Fig. 3.3 A simplified model of craniovertebral junction and upper cervical vertebral development based on O'Rahilly and Müller [9], Müller and O'Rahilly [13], and Sensenig [5]. (**a**) With ventromedial somital cells migration toward the notochord, segmented sclerotomes are formed. The longitudinal *dashed lines* represent the notochord. (**b**) The lower half of the occipital sclerotomes 2, 3, and 4 and cervical sclerotomes undergo condensation (*dark regions*). Segmental ganglia and nerves, represented by *circles*, develop from the neural crest. (**c**) The cells from the caudal half of the sclerotome migrate dorsolaterally through the interganglionic space. Note the craniocaudal gradient in the development of the neural arches, with more dorsolateral extension of the hypochordal bows in the occipital region than in the cervical region. At this stage, the median (central) and lateral segments, roughly representing the centrum and neural arch of a developing vertebra, are established. The median part of the hypochordal bow of S2 begins disappearing. The median segments of S3–8 are still composed of dense caudal and loose rostral parts. (**d**) The dense caudal parts of centra of S2 (or O2) and S5 (C1) disappear. The dense caudal parts of the other sclerotomes are now diminished in size. The fissures of von Ebner (*horizontal gray bars*) separate the caudal and loose rostral parts of S7 and S8 (C3 and C4, respectively). The median portion of the hypochordal bow of S3 disappears. The lateral mass derived from the hypochordal bow of S2 is fused with the hypochordal bow of S3 laterally, leaving the two hypoglossal nerve rootlets within in a single canal. (**e**) The rearrangement at S7–9 centra occurs in a way that the dense caudal part of S7 joins the loose rostral part of S8 (S7–8 fusion or future C3 vertebra) and dense caudal part of S8 joins the loose upper part of S9 (S8–9 fusion or future C4 vertebra). S9 is not shown in (**a**–**d**). The centra of S1–S4 fuse to form the basiocciput. The centra of S5 and S6 and loose rostral part of S7 centrum fuse to form the dens and body of the C2 vertebra. Note the hypochordal bows of S3 and S4 are fused laterally. (**f**) The final rearrangement of the occipitocervical junction is achieved. Note the hypoglossal nerve within the exocciput formed by the fusion of the lateral bars (or extensions) of the hypochordal bows of O2–O4. The lateral bars of S7 and S8 form the neural arches of C3 and C4. The upper dense part of S7–8 fusion forms intervertebral discs C2–3 and the upper dense part of S8–9 fusion forms intervertebral discs C3–4. The development of the remaining vertebrae is similar to that of C3 and C4 vertebrae

packed region of S5. Once chondrification has taken place in the occipital region, the basiocciptal and exoccipital segments are united. Then, the ossification centers appear independently within these segments. By the ventral and dorsal growth of the exoccipital and suboccipital ossification centers, they meet each other but remain separated by a synchondrosis (known as the anterior intraoccipital synchondrosis). This synchondrosis traverses the occipital condyle; the portion of condyle anterior to the synchondrosis is basioccipital and the portion posterior to it is

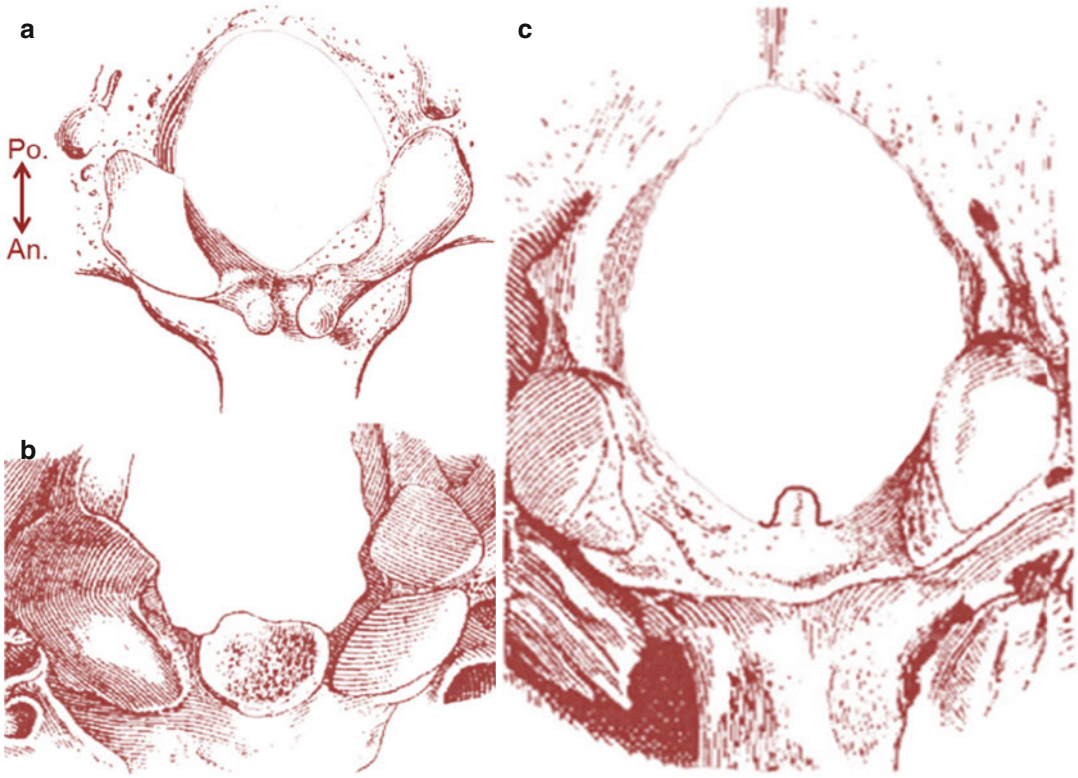

Fig. 3.4 The remnants of the anterior arch of the proatlas. The *arrow* shows the orientation of the specimens: *An*. anterior, *Po*. Posterior. (**a**) Shows two basilar processes. Some may regard these as the paramedian precondylar processes. (**b**) Shows a single large condylus tertius. (**c**) Shows a backward spur-like projection from the median portion of the anterior margin of the foramen magnum. Some advocate that this spur-like projection is not derived from the proatlas, but represents ossification of the attachment of the apical ligament [23] (Reproduced from Oetteking [21] with permission from John Wiley and Sons)

exoccipital in origin [15]. In infants and children, the occipital condyle is thus divided by a cleft corresponding to the unossified anterior intraoccipital synchondrosis [15]. The exoccipital portion of the condyle is larger than its basioccipital portion. The anterior intraoccipital synchondrosis ossifies in a mediolateral direction [15], commencing at 1–2 years of age and being completed by the age of 7–10 years [16]. Henceforward, the occipital condyle manifests as a single osseous prominence with a uniform articular facet. Occasionally, the articular facet may be transversely divided in the adults. The division of the articular facet in adults is attributed to its maceration in its midportion [15].

The anterior ends of the occipital condyles are occasionally connected together by a horizontal bony ridge, the so-called prebasioccipital arch, in front of the anterior rim of the foramen magnum [17–21]. If the medial part of this ridge vanishes, its lateral part is retained either unilaterally or bilaterally [18]. The lateral part may retain its ridgelike appearance or become bumpy and in the latter case, it is called the basilar process. Likewise, if the lateral part vanishes, the medial part of the ridge may be retained as a single median or two paramedian projection(s) [18, 22]. The latter variants include the pseudocondylus tertius [18, 19] or precondylar process [22] and the true condylus tertius [19, 20] (Fig. 3.4). The true condylus tertius is located just at the anterior rim of the foramen magnum. The precondylar process, as a continuation of the anterior end of the occipital condyle [18], is located slightly anterior to the foramen magnum. Embryologically, both the precondylar process and condylus tertius

are derivatives of the hypochordal bow of the proatlas [18]. These bony excrescences at the anterior margin of the foramen magnum are thus remnants of the anterior arch of the proatlas.

Proatlas Segmentation Malformation and Variable Manifestations of the Proatlas

The proatlas found in some lower vertebrates is a separate atlas-like vertebra between the occipital bone and atlas [24, 25]. Unlike a typical developing vertebra, the hypochordal bow of S4 never fuses with the centrum of S5 under normal circumstances in man. Instead, the hypochordal bow of the primary sclerotome 4 (S4) partially regresses and as mentioned earlier, it normally only contributes to the inferior portion of the basiocciput and the caudal part of exocciput. The centrum of the primary sclerotome 5 (S5) forms the apex of the dens as well as the apical ligament medially and also contributes to the formation of the occipital condyles laterally. This unique craniovertebral sclerotomal segmentation pattern dictates that the mesodermal constituents of the proatlas in man should be integrated into the occipital bone and axis. If (a) this pattern of segmentation in the craniocervical junction is disordered, (b) the mesodermal constituents of the proatlas are distributed abnormally, (c) the hypochordal bow of S4 hypertrophies or fails to partially regress, or (d) the centrum of S5 abnormally tends to be liberated from the axis or fuses with the hypochordal bow of S4, then a series of osseous anomalies or variations arises in the craniovertebral junction. The term "proatlas segmentation failure or malformation" has been applied to this ontogenetic error by several authors [26–28]. The associated anomalies or variations are collectively referred to as "proatlas remnants" or "manifestations of the proatlas" and are grouped under a broader category of "manifestations of the occipital vertebrae" (Table 3.1) [19, 27, 28, 54–56]. In an evolutionary sense, the proatlas segmentation malformation represents a phylogenetic regression in the ontogeny of the craniovertebral junction with an attempt to retain the proatlas and liberate it from the occipital region [44, 45]. To the best of our knowledge, only one case of a persistent proatlas as an additional atlas-like vertebra has been reported in man [57, 58].

With such a complicated genesis, it is not surprising that anatomical presentations of the proatlas segmentation malformation are quite variable, with some being clinically significant and others not. Some of the clinically insignificant remnants of the proatlas, including the basilar and precondylar processes and prebasioccipital arch, were discussed earlier. The clinically significant anomalies have an incidence of about 1.4 % and may result in lower brain stem compression [26], and these usually, but not always, manifest as anomalous bony excrescences around the foramen magnum [26, 44]. Typically, the tip of the odontoid process is absent and the basiocciput is elongated and protruded posteroinferiorly into the foramen magnum [26, 54]. The basioccipital protrusion is embryologically derived from the centrum of S5. Occasionally, the apex of the dens is present but is small and malformed. If the odontoid process is not hypoplastic, the posteroinferiorly directed median bony projection at the anterior margin of the foramen magnum is the third occipital condyle (condylus tertius), which sometimes articulates with the apex of dens or anterior arch of the atlas [19]. As the notochord travels posteriorly to the hypochordal bow of S4, the osseous anomalies in front of the apical ligament, such as the condylus tertius, represent the derivatives of the hypochordal bow. The apical ligament attaches to the basion over the condylus tertius [10]. A triangular or spikelike horizontal median projection from the anterior margin of the foramen magnum, medial indentation from the occipital condyle and non-fusion, inward displacement and hypertrophy of the condyle, os terminale persistens (Fig. 3.5), and os odontoideum are among the clinically significant variants of proatlas remnants [20, 26, 44]. Notably, in a series of 100 patients with Chiari malformation and craniovertebral junction anomalies, clinically significant proatlas segmentation malformations were found in eight patients (8 %) [54]. Likewise, hindbrain herniation was associated with proatlas segmentation malformations in 33 % of the cases [26].

Table 3.1 Some of the developmental anomalies and osseous variations of the occipital bone including the manifestations of occipital vertebrae

Anomaly or variation	Description	Reference(s)
Canalis basilaris medianus	The postnatal remnant of the cephalic notochord; presents as a well-corticated longitudinal canal in the midline of the basiocciput	Madeline and Elster [29]
Median basioccipital raphe	Midline trace of the median fusion of the parachordal plates	Madeline and Elster [29]
Longitudinal basioccipital cleft	Partial midline cleft in the basiocciput; is reminiscent of midline fusion of the bilateral parachordal plates	Madeline and Elster [29]
Cruciform sphenooccipital synchondrosis	Longitudinal anterior basioccipital and postsphenoidal clefts in conjunction with unossified sphenooccipital synchondrosis	Madeline and Elster [29]
Transverse (coronal) basioccipital cleft	Results from the retention of the segmented nature of the basioccipital primordium; may traverse the basiocciput partially or completely; may be an incomplete groove or a complete gap; is similar in appearance to the sphenooccipital synchondrosis radiographically but is actually filled with fibrous tissue not cartilage; very rare	Kruyff [30], Johnson and Israel [31], Prescher [19]
Basioccipital hypoplasia	A consequence of paraxial mesodermal insufficiency in the occipital region or premature closure of the sphenooccipital synchondrosis; associated with basilar invagination	Smoker [32], Nishikawa et al. [33], Noudel et al. [34]
Fossa navicularis	A shallow depression measuring ~3 × 5 mm on the undersurface of the anterior portion of the basiocciput	Cankal et al. [35]
Pharyngeal tubercle	A median tuberosity on the undersurface of the basiocciput about 1 cm anterior to the foramen magnum; is the point of attachment of the pharyngeal raphe; a tubercle of 1.5–2 cm diameter is radiographically apparent in 3.8 % of cases	Robinson [7], Hauser and De Stefano [36], Finke [37]
Bipartite hypoglossal canal	Division of the hypoglossal canal by a bony spicule; is a remnant of the hypochordal bow of S3	O'Rahilly and Müller [9], Müller and O'Rahilly [14]
Divided (bipartition of) occipital condyle	The partial or complete subdivision of the articular facet; may be unilateral or bilateral; associated with division of the superior articular facet of the atlas; has an incidence of ~5 %	Tubbs et al. [38], Kunicki and Ciszek [39], Tillmann and Lorenz [15]
Condylar hypoplasia	Underdevelopment of the occipital condyles; associated with a more horizontal than oblique orientation of the atlantooccipital joint and basilar invagination	Smoker [32]
Occipitocondylar hyperplasia	Hypertrophy of the occipital condyles; may cause cervicomedullary compression	Ohaegbulam et al. [40], Halanski et al. [41]
Paracondylar (paramastoid or jugular) process	A pneumatized osseous process in the lateral condylar area (jugular process of the occipital bone) located between the occipital condyle and mastoid process at the point of insertion of the rectus capitis lateralis muscle; may be unilateral or bilateral; may or may not fuse with the transverse process of the atlas; has an incidence of 2–4 %	Lang [42], Tubbs et al. [38], Anderson [43], Taitz [17], Prescher [19]
Lateral (transverse) process of the occipital condyle	Is homologous to the transverse process of the atlas arising from the its lateral mass; is a proatlas remnant	Stratemeier and Jensen [44], Gladstone and Erichsen-Powell [45]
Prebasioccipital arch or anterior lip of the foramen magnum	A U-shaped ridge connecting the end of the occipital condyles; manifests as the ventral arch of proatlas	Prescher [19], Taitz [17], Oetteking [21]
Basilar process	Lateral tubercle and the remains of the prebasioccipital arch; a proatlas remnant; is sometimes considered a variant of or the same as the precondylar process	Prescher [19], Oetteking [21]
Condylus tertius	A downward bony projection located just at the anterior margin of the foramen magnum; associated with an increased prevalence of os odontoideum; has an incidence of ~1 %	Smoker [32], Prescher [19, 46]

Table 3.1 (continued)

Anomaly or variation	Description	Reference(s)
Precondylar process or pseudocondylus tertius	A single median or two paramedian projection(s) from the inferior surface of the basiocciput located a few millimeters in front of the anterior margin of the foramen magnum; has an incidence of up to 25 % in adults; is a proatlas remnant; is also regarded as an ossification in the median portion of the anterior atlantooccipital ligament; unlike condylus tertius, it contains a sagittal canal	Vasudeva and Choudhry [22], Prescher [19], Hauser and De Stefano [36]
Anteromedian tubercle of foramen magnum	A small median triangular tubercle projected horizontally backward from the anterior border of the foramen magnum; is distinct from the condylus tertius, which projects downward; may represent ossification of the attachment of the apical ligament	Lakhtakia et al. [47], Prescher [19], Oetteking [21]
Posterior lip of the foramen magnum	A bony ridge extending from the posterior end of one or both occipital condyle(s) along the posterior foraminal margin; does not fuse posteriorly; may be hypertrophied and manifest as the bony excrescences around the posterior margin of the foramen magnum; remnants of the dorsal arch of the proatlas	Gladstone and Erichsen-Powell [45], Prescher [19], Menezes and Fenoy [26], Oetteking [21]
Kerckring or Kerckring-like ossicle(s)	A single median or paramedian ossicle at the lower edge of the supraocciput; there may be two paramedian ossicles which then fuse to form a single median ossicle; appears in the fourth and fifth fetal months and usually fuses with the supraocciput before birth; rarely remains completely separated; although controversial, some have regarded it as the neurapophysis of the proatlas	Piersol [48], Le Double [49], Caffey [50], Madeline and Elster [29]
Accessory ossicle(s) of the innominate (posterior intraoccipital) synchondrosis	Is seen in 0.4 % of newborns as one to four ossicles within the synchondrosis between the supraocciput and exocciput; may be large and protrude externally and internally; fuses with the supraocciput in the first year of life; the medially located ossicles may be considered as proatlas remnants	Caffey [50]
Persistent transverse occipital fissure/suture	A fissure/suture between the intermediate and interparietal parts of the occipital squamous; is sometimes misnamed the mendosal suture	Lochmuller et al. [51], Nayak et al. [52], Tubbs et al. [53]
Atlantooccipital assimilation	Partial or complete fusion of the atlas and occipital bone along the margin of the foramen magnum; associated with basilar invagination	Smoker [32]

Ossification of the Atlas

As mentioned earlier, the mesodermal primordium of the atlas is derived from the hypochordal bow of S5. Ganguly and Roy [10] believed that before the embryo attains a CRL of 30 mm (in the eighth week of the fetal period), the precartilaginous proatlas is divided and its dorsal caudal half incorporates into the cartilaginous primordium of the atlas and its ventral cranial part incorporates into the occipital cartilage at the anterior margin of the foramen magnum. The accuracy of this view, which has been held by some recent authors [26, 60], is uncertain. This is because the embryonic specimens presented by Ganguly and Roy [10] lack stages 11–30 mm CRL embryos, an embryonic period in which substantial development takes place in the craniovertebral junction. The developmental anatomy of the atlas has been well studied by Macalister [61]. Accordingly, the ring of the atlas is completely chondrified at the fifth week of gestation. By the seventh week, two ossification centers appear at the root of the posterior arch close to the lateral masses. These centers essentially grow backward to form the right and left posterior bony hemi-arches. This growth continues postnatally until about 4 years of age when the posterior arch closes by the fusion of right and left hemi-arches in the dorsomedian plane. The bilateral ossification centers also extend forward into the lateral masses and outward into the transverse processes [61]. The ossification of the anterior arch is delayed in a way so that it begins during the first year of postnatal life. Initially, two ossification centers of unequal

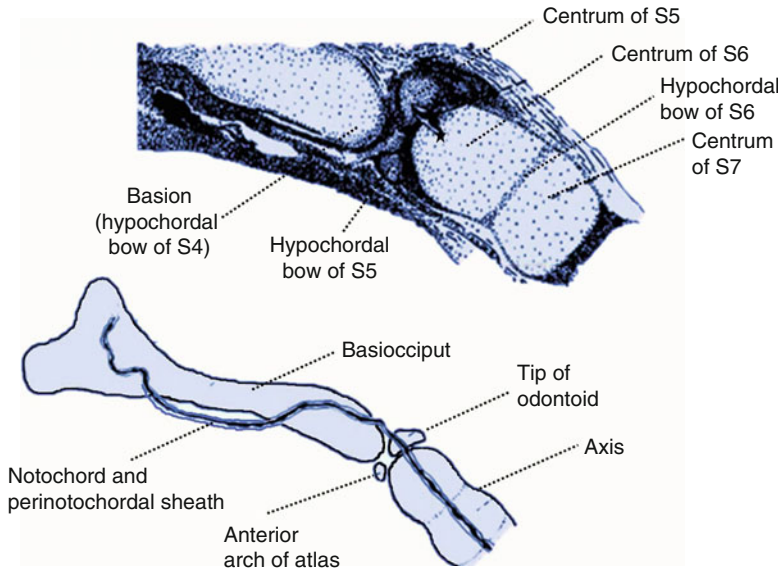

Fig. 3.5 The embryogenesis of proatlas segmentation malformation – os terminale persistens (Bergman's ossicle) variant. The *upper and lower images* show the mesenchymal/chondrified and osseous stages of the craniocervical junction, respectively. In the *upper image*, a small segment of notochord (*star*) is shown traversing between the centra of S5 and S6. In the *lower image*, the original fetal position of the notochord is superimposed on the components of the craniocervical junction. Note that hypochordal bow of S4 contributes to the basion and the centrum of S5 to the tip or apophysis of the odontoid. Normally, the centra of S5–7 fuse to form the dens and body of the axis. The failure of fusion leads to the formation of an independent center for chondrification and ossification in the S5 centrum and results in the tip of the odontoid being isolated giving rise to the os terminale persistens. On the other hand, if the mesenchymal fusion and chondrification of the dens occurs normally, the tip of the odontoid may be separated from the dens by an intervening synchondrosis, derived from the vestigial remnant of the S5 hypochordal bow. This synchondrosis usually ossifies, and a failure in its ossification also gives rise to the os terminale persistens. The notochord has an S-shaped course through the basiocciput and passes through the os terminale persistens; it is located on the ventral surface of the basiocciput at its midportion and runs obliquely within its rostral and caudal parts [59] (Reproduced with modification from Gladstone and Erichsen-Powell [45])

sizes appear in the median part of the cartilaginous anterior arch, which then rapidly fuse to form a single dominant ossification center. This median ossification center grows backward and laterally to join the lateral mass by the fifth year [61]. If the median ossification centers of the anterior arch fail to develop, ossification proceeds to the midline from the lateral masses of the atlas [62].

Atlantooccipital Assimilation and Other Developmental Anomalies of the Atlas

The atlas may be completely or partially fused with the occipital bone in a process referred to as occipitalization of the atlas or atlantooccipital assimilation or fusion. This congenital assimilation is one of the most common anomalies of the craniovertebral junction [63] and has most likely a multifactorial causation that often is aggregated in families [64]. The general prevalence ranges from 0.5 to 3 % in different series [65–67]. The syndromic forms of atlantooccipital assimilation are associated with Klippel-Feil syndrome and DiGeorge (22q11.2 deletion) syndrome among others [61, 66]. Embryologically, the assimilation takes place when the primordia of atlas and occiput are still cartilaginous [61]. Whether or not this fusion may also occur in the early mesodermal stage is questionable. The anterior arch of the atlas fuses with the basion at the anterior margin of foramen magnum, the posterior arch with the lower end of the supraocciput at the posterior

margin of the foramen magnum, the superior articular facet with the occipital condyles anterolateral to the foramen magnum, and the transverse process of the atlas with the jugular process of the occipital bone [61, 62]. Atlantooccipital assimilation results in a 15–35 % reduction in the surface area of the foramen magnum [68] and is occasionally associated with os odontoideum and basilar invagination [66]. An animal model has indicated that the aberrations in homeobox (*Hox*) gene expression are associated with atlantooccipital assimilation [69]. The family of highly conserved transcription regulatory proteins encoded by *Hox* genes plays a key role in patterning and determining the segmental fate of the axial skeleton in vertebrates [70–72]. In an evolutionary sense and unlike the proatlas segmentation malformation, atlantooccipital assimilation represents phylogenetic progression in the ontogeny of the craniovertebral junction with an attempt to integrate an additional vertebra into the occipital region [44, 45].

Several other developmental anomalies of the atlas have been reported [20, 61, 62]. Hypoplasia, dysplasia, agenesis, or midline cleft of the anterior arch is less common than that of the posterior arch. In a series of 21 patients with proven or suspected Chiari I malformation, agenesis of the anterior or posterior arches of the atlas or variable degrees of atlantooccipital assimilation were the most common osseous anomalies at the craniovertebral junction [73]. In another series of 100 patients with Chiari malformation and concomitant craniovertebral junction anomalies, atlantooccipital assimilation was found in 92 patients (92 %) [54]. These observations imply that the anomalies of the atlas are commonplace in patients with hindbrain herniation and that they may be the manifestations of a common underlying ontogenetic error or may actually have a cause and effect relationship.

Basicranial Development

The basicranium is composed of a flat anterior part and an oblique posterior part (clivus). The clivus is made up of basisphenoidal (anterosuperior) and basioccipital (posteroinferior) segments joined by an intervening sphenooccipital synchondrosis. The rostral end of the notochord marks the caudal part of the sphenooccipital synchondrosis. Development of the basicranium follows successive stages of mesenchymal condensation, chondrification, and ossification [74, 75]. Once the mesenchymal (desmal or blastemal) basicranium is laid down, chondrification and ossification takes place in a posteroanterior direction with the posterior cranial fossa being the first and the anterior fossa being the last to chondrify or ossify [74]. During the third month of fetal life, the chondrification is almost completed. Chondrification and ossification are overlapping stages separated in space. Hence, while chondrification is occurring in the anterior portion of the basicranium, the posterior basicranium begins ossifying [74]. What follows relates to the posterior basicranium, which contributes to the formation of the posterior cranial fossa.

The segmented (sclerotomal) nature of the developing basiocciput was first discovered by Froriep in calves, Weiss in rats, and Levi in humans (cf. 76). The initial mesenchymal primordium of basicranium is established in the first month of gestation. This process has been discussed. Chondrification appears in the basiooccipital region during the second month [76]. Initially, two longitudinal cartilaginous plates (the so-called parachordal plates) are formed on each side of the cephalic notochord around the fifth week of fetal life [59, 74, 76]. At about the same time, the cartilaginous otic capsule is also developing but remains separate from the parachordal cartilage [74, 76]. The two parachordal plates fuse across the midline to form a single plate, known as the basal or chordal plate, surrounding the notochord [74, 76]. The cartilaginous otic capsule is then incorporated into the basal plates laterally [76]. The segmented nature of the basiocciput begins disappearing during the late mesenchymal stage and is totally lost with fusion of the cartilaginous centers [76, 77]. The basal cartilage is divided caudally and each division extends dorsolaterally in a horizontal plane and on either side of the foramen magnum as the exoccipital plate,

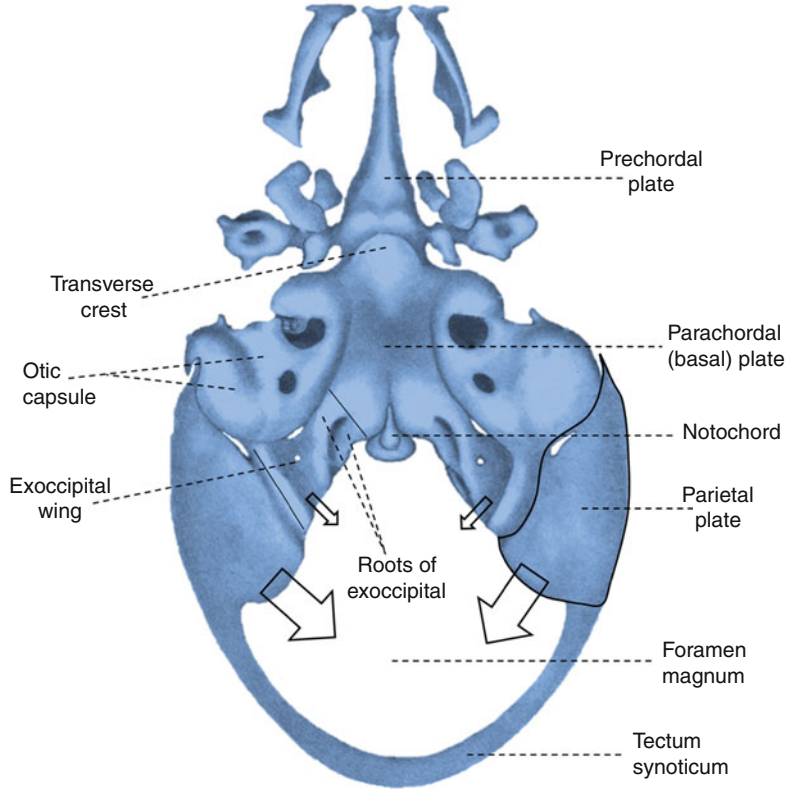

Fig. 3.6 Basichondrium of a 20 mm CRL embryo, ~8th week of fetal life. The foramen magnum is very large at this stage. The exoccipital is shown between two *solid lines* on the *left side*. The territory of the parietal plate is marked on the right side. The parietal plate of the occipital bone is anteroinferiorly fused with the otic capsule, posteroinferiorly with the exoccipital, and posteriorly extends as the tectum synoticum. The caudal portion of the prechordal cartilage contributes to the basisphenoid, and the rest of it and the appendages develop into the anterior basicranium [77] (Reproduced with some modifications from Kernan [78])

i.e., the cartilaginous primordium of the exoccipital [76–78]. The hypoglossal nerve passes through a foramen in the cartilaginous exoccipital; this foramen is large in the cartilaginous stage but becomes smaller with ossification. In front of the rostral end of the notochord, which also marks the rostral border of the parachordal plates, chondrification occurs in the prechordal cartilage and its appendages [77].

In an embryo of 20 mm CRL (about the eighth week of fetal life), the basichondrocranium attains a considerable degree of maturity and is composed of four regions: occipital, otic, orbitotemporalis, and ethmoidal [78]. The following account of basichondrocranial development is derived from Kernan's study: The central portion of the basichondrocranium is made up of two continuous ventral and dorsal bars marked by a transverse crest between the two bars (Fig. 3.6). The transverse crest is the primordium of the dorsum sellae. The dorsal cartilaginous bar is the chordal (basal) plate and the ventral bar is the prechordal plate. The cartilaginous otic capsule is fused with the lateral border of the basal plate, and the line of fusion is marked as the basicapsular commissure or sulcus. The caudal end of the basal plate marks the anterior margin of the foramen magnum. Ventrally, each exoccipital plate is composed of two cranial and caudal roots with an intervening foramen through which the hypoglossal nerve travels. These roots represent the pedicles (neural arches) of the occipital vertebrae. Dorsally, the two roots join to form a single, flat cartilaginous plate, known as the exoccipital wing. The lateral border of the exoccipital plate is ventrally separated from the otic capsule by the jugular foramen and is dorsally fused with it at the

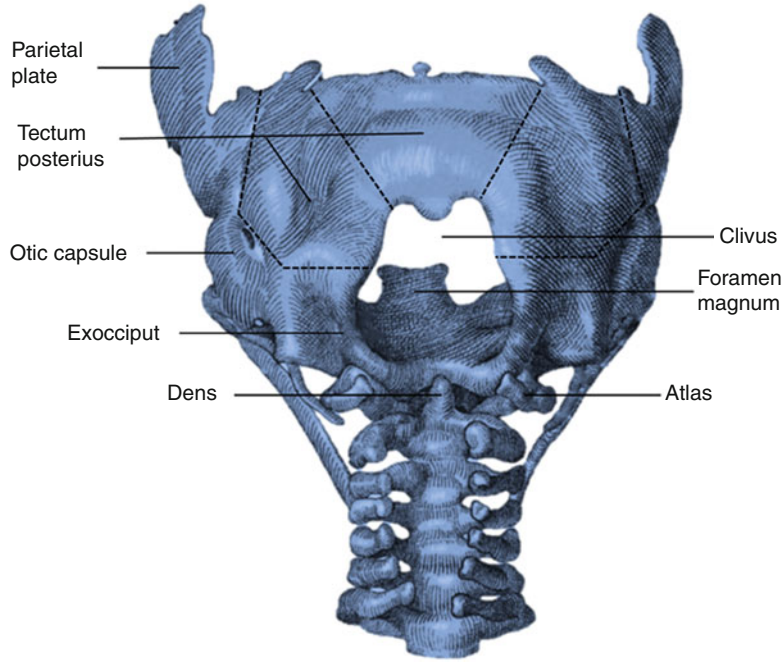

Fig. 3.7 The posteroinferior aspect of the basichondrocranium and occipital region of a 43 mm CRL fetus, ~12th week of fetal life. The tectum synoticum is regressed and the upper part of the posterior border of the parietal plates is free. The tectum posterius is derived from the parietal plates and exoccipital wings and is arbitrarily composed of two lateral pieces and a central piece (marked by *dashed lines*). At this stage, ossification progresses in the central part of the tectum posterius, anterior (root) portion of the exocciput, and caudal portion of the basiocciput (Reproduced with modifications from Macklin [80])

capsulooccipital commissure. At its posterior border, the exoccipital wing joins a thin plate of triangular cartilage known as the parietal plate of the occipital bone, the apex of which is pointed anteriorly toward the otic capsule. The inferior border of the parietal plate fuses with the otic capsule anteriorly and the exoccipital wing posteriorly. Its superior border is free. From the upper part of the posterior border of the parietal plate, a narrow band of cartilage extends from either plate dorsally and fuses with the contralateral counterpart to form a thin ribbon of cartilages known as tectum synoticum of "Kernan" or tectum cranii anterius of "Fawcett" (Fig. 3.6). At this stage, the basichondrocranium contains a very large foramen magnum.

The later stages in basichondrocranial development are prominently characterized by development in the posterior occipital region between the parietal plates and exoccipital wings of both sides. This region corresponds to the cartilaginous supraoccipital part of the occipital squamous bone. As indicated by the arrows in Fig. 3.6, the parietal plates (below the tectum synoticum) and exoccipital wings of the right and left sides extend dorsomedially, ultimately fusing in the dorsal midline to form a wide, trapezoidal cartilaginous plate posterior to the foramen magnum, known as the tectum posterius of "Kernan" or "tectum cranii posterius of Fawcett." Simultaneously, the tectum synoticum undergoes regression. This view has been supported by Levi [79], Macklin [80], and Kernan [78] and more recently by Müller and O'Rahilly [81]. With regression of the tectum synoticum, the parietal plate simultaneously diminishes in size [78]. The posterior aspect of the basichondrocranium and occipital region in a fetus of 43 mm CRL (~12th week of fetal life) is shown in Fig. 3.7. The final fate of the parietal plate of the occipital bone is not well described in the literature, but most likely is retained as the mastoid fontanelle and gives rise to the superolateral part of the cartilaginous supraocciput next to the fontanelle. In fact, it has been shown that the mendosal fissure, which postnatally is connected to the mastoid fontanelle, is the remnant

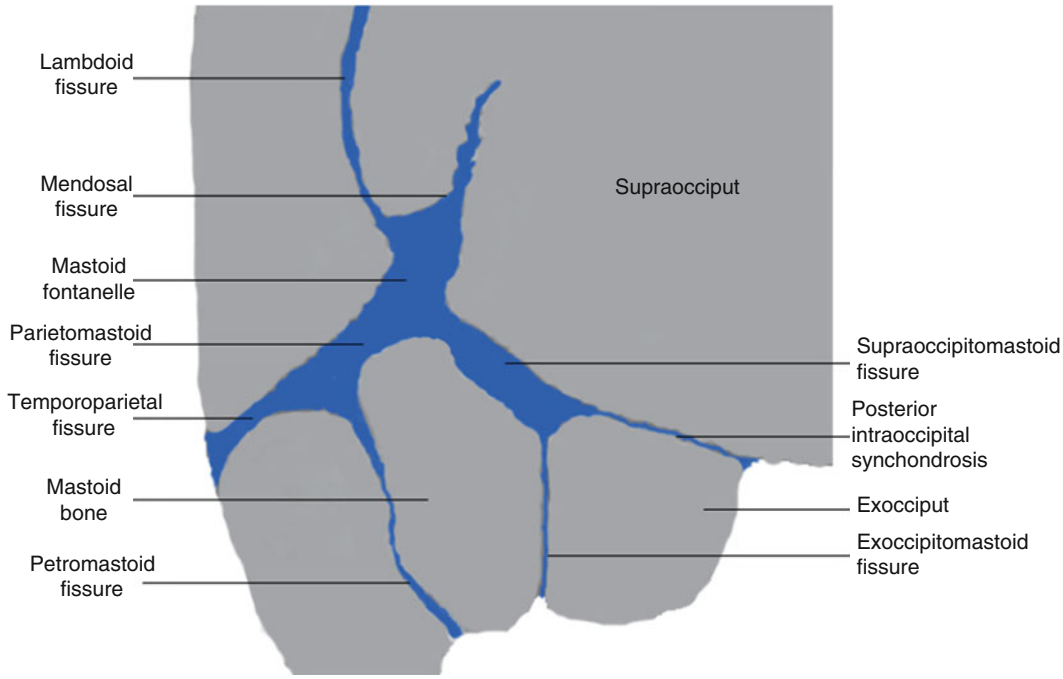

Fig. 3.8 A schema showing the mastoid fontanelle and its related cartilaginous fissures at birth. The fissures are replaced by the sutures in the adult skull, and some sutures obliterate completely with fusion of the bones. The mastoid fontanelle seems to be the remnant of the fetal parietal plate. The mendosal fissure is the remnant of the tectum synoticum [82]

of the tectum synoticum of the parietal plate [82]. Figure 3.8 shows the mastoid fontanelle and its relationship with the supraocciput and exocciput at birth. The different components of the posterior basichondrocranium and their relationships are schematized in Fig. 3.9.

By the 14th week of fetal life, the basichondrocranium attains its complete maturation (Fig. 3.10), and endochondral ossification has already begun in several other centers [74, 76]. The ossification of cartilaginous basicranium occurs sequentially and in a consistent direction [84]. The first ossification centers in the supraoccipital, exoccipital, and basioccipital regions appear in 30, 37, and 51 mm CRL embryos, respectively [42]. The basioccipital and exoccipital segments have one ossification center each; however, the supraoccipital segment develops from multiple ossification centers [85]. Radiographically, the ossified basiocciput is easily recognizable when the fetus attains a CRL of 80–100 mm [84], as is the basisphenoid and anterior basicranium in fetuses of 100–150 mm CRL [84]. During the second trimester of pregnancy, the rate of longitudinal growth of the posterior basicranium is about half that of the anterior basicranium [86]. The details on the development of the anterior basicranium are beyond the scope of this chapter.

Contribution of Cells of Neural Crest Origin to the Basicranium

In their seminal work, McBratney-Owen and colleagues [87] showed that in a mammalian (mouse) model, the basicranial mesenchyme rostral and caudal to the sphenooccipital synchondrosis is derived from neural crest and mesoderm, respectively (Fig. 3.11). The sphenooccipital

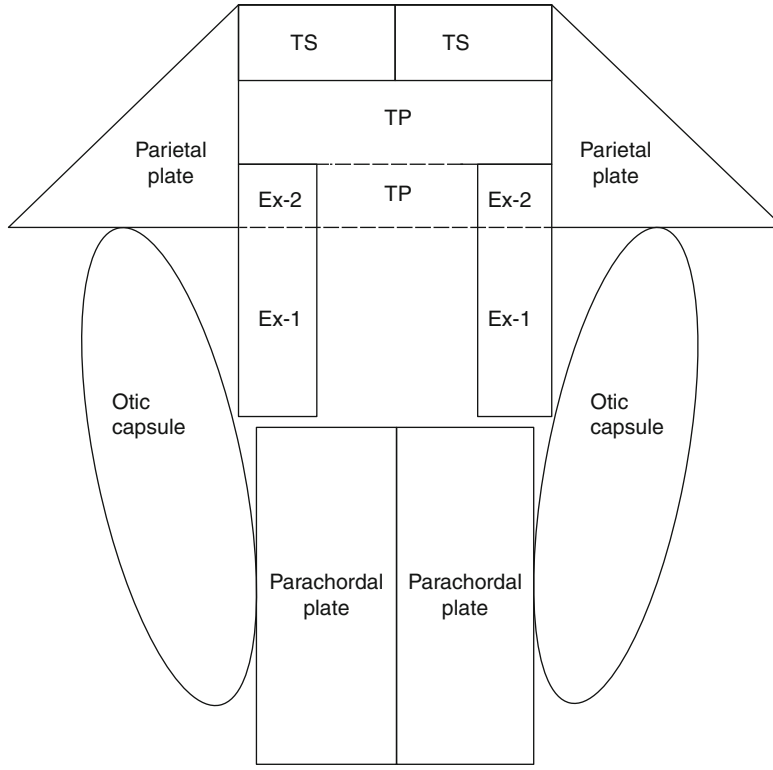

Fig. 3.9 A schematic drawing of the posterior basichondrocranium. The parachordal plates fuse to form a single basal plate. The exocciput is composed of a root (*Ex-1*) and a wing (*Ex-2*). The otic capsule is located lateral to the exocciput and basal plate. Note this schema is a simplified drawing and lacks some details of anatomical relationships between the related parts. The tectum synoticum (*TS*), which is a temporary structure, originates from the upper part of the base of the parietal plate. The tectum posterius (*TP*) originates from the lower part of the base of the parietal plate and exoccipital wing

synchondrosis is initially of dual origin, with its rostral half being from the neural crest-derived prechordal cartilage and the caudal half from mesoderm-derived basiocciput [87]. Postnatally, the neural crest-derived cells in the synchondrosis disappear, and the synchondrosis becomes entirely mesodermal. Later, the mesoderm-derived osteoblasts are introduced into the caudal basisphenoid through the endochondral ossification of the sphenooccipital synchondrosis [87]. The boundary of the neural crest- and mesoderm-derived basicranium – only roughly correlating with the prechordal-chordal boundary – is ontogenetically and phylogenetically important as it marks the transition from the mesoderm-derived basicranium (posteriorly) to neural crest-derived basicranium anteriorly. It is believed that by their contribution to the formation of head including the basicranium, cells of neural crest origin play a dominant role in the evolution of vertebrates from chordate-like ancestors [88].

Development of the Occipital Bone

At birth, the occipital bone is composed of a squamous portion and a basioccipital and two exoccipital segments (Fig. 3.12). The developmental anatomy of the basioccipital and exoccipital segments has been discussed. The squamous portion is derived from a lower cartilaginous plate (the origin of this plate from the

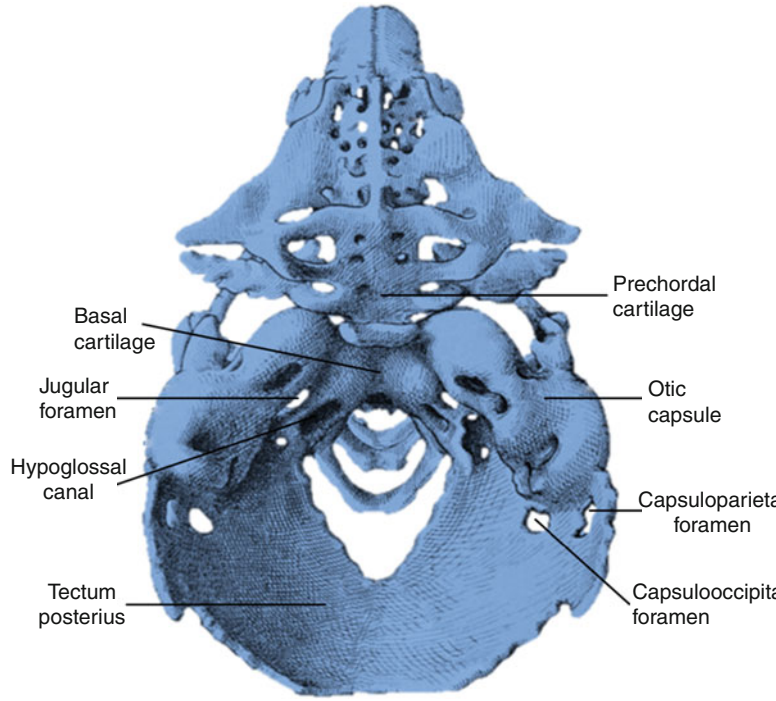

Fig. 3.10 The superior aspect of the basicranium in the fetus of 80 mm CRL, ~14th week of fetal life. The jugular foramen is located between the otic capsule and exocciput. Two other foramina are visible, one between the otic capsule and the tectum posterius (capsulooccipital foramen) and one between the otic capsule and the parietal plate (capsuloparietal foramen). These foramina transmit emissary veins. They disappear or are retained as the mastoid foramina in adults (Reproduced with slight modifications from Hertwig [83])

parietal plates and exoccipital wings has been discussed) and an upper membranous part. The upper membranous part is composed of ribbon-like intermediate and triangular interparietal segments (Fig. 3.13). The membranous interparietal segment is formed by two medial and two lateral plates, one on either side of the midline [89, 90]. A median fissure separates the medial plates. Each plate as well as the intermediate segment demonstrates two ossification centers [90]. At 12–15 weeks of gestation, the lateral plates of the membranous interparietal region grow medially and fuse with each other to form a single hybrid between the intermediate segment below and the medial plates of the interparietal segment above [90, 91]. A transverse occipital fissure separates the intermediate segment from the interparietal segment. Later, the transverse fissure is obliterated medially by the fusion of the intermediate and interparietal segments, and henceforward, it is called the lateral (or mendosal) fissure. The lateral fissure is well distinguishable at 16 weeks of gestation [90]. At this time, the median fissure mostly disappears following the fusion of the two medial plates [90].

In a developed skull, the highest nuchal line represents the border between the intermediate segment and interparietal bone and the superior nuchal line represents the border between the intermediate segment and cartilage-derived supraocciput. Initially, the lateral fissure transforms into a suture (the so-called mendosal suture) at the lateral part of the highest nuchal line [92]. With complete fusion of bones, the mendosal suture usually disappears between the second and fourth years of life. However, it may persist in 16 % of adult skulls [53]. Very rarely, the entire transverse fissure/suture between the intermediate and interparietal segments may persist; a persistent transverse occipital fissure/suture should not be confused with the mendosal suture [51]. It should be noted here that the terms "fissure" and "suture" are often used interchangeably, with some authors favoring one over the others [93].

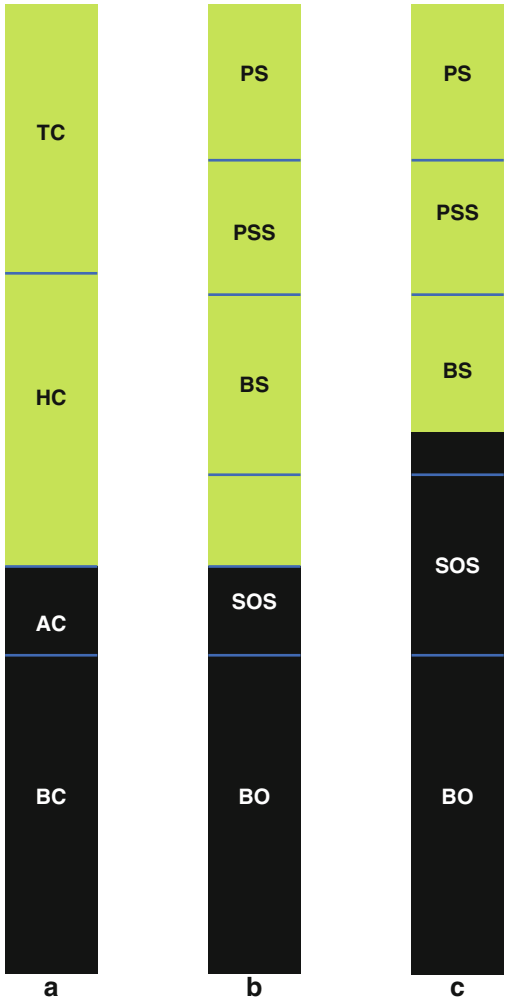

Fig. 3.11 Dynamic changes in the boundary of the neural crest- and mesoderm-derived basicranium based on a mouse model. *AC* acrochordal cartilage, *BC* basal cartilage, *BO* basiocciput, *BS* basisphenoid, *HC* hypophyseal cartilage, *PS* presphenoid, *PSS* presphenoidal synchondrosis, *TC* trabecular cartilage, *SOS* sphenooccipital synchondrosis. (**a**) The fetal period. The acrochordal cartilage is the rostral part of the basal cartilage surrounding the tip of the notochord. The *black* region is a mesodermal derivative and the *yellow* region is a neural crest derivative. (**b**) The early postnatal period. Note the sphenooccipital synchondrosis has a dual origin. (**c**) The late postnatal period. With apoptosis of neural crest cells and introduction of mesoderm-derived osteoblasts into the caudal basisphenoid, the mesoderm-neural crest boundary moves anteriorly. The entire sphenooccipital synchondrosis is now mesodermally derived (Reproduced, with permission from Elsevier, from McBratney-Owen et al. [87] with modifications)

In a morphological sense, they are different stages of a same structure; ontogenetically, the fissure is replaced by the suture, and the suture may become completely obliterated following ossification.

The appearance of ossification centers in the supraoccipital cartilage has long been a controversial issue. According to Mall [85], two paramedian ossification centers appear in the 55-day-old embryo and these speedily fuse into a single median center. Simultaneously, two new ossification centers appear lateral to the fusing paramedian centers to which they also join by day 57. On day 58, thus, there is a single ossifying mass across the supraoccipital midline. As mentioned earlier, the supraoccipital cartilage can be arbitrarily divided into a central plate and two lateral plates (Fig. 3.7). The paramedian centers occupy the central plate and lateral centers occupy the upper parts of the lateral plates [94]. Srivastava [94] also speaks of another independent ossification center in the lower part of the lateral plate of the supraoccipital cartilage on either side. The different segments and plates of the developing supraoccipital squama are schematized in the Fig. 3.13. The rapid formation and fusion of the supraoccipital ossification centers may account for the discrepancies in the literature regarding the number and arrangement of these centers.

Basicranial Angle, Platybasia, and Basilar Kyphosis

The basal angle is formed between the axes of the anterior and posterior basicranium. For practical purposes, the center of the pituitary fossa [95], tuberculum sellae [96, 97], or dorsum sellae [95] is used as a landmark for the basicranial hinge around which the posterior basicranium rotates. The basion is invariably used as the inferior limit of the posterior basicranium [95–97] and foramen cecum [97, 98] or nasion [95] is used as the front limit of the anterior basicranium. Figure 3.14 shows different

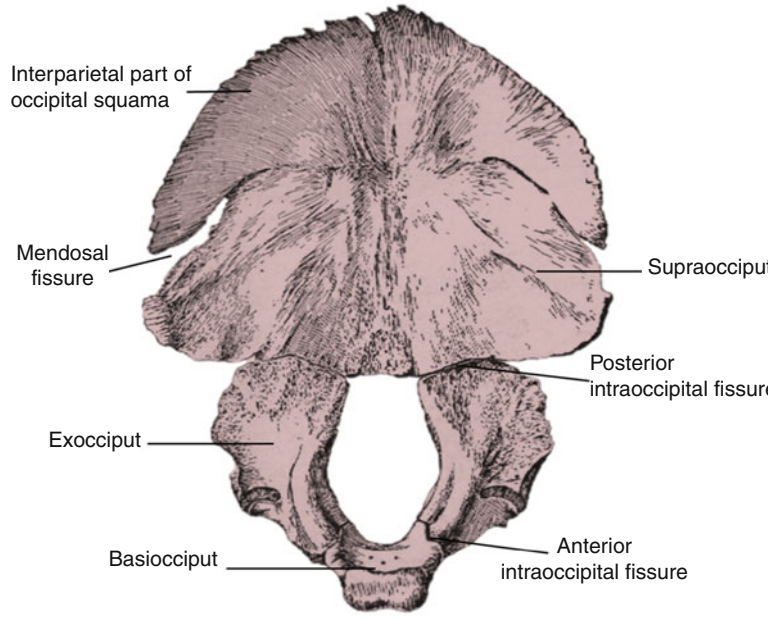

Fig. 3.12 The occipital bone at birth (Reproduced from Piersol [48])

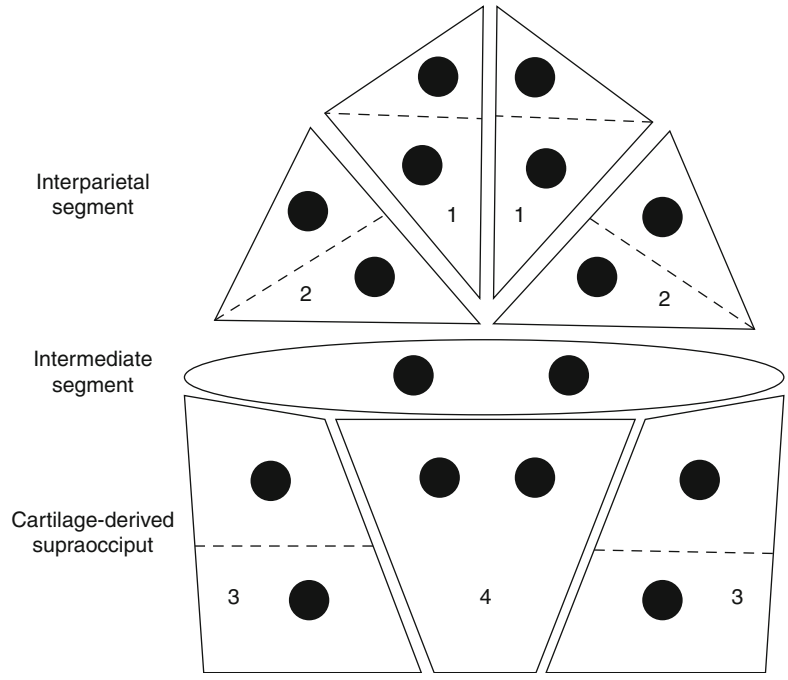

Fig. 3.13 A line diagram showing the different segments contributing to the development of the squamous portion of the occipital bone and their respective ossification centers. *1* medial plates of the interparietal segment, *2* lateral plates of the interparietal segments, *3* lateral plates of the supraoccipital cartilage, *4* central plate of the supraoccipital cartilage. The intermediate segment and cartilage-derived supraocciput together form the supraoccipital part of the occipital squama. The ossification centers are shown by the *black* circles. The *dashed lines* represent the boundaries between the ossification centers. The variable separation and fusion of the different plates and/or ossification centers may result in the formation of variant sutures and sutural (inca) bones in the adult skull [89]

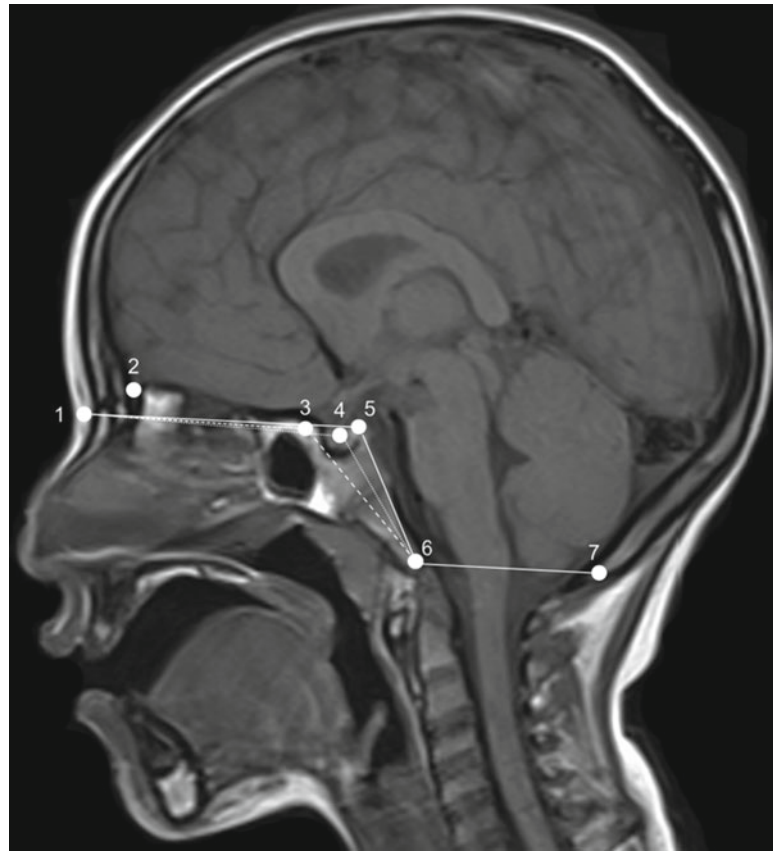

Fig. 3.14 Midsagittal magnetic resonance imaging of the head. The different landmarks used for measuring the basicranial angle are shown. *1* nasion, *2* foramen cecum, *3* tuberculum sellae, *4* center of pituitary fossa, *5* dorsum sellae, *6* basion, *7* opisthion. Note the opisthion-basion-tuberculum sellae angle is known as Boogard's angle. The size of the posterior cranial fossa decreases with an increase in Boogard's angle [96]

landmarks and methods used for measuring the basicranial angle. The posterior basicranium retroflexes during the fetal period, and thus, the basicranial angle simultaneously increases [97, 98]. This retroflexion moves the basion upward and dorsally, flattens the basicranium [99], and decreases the ventral depth of the posterior cranial fossa. Two hypotheses concern the mechanism of posterior basicranial retroflexion: enlargement of the intracranial space and, more importantly, expansion of the developing upper airways may act from above and below to flatten the skull base [97, 99]. More than normal and less than normal retroflexion of the posterior basicranium result in the conditions, respectively, known as platybasia and basilar kyphosis. Although the angle varies slightly depending on the method and landmarks used for its measurement, an angle between 125° and 143° is generally considered normal [95]. A basicranial angle greater than 143° indicates platybasia and one less than 125° indicates basilar kyphosis [95]. Isolated and mild platybasia is asymptomatic and insignificantly affects the posterior fossa volume [100]. Moderate to severe platybasia is often associated with basilar invagination [32]. The basicranial angle increases in patients with Chiari I malformation [96].

Basilar Invagination and Basilar Impression

Basilar invagination, one of the most common anomalies of the craniovertebral junction, is when the caudal part of the occipital bone is displaced

inward and upward and the vertebral column and skull base abnormally approximate each other. In severe cases, the odontoid process is prolapsed into the foramen magnum [96]. Basilar invagination may be congenital or secondary to such conditions as Paget's disease, osteogenesis imperfecta, hyperparathyroidism, and rickets [32]. The secondary or acquired forms of basilar invagination are referred to as basilar impression [32]. The congenital forms of basilar invagination are associated with hypoplasia of the atlas, basiocciput, and/or occipital condyle; platybasia; and atlantooccipital assimilation [32, 101], as well as a higher incidence of hindbrain herniation [96, 101]. Such associations do not necessarily reflect, at least in some cases, a cause and effect relationship. Instead, they may represent consequences of the same pathological mechanism. The craniocervical growth collision theory of Roth is worth mentioning here as a potential embryologic explanation for the occurrence of basilar invagination and associated anomalies. According to Roth [102], following an early embryonic period of predominant neural growth, the proliferation of skeletogenic tissue and vertebral growth ultimately overtake growth of the spinal cord. Normally, the vertebral column grows in a craniocaudal direction resulting in expansion of the vertebrae below the distal end of the spinal cord. If the distribution of skeletogenic tissue is reversed for any reason and the vertebral growth occurs in a caudocranial direction, the growing vertebral column collides with the developing skull base [102]. This collision pushes the posterior skull base and the margin of the foramen magnum upward and compresses the primordia of the occipital and cervical vertebrae against each other, potentially leading to abnormal segmentation at the craniovertebral junction, fusion of the atlas and occipital bones, platybasia, and prolapse of cervical vertebral column into the skull base.

There are several morphometric criteria for diagnosing basilar invagination [103]. Figure 3.15 shows some of the reference lines used for this purpose. Basilar invagination is divided into two groups, without (group 1) and with (group 2) associated Chiari I malformation [105, 106]. So far, only about 20 % of patients with basilar invagination have Chiari malformation [105]. Pure basilar invagination has clinically acute manifestations with pyramidal motor and proprioceptive deficits, whereas basilar invagination with Chiari malformation usually manifests chronically with cerebellar and vestibular deficits [106, 107]. The familial form of basilar invagination has been reported and an autosomal dominant pattern of inheritance with incomplete penetrance and variable expressivity has been suggested [108].

Shallowness of the Posterior Cranial Fossa in Chiari I Malformation

Various linear morphometric measurements have been defined to evaluate the dimensions and size of the posterior cranial fossa and occipital bone (Fig. 3.16). In a study comparing the depths of the posterior cranial fossa among Chiari I patients aged above 15 years and normal controls, the height of the supratentorial occipital region (*H*) was similar among Chiari I patients and normal individuals [109]. However, the posterior fossa height or depth (*h*) was ~16 % less among Chiari I patients. This observation, which has been confirmed by several other studies [96, 111], implies that patients with Chiari I malformation have a shallow posterior fossa. As the supratentorial and infratentorial parts of the squamous occipital bone are, respectively, composed of membranous and cartilaginous origins, the shallowness of the posterior fossa reflects an abnormality of the occipital squamous bone restricted to its cartilage-derived lower part.

Underdevelopment of the Occipital Bone and Basioccipital Hypoplasia in Chiari I Malformation

In their seminal work, Nishikawa et al. [33] compared occipital bone morphometry among patients with Chiari I malformation aged over 15 years and age- and gender-matched healthy controls. The supraocciput and exoccipital heights (measured from the jugular tubercle to the atlantooccipital

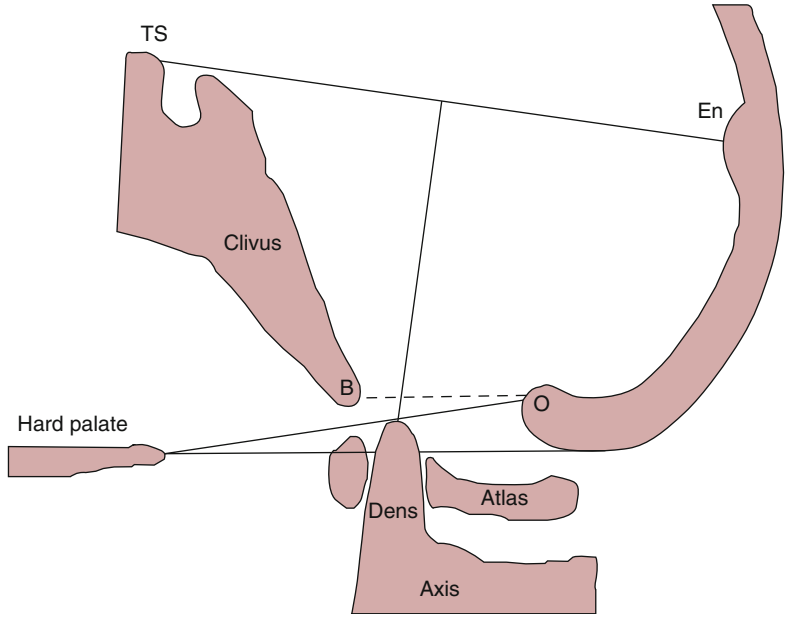

Fig. 3.15 The reference lines used for diagnosing basilar invagination. Chamberlain's line connects the posterior end of the hard palate to the opisthion (*O*). McGregor's line extends from the posterior end of the hard palate to the lowest point on the midline supraoccipital curve [103]. Note the posterior margin of the foramen magnum is curved upward into the posterior cranial fossa, which is usually the case in basilar invagination. McRae's line extends from the basion (*B*) to the opisthion (*O*). Twining's line connects the tuberculum sellae (*TS*) and the endinion (*En*). A line perpendicular to Twining's line, which passes through the apex of the dens, is the Klaus height index line [103]. Normally, the apex of the dens should lie below McRae's line. Severe basilar invagination is diagnosed when the odontoid process violates McRae's line. The diagnosis of basilar invagination is considered if the odontoid process extends beyond 5 and 7 mm above Chamberlain's and McGregor's lines, respectively. The Klaus height index less than 30 mm indicates basilar invagination and a value between 30 and 36 mm indicates a tendency toward basilar invagination [103]. It should be mentioned that opinions differ on the cutoff value of these measurements for the diagnosis of basilar invagination [104]

joint) were reduced by ~20 % in patients with Chiari I malformation. In another study, Noudel et al. [34] compared the basioccipital lengths (measured from the sphenooccipital synchondrosis to the basion) among 17 patients with Chiari I malformation aged over 16 years and healthy controls. Notably, the basioccipital length was reduced among Chiari I patients. The association of a short clivus with Chiari I malformation has been confirmed by other studies [109, 112]. The bulk of evidence, thus, indicates that the supraoccipital, exoccipital, and basioccipital segments of the occipital bone are underdeveloped and hypoplastic, albeit to varying degrees, in the Chiari I malformation. Severe basioccipital hypoplasia or dysgenesis is associated with basilar invagination [33]. Dysgenesis of the basiocciput may be associated with a normal appearing basisphenoid [113]. Basioccipital dysgenesis (with scalloping, concavity, and thinness) has also been reported in the Chiari II malformation [96].

Nonlinear Nature of Occipital Bone Dysplasia in the Chiari I Malformation

In order to elucidate the nature of occipital bone dysplasia in Chiari I malformation, a meta-analysis was performed. Figure 3.17 shows the results of this meta-analysis for four studies that reported the values for mean and standard deviation of the clival or supraoccipital length or size of the foramen magnum in adult patients with Chiari I malformation [109, 114–116]. Although there are significant reductions in the lengths of the

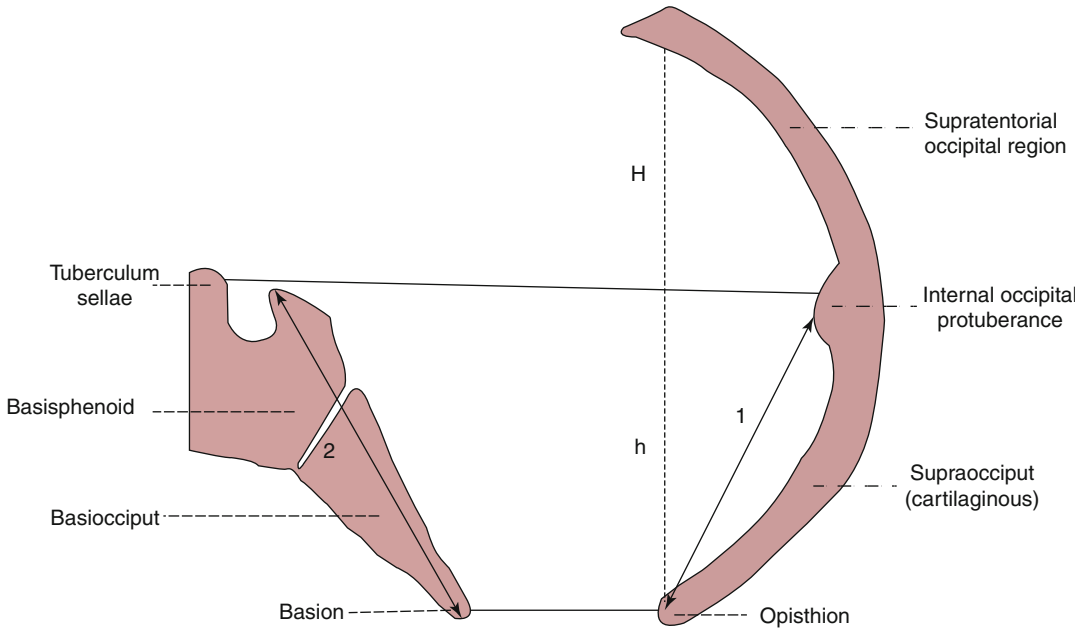

Fig. 3.16 The linear morphometry of the posterior cranial fossa and occipital bone. McRae's and Twining's lines are shown. A line perpendicular to Twining's line is drawn at one-fourth of its distance from the endinion (internal occipital protuberance) connecting the inner table of bones in the infra- and supratentorial compartments. The distances between Twining's line and the inner table of the skull in the supratentorial and infratemporal regions, respectively, indicate the depth of the posterior fossa in the supraoccipital region and the height of the supratentorial occipital region [109]. The lengths of the supraocciput and clivus are represented by the *two-headed arrows 1* and *2*, respectively [110]

supraocciput and clivus, the meta-analysis indicated that the overall reduction in size is more prominent in the supraocciput than in the clivus. This is in line with the observation made by Nishikawa et al. [33] and Dagtekin et al. [117] in adult Chiari I patients in whom the supraocciput was significantly more underdeveloped than the clivus. The meta-analysis also indicated that there is a tendency for the foramen magnum to widen anteroposteriorly; however, this increase in the size of the foramen magnum is not proportionate to the retardation of the supraocciput and clivus. Overall, it seems that occipital bone dysplasia in Chiari I malformation is nonlinear in nature and different parts of this bone are disproportionately affected. As mentioned earlier, the supraocciput develops through a morphologically complex process of chondrification and ossification. The chondrified supraocciput is derived from the parietal plate and exoccput and is composed of lateral and central plates. The lateral plates ossify by two upper and lower ossification centers and the central plate ossifies by two centers that rapidly fuse. The parietal plate undergoes partial reversion during fetal life rendering the upper part of the chondrified supraocciput derived from this plate vulnerable to regression as well. This could potentially provide an embryological basis for shortening of the supraocciput in Chiari malformation.

Midface Retrocession in Chiari Malformation

In an experimental fetal animal model of Chiari malformations and spinal dysraphism induced by a single maternal dose of vitamin A, Marin-Padilla and Marin-Padilla [118] noted that the underdevelopment of the occipital bone and posterior cranial fossa causes the maxilla to take a more posterior position within the viscerocranium,

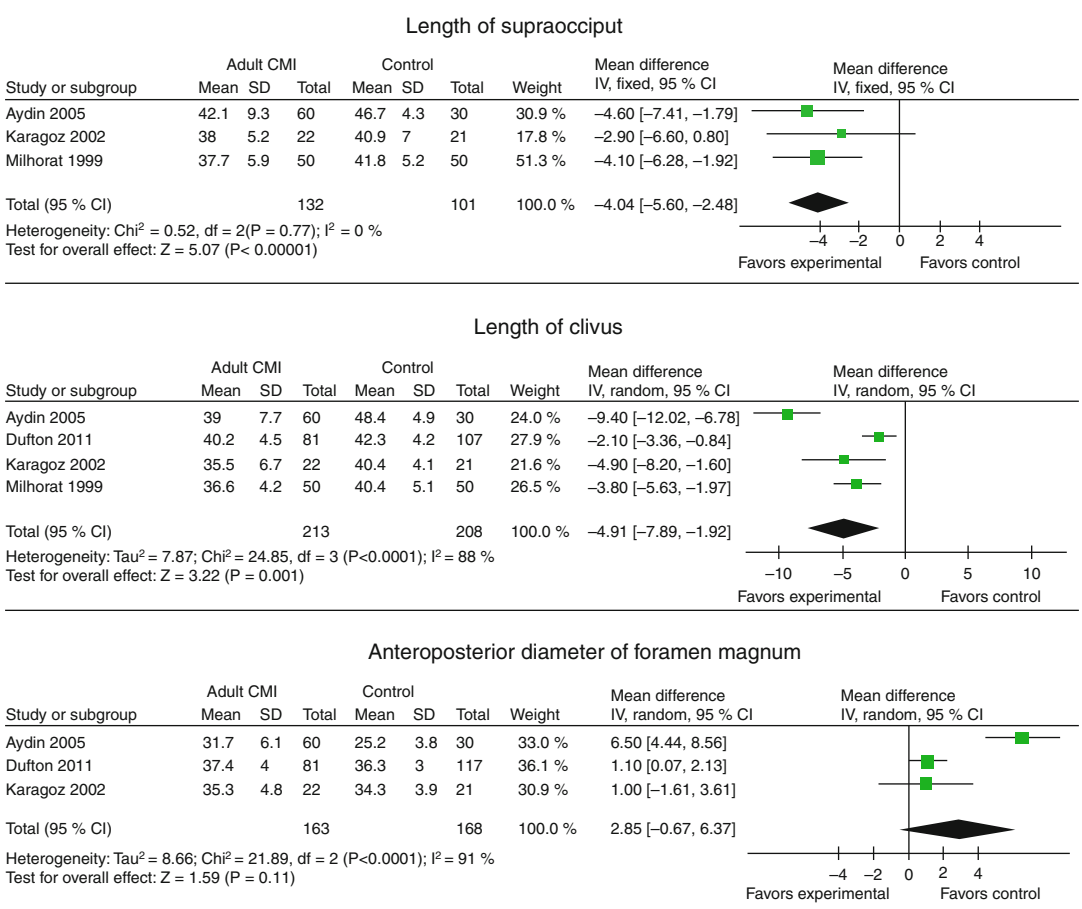

Fig. 3.17 Forest plots comparing the clival and supraoccipital lengths and anteroposterior diameter of the foramen magnum among adult patients with Chiari I malformation and controls. Homogeneity-based method of meta-analysis was performed using Review Manager Version 5 for Windows (Cochrane Collaboration and Update Software). Homogeneity between studies was assessed by means of standard Cochran's Q statistic and I^2 statistic. A fixed effect model (for data set with nonsignificant heterogeneity) or random effect model (for data set with significant heterogeneity) was used to merge odd ratio values and to estimate the overall effect size. Overall effect, odds ratio, and confidence interval are presented

leading to retrocession of the midface. In humans, a subtle midface retrocession can be best evaluated by the length of Chamberlain's line; a short Chamberlain's line reflects midface retrocession with respect to the occipital region. The length of Chamberlain's line is reduced in patients with Chiari I malformation, reflecting a subtle abnormality in the midface [96]. Interestingly, patients with greater midface retrocession have smaller posterior fossae [96]. Further studies are required to elucidate the potentially more pervasive, albeit subtle, abnormalities of the viscerocranium among Chiari patients.

Embryogenesis of the Hindbrain

The Developmental Anatomy of the Cerebellum

The current understanding of the embryogenesis of the cerebellum is indebted to the observations made during the late nineteenth to early twentieth centuries. The following discussion is based on the studies of Bailey and Miller [119], Dow [120], Frazer [6], Hamilton et al. [121], Heisler [122], Hochstetter [123], Keibel and Mall [124], Keith [125], Minot [126], Patten [127], Piersol [48],

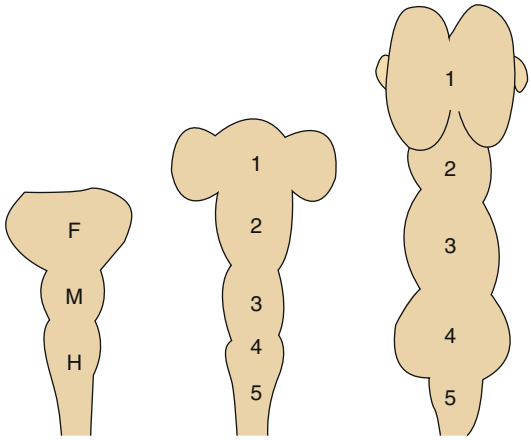

Fig. 3.18 Schema of the cranial neurocele at three-vesicle and five-vesicle stages. The expansion of the cranial neurocele initially yields the forebrain (*F*), midbrain or mesencephalon (*M*), and hindbrain (*H*). With further subdivision, the telencephalon (*1*), diencephalon (*2*), mesencephalon (*3*), metencephalon (*4*), and myelencephalon (*5*) are formed (Reproduced from Heisler [122] with slight modifications)

and Stroud [128]. More recent observations have been made by means of in vitro and in vivo fetal sonography and magnetic resonance imaging [129–133].

The primary neural tube expands cranially to form three vesicles separated by two constrictions: one between the forebrain and midbrain vesicles and the other between the midbrain and hindbrain vesicle. The constriction between the midbrain and hindbrain is called the *isthmus* and appears even before the cranial closure of the neural tube [122]. Subsequently, two other constrictions appear in the region of the forebrain and hindbrain yielding a five-vesicle neural tube composed of the telencephalon, diencephalon, mesencephalon, metencephalon, and myelencephalon (Fig. 3.18). The transfer from three-vesicle to five-vesicle neural tube is associated with bending of the neural tube at three levels (midbrain, midportion of the hindbrain, and cervicomedullary junction) and a spatial change occurs from a craniocaudal to ventrodorsal orientation of the vesicles [122].

The rhombencephalon (hindbrain) extends from the isthmus to the cervical flexure [126]. In the midportion of the rhombencephalon, the basal and alar plates lie in the same plane. Moving upward and downward, the alar plates on both sides approximate each other in the dorsal midline (Fig. 3.19) and tend to attain a dorsal position in much the same way as in the spinal cord [6]. Thus, the roof plate is wider in the midportion and narrower in the cranial and caudal portions of the rhombencephalon. Just beneath the isthmus and as a result of rapid initial growth of the midbrain, the rostral ends of the right and left metencephalic alar plates, which are in a close proximity in the dorsal midline, are pushed downward. This creates an internal bend in the metencephalic alar plate (Fig. 3.19). A medial portion located rostrally lies transversely beneath the isthmus. The lateral arms located caudal to this bend are initially longitudinally oriented [6].

At the fourth week of fetal life, the roof of the rhombencephalon is bounded laterally by the rhombic lip, inferiorly by the obex, and superiorly by the metencephalic alar plates [125]. The dorsal extension of the metencephalic alar plate over the roof plate forms a thickened *metencephalic rhombic lip* at the junction between the roof plate and alar plates [121]. The metencephalic alar plates then thicken and bulge internally toward the fourth ventricle and externally toward the cisterna magna to form the intraventricular and extraventricular parts of the cerebellar plates, respectively [121]. At this stage, the cerebellar plates have three layers: ependymal, mantle, and marginal layers from inside out [121]. Between the sixth and eighth weeks, the pontine flexure is maximized. The metencephalic rhombic lip and cerebellar plates including the previously longitudinal arm caudal to its internal bend are now in a transverse plane. At the second month, the growth of the intraventricular part dominates due to the proliferation of precursor neural cells (neuroblasts) in the subependymal region to form a mantle layer.

The growth of the cerebellar plates (and later, primordium) demonstrates a considerable heterogeneity in space and time, which results in the appearance of several topographically distinguishable regions in the course of its development (Fig. 3.20). Initially, the cerebellar plates grow in a transverse direction expanding them laterally

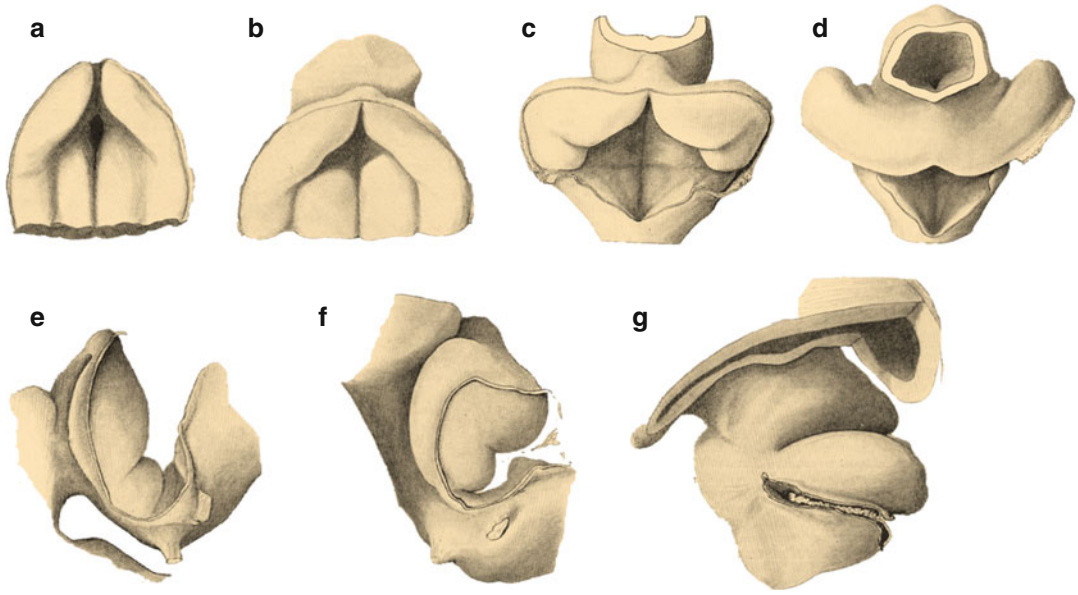

Fig. 3.19 Schema of the posterior (**a**–**d**) and lateral (**e**–**g**) views of the developing cerebellum. (**a**) The right and left metencephalic alar plates approximate each other rostrally and are in an inverted V-shaped position. (**b**) The enlarging mesencephalon pushes the metencephalic alar plates downward. This creates an internal bend in each alar plate, which is best visible in (**c**, **f**). (**c**) The cerebellar plates are composed of longitudinal and transverse parts marked by the internal bend. The transverse parts begin to fuse rostrally and externally beneath the mesencephalic isthmus. (**d**) The dorsomedian fusion of the cerebellar plates progresses caudally. (**e**) The lateral view corresponding to (b) shows the intraventricular growth of the cerebellar plates at this stage. (**f**) The lateral view corresponding to (c) shows the transverse and longitudinal parts of the cerebellar plates. The internal bend is maximized. The extraventricular part of the cerebellum is enlarging. (**g**) The lateral view corresponding to (d) shows that the extraventricular part of the cerebellum has grown considerably. The growth rate of the longitudinal part of the cerebellum is lower than that of the transverse part, and the intraventricular part of the cerebellum is now substantially regressed (Reproduced from Frazer [6] with slight modifications)

[119]. The transverse growth coincides with the growth of the intraventricular part in the early stages of the embryo. The lateral parts of cerebellar plates corresponding to cerebellar peduncles grow in a rate lower than in its medial parts [124]. During the third month, the two transversely lying cerebellar plates fuse in the dorsal midline to form a single cerebellar primordium [124]. The fusion of the two cerebellar plates occurs externally, leaving the two intraventricular parts separate in the midline [119]. The cerebellar primordium is connected to the roof of the midbrain anteriorly and the choroid plexus of the fourth ventricle posteriorly by two thin membranes, namely, anterior and posterior medullary vela. Subsequently, the greatest growth of the cerebellar primordium occurs through a longitudinal expansion of its extraventricular part [119]. The neuroblasts migrate from the metencephalic rhombic lip and mantle layer of the intraventricular part and contribute to the formation of cerebellar gray matter within the extraventricular part [121]. The development of cerebellar gray matter follows several successive stages: (1) first, neuroblast migration yields the superficial cerebellar cortex; (2) a group of neuroblasts migrates toward the surface deep to the superficial cerebellar cortex to form Purkinje cells; (3) neuroblasts of superficial cerebellar cortex migrate deeply beneath the Purkinje cell layer; and (4) the remaining mantle zone neuroblasts form the deep cerebellar nuclei [121]. Ultimately, subependymal neuroblast proliferation ceases. The migration of precursor neuronal cells and cessation of subependymal neuroblast proliferation are associated with gradual disappearance of the intraventricular part of

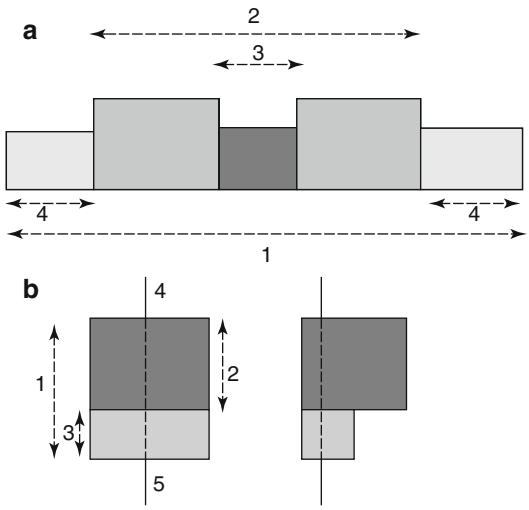

Fig. 3.20 A schematic representation of the heterogeneous growth of the cerebellar primordium. The transverse section (**a**) through the cerebellar primordium (*1*) shows a medial region (*2*) and two lateral arms (*4*). The medial region is composed of a median vermis (*3*) and lateral (hemispheric) masses between the vermis and lateral arms. The lateral arms form the cerebellar peduncles [124]. The sagittal section (**b**) through the cerebellar primordium (*1*) shows the cranial and caudal parts derived from the metencephalic alar plates (*2*) and thickened rhombic lip (*3*), respectively. The superior and inferior medullary vela are attached to the cerebellar primordium and arbitrarily divide it into intra- and extraventricular parts marked by the *dashed lines*. As depicted here, the median vermis, lateral arms, and caudal region of the cerebellar primordium grow in lower rates

the cerebellar primordium, a process referred to as *eversion of the cerebellum* [121] (Fig. 3.21). The eversion is thus mainly due to a shift in the pattern of cerebellar growth from intraventricular to predominantly extraventricular growth. The cerebellar primordium is mainly extraventricular in an 80 mm CRL embryo corresponding to ~14th week of fetal life [121]. Despite cessation of subependymal neuroblast proliferation, the metencephalic rhombic lip continues to generate new neuroblasts destined for the extraventricular part of cerebellum [124]. The longitudinally growing extraventricular part then overlaps the superior and inferior medullary vela [119].

In brief, the transverse growth of the cerebellar plates precedes the longitudinal growth of the primordium, and the growth of intraventricular part precedes that of the extraventricular part. The fusion of cerebellar plates into a single cerebellar primordium marks the shift in the pattern of early cerebellar development and growth. The longitudinal growth of the cerebellar primordium during the second trimester results in the appearance of several cortical sulci and fissures. After the initial rapid transverse growth of the cerebellar plates (before fusion and during the second month of fetal life), transverse growth of the cerebellar primordium during the third to fifth months continues at slower rates. Following the fifth month of fetal life and mainly during the third trimester, the cerebellum experiences its most rapid transverse growth compared to any other parts of the brain. What follows below is a discussion of the development of the vermis and cerebellar hemispheres.

Dorsomedian fusion of the cerebellar plates begins rostrally at the ninth week of fetal life [134]. The region of median fusion gives rise to the vermis. The embryogenesis of the vermis has two stages. Following the rostral fusion of the extraventricular part of the cerebellar plates through their thickened rhombic lips, the anterior vermis is the first to form. Until the 18th week of gestation, the vermis covers only the rostral half of the fourth ventricle [129]. The anterior vermis is anatomically continuous with the germinating rhombic lip laterally and the rhombic roof inferiorly. The anterior vermis progressively grows in a caudal direction, closing the posteroinferior interhemispheric cleft and entirely covering the fourth ventricle between the 18th and 21st weeks of fetal life [129]. The progressive caudal growth of the vermis occurs by the specialization of the adjacent part of the rhombic roof as well as, mainly, by the growth of the rhombic lips toward the midline and their fusion favored by the mechanical effects of the transversely expanding lateral hemispheres. Once closure of the vermis is completed, it continues to grow linearly in both the longitudinal and anteroposterior directions after the fifth month of fetal life. This growth is closely proportionate to the transverse growth of cerebellum [133]. While the vermis grows in a craniocaudal direction during the first half of the fetal life, its further growth in the second half of

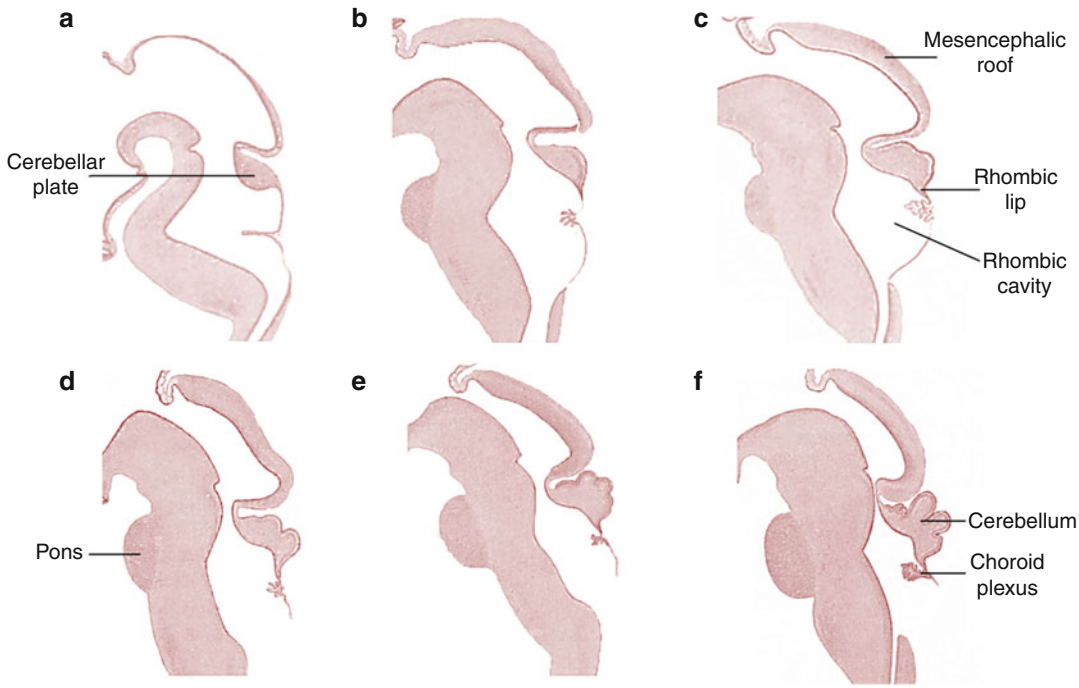

Fig. 3.21 Parasagittal sections through the midbrain/hindbrain showing the successive stages of cerebellar development and the process of cerebellar eversion. The cerebellar primordium is mainly intraventricular in (**a**) and is extraventricular in (**b**–**f**). The fusion of the cerebellar plates (not shown here) marks the transition from intraventricular to extraventricular development of the cerebellum. Note that the ventral pons, which contains corticopontocerebellar fibers, grows and the pontine flexure straightens concomitantly with the development of the extraventricular cerebellum (Reproduced with modifications from Hochstetter [123])

fetal life and occurs circumferentially, ultimately leaving two notches between the cerebellar hemispheres, one anteriorly and one posteroinferiorly.

At the end of the third month, the cerebellum is dumbbell-shaped with two lateral masses and a relatively thin median vermis [125]. As mentioned earlier, the cerebellar primordium is composed of metencephalic alar plates, which partially extend into the roof plate forming a thickened metencephalic rhombic lip. The metencephalic rhombic lip continues to yield neuroblasts, and the neuroblasts originating from it migrate superficially to the cerebellar cortex [124]. As a result of the differential growth of the metencephalic alar plate and rhombic lip, three sulci successively appear between them: one in the median area (sulcus postnodularis) and then two in the lateral areas (sulcus floccularis). These sulci (postnodularis and floccularis) later become continuous to form the posterolateral fissure, which is the first fissure to appear in the developing cerebellum [121]. The posterolateral fissure separates the flocculonodular lobe from the rest of the cerebellum (corpus cerebelli) [48]. In this way, the thickened rhombic lip gives rise to the nodulus and flocculus [124].

During the fourth and fifth months, the cerebellar cortex grows rapidly in the longitudinal axis resulting in the appearance of several other transverse sulci or fissures and intervening lobules [124, 127]. The longitudinal growth of the cerebellum occurs superficially first in the median region corresponding to the vermis and later to a greater extent in the lateral regions corresponding to the cerebellar hemispheres. The first fissure to appear in the median (vermian) region of the corpus cerebelli is the fissura prima of Elliot-Smith or sulcus primarius of Bolk, which separates the anterior and posterior cerebellar lobes during the

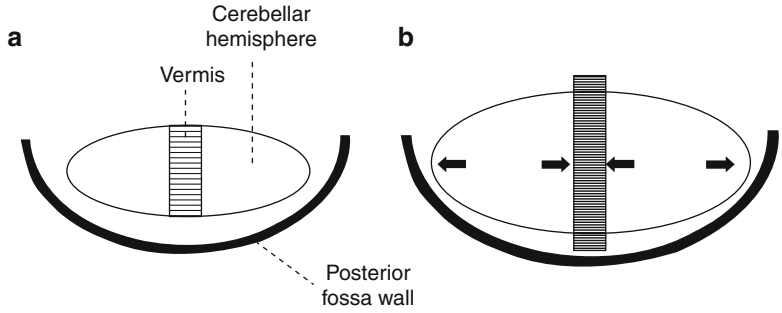

Fig. 3.22 Schema depicting the relative overcrowding of the posterior cranial fossa from the early (**a**) to the late (**b**) second trimester. *Arrows* indicate the conflict between the growing cerebellar hemispheres and the midline vermis and the wall of the posterior fossa. Slight degrees of overcrowding are favored by the relatively greater transverse growth rate of the cerebellar hemispheres compared to that of the posterior cranial fossa. The relative overcrowding is a normal event beginning during the second trimester and continuing to the third trimester and early postnatal life. An exaggerated overcrowding as a result of a small posterior fossa may result in the upward and downward herniation of the vermis

fourth month of fetal life [48, 127, 132]. Initially, the growth rates of the anterior and posterior cerebellar lobes are proportionate, and the volumes of the two lobes are rather similar. Beginning from week 16, the posterior lobe grows faster [132]. The minor cerebellar fissures appear until the seventh month of fetal growth [125].

The fourth month of fetal life is marked by the cortical growth of the median vermis [124]. At this time, the lateral masses of the corpus cerebelli are smooth [124]. The subdivision of the hemispheric masses occurs during the fifth month of fetal life once the basic subdivision of the vermis has taken place [48]. With the rapid longitudinal growth of the cerebellum within the posterior fossa during the second trimester, the cerebellar primordium gradually becomes wedge-shaped with the apex posterior as a result of mechanical factors [125]. At this time, transverse growth occurs at a relatively lower rate, and the expanding lateral hemispheres roll in toward the midline overlapping the vermis [124]. This results in the formation of a median longitudinal fissure between the two hemispheres. The transverse length of the cerebellum is three times the longitudinal length of the vermis in the early part of the second trimester [132]. However, by the end of the second trimester, the transverse length is about two times the longitudinal length of the vermis [132]. This may have some potential implications: first, the longitudinal growth of vermis overrides the transverse growth of the cerebellar hemispheres during the second trimester. Secondly, the rate of transverse cerebellar growth is greater than the rate of expansion of the confined posterior cranial fossa, which brings about a state of relative posterior fossa overcrowding. The overcrowding results in the compression and spreading out of the vermis sandwiched between the two cerebellar hemispheres. This mechanism is depicted in Fig. 3.22.

The fetal cerebellum goes through a phase of rapid growth after 28 weeks of fetal life [131] and the third trimester is marked by the transverse growth of the cerebellar hemispheres [133]. This contributes further to the overcrowding of the posterior fossa. Wedging of the cerebellum becomes more evident toward the end of pregnancy, probably because the posterior fossa is more yielding anteroposteriorly than transversely late in the fetal period. During this phase of growth, which is mainly due to the massive proliferation and migration of the cortical granule cells, the cerebellar volume increases by ~2.8-fold [131]. The intracranial and cerebral volumes increase by ~twofold during the same period [131].

The embryogenesis of the cerebellar lobules is beyond the scope of the current chapter. The reader is referred to the review by Dow [120] for details on the ontogeny and phylogeny of cerebellar lobulation. So far, several different systems of nomenclature and subdivision have been

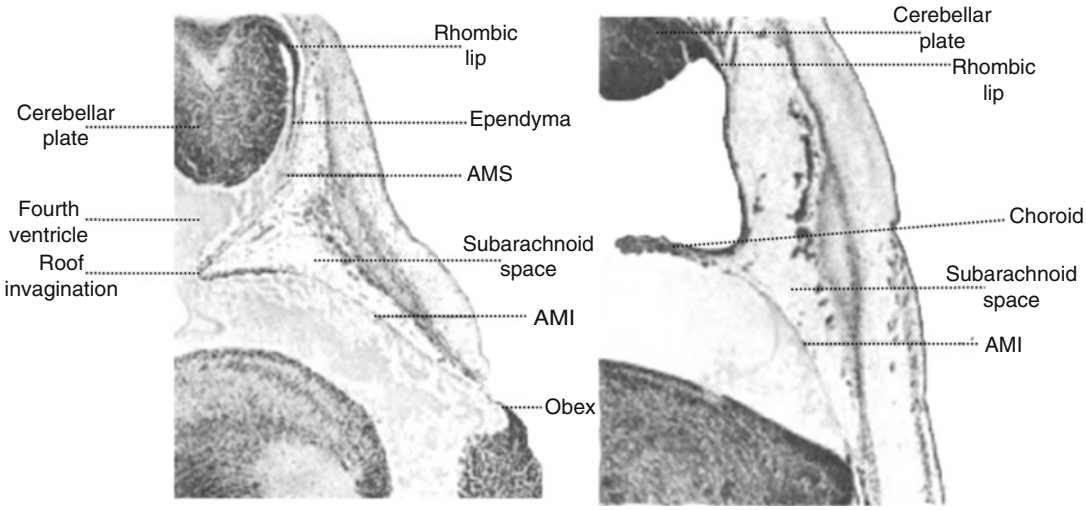

Fig. 3.23 The embryogenesis of the rhombic roof. *AMS* area membranacea superior, *AMI* area membranacea inferior. Note the developing cerebellum is mainly intraventricular at these stages (Reproduced from Weed [137] with slight modifications)

proposed. Ingvar (as cited by Dow [120]) noted that the region in front of the primary fissure and the one behind the prepyramidal fissure are morphologically the most constant regions in the mammalian cerebellum. However, the region between the primary and prepyramidal fissures demonstrated considerable phylogenetic variation. This phylogenetically variable region of the cerebellum (the middle lobe of Ingvar) receives the corticopontocerebellar afferents and, according to Dow, should be designated as neocerebellum. Phylogenetically, the flocculonodular lobe and the lingula (the so-called archicerebellum) are the oldest parts of the cerebellum. This is followed by the appearance of the paleocerebellum, composed of the anterior lobe (except lingula), pyramis, uvula, and paraflocculus, and subsequently the appearance of the neocerebellum (the rest of the cerebellum). According to Ingvar, while the archicerebellum essentially receives vestibular inputs, the paleocerebellum and neocerebellum receive spinal and cortical inputs, respectively. In lower primates, the paraflocculus is larger than the flocculus, projects between the latter and lateral part of the corpus cerebelli, and is connected by a stalk with the uvula and pyramis [120, 128]. The paraflocculus is retained as a small and vestigial structure in man [128] and is often referred to as the accessory paraflocculus [135]. The accessory paraflocculus lies in close vicinity to the flocculus and grossly varies in shape from a flat lamella to a rosette-like cluster of folia akin to the flocculus [136]. There are controversies around the origin of the tonsils (the lowest part of the corpus cerebelli) in humans. While some advocate that it is a part of the middle lobe in front of the prepyramidal fissure that grows downward and secondarily becomes contiguous to the uvula, others believe that it represents the growth of the stalk of the paraflocculus intervening between the uvula/pyramis and vestigial paraflocculus in humans [120].

Development of the Rhombic Roof

A discussion on the embryogenesis of the roof of the fourth ventricle is not complete without referring to the outstanding work of Weed [137]. In human embryos and other mammals, Weed identified an oval thinned-out area of epithelial differentiation (the so-called area membranacea superior) in the superior portion of the ependymal roof of the fourth ventricle (Fig. 3.23). The superior and inferior borders of this area were continuous with the ependymal layer, and its

lateral borders were flanked by a hypercellular region of ependyma on either side. With further development of the rhombencephalon and formation of the pontine flexure, the rhombic roof is invaginated at its midpoint of its caudocephalic axis to be developed into the choroid plexus. At this stage, the area membranacea superior is separated from the inferior portion of the rhombencephalic roof by the primordium of the choroid plexus. Shortly thereafter, the area membranacea superior in the human embryo is replaced by the growth of ependymal cells originating from its proliferative lateral borders. At the same time, the ependymal lining below the invaginated roof also thins out and undergoes epithelial differentiation to form the *area membranacea inferior* (Fig. 3.23). The latter extends from the choroid plexus primordium superiorly to the obex inferiorly. The mesenchyme posterior to the area membranacea inferior is broken down retaining only a pial layer and arachnoid strands extending from the condensed mesenchymal layer of dura mater to the area membranacea inferior. The space between the dura and area membranacea inferior develops into the cisterna magna. The inferior membrane, which separates the fourth ventricle from the developing cisterna magna, bulges backward and is covered internally by a thin ependymal layer.

The embryonic fate of the saccular invagination (outpouching or diverticulum) at the caudal portion of the rhombic roof was once a controversial topic [138]. Wilson cited Blake [139] as stating that the saccular invagination gradually becomes larger and ultimately disappears in humans, but not in lower mammals. With the degeneration of a considerable part of the caudal sac, its neck is retained at the margin of the foramen of Magendie [138]. Thus, in adults, the rhombic roof is made up of the inferior medullary velum, tela choroidea, and area membranacea inferior of Weed with the foramen of Magendie being found in the middle portion of the latter. The inferior medullary velum flanks the nodulus of the cerebellum [138] and is in fact derived from the most caudal part of the metencephalic rhombic lip, the rostral part of which contributes to the flocculus.

Abnormal Cerebellar Development and Morphology Associated with Neural Tube Defects and the Chiari II Malformation

Prenatal Period

In twin embryos of ~25 mm CRL (7–8 week), Padget [140] made an interesting observation: one of the embryos had a lumbosacral spina bifida aperta, and the other was normal. The posterior fossa and fourth ventricle (rhombic cavity) were smaller in the embryo with the neural tube defect. The cerebellar plates, which were intraventricular at this stage, were of a similar size in both embryos. The intraventricular cerebellar plates approximated each other in the dysraphic embryo with a small rhombic cavity and tended to prematurely fuse. Thus, the transverse diameter of the intraventricular cerebellum in the dysraphic embryo was diminished in the late embryonic period as a consequence of a small and unyielding posterior fossa. It may be assumed that if the later longitudinal growth of the extraventricular cerebellum occurs about a restricted transverse axis, the disproportionate longitudinal expansion (especially of the midline vermis) would then result in its upward or downward herniation. A later stage of cerebellar development has been studied by Van Hoytema and Van den Berg in a fetus of 140 mm CRL with spina bifida aperta. In normal fetuses of this stage, the rhombic roof is perforated and the cerebellum simultaneously undergoes an inward rotation in a way that its caudal part (i.e., caudal vermis) turns inside and into the fourth ventricle. In the fetus with spina bifida, however, the rhombic roof is thick and infiltrated by the choroid plexus and is only partially perforated; the inward rotation of the caudal cerebellum does not happen, and the lower part of the vermis is pulled down by its arachnoidal attachments to the overcrowded choroid plexus and thick rhombic roof [141]. A substantially reduced transverse cerebellar diameter and obliterated cisterna magna have also been detected by ultrasound examination of fetuses older than 15 weeks with spina bifida [142]. Taken together, the subnormal cerebellar development in fetuses with spina bifida is characterized by a tendency for early fusion of the cer-

ebellar plates, restricted transverse growth, and failure of inward rotation of the caudal cerebellum.

Postnatal Period

The total and lateral (hemispheric) cerebellar volumes are reduced in pediatric patients with Chiari II malformation [143]. The vermian volume is near normal, but the midsagittal vermis area and longitudinal and anteroposterior diameters of the vermis are increased [143]. This implies that (1) the cerebellum in patients with Chiari II malformation is reduced in size (secondary to hypoplasia or atrophy), (2) the hypoplasia or atrophy preferentially affects the lateral cerebellar hemispheres, and (3) elongation and expansion of the cerebellar vermis probably results from side-to-side compression by the two cerebellar hemispheres in an unyielding posterior cranial fossa. Moreover, while the absolute and relative (i.e., fraction of total) volumes of the posterior cerebellar lobe are reduced in Chiari II malformation, the absolute and relative volumes of the anterior cerebellar lobe are increased [144]. This also implies that the overall reduction in the size of the cerebellar hemispheres in Chiari II malformation is related to a subnormal growth of the posterior cerebellar lobe. The enlarged anterior cerebellar lobe may be a secondary compensation for the compromised posterior lobe [144].

Rhombencephalosynapsis

Complete and partial rhombencephalosynapsis occurs rarely in association with the Chiari II malformation [145, 146]. Rhombencephalosynapsis is an uncommon anomaly in which the two cerebellar hemispheres are fused. In its most complete form, the vermis is totally absent and the two cerebellar hemispheres and the dentate nuclei are fused or are in opposition with each other [145]. In partial rhombencephalosynapsis, the anterior vermis is usually absent and the posterior vermis is hypoplastic [146]. The developmental origin of this malformation is controversial. It has been mentioned that the cerebellar primordium demonstrates a heterogeneous pattern of growth following the midline fusion of the cerebellar plates. Generally, the growth of the vermis occurs at a lower rate compared to that of the lateral hemispheres. This differential growth pattern results in the median fused region (vermis) being topographically distinct from the cerebellar hemispheres. Rhombencephalosynapsis is expected to occur if the growth of the vermis is either retarded following the early fusion or paradoxically enhanced to a level comparable to that of the cerebellar hemispheres. However, there are no direct observations to prove or disprove this statement.

Agenesis or Occlusion of the Foramen of Magendie in Chiari I Malformation

In 1950, Gardner and Goodall reported 17 patients with Chiari I malformations with or without associated hydromyelia or basilar impression. All patients had an occluded foramen of Magendie either due to atresia or arachnoid adhesions between the impacted cerebellum and medulla oblongata [147]. Symptoms were relieved following release of this obstruction. Gardner et al. [148] posited that the atresia or agenesis of the foramen of Magendie resulted from persisting remnants of the embryonic rhombic roof, which not only cover the foramen of Magendie but also occlude the foramina of Luschka laterally. Depending on the elasticity and permeability of this occluding membrane, a unified embryological theory was proposed accounting for Chiari malformation, Dandy-Walker syndrome, arachnoid cysts of the cerebellum, and hydromyelia/syringomyelia. Accordingly, if the occluding membrane is not permeable, the anomaly is severe. If the membrane is elastic, the fourth ventricle bulges into the cisterna magna and Dandy-Walker syndrome results. If the membrane is not elastic, the Chiari malformation occurs. If the membrane is split, an arachnoid cyst appears in between the two layers of the rhombic roof. Gardner et al. [148] postulated that occlusion of the foramen of Magendie is physiologically more significant than that of the foramina of Luschka as the former is located in the midline and acts to substantially dissipate the ventricular pulse wave

into the subarachnoid space. These findings faced skepticism by subsequent studies showing occlusion of the foramen of Magendie in only a small proportion of Chiari I patients [149].

The Development of the Tentorium Cerebelli

At the eighth week of fetal life, the mesenchymal condensation of the cerebrocerebellar fissure intervening between the cerebellum and occipital lobe of the cerebrum forms a small transverse fold on either side of the midbrain [74, 140, 150]. These tentorial folds attach to the otic capsules laterally [74] and are symmetric, initially separate, transparent, and histologically composed of a central core of loosely packed mesodermal cells sandwiched between two layers of flattened mesodermal cells [150]. The median fusion of the bilateral tentorial folds begins dorsally during the third month of the fetal period to form a single tentorium cerebelli. Once the dorsal tentorial fusion attains a considerable length (10 mm) at about the fifth week of gestation, the fusion is completed leaving a notch (i.e., tentorial incisura) between the ventral nonunited portions of the tentorium through which the midbrain traverses [150]. Henceforward, the growth of different parts of the tentorium continues rather proportionally and the loosely packed mesenchymal core is gradually replaced by a dense collagenous tissue [150]. The tentorium is subject to a continuous traction as a consequence of differential encephalization (disproportionate growth of the cerebrum and cerebellum) [74, 98]. This stretches the tentorial insertion over the otic capsules and results in an enhanced bone deposition along its basicranial attachments corresponding to the crest of the petrous temporal bone, which marks the boundary of the posterior cranial fossa with the middle fossa [74].

From an evolutionary point of view, the fusion of tentorial folds happened relatively late in the evolution of mammals, and the ratio of the length of fused tentorium to the length of the incisura (known as the tentorial index) is greater among higher mammals [151]. The tentorium cerebelli in man has two other characteristics: it has the largest surface area in relation to body size among primates and mammals and, comparatively, is the most posteroinferiorly positioned [98, 150, 151]. Notably, in patients with Chiari II malformation, the tentorium is often dysplastic, its calvarial attachment is displaced inferiorly toward the foramen magnum, and the tentorial index is low [152, 153].

Posterior Cranial Fossa Volume and Its Determinants

Assuming that the posterior cranial fossa is a triaxial ellipsoid, its volume can be estimated by the following formula:

$$V = \frac{1}{6}\pi xyz$$

where π is a constant approximately equal to 3.14 and x, y, and z are, respectively, the width (maximum transverse diameter), length (distance from the dorsum sella to the internal occipital protuberance), and height (distance from the basion to the peak of the tentorium cerebelli corresponding to its ventral edge on the midsagittal plane) of the posterior cranial fossa [111]. Any factor affecting the width, length, and height of the posterior cranial fossa proportionately affects its volume. The bulk of evidence indicates that patients with Chiari I malformation have a small or overcrowded posterior fossa, albeit to a varying extent and pattern. It seems that a reduction in the height of the posterior fossa is the main culprit in the majority of patients with Chiari I malformation [96, 109, 111, 154]. The shallowness of the bony posterior fossa is a consequence of supraoccipital and basioccipital hypoplasia, platybasia, and basilar invagination. The length of the fossa may be reduced or normal in pediatric patients [111, 155] and is occasionally increased in adult patients [109]. Some have advocated that the

increase in the length of the posterior fossa in adult patients with Chiari I malformation is a compensation for the reduced height [109, 156]. Only a few studies have evaluated the width of the fossa, and both reduced and normal widths among pediatric patients have been reported [111, 155]. As mentioned earlier, the size of the foramen magnum tends to slightly increase in Chiari I malformation. On the other hand, the small posterior fossa in Chiari II malformation is associated with a prominently enlarged foramen magnum [157]. The embryological basis of the Chiari I and II will be discussed in greater details in a separate chapter.

The boundary of the posterior cranial fossa is established by the end of the embryonic period. Initially, the posterior fossa is larger and partially opened posteriorly. During the third month, the posterior boundary of the fossa is completed. Ventricular distension and cerebellar growth are among the main factors expanding the posterior fossa during the embryonic period and even later. Subsequently, the volume of the fossa is reduced by two main mechanisms, namely, rotation of the tentorium and petrous bone during the second and third trimesters. Cerebellar growth is well accommodated and the reduction in volume is compensated for by the growth of the basicranial synchondroses and upward reflection of the extensible tentorium. Hormonal factors also play a key role in the growth of the posterior fossa. Any discordance between the mechanisms tending to reduce the volume and those tending to expand the posterior cranial fossa can potentially lead to a small fossa or more than normal crowding (i.e., overcrowding), with the hindbrain herniation being a consequence. We conclude with a discussion on some factors affecting the size of the posterior fossa during the embryonic, fetal, and early postnatal periods.

Ventricular Distension

The role of ventricular distention in expanding the posterior cranial fossa has been studied by McLone and Knepper [158] in a mouse embryo model with a caudal neural tube defect. With cerebrospinal fluid drainage through a defect in the neural tube, the cranial neurocele including the hindbrain vesicle partially collapses. The incomplete distension of the hindbrain vesicle leads to the formation of a small posterior fossa from lack of adequate forces and mechanical induction necessary to expand the surrounding mesenchymal or chondrified primordium. McLone and Knepper [158] postulated that a decrease in ventricular distension explains the occurrence of a small posterior fossa in Chiari II malformation. It should be noted that ventricular distension is only one of the factors that influence the size of the posterior fossa and affects its dimensions during the embryonic and early fetal periods. Therefore, the antenatal repair of the neural tube defect between 19 and 25 weeks of gestation does not affect the overall posterior fossa size during the late fetal period [159].

Rotation of the Intracranial Attachment of the Tentorium Cerebelli

During the fetal period, the tentorium rotates backward and downward toward the foramen magnum [98]. The tentorial rotation ranges from 90° to 180° and mainly occurs in a fetus less than 160 mm CRL (before 22 weeks of fetal life), a period when the otic capsule is still precartilaginous or cartilaginous [75, 160–163]. The differential encephalization (i.e., greater expansion of the cerebrum in relation to the cerebellar expansion) is the main factor influencing this rotation and determines the final intracranial tentorial attachment [98, 161]. With the expansion of the supratentorial space and posteroinferior rotation of the tentorium, the infratentorial angle (the angle formed between the lines extending from the calvarial attachment of the tentorium to the center of the pituitary fossa and from the latter to the basion) reduces by ~40 % between 10 and 22 weeks and by ~10 % between 22 and 29 weeks of the fetal period [98]. The gradual cessation in tentorial rotation after 22 weeks of the fetal period temporally corresponds to the stage in which the

ossification of the otic capsule has just begun and is progressing. The posteroinferior tentorial rotation diminishes the volume of the posterior cranial fossa by reducing its height.

Rotation of the Otic Cartilage and Petrous Temporal Bone and Shift in the Pattern of Posterior Cranial Fossa Growth

By the end of the third month of fetal life, the width and length of the posterior cranial fossa are similar, and the fossa is rather circular or funnel-shaped in its outline. During the second trimester, the posterior fossa grows in width more than in length and gradually becomes broader [86]. The preferential transverse growth of the posterior fossa during the second trimester is concomitant with and probably favored by the predominant transverse growth of the cerebellum. The late phase of fetal posterior fossa growth is characterized by a more longitudinal growth concomitant with the expansion of the middle cranial fossa. During the second half of fetal life, the otic cartilage and petrous temporal bone rotate backward [164] (Fig. 3.24). This rotation is temporally and mechanistically distinct from the tentorial rotation. While the latter ceases around 20–22 weeks of fetal life, the petrous rotation actually becomes more prominent following this period. The posteroinferior tentorial rotation occurs on a vertical plane and about a horizontal axis. In contrast, the backward rotation of the petrous bone is essentially on a horizontal plane and around a vertical axis. The petrous rotation results from expansion of the floor of the middle cranial fossa, which lodges the temporal lobe of the cerebrum [164]. The squeezing of the posterior fossa tends to diminish its width along with the posterior rotation of the petrous bones. However, rapid anteroposterior elongation of the posterior fossa accommodates the growing cerebellum during the late fetal period [164].

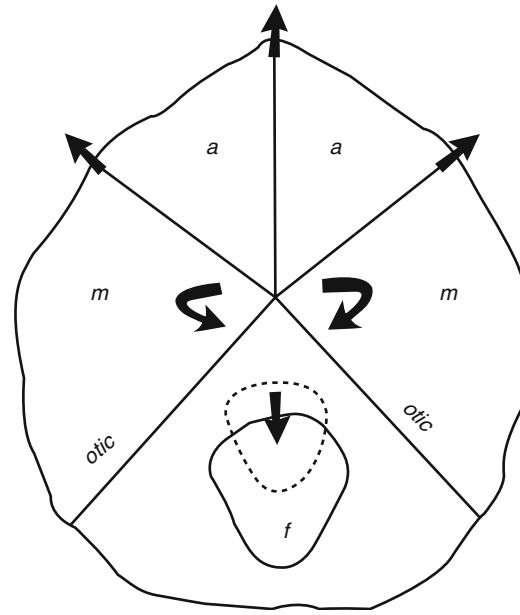

Fig. 3.24 The pattern of basicranial growth and rotation of the otic capsule (petrous temporal) during the second and third trimesters [164] with slight modifications (Reproduced with permission from John Wiley and Sons). Note the anterior cranial fossa (*a*) extends forward, the middle cranial fossa (*m*) expands with backward rotation of the petrous, and the foramen magnum (*f*) enlarges and is displaced posteriorly with the fetal growth

Growth of the Basicranial Synchondroses

At the fifth month of fetal life, the wall of the posterior cranial fossa is composed of several osseous segments (basiocciput anteriorly, supraoccipu t posteriorly, and exoccipuits and portions of the petromastoid temporal bone laterally) joined by the intervening synchondritic cartilages (Fig. 3.25) [74]. A synchondrosis is a cartilaginous growth plate made up of a middle resting zone of quiescent chondrocytes sandwiched between pairs of proliferating and hypertrophic zones [87]. The growth of a synchondrosis results in the deposition of new bone at the flanking osseous segments and growth of the basicranium (Fig. 3.25). The petrooccipital and occipitomastoid synchondroses contribute to the transverse growth of the posterior fossa, and the sphenooccipital, anterior, and posterior intraoccipital and occipitomastoid synchondroses contribute to growth in length [74]. This growth, beginning as early as the fourth to fifth month of fetal life [164], continues in postnatal life until the synchondroses become nonfunctional and

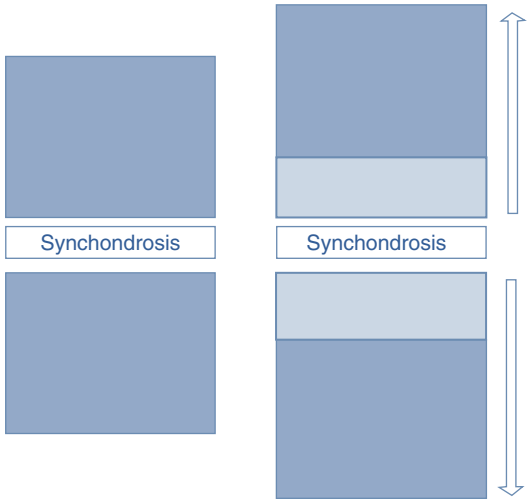

Fig. 3.25 A schema showing the growth of a synchondrosis with introduction of new bone into the flanking osseous segments and centrifugal displacement of these segments [74]

replaced by sutures, which then are ossified and fully obliterated with the concomitant fusion of the adjacent bones [16]. The synchondroses show variable rates of growth and timing for closure between genders [16]. Generally, the posterior intraoccipital synchondrosis is the first to close, followed by the anterior intraoccipital synchondrosis, and then the petrooccipital, occipitomastoid, and sphenooccipital synchondroses [16]. Closure of the anterior and posterior intraoccipital and sphenooccipital synchondroses is usually delayed in males compared to females [16].

Histologically, the middle resting zone contains the precursor cells of proliferating chondrocytes and is maintained by bone morphogenetic protein (BMP)-3 [165]. The maintenance of synchondrosis depends on the proliferation of chondrocytes [166] and the balance between the zones of proliferating and hypertrophied chondrocytes [167]. The phenotypic transition from the proliferating chondrocytes to hypertrophic chondrocytes and later to osteoblasts occurs toward the chondro-osseous junction of the synchondrosis and results in the introduction of new bone around the synchondrosis [166]. Several mediators and signaling pathways control this transition. The fibroblast growth factor receptor isoform 3 (FGFR3) is expressed in the proliferating chondrocytes of the basicranial synchondroses [168]. In a mouse model, the overactivation of FGFR3 signaling results in a rapid phenotypic transition and accelerated closure of synchondroses [166]. BMP4 also exerts a biphasic effect on the basicranial synchondroses characterized by an early phase of enhanced proliferation of chondrocytes followed by an accelerated phase of transition into the hypertrophic phenotype [167]. In humans, the sphenooccipital synchondrosis demonstrates a characteristically delayed postnatal closure. Its closure starts at 8 years of age, and the closure is almost complete in 50 and 95 % of individuals by the ages of 14 and 16–18 years, respectively [16]. The premature closure of the sphenooccipital synchondrosis is suggested as a cause of clival hypoplasia (shortened clivus) in patients with Chiari I malformation [34].

Upward Reflection of the Tentorium Cerebellum

Although generally considered as a stiff membrane, the dura mater has considerable viscoelastic properties [169, 170], enabling it to react to the tensions and forces applied to it with a rapid phase of expansion mediated by the elastic component and a slow phase mediated by the viscous component. In a cadaveric study, the dura mater was found to have an extensibility of 10–30 % [171]. Connective tissues containing collagen fibers and elastin also have the capability of remodeling by changing the intermolecular crosslinks to maximally adapt to mechanical stresses [172, 173]. These properties of the tentorium enable it to reflect upward and expand to compensate for the increased volume of the infratentorial contents. Although the short-term tentorial expansion is restricted by its viscoelasticity, the remodeling of its fibers as a result of prolonged stress may lead to greater tentorial expansion in the long term.

Tentorial extensibility has important anatomical relevance. As mentioned earlier, the slight degree of overcrowding in the posterior cranial fossa is a normal event during fetal development.

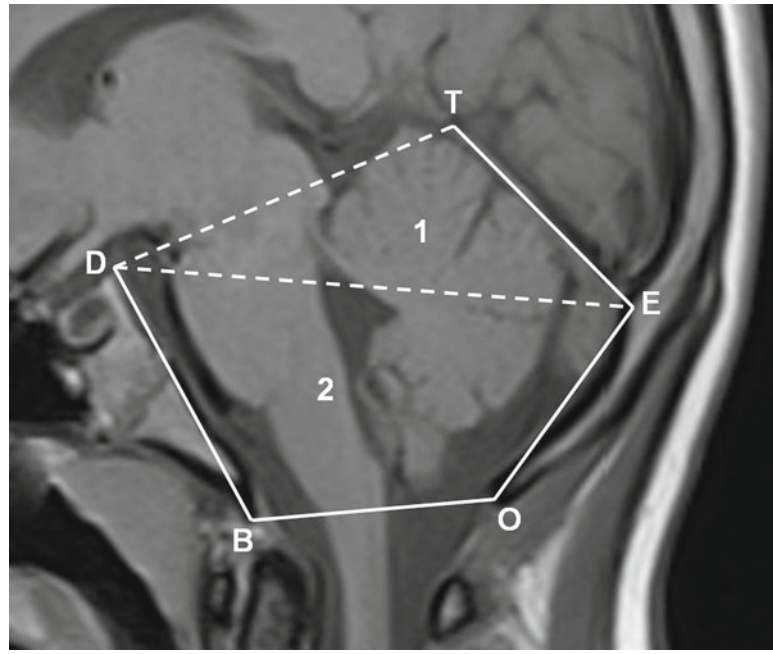

Fig. 3.26 A midsagittal plane of the posterior cranial fossa shows its division into tentorial (*1*) and bony (*2*) regions. *B* basion, *D* dorsum sellae, *E* endinion, *O* opisthion, *T* apex or peak of the tentorium. The T-E-O angle is the tentorial angle, T-E-D the angle of the tentorium to Twining's line, D-E-O the supraoccipital angle, E-D-B the clival angle, and D-B-O Boogard's angle

This overcrowding pushes the expanding tentorium upward. As the tentorium is peripherally attached to the inner surface of the occipital bone and the superior crest of the petrous bone and its attachments are fixed after the second trimester, tentorial expansion makes it concave downward. In the midsagittal plane, the ventral edge (apex) of the tentorium is the peak of this structure and is located above the upper level of the bony posterior fossa. Thus, the posterior fossa can be divided into two regions as shown in the Fig. 3.26. Unlike the lower bony region, the upper tentorial region ought to be expansile owing to the extensibility of the tentorium. In adult patients with Chiari I malformation, the tentorial region expands to compensate for overcrowding of the posterior fossa [33].

Hormonal Influences

The basicranial synchondroses are homologous to the epiphyseal growth plates of the long bones. In experimental and human studies, endochondral and periosteal bone growth as well as bone turnover and remodeling are influenced by such hormones as thyroxine, cortisol, estrogen, testosterone, parathyroid hormone, growth hormone, and activated vitamin D (cholecalciferol) [174–180]. To what extent the growth of the posterior fossa is affected by these hormones and their disturbances remains to be fully understood. In vitro, hydrocortisone and parathyroid hormone doses dependently enhance glycosaminoglycan synthesis by the chondrocytes derived from the sphenooccipital synchondrosis of the rabbit [181, 182], and hydrocortisone and cholecalciferol increase the proliferation of these chondrocytes [182, 183]. The sphenooccipital synchondrosis may remain open up to the fourth decade of life in patients with hypothyroidism [184]. The basiocciput is shorter in patients with growth hormone deficiency [184]. In a series of patients with rickets, the posterior fossa was significantly smaller compared to healthy controls, and ~30 % of the patients had Chiari I malformation [185]. These data indirectly indicate that various hormones regulate posterior fossa growth. Further studies are required to elucidate this aspect of development and specially the role of sex hormones.

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Embryology and Pathophysiology of the Chiari I and II Malformations

4

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Abstract

Hindbrain herniation is only one component of the Chiari malformations. These malformations often have other associated intracranial anomalies and malformations of the vertebral column. Depending on embryologic timing, herniation of the cerebellar vermis or tonsils occurs. Additionally, the herniated hindbrain may include the medulla oblongata and fourth ventricle. Currently, no single theory explains all of the malformations seen in the Chiari I and II malformations. These pathologic derailments seem to result from a heterogeneous spectrum of ontogenetic errors and pathological mechanisms, which share some common phenotypical presentations. In this chapter, the theories pertinent to the embryology and pathophysiology of Chiari I and II malformations and their associated anomalies are discussed.

Although Chiari I and II malformations have hindbrain herniation into the upper cervical spinal canal, both are also often associated with other anomalies of the craniofacial skeleton, vertebral column, and central nervous system. Table 4.1 lists some of these associated anomalies. The herniated hindbrain may include the medulla oblongata, fourth ventricle and caudal vermis, and cerebellar hemispheres (usually tonsils) to varying extents. An efficient theory with high explanatory power should be able to provide a rational basis for the occurrence of not only hindbrain herniation but also that of other associated anomalies. Currently, no single theory explains each of these malformations as the Chiari malformation seems to result from a heterogeneous spectrum of ontogenetic errors and pathological mechanisms, which share some common phenotypical presentations [59]. In this chapter, the theories pertinent to the embryology and pathophysiology of Chiari I and II malformations and their associated anomalies are discussed.

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Table 4.1 Some of the anomalies associated with Chiari malformation

Anomaly	Description	Reference(s)
Cranium bifidum	Is the cranial counterpart of spina bifida and is likewise comprised of occulta, cystica, and aperta variants	Padget [40]; Ingraham and Scott [20]; Anegawa et al. [2]
Lacunar skull	Is characterized by rounded (punched-out) defects in the inner table of skull separated by whorl-like bony ridges	Ingraham and Scott [20]; Peach [43]
Platybasia	Flattening of the angle between clivus and anterior basicranium; severe form is associated with basilar invagination	Schady et al. [52]; Smoker [53]
Small posterior cranial fossa	Reduction in the size of posterior cranial fossa in relation to the cranial dimensions	Schady et al. [52]
Basilar invagination	Abnormal approximation of the odontoid process and skull base	Schady et al. [52]
Proatlas segmentation malformation	Most often present as osseous anomalies around the foramen magnum	Muhleman et al. [34]; Menezes [32]
Atlantooccipital assimilation	Partial or complete fusion of atlas and occipital bone; is seen in about 8 % of pediatric patients with Chiari I malformation	Tubbs et al. [60]
Klippel-Feil syndrome	Fusion of two or more cervical vertebrae; is seen in about 3 % of patients with Chiari I malformation	Tubbs et al. [60]
Spina bifida	Is composed of spina bifida occulta, cystica, and aperta variants; the latter two are comprised of meningocele, meningomyelocele, myelocystocele, and myeloschisis; is often but not always associated with hydrocephalus and Chiari II malformation	Pooh and Pooh [48]; Russell and Donald [51]; Ingraham and Scott [20]
Dysplastic tentorium cerebelli	Decreased length of the fused tentorium and increased length of the incisura	Peach [43]
Low-lying tentorium cerebelli	Downward displacement of intracranial attachment of the tentorium; contribute to a small posterior cranial fossa	Gardner [16]
Hypoplasia or absence of falx cerebri and falx cerebelli	Is related to overcrowding of the intracranial and posterior cranial fossae	Peach [43]; Tubbs et al. [56]
Hydrocephalus	Often communicating; may be a primary event or secondary to hindbrain herniation	Ingraham and Scott [20]
Microgyria	The cerebral gyri are smaller but numerous giving rise to a "wormy" appearance of the cerebral cortex	Ingraham and Scott [20]
Gray matter heterotopia	Collection of neural cells in abnormal *locations within the white matter*; has been reported in patients with spina bifida and Chiari II malformation	Gilbert et al. [18]
Large massa intermedia	Excessive approximation and adhesion of the thalami and thickening of the interthalamic adhesion	Gardner [17]; Naidich et al. [35]; Peach [43]
Stenosis of aqueduct of Sylvius	May be primary or secondary to midbrain compression by hydrocephalus or overcrowded brain	Masters [29]; Russell and Donald [51]
Tectal beaking	The quadrigeminal plate of the midbrain is fused into a conical mass, the apex of which projects between the cerebellar hemisphere	Peach [43]
Dorsal wedging of brain stem	Dorsal part of pons and/or upper medulla protrudes into the fourth ventricle	Lichtenstein [27]
Imperforated rhombic roof	Primary agenesis or secondary occlusion of the outlets of the fourth ventricle by a fibrovascular membrane or arachnoid veil	Gardner [15]; Tubbs et al. [57]

Table 4.1 (continued)

Anomaly	Description	Reference(s)
"Tight" cisterna magna	The cisterna magna is small or obliterated; is due to overcrowding of the posterior cranial fossa, downward displacement of cerebellum, fibrovascular adhesions of the meningeal layers, or dysgenesis during embryonic and early fetal periods	Gardner [16]; Masters [29]
Low-lying and obliterated fourth ventricle	The fourth ventricle is slit-like and compressed and partly or entirely extends below the foramen magnum	Russell and Donald [51]
Upslanting cervical spinal nerves	Upper cervical spinal nerves with an ascending intradural course; these spinal nerves normally have a rather horizontal course	Barry et al. [3]
Syringomyelia	The cavitation within the spinal cord tissue; is more common in Chiari II than in Chiari I malformation	Josef and Fehlings [23]
Hydromyelia	Dilated central spinal cord canal	Ingraham and Scott [20]

Hydrocephalic Brain or Pressure Coning Theory

The question of whether hydrocephalus is the cause or effect of hindbrain herniation has been considered since Chiari's initial description and is complicated by the fact that hydrocephalus may occur without associated hindbrain herniation and vice versa [4]. Therefore, it is reasonable to assume that the developmental or postnatal factors leading to hydrocephalus and hindbrain herniation are mechanistically distinct but also partially overlap. A historical account of the discourses on the relationship between hydrocephalus and hindbrain herniation would best aid in clarifying this concept. In his classic paper of 1891, Hans Chiari wrote: "Since giving more attention to these relationships [in both type I and II malformations], I have had the impression that the extension of the tonsils and medial side of the inferior lobes [of the cerebellum] *probably* always is the result of chronic and the very early onset of cerebral hydrocephalus. I have found it in a relatively large percentage of cases of chronic congenital hydrocephalus, but never without hydrocephalus or in cases of acute or later developing hydrocephalus" (quoted from English translation of Radkowski [49]). The presence of hydrocephalus was not appreciated by Arnold, but Chiari assumed that it might have been, in some cases, a transient event in the fetal period [25]. The hydrocephalic brain theory, later known as "pressure coning effect" [16], dominated thoughts and still stands as a plausible – albeit not the sole – mechanism behind hindbrain herniation.

The validity of the pressure coning theory has been questioned by the forerunners of caudal traction, posterior fossa overcrowding, the so-called neural tube overgrowth theory, and inadequate ventricular distension theories (see below). It has been noted that only ~15 % of patients with meningomyelocele had externally recognizable hydrocephalus at birth and that majority of them develop hydrocephalus during the first 3 years of life [54], casting doubt on the presumed role of primary fetal hydrocephalus in Chiari II malformation. The idea that hydrocephalus and hindbrain herniation "may be causally independent of each other" was emphasized by Bell et al. [4]; in their study of 21 human fetuses with spina bifida, 3 of 12 fetuses with Chiari II malformation lacked hydrocephalus. Instead, hindbrain herniation was closely linked with the size and location of the spinal defect: "the more cephalad and extensive the spinal lesion, the more likely it was to be accompanied with Chiari II malformation" [4]. It also has been suggested that a high cerebrospinal fluid (CSF) flow rate through the fistulous communication between the neurocele and amniotic cavity at the level of neural tube defect may induce a high craniospinal pressure gradient (by reducing the pressure of the spinal neurocele

without increasing the intracranial pressure), which by itself causes the hindbrain to herniate into the spinal canal [8]. The latter findings indicated that hindbrain herniation may be either a direct or an indirect consequence of the spina bifida defect, shedding light onto the plausibility of other theories (e.g., caudal traction, posterior fossa overcrowding, and inadequate ventricular distension), which are mechanistically favored by the spina bifida defect.

The findings of Bell et al. [4] and others could, however, by no means totally exclude the possibility that hydrocephalus is of a direct cause-and-effect relationship with hindbrain herniation at least in some cases. If one accepts the hydrocephalic brain theory, then an account of the etiologies of the *primary* fetal hydrocephalus would be necessary. It has been suggested that CSF absorption pathways are underdeveloped in patients with spina bifida cystica [51]. Atresia of the aqueduct of Sylvius [51], cranial venous outflow insufficiency and venous blood backflow [66], lack of elasticity and reduced permeability of the embryonic rhombic roof [14], primary agenesis of the outlets of the fourth ventricle or occlusion of the rhombic roof foramina by a membrane [15, 51], hyperfunctioning choroid plexus of the lateral ventricles and overproduction of CSF [17], and dysgenesis of the cisterna magna [17, 29] all hinder normal CSF balance and circulation and are among the known etiologies of primary fetal hydrocephalus in Chiari malformation. In the context of hydrocephalic brain theory, a differentiation should ideally be made between the factors initiating hydrocephalus and those maintaining or aggravating it once it develops. However, such a distinction remains arbitrary in the majority of cases as multiple interrelated anomalies often coexist at the same time in the same subject.

Ultimately, evidence exists for hydrocephalus being either a primary event causing hindbrain herniation (per hydrocephalic brain theory) or a secondary event caused by hindbrain herniation. This may in fact reflect the heterogeneous nature of the pathogenesis of hindbrain herniation across patients with or without spina bifida, and it is safe to assume that the relationship between hydrocephalus and hindbrain herniation is bidirectional, one causing or aggravating the other. Figure 4.1 shows a self-perpetuating cycle; irrespective of the factor(s) initiating the cycle, hydrocephalus reduces the compliance of the intracranial cavity [66]. Therefore, with slight elevation of the CSF and intracranial blood volumes, the intracranial pressure increases quickly, pushing the hindbrain down through the foramen magnum. Obstruction of CSF flow through the foramen magnum aggravates the hydrocephalus, and the cycle continues resulting in increasing hydrocephalus and hindbrain herniation [66]. If hindbrain herniation is the inciting event, then CSF flow blockage would secondarily lead to hydrocephalus, which by itself aggravates hindbrain herniation by increasing intracranial pressure. Several mechanisms have been recognized for CSF blockage in the Chiari malformation. Partial blockage of the foramen magnum with herniated hindbrain is commonly observed in patients with meningomyelocele and Chiari II malformation [51]. Usually, the outlet of the fourth ventricle is below the foramen magnum, and CSF drains into the spinal subarachnoid space. But because of partial blockage at the level of foramen magnum, an accumulating amount of CSF does not circulate into the cranial subarachnoid space [51]. The spinal compartment has a capacity of CSF absorption that is only one sixth that of the cranial compartment [47]. Although the dural sac of the spina bifida cystica has abnormally high absorptive capacity [45], this may not compensate for exclusion of the intracranial CSF absorption in severe cases of foramen magnum blockage. Thus, if the accumulated spinal CSF

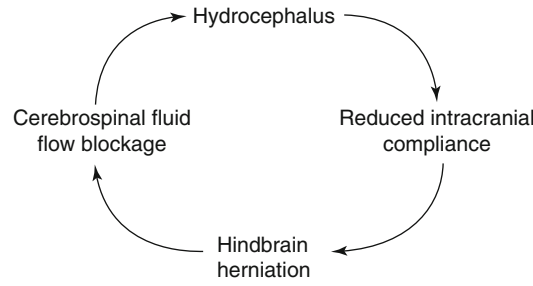

Fig. 4.1 The self-perpetuating cycle linking hydrocephalus with hindbrain herniation

overwhelms the absorptive capacity of the spinal compartment, it reenters the ventricular cavity, leading to a communicating hydrocephalus [51], or penetrates into the substance of the spinal cord, leading to syringomyelia [37]. Alternatively, the outlets of the fourth ventricle may become secondarily obliterated between the impacted cerebellum and brain stem, causing a noncommunicating hydrocephalus [20]. Mechanical irritation of the basal cistern can also induce an aseptic inflammatory reaction and fibrosis within the subarachnoid space, which hinders CSF circulation in the posterior cranial fossa [20].

External Compression Theory

The external compression theory was proposed by Cameron [7] to provide a mechanical basis for hindbrain herniation aside from hydrocephalus in the fetuses with spina bifida defect. Cameron believed that, ontogenetically, the spina bifida cystica is, at the initial stage, an aperta (myeloschisis) lesion, later epithelialized to form a cystic lesion. Thus, in embryonic and early fetal life, there is a fistulous communication between the neurocele and amniotic cavity. Cameron [7] opined that increased intra-amniotic pressure (perhaps due to fetal and maternal maneuvers) is transmitted onto the developing skull, squeezing the cranial neurocele to drain out through the hydromyelic cord. Leakage of the neurocele fluid into the amniotic space and squeezing of the developing brain would thereby induce a Chiari II malformation and produce a variety of associated anomalies including stenosis of the aqueduct of Sylvius, hypoplasia of the falx cerebri, tectal beaking, and large massa intermedia. This theory, however, was refuted by Peach [44] on the grounds that according to Pascal's law, the pressure exerted by the amniotic fluid on the embryo or fetus is equal at the skull and defective spinal lesion. Thus, the intra-amniotic pressure cannot induce a pressure gradient between the cranial neurocele and the hydromyelic cord. Moreover, in a study of infants less than 3 months of age with lumbar meningomyelocele, about half of them were found to have amniotic fluid debris (squama, lanugo hair, and mucin) in the spinal cord tissues, central spinal cord canal, and spinal subarachnoid space, i.e., vernicomyelia [21]. The presence of vernicomyelia in meningomyelocele infants implies that the direction of flow between the amniotic cavity and neurocele is not always caudad and that a degree of rostral flow from the amniotic cavity to the neurocele also exists in some if not all of the affected fetuses [21].

Although the external compression theory has not been accepted, its invalidation does not contradict the hydrodynamic theory or other theories, which emphasize that hindbrain herniation is a consequence of neurocele fluid leaking through the defect in the neural tube. This leakage could instead be mechanically favored by a normally higher neurocele pressure than amniotic pressure in the embryonic and early fetal neural tube [17]. However, when the hindbrain herniates, the spinal compartment is isolated – partially or completely – from the cranial compartment and becomes in equilibrium with the amniotic cavity. As a result, a to-and-fro flow through the spina bifida defect is established: The in utero maneuvers compressing the head causes caudad egress of the fluid through the defect, while subsequent release of head compression causes the amniotic fluid to pass rostrad into the spinal compartment [21].

Posterior Cranial Fossa Overcrowding in Chiari Malformation

The phenomenon of posterior cranial fossa overcrowding is an integral part of the modified hydrodynamic theory of Gardner, occipital dysplasia theory, disorganized neural tube growth theory, and inadequate ventricular distension theory (see below). In fact, these theories have been proposed to explain the overcrowding phenomenon on the grounds of either a small posterior cranial fossa or increased size of the hindbrain (see below). Accordingly, normal growth of the posterior fossa brain within a confined, unyielding fossa or abnormally large size of the posterior fossa brain in an apparently normal fossa results in the state of "overcrowding." The overcrowded posterior fossa brain herniates upward through the tentorial

incisura and downward through the foramen magnum and also hinders CSF circulation, leading to the hydrocephalus. A point of importance here is that the relative ratio of the posterior fossa brain volume to total fossa volume is above normal but less than one in this state, and overcrowding by no means indicates that the posterior fossa brain volume is greater than the total posterior fossa volume. In one study, the posterior fossa brain occupied 83.3 % of the posterior fossa space in adult patients with Chiari I malformation and 79 % of the fossa space in healthy individuals [36]. Whether such a degree of posterior fossa overcrowding (~5 %) is by itself sufficient to cause hindbrain herniation or not is not clear. However, it is more likely that the overcrowding phenomenon works in concert with other factors to induce hindbrain herniation.

Hydrodynamic Theory

The hydrodynamic theory was suggested by Gardner et al. [14], and in 1977, he modified it to explain the smallness of the posterior cranial fossa as well as formation of the neural tube defect in Chiari II malformation. Consulting the works of Weed [63], Padget [39], and Bering [6], Gardner [17] attested that (1) the development of the area membranacea superior of Weed coincides with development of the posterior choroid plexus of the rhombic cavity and that of the area membranacea inferior of Weed coincides with development of the anterior choroid plexus of the lateral ventricles, (2) the area membranacea superior and inferior filter the CSF out of the brain ventricles in normal fetuses, and (3) the anterior choroid plexus expands rapidly and out of proportion to the posterior choroid plexus; thus, the CSF pressure generated by the anterior choroid plexus in the supratentorial space overrides the pressure generated by the posterior choroid plexus, and this pressure gradient pushes the tentorium downward. If the second mechanism fails due to abnormal thickening or reduced permeability of the rhombic roof [14], then the CSF cannot egress from the ventricular cavity through the rhombic roof. If the third mechanism becomes exaggerated due to hyperfunctioning or markedly enlarged anterior choroid plexus [16, 17], the filtering capacity of the rhombic roof is overwhelmed and the neural tube expands to a greater extent than normal. Under both these circumstances, a state of fetal hydrocephalus and hydromyelia ensues. The fetal hydromyelia leads to rupture of the weakest part of the closed neurocele in the caudal region (or occasionally in the cephalic region such as in the mesencephalon) leading to a variety of neural tube defects [17]. When the caudal neurocele opens, CSF drains out of the fourth ventricle through the hydromyelic central spinal cord canal and from the spina bifida defect into the amniotic cavity; this results in dissipation of the CSF pressure generated by the posterior choroid plexus within the infratentorial space. The supratentorial CSF pressure generated by the anterior choroid plexus and the hydrocephalic cerebrum pushes the tentorium downward to a greater extent than in normal, leading to a small posterior cranial fossa. Ultimately, the growing hindbrain herniates out of the small posterior fossa [17]. The sequence of the events per Gardner's hydrodynamic theory (Fig. 4.2) occurs in the embryonic and early fetal period when the otic capsule is still cartilaginous and tentorial rotation is feasible. Gardner [15] outlined the differences in pathogenesis of the Chiari I and II malformations in an interesting manner, "if the size of the posterior fossa is severely reduced by this process, the cerebellar portion of the resulting hernia will consist of the earlier developing vermis (Chiari II); if its size is reduced to a lesser degree, the cerebellar hernia will consist of the later developing tonsils (Chiari I)".

Gardner [15] elaborated upon the hydrodynamic theory to explain the co-occurrence of hydromyelia and syringomyelia with Chiari malformation and hydrocephalus. He postulated that with any restriction in the outflow of the fourth ventricle, either due to complete or partial obstruction of the foramen of Magendie, the CSF pulse wave generated by the pulsating choroid plexus (synchronous with cardiac beat) cannot be dissipated at the level of the foramen of Magendie but is directed downward toward the obex of the medulla and central canal. The "water hammer

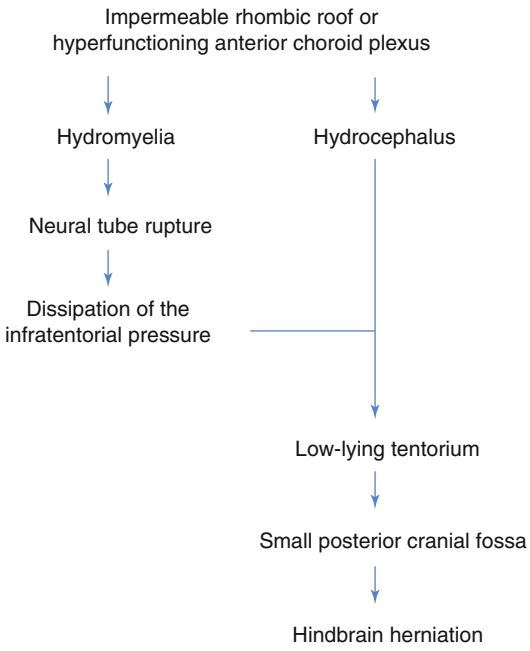

Fig. 4.2 A flow diagram depicting Gardner's hydrodynamic theory

effect" of the CSF pulse pressure causes funnel-shaped dilation at the obex, dilation of the central canal, and/or hydrodissection of the lower medulla or spinal cord along the nerve fiber tracts. Notably, the foramen of Magendie was completely obliterated by an arachnoid veil in at least 30 % of patients with syringomyelia and Chiari malformation examined by Gardner [15] and was also partially closed in more than 10 % of patients.

Ultimately, in the hydrodynamic theory of Gardner, overdistension of the supratentorial ventricles and/or imperforation of the roof of the fourth ventricle are the inciting events, which independently lead to hydrocephalus, hydromyelia, and syringomyelia. The induction of hindbrain herniation is secondary to *early fetal* hydrocephalus and growth of the hindbrain within a small posterior cranial fossa. Moreover, this theory maintains that the expansion of the syrinx is due to a pulsatile CSF flow wave (hammer effect), which is transmitted into the syrinx through a patent upper cervical central canal. Hence, it predicts that the syrinx should expand during cardiac systole and should constrict during diastole. The latter assumption has been invalidated by Oldfield et al. [37] who put forth another theory for the pathogenesis of the syringomyelia (see below).

Occipital Dysplasia Theory

The size of the posterior cranial fossa is determined by several factors effective in fetal and postnatal life, including (1) ventricular distension, (2) rotation of the intracranial attachment of the tentorium cerebelli, (3) rotation of the otic cartilage and petrous temporal bone, (4) growth of the basicranial synchondroses, (5) upward reflection of the tentorium cerebellum, and (6) various hormonal influences (see Chap. 3). The occipital dysplasia theory implies that failure of the occipital bone to develop normally, primary axial skeletal defect, paraxial mesodermal insufficiency, or altered morphogenesis of the occipital bone gives rise to a small posterior cranial fossa and contributes to the overcrowding phenomenon.

This theory was emphasized by Marin-Padilla and Marin-Padilla [28] in an animal embryo model of Chiari I and II malformations induced by maternal administration of vitamin A and was later supported by the morphometric data obtained from patients with Chiari malformation. Marin-Padilla and Marin-Padilla's model expressed a constellation of craniofacial anomalies and dysraphic states. In this model, (1) there was a reduction in the length of the skull base essentially as a result of an underdeveloped occipital region. Underdevelopment and shortening of the basiocciput was more pronounced in animal fetuses with a spina bifida defect (corresponding to Chiari II malformation) than in those without a spina bifida defect (corresponding to Chiari I malformation), (2) the odontoid process was apparently protruded into the posterior fossa with its tip located above the plane of the depressed basion of the underdeveloped basiocciput, and (3) shortening of the basiocciput resulted in a small posterior cranial fossa and subsequent compression of the brain stem and cerebellum and partial reduction in the ventricular size and

slight compression of the aqueduct of Sylvius. Therefore, Marin-Padilla and Marin-Padilla [28] suggested that Chiari I and II malformations are "complex developmental disorders" or sequence anomalies initiated by "primary axial skeletal defects" (invariably involving the craniocervical junction and occipital region) leading to "secondary neurological anomalies."

The nature of occipital dysplasia leading to a small posterior cranial fossa in Chiari I malformation is already discussed (see Chap. 3). In brief, the supraocciput is affected more than the basiocciput, the foramen magnum tends to enlarge, and the height of the posterior fossa is reduced. There may be a compensatory increase in the length of the posterior fossa in adults. Further studies comparing adult and pediatric patients are required to fully elucidate the dynamic and potentially age-related pattern of the occipital dysplasia in the Chiari I malformation. Patients with Chiari II malformation also have a small posterior cranial fossa, but the pattern of occipital dysplasia shows some differences from that of the Chiari I malformation. A reduced clivus-supraocciput angle (the angle formed between the lines drawn along the axes of the clivus and supraocciput) has been reported among Chiari II patients [10]. The following equations reflect the morphological significance of the clivus-supraocciput angle:

$$\text{Basicranial angle} + \text{Clival angle} = 180^{\circ} \quad (4.1)$$

The clival angle is between Twining's line and the axis of the clivus, and the basicranial angle is formed between the axis of the clivus and horizontal plane of the anterior basicranium.

$$\begin{aligned} &\text{Supraoccipital angle} + \text{Clival angle} \\ &+ \text{Clivus-Supraocciput angle} = 180^{\circ} \end{aligned} \quad (4.2)$$

The supraoccipital angle is between Twining's line and the axis of the supraocciput. Based on Eqs. 4.1 and 4.2, Eq 4.3 can be obtained.

$$\begin{aligned} &\text{Clivus-Supraocciput angle} \\ &= \text{Basicranial angle} - \text{Supraoccipital angle} \end{aligned} \quad (4.3)$$

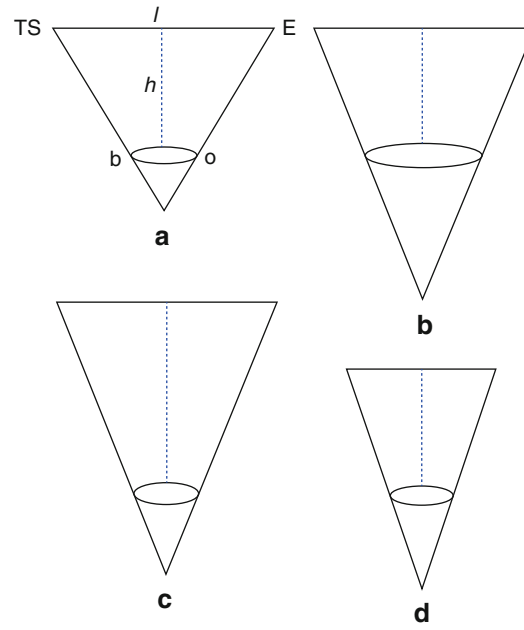

Fig. 4.3 *Line diagrams* showing the morphological implications of the reduced clivus-supraocciput angle in the posterior cranial fossa of patients with Chiari II malformation. *TS* tuberculum sellae, *E* endinion, *b* basion, *o* opisthion. *l* and *h* indicate the length and height of the bony posterior cranial fossa. The *oval circle* represents the foramen magnum, (**a**) is the reference diagram representing the normal condition, (**b**) increase in the size of the foramen magnum, (**c**) increase in the height of the posterior fossa, and (**d**) decrease in the length of the posterior fossa

Equation 4.3 indicates that a decrease in the clivus-supraocciput angle is associated with (and in a mechanistic term, caused by) a reduction in the basicranial angle and an increase in the supraoccipital angle. Therefore, the clivus and supraocciput tend to lie perpendicular to Twining's line when the clivus-supraocciput angle is reduced. Figure 4.3 shows the three morphological changes in the posterior cranial fossa, which can potentially explain a reduced clivus-supraocciput angle. These include increased size of the foramen magnum as well as an increased height and reduced length of the posterior fossa. The possibility of an increase in the posterior fossa height in Chiari II malformation is not supported by the literature as the reduction in the posterior fossa volume is recognized as an etiopathogenic factor. Thus, a combination of increased foraminal size

and reduced length of the posterior fossa can best explain the co-occurrence of a small posterior fossa with the reduced clivus-supraocciput angle in the Chiari II malformation.

The Neural Tube Overgrowth or Disorganized Neural Tube Growth Theory

This theory was proposed by Barry, Patten, and Stewart [3] in an attempt to link the co-occurrence of neural tube non-closure, Chiari malformation, and other cerebral anomalies with an earlier observation by Patten [41] of a curious neural tube maldevelopment, the so-called overgrowth of the neural tube. The neuroepithelium in such cases was characterized by an enhanced growth, folding and refolding on itself, and crowding into the apparently normal surrounding space and ventricular cavity [41]. Later, Patten [42] reported that a local overgrowth may lead to non-closure of the neural tube. Examining the fetuses with caudal neural tube defects and Chiari II malformation, Barry and colleagues observed that (1) the spinal cord segments immediately proximal to the defect were larger than normal, (2) the cerebrum and hindbrain were enlarged, and (3) the proximal cervical spinal cord segments were also larger but were compressed cephalocaudally [3]. They subsequently posited that the neural tube overgrowth phenomenon observed in the fetuses with spina bifida involves distant regions of the developing central nervous system as well and occurs before differential growth of the vertebral column begins. Such a phenomenon, Barry et al. [3] opined, leads to neural tube non-closure (spina bifida), downward displacement of the overgrown hindbrain into the cervical spinal canal (Chiari II malformation), and multiplicity of the cerebral cortical gyri (microgyria). In a rat fetal model of Chiari II malformation induced by maternal dose of ethylenethiourea, hydrocephalus was absent but overgrowth of the neural tube was evident, indicating that Chiari malformation can develop without hydrocephalus and with crowding of the cranial space by the overgrown brain [19]. The neural overgrowth theory was faced with skepticism as the cerebellum in the Chiari II malformation has often been found atrophied and small postnatally. However, an unbiased revisit of this theory in the light of earlier accounts and most recent observations implies that this theory may indeed be relevant and has the power of explaining such associated anomalies as microgyria, neural dysgenesis, and gray matter heterotopia in the cerebrum and cerebellum of patients with Chiari II malformation. The so-called neural tube overgrowth theory is supported by findings that the brain in the Chiari II malformation is heavier than normal despite the presence of hydrocephalus [21].

Perhaps, the main barrier to the popularity of the neural overgrowth theory is its name, giving rise to a misunderstanding of its pathological nature. Barry and colleagues stated that this term is "a purely descriptive morphological term," thus, testifying that it may or may not reflect the underlying histopathogenesis. Experimentally, this phenomenon can be induced by manipulation or extirpation of the notochord, hypoxia, and various nonspecific chemical insults in animal embryos [5] and is characterized by disorganized neuroepithelial cell migration and formation of the rosette-like accumulation of cells within the overgrown regions [24] as well as shrinkage of the brain vesicles [22]. Splotch-delayed mouse embryos harboring Pax-3 gene mutation [62] are predisposed to neural tube defects and also demonstrate features of an overgrown neural tube [33]. The so-called overgrowth is associated with mesodermal insufficiency, notochordal abnormality, alterations in the neuroepithelial basal lamina, loss of cellular polarity, disorganized cell orientation, and increased neuroepithelial intercellular space rather than true neuroblast proliferation [38, 67]. Overgrowth of the neural tube in the chicken embryo overexpressing the fork head transcription factor *FoxG1* is also associated with decreased neuroepithelial apoptosis mainly in the telencephalon and mesencephalon [1].

The data above imply that the phenomenon of "neural tube overgrowth" mentioned by Patten [41] and Barry et al. [3] is in fact a generalized

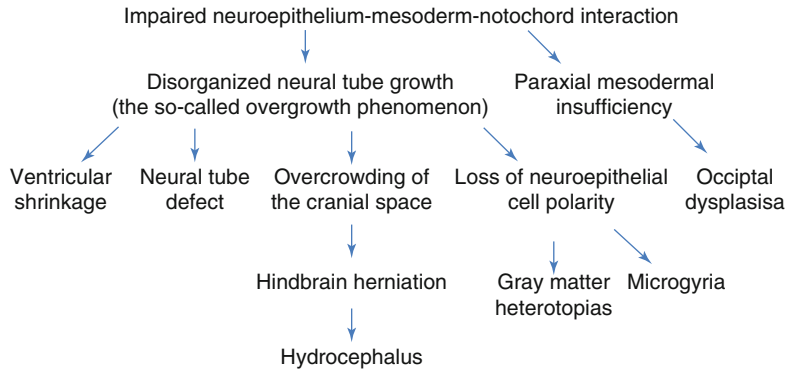

Fig. 4.4 The proposed sequence of events in the disorganized neural tube growth theory. In splotch-delayed animal models, impaired neuroepithelium-mesoderm-notochord interaction was associated with mesodermal insufficiency and disorganized neural tube growth (Adapted from Yang and Trasler [40])

disorder of neuroepithelial organization manifesting as an enlarged, folded, or crowded neural tube in the embryonic or early fetal periods. The manifestation of *disorganized neural tube growth* in late fetal and postnatal life, especially in connection with hindbrain development, remains to be elucidated in experimental studies or studies of aborted human fetuses. If *disorganized neural tube growth* is the underlying factor in the pathogenesis of a neural tube defect (as suggested by Patten [42]), one should look for distant abnormalities in the central nervous system derived from a fused but still disorganized neural tube in patients with a spina bifida defect. Barry et al. [3] proposed that such a pathological phenomenon leads to hindbrain enlargement and herniation and microgyria. It is not unlikely that the structures similar to rosette-like neuroepithelial cell accumulations seen in animal embryos with a disorganized neural tube give rise to the masses of gray matter heterotopia, which are often located periventricularly in patients with Chiari II malformation. There is no direct evidence in the literature as to whether the mesodermal and notochordal abnormalities seen in the experimental models of a disorganized neural tube also contribute to the constellation of axial skeletal anomalies and occipital dysplasia in human fetuses with Chiari II malformation. However, such a possibility is likely, and further studies should address this aspect of maldevelopment. Figure 4.4 shows the proposed sequence of events per the disorganized neural tube growth theory leading to hydrocephalus and hindbrain herniation.

Neuroschisis Theory

This theory was formulated by Padget [40] and, in fact, represented an early attempt to put forth the foundations of an inadequate ventricular distention theory and merge it with the disorganized neural tube growth theory. The neuroschisis or neural cleft is the splitting open of the neural plate. The mesencephalon is the most common site of the cleft. The irregular margins of the cleft are composed of pyknotic cells and occasionally tend to join in an end-to-end manner sometimes with an everted or inverted fusion of the cleft walls. A neuroschisis bleb is formed at the site of the cleft by escape of neurocele fluid into the surrounding mesoderm; this bleb is walled by a membrane and mesoderm and is often covered by an intact cutaneous ectoderm (primitive skin), but occasionally the skin is also damaged and interrupted by pyknotic, degenerated cells. Padget [40] noted that the process of neuroschisis was associated with folding of irregularly widened neural tube walls into the neurocele cavity and secondary fusion of these folds as well as narrowing of the neurocele cavity. These features are reminiscent of disorganized neural tube growth and, according to Padget [40], are most prominent at the mesencephalon and hindbrain regions, which are relatively voluminous in normal embryos. Padget [40] added that narrowing of the neurocele cavity arises from abnormal folding and fusion of the neural tube walls and partial collapse of the neurocele following rupture of the neural clefts.

Padget [40] postulated that the neuroschisis blebs (1) may undergo healing with some

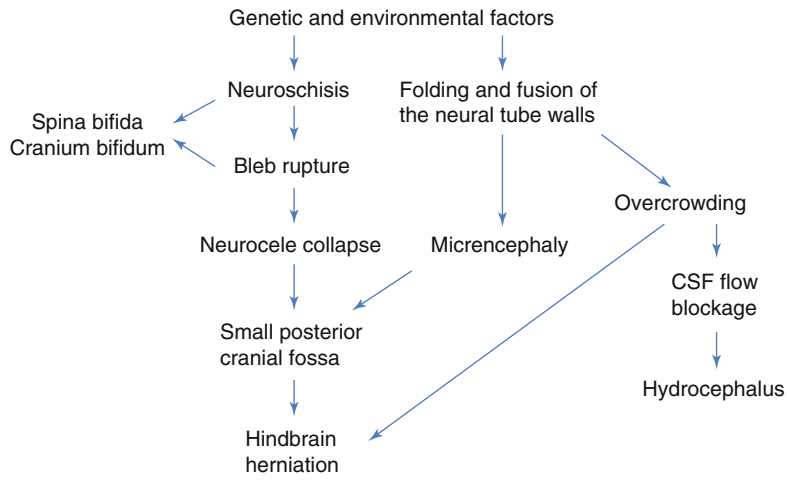

Fig. 4.5 The sequence of events in the neuroschisis theory of Padget leading to a neural tube defect, hindbrain herniation, and hydrocephalus

scarring left at the site of the healed neuroschisis, (2) may remain intact as a loculated fluid collection with a mesodermal periphery, or (3) may rupture with eversion of the neural cleft margins, leading to the spectrum of cranium bifidum and spina bifida anomalies, respectively, comprising occulta, cystica, and aperta variants. Reduction in the size of the neurocele secondary to partial neurocele collapse and folding and fusion of the neural tube walls results in micrencephaly. Subsequently, a small posterior cranial fossa ensues as the neural tube folding process is more conspicuous in the voluminous mesencephalic and hindbrain regions of the embryonic neural tube. Neural wall folding and fusion at the mesencephalon leads to stenosis and forking of the aqueduct of Sylvius, and crowding of the metenmyelencephalic junction blocks the outlets of the fourth ventricle, leading to hydrocephalus. Subsequent development of the crowded cerebellum within a small posterior cranial fossa results in a Chiari malformation. Figure 4.5 shows the sequence of events proposed by the neuroschisis theory.

Cord Traction or Tethered Cord Theory

This theory was proposed by Penfield and Coburn [46] based on surgical and autopsy findings in an adult patient with hindbrain herniation and a history of operation for a thoracic meningomyelocele in childhood. At the level of the bifid vertebral arch, the dura mater and spinal cord were dorsally attached to the soft tissues by fibrous adhesions. The brain stem was elongated, and the lower brain stem and cerebellum were herniated downward through the foramen magnum. The cisterna magna was obliterated, and the space between the cerebellum and tentorium was enlarged to form a supracerebellar cisterna. The lower cranial nerves and cervical nerves demonstrated a prominent ascending course rather than their expected descending or horizontal course. The tip of the herniated cerebellum was firmly adherent to the spinal cord by meningeal adhesions, and upon release of these adhesions, the herniated cerebellum retracted upward for a significant distance. Penfield and Coburn [46] then proposed that spinal cord fixation at the level of the bifid vertebral arch produces traction on the cord during vertebral growth. This traction interrupts the normal ascent of the spinal cord and results in downward traction of the brain stem and spinal cord and nerves above the point of fixation.

Lichtenstein [27] expounded upon the cord traction theory to explain the co-occurrence of Chiari II malformation with hydrocephalus and syringomyelia. He posited that spinal cord stretching secondary to various dysraphic conditions results in hindbrain herniation early in life and spinal cord degeneration later in life. Secondary to spinal cord stretching, the brain stem is elongated. The medulla oblongata, fourth ventricle, choroid plexus, and vermis are pulled

downward. Midbrain traction results in the elongation, flattening, and stenosis of the aqueduct of Sylvius, which subsequently leads to hydrocephalus of the third and lateral ventricles. The herniated choroid plexus produces CSF. As the fourth ventricle is collapsed and restricted at the foramen magnum, the CSF escapes into the substance of the upper cervical spinal cord through a diverticulum or fissure along the intramedullary path of least resistance, leading to syringomyelia. Penfield and Coburn [46] and Lichtenstein [27] noted that with distal cord tethering, the fourth ventricle is obliterated by a wedge-shaped protrusion of the upper medulla or pons into the ventricle. Such brain stem deformation also blocks the fourth ventricle leading to hydrocephalus. In order to explain this finding, Lichtenstein [27] proposed that the dorsal part of the spinal cord is often fixed in the midline in cases of tethering. Thus, the ventral part of the spinal cord and hindbrain ascends to a greater extent than does the dorsal part. This results in a relative overcrowding of the ventral hindbrain, which wedges backward into the fourth ventricle.

Ultimately, the cord traction theory states that hindbrain elongation/herniation is due to impediment of normal ascent of the spinal cord during axial growth and subsequent downward pulling of the cord. Protracted spinal cord traction should be present since the fetal or early postnatal growth period to sufficiently interfere with spinal cord ascent and cause hindbrain herniation [58]. The spinal ascent is a passive process related to the disproportionate growth rates of the vertebral column and spinal cord. Failure of cord ascent is due to the fixation of the spinal cord against the elongating vertebral column. This theory explains the occurrence of brain stem gross abnormality, stenosis of the aqueduct of Sylvius, hydrocephalus, and syringomyelia in patients with spinal dysraphism and a tethered cord. However, the validity of the caudal traction theory was doubted by Barry et al. [3] as they noted that the tension exerted by the anchorage of the spinal cord at the level of the spina bifida defect is dissipated within five spinal cord segments. The ascending course of the upper cervical spinal nerves attributed to caudal cord traction by Penfield and Coburn [46] and Lichtenstein [27] was instead attributed to the compression of the cervical cord by the enlarged and herniated hindbrain [3].

Developmental Arrest Theory

This theory was suggested by Daniel and Stritch [11]. They postulated that hindbrain abnormalities in Chiari malformations are a consequence of failure in normal development of the pontine flexure. The pontine flexure together with the mesencephalic and cervical flexures develops late in the first month of embryonic life as the brain grows rapidly [26]. Therefore, the flexures reduce the length of the neural tube along the longitudinal axis of the body. According to Daniel and Stritch [11], if the pontine flexure does not develop, the vascularized rhombic roof fails to normally invaginate into the rhombic cavity. Therefore, it is retained as a thick fibrovascular band connecting the caudal vermis to the obex and dorsal medulla. The cerebellum wraps around the brain stem, and the elongated hindbrain herniates through the foramen magnum. In this theory, the elongated brain stem is a primary event central to the pathogenesis of Chiari malformation. In contrast, brain stem elongation is secondary to tethering of the cord in the caudal traction theory. This theory has major shortcomings. First, formation of the pontine flexure is necessary for cerebellar anlages and primordium to come into a horizontal plane securing the normal development of the cerebellum in such a way that in the mature cerebellum, the vermis is located medially and the hemispheres laterally. If the pontine flexure does not develop normally, then it is reasonable to assume that the cerebellar anlages would retain a rather angular position. Therefore, in the mature cerebellum, the cerebellar vermis and hemispheres would, respectively, be superiorly and inferiorly positioned. This pattern is not appreciated in cases of Chiari malformation. Secondly, the fibrovascular adhesions between the cerebellum and medulla are in fact due to failure of the area membranacea inferior to differentiate and thin out. As a result, the choroid plexus does not normally grow into the rhombic cavity but infiltrates the thickened rhombic roof [61]. Finally, like the mesencephalic and cervical

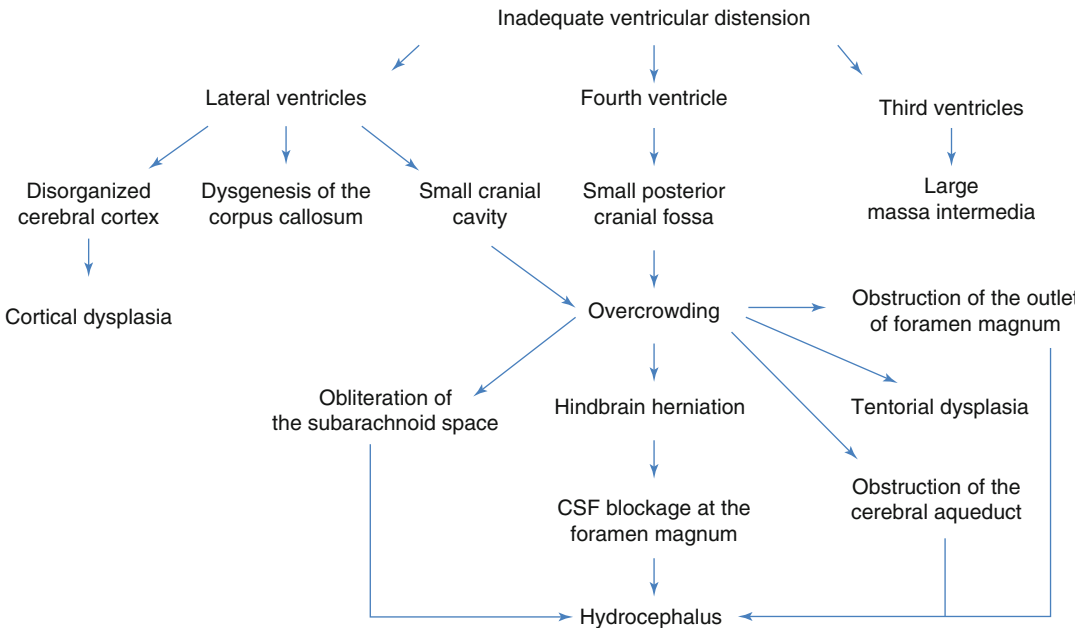

Fig. 4.6 A flow diagram showing the sequence of pathological events favored by inadequate distension of the lateral, third, and fourth ventricles

flexures, the pontine flexure straightens during brain development [26]. Although the pontine flexure initially leads to invagination of the rhombic roof, it could not be a main factor in maintaining the intraventricular position of the choroid plexus. Instead, it has been shown that intorsion of the choroid plexus is associated with inward rotation of the caudal vermis favored by regression of the area membranacea inferior and perforation of the rhombic roof [61].

Inadequate Ventricular Distension Theory

This theory was suggested by McLone and Knepper [31] and was based on the observation that the spinal neurocele undergoes a transient and partial collapse early in the developing embryo. McLone and Knepper [31] found a temporal association of this partial neurocele occlusion with distension of the cranial vesicles in a mouse embryo model. They attested that in the embryo with a neural tube defect, the occlusion process is defective in a way that the ventral portion of the spinal neurocele fails to collapse in the midline and the medial walls do not come into opposition. The latter results in less-than-normal distension of the cranial vesicles, which leads to the formation of a small posterior fossa from lack of the adequate forces necessary to expand the surrounding mesenchymal primordia of the chondrocranium. Subsequently, the development of the rhombencephalon in an inadequate and fixed space results in the downward displacement of the brain stem and cerebellum.

McLone [30] further expounded upon this theory in an attempt to link the co-occurrence of pan-brain and calvarial anomalies with the Chiari II malformation. Figure 4.6 shows the sequence of events led by an inadequate ventricular distension. Hydrocephalus is not a primary event in this theory but is secondary to hindbrain herniation and overcrowding of the intracranial cavity resulting in blockade of CSF flow through the restricted foramen magnum and obliterated subarachnoid space as well as occlusion of the fourth ventricular outlet and aqueduct of Sylvius. The cortical dysplasia and gray matter heterotopias are attributed to lack of the inductive ventricular

forces necessary for normal development and organization of the telencephalon. A large massa intermedia is due to abnormal approximation and fusion of the thalami in a collapsed third ventricle. McLone [30] also posited that normal orientation of calvarial ossifying collagen bundles requires distension of the lateral ventricles; the inadequate ventricular distension causes these ossifying bundles to abnormally whorl, leading to the appearance of the lacunar skull (craniolacunia). The inadequate ventricular distension theory has been supported by experimental data. In the fetal rat model of dysraphism induced by a midline dorsal incision deep into the medulla oblongata during late pregnancy, hindbrain herniation consistent with Chiari type II malformation was noted in surviving animals [9]. This observation indicated that *significant* leakage of CSF distal to the brain stem is sufficient to result in hindbrain herniation. Although this theory explains the small posterior cranial fossa in Chiari II malformation, it fails to provide a clue to the pathoembryogenesis of Chiari I malformation.

Craniocervical Growth Collision or Caudocranial (Reversed) Vertebral Growth Theory

This theory, suggested by Roth [50], is pertinent to the pathogenesis of Chiari malformation in the case of lumbar tethering of the spinal cord such as observed in patients with a caudal meningomyelocele. Craniocervical growth collision theory claims that hindbrain herniation is essentially secondary to maldevelopment of the vertebral column. Roth maintained that (1) the developing neurocele is always separated from the surrounding skeletogenic tissues (primordia of axial skeleton) as the subarachnoid space is apparent as early as when chondrification takes place, (2) the availability of space along the developing central nervous system determines the distribution of and relative quantity of the skeletogenic mesoderm, (3) with the onset of a neuro-vertebral growth differential, the relatively faster growth of the vertebral column overrides the growth of the spinal cord, and finally (4) with upward retraction of the spinal cord, more space is available caudally for distribution of skeletogenic tissue; thus, the vertebral column grows caudally below the level of the spinal cord. This pattern is referred to as a cranio-caudal direction of vertebral growth, which, according to Roth, is a *basic growth law.* With fixation of the spinal cord to the caudal vertebrae, upward ascent of the cord is restricted. Therefore, skeletogenic materials are distributed cranially, colliding with the developing skull base. This pattern is referred to as a caudocranial direction of vertebral growth (reversed cervical growth or reversal of cranio-caudal vertebral growth), which, according to Roth, leads to the following abnormalities:

1. "Sucking-up" of hindbrain into the upper cervical spinal canal
2. Upward rather than downward slanting of the upper cervical spinal nerves, giving rise to the impression of a *cervicocranial cauda equina*
3. Funneling of the upper cervical spinal canal and widening of the foramen magnum
4. Secondary hydrocephalus
5. Basilar invagination

Per this theory, the sequence of events leading to Chiari malformation begins with a primary neural tube defect, which then alters the development of the vertebral column, secondarily leading to the malformation of the hindbrain at the craniocervical junction. Although the craniocervical growth collision theory essentially associates Chiari malformation with dysraphism, Roth attempted to attribute the Chiari malformation of non-dysraphic states to a *genuine* (i.e., primary or intrinsic) abnormality of axial growth. Roth further mentioned the phenomenon of *postembryonic neural growth* (especially that of the cerebellum), which contributes to the pathogenesis of hindbrain herniation by caudal displacement of the growing neural tissue within the collided craniocervical junction. Not mentioned by Roth, however, is the adaptability of the craniocervical growth collision theory for explaining the occurrence of atlantooccipital or cervical-vertebral fusion in Chiari patients. These abnormalities may represent a reaction to the cranially directed colliding force stimulating abnormal osteogenesis and fixing the derivatives of the occipital and cervical somites.

Theory of "Suck and Slosh" Effect as the Cause of Origin and Expansion/ Maintenance of a Spinal Cord Syrinx

This theory was formulated by Williams [64, 65] to provide a mechanism for formation and maintenance of communicating and noncommunicating spinal cord syrinx seen with Chiari malformations. This theory maintains that under physiologic conditions and at rest, the pressure within the spinal canal is equal to the intracranial pressure. With maneuvers that increase thoracoabdominal pressure, the spinal CSF pressure initially goes up but soon equalizes with the intracranial pressure by the shift of CSF from the spinal to the intracranial compartment. Following the cessation of the straining maneuver, the spinal CSF pressure goes down, which also rapidly equalizes with the intracranial pressure by the shift of CSF between the two compartments. If the pressure within the spinal canal becomes substantially lower than the intracranial pressure for a prolonged time (the so-called phenomenon of craniospinal pressure dissociation), the relative negative pressure within the spinal cord tends to *suck* the CSF from the fourth ventricle down into the spinal cord central canal and tissues, leading to the formation of hydromyelia and syringomyelia. This "suck" effect occurs in Chiari patients and causes further downward displacement of hindbrain through the foramen magnum. Once a significant hindbrain (tonsillar) herniation is established and the upper cervical spinal cord central canal is secondarily impacted at or below the level of foramen magnum by the herniated tonsils, the anatomical communication between the fourth ventricle and syrinx closes off. Next, the maintenance or further expansion of the syrinx takes place by another mechanism, the so-called "slosh" effect. Accordingly, the fluctuation in the CSF pressure within the spinal subarachnoid space is transmitted to the spinal cord and the wall of the syrinx externally. The increased spinal CSF pressure compresses the syrinx leading to the egress of the intrasyrinx fluid rostral and/or caudal to the site of its maximum compression. This potentially forceful pulsatile and bidirectional movement of intrasyrinx fluid extends the syrinx at its proximal and distal ends without the need for any anatomic communication between the syrinx cavity and the intracranial ventricular system. Expansion and maintenance of the syrinx is further contributed to by the perivascular transport of spinal CSF into the syrinx cavity.

Thus, the "suck" effect is driven by the craniospinal pressure dissociation and the "slosh" effect is driven by the isolated spinal CSF pressure fluctuation. In an attempt to explain the mechanism underlying the fluctuations in the spinal CSF pressure, Williams stressed that the spinal CSF pressure is mainly a result of extradural spinal venous pressure. Increases in the extradural spinal venous pressure with Valsalva maneuver lead to an increase in spinal CSF pressure. Following the cessation of the restraining maneuver, an abrupt increase in the spinal venous outflow leads to a rebound decrease in the spinal CSF pressure. In this way, fluctuations in the spinal CSF pressure reflect the pressure fluctuations of the spinal venous system. The mechanism behind the "suck" effect and craniospinal pressure dissociation is slightly more complex. In patients with hindbrain herniation not significant enough to cause impaction of the cord, the herniated hindbrain (tonsils) acts as a unidirectional valve. The CSF can move in an upward direction from the spinal to the cranial compartments; however, downward movement of CSF from the cranial to the spinal compartment is dampened by the synchronous downward movement of the herniated hindbrain and partial obstruction at or below the level of the foramen magnum. Such dampening of CSF flow in the craniospinal direction results in an aggravated and protracted (rebound) decline in spinal CSF pressure in relation to the intracranial pressure.

The "suck and slosh" effect of Williams is pervasive and can explain the occurrence of communicating and noncommunicating syringomyelia as well as their temporal relationship. In this theory, the communicating syringomyelia is the precursor for the noncommunicating syringomyelia, and temporally, these two are separated by the timing of *significant* hindbrain herniation through the foramen magnum. At first, the *internally* acting "suck" effect leads to formation of syringomyelia, and once a significant hindbrain

herniation occurs, the syrinx is maintained or expanded by the *externally* acting "slosh" effect. However, this theory cannot explain and was not proposed to explain the events leading to the occurrence of initial hindbrain herniation, which are necessary to generate the "suck" effect. Notably, in patients with Chiari I malformation, syringomyelia is more commonly found in patients with moderate cerebellar herniation (9–14 mm) than in those with smaller or larger herniation [55]. Thus, it is reasonable to assume that the valve-like mechanism imposed by the herniated hindbrain is more efficient at the moderate degrees of herniation. While the smaller herniation may not be sufficient enough to induce a valve-like mechanism, the larger herniation hinders this mechanism by blocking the CSF flow through the foramen magnum in both upward and downward directions and eliminating the "suck" effect.

Exaggerated Spinal CSF Systolic Wave Theory for Syringomyelia

This theory proposed by Oldfield et al. [37] only deals with the pathogenesis of syringomyelia in patients with Chiari malformation. The theory stresses the earlier observations of du Boulay et al. [12, 13] that in normal individuals and during the cardiac systole, CSF moves downward from the cranial into the spinal subarachnoid space through the foramen magnum to accommodate for the increased intracranial blood volume. During diastole and when blood rushes out of the cranial cavity, the CSF flow is reversed back into the cranial subarachnoid space. This waveform or pulsatile flow of CSF across the foramen magnum is approximately ten times greater than the synchronous CSF flow through the fourth ventricle. In the cases examined by Oldfield et al. [37], they noted that the communication between the spinal syrinx and fourth ventricle (i.e., upper cervical spinal cord central canal) in Chiari I patients was invariably closed. Contrary to the prediction of Gardner's theory, they also noted that, in fact, the syrinx constricts during cardiac systole and expands during diastole. The systolic constriction of the syrinx was synchronous with the downward excursion of the herniated tonsils. The CSF "to-and-fro" flow between the cranial and spinal compartments was dampened as a result of partial occlusion of the subarachnoid space at the level of the foramen magnum (secondary to hindbrain herniation). Based on these findings, Oldfield et al. [37] concluded that (1) the sudden, pistonlike excursion of the herniated tonsils transmits an accentuated pressure wave on the spinal CSF and creates an exaggerated CSF pulsatile pressure in the spinal canal during systole, (2) the exaggerated spinal CSF pulse pressure acts on the syrinx externally causing its compression, and (3) by diastole, the spinal CSF pressure suddenly ceases, leading to sudden expansion of the syrinx during diastole. Ultimately, Oldfield et al. [37] formulated a new theory to compensate for the inadequacy of Gardner's hydrodynamic theory of syringomyelia: the exaggerated CSF wave pressure during cardiac systole leads to a greater than normal passage of CSF along the perivascular spaces of the spinal cord into the cord substance. Intramedullary accumulation of CSF leads to the formation of syringomyelia. The pathophysiology of syringomyelia in Chiari I malformations is further discussed in another chapter (see Chap. 13).

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Surgical Anatomy of the Craniocervical Junction Relevant to Chiari Malformations

5

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Abstract

The anatomy of the craniocervical junction is complex with an intricate intersection between lower cranial and upper cervical nerves and the osteology of the posterior fossa skull and the atlanto-axial joints. A comprehensive understanding of this morphology is important to those treating patients with hindbrain herniation. In this chapter, the surgical anatomy of the posterior fossa and its contents (cerebellum, brainstem, lower cranial nerves, vertebrobasilar arteries, cranial venous sinuses) and upper cervical spine and its related neurovascular structures are reviewed and in special regard to the anatomy encountered in posterior fossa decompression for the Chiari malformations.

The anatomy of the juncture between the skull base and the upper cervical spine is complex and compact. Superiorly, the posterior cranial fossa houses not only the derivatives of the rhombencephalon (hindbrain) but also vessels that serve this structure, its outgrowths (lower cranial nerves), meninges with their vascular and nervous supply, and CSF within the ventricle and related subarachnoid spaces and cisterns. As the anatomy of the posterior cranial fossa is rich, the chapter will focus on the specific and germane morphology related to approaches to the posterior fossa for Chiari malformations. As by definition this embryologic derailment extends into the upper cervical region, anatomy of the craniocervical region will be focused on from a surgical perspective.

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Soft Tissues of the Posterior Craniocervical Junction

Advancing through the soft tissues overlying the craniocervical junction, a standard midline incision through the skin advances through the tela subcutanea and then the upper fibers of the trapezius muscle inserting on either side of the occipital bone near the most posterior aspect of the external occipital protuberance referred to as the inion. Deep to the trapezius muscle is the splenius capitis muscle, which has a fiber course that is opposite to that of the overlying upper fibers of the trapezius muscle (Fig. 5.1). The splenius capitis arises from the lower half of the nuchal ligament and spinous processes of the last cervical and upper three to four thoracic vertebrae and attaches to the mastoid process and lateral aspect of the superior nuchal line. Below the splenius capitis lies the semispinalis capitis muscle (Fig. 5.1), which at this point is composed of vertical fibers traveling cephalad to insert onto the occipital bone between the superior and inferior nuchal lines. Along with their bony attachments, the above-noted muscles also travel along and attach to the midline nuchal ligament, which is a continuation of the supraspinous ligament of the thoracic spine. As the deepest muscular layer, the suboccipital muscles are four in number. Of these the suboccipital triangle is composed of the rectus capitis major and inferior capitis inferior and superior (Fig. 5.1). The rectus capitis minor is found just medial to the rectus capitis major attaching the posterior tubercle of the atlas to the occiput. For the suboccipital triangle muscles, the rectus capitis major travels between the occiput and spinous process of C2. The superior oblique arises from the transverse process of the atlas and inserts onto the occiput. The inferior oblique originates from the spinous process of C2 and attaches to the transverse process of the atlas. Except for the trapezius, which receives its innervation via the spinal accessory nerve, the other above-noted muscles are all innervated by adjacent dorsal rami of spinal nerves. In unison, the trapezius, splenius capitis, and semispinalis capitis aid in extending the neck. The suboccipital triangle muscles and rectus capitis posterior minor although theoretically these may move the atlas and axis, practically they may act more as proprioceptive structures. This assumption is strengthened by the fact that many of these small muscles are removed with posterior fossa decompression, and in our experience, no patient has ever complained of a functional deficit postoperatively that would be related.

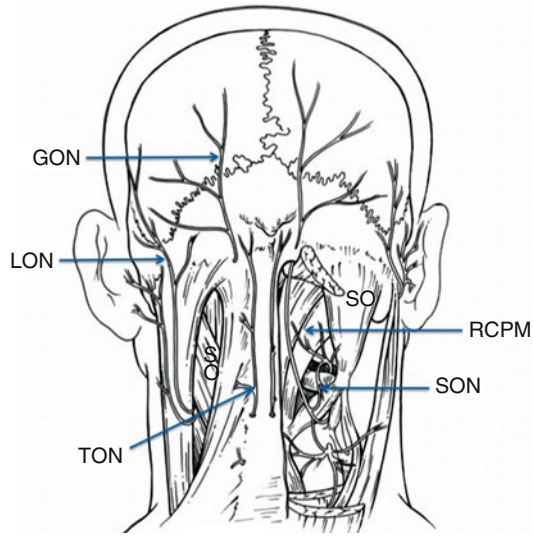

Fig. 5.1 Posterior craniocervical junction noting the third occipital (*TON*), greater occipital (*GON*), and lesser occipital nerves (*LON*). Also note the splenius capitis (*SC*), superior oblique (*SO*), and rectus capitis posterior major (*RCPM*) muscles. The suboccipital nerve (*SON*) is seen emerging below the horizontal segment of the vertebral artery

Cervical Nerves

With midline dissection of the suboccipital region, one often encounters the third occipital nerve (Fig. 5.1). One of many nerves in this region, the third occipital nerve is a derivative of the dorsal ramus of the third spinal nerve. Like the majority of other spinal nerves, the third spinal nerve divides into lateral and medial branches, the latter of which ramifies into deep and superficial divisions. The superficial medial branch (third occipital nerve) curves around the dorsolateral surfaces of the C2–C3 facet joint, which it innervates. The third occipital nerve then courses under the inferior

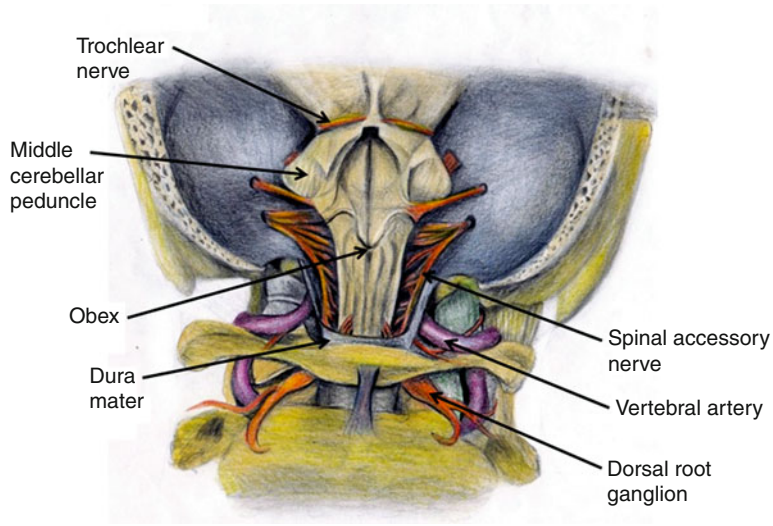

Fig. 5.2 Schematic drawing of the craniocervical junction following removal of the overlying occipital bone and cerebellum. Note the floor of the fourth ventricle with an apex at the obex, the suboccipital nerve coursing below the horizontal segment of the vertebral artery, and the dorsal root ganglion of C2 just inferior to the posterior arch of the atlas

capitis oblique muscle and supplies the semispinalis capitis, and travels deeply along the muscle before sending a communicating branch to the greater occipital nerve. At the level of the superior surface of the second cervical spinal process, the third occipital nerve turns dorsally and pierces the semispinalis capitis, splenius capitis, and trapezius muscles. After exiting these overlying muscles, the nerve becomes cutaneous and supplies a small area near the inion.

About 3 cm lateral to the inion, one finds the greater occipital nerve (Fig. 5.1), which is a branch of the medial division of the dorsal ramus of the second spinal nerve. As does the third occipital nerve, the greater occipital nerve emerges below the inferior capitis oblique muscle to ascend up through the soft tissues of the suboccipital region (semispinalis, splenius capitis, semispinalis capitis, and trapezius muscles) before it exits lateral to the inion to travel parallel to the occipital artery, which is usually lateral to it, and innervate skin anteriorly to at least the vertex of the skull. The greater occipital nerve will usually communicate medially with branches of the third occipital nerve and laterally with branches of the lesser occipital nerve. This latter nerve is unusual compared to the other nerves supplying the suboccipital and occipital regions in that it is derived from the ventral ramus of the second and third cervical nerves (i.e., the cervical plexus) and does not innervate the muscles that it travels by as does the third and greater occipital nerves. The lesser occipital nerve (Fig. 5.1) can be found approximately 7 cm lateral to the inion and branches into medial and lateral parts at approximately a midpoint between the inion and an intermastoid line.

Upper Cervical Spine Vasculature

Vascularly, in this region, and from superficial to deep, one finds branches to the overlying skin and muscles derived from the transverse cervical branch of the thyrocervical trunk (arising from the first segment of the subclavian artery, that is, the portion medial to the anterior scalene muscle), which supplies the trapezius muscle, branches of the occipital artery, a posterior branch of the external carotid artery, muscular branches of the vertebral artery, the first branch of the subclavian artery, and segmental branches feeding spinal nerve segments. Anastomoses are usually strong between the descending branch of the occipital artery and the vertebral arteries. The third part of the vertebral artery can be localized as one of the contents of the suboccipital triangle (Fig. 5.2). This horizontal or pre-intracranial segment of the artery and the suboccipital nerve (dorsal ramus of C1) are both found in this geometrically arranged region with the nerve being located inferior to the artery at the posterior arch of the atlas, which is in

the floor of this triangle (Fig. 5.2). Regionally, accompanying veins are found, as is the deep cervical vein, which travels at the level of and lateral to the semispinalis cervicis muscle and feeds into the suboccipital venous plexus, which has been compared to the cavernous sinus in regards to its composition. This plexus has rich connections with the vertebral venous plexus.

Posterior Cranial Fossa

The posterior cranial fossa is limited inferiorly by the occipital and sphenoid bones. The posterior aspect of the temporal bones makes up the lateral walls of the posterior cranial fossa (Fig. 5.3). Overlying these bones making up the inferolateral walls is a layer of dura mater, which extends superiorly to form one of the many intracranial dural specializations, the tentorium cerebelli, which acts as the non-ridged roof of the posterior cranial fossa.

Venous Sinuses

The mostly valve lacking vertebral venous plexus (Batson's) communicates superiorly with the marginal sinus. This sinus encircles the foramen magnum and receives, among others, the basilar venous plexus anteriorly, veins traveling through the hypoglossal canal laterally, and the occipital sinus posteriorly. This latter sinus will often be encountered in midline decompression of the posterior fossa and is usually enlarged in children. Superiorly, it joins the torcular Herophilus (Fig. 5.4). Interestingly, in the upright position, most intracranial blood travels via the marginal sinus and then into the vertebral venous plexus and through the internal jugular veins in recumbence. The basilar venous plexus also communicates with the inferior petrosal sinus that then drains into the internal jugular vein either intra- or extracranially. The superior petrosal sinus unites the cavernous sinus anteriorly to the transverse sinus posteriorly and runs in the attached edge of the tentorium cerebelli, which will often house several venous lakes (tentorial sinuses).

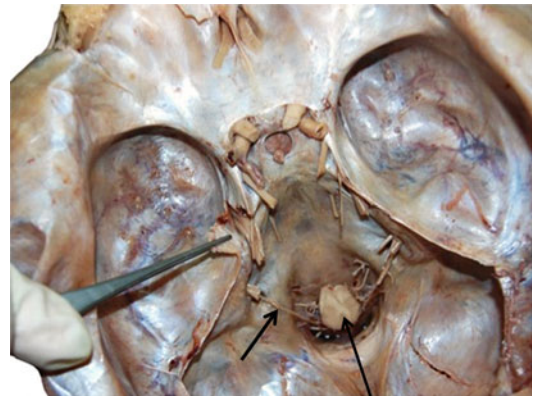

Fig. 5.3 Superior view of the skull base following removal of the brain. The medulla oblongata is in place (*long arrow*). For reference, note the spinal accessory nerve (*short arrow*) ascending through the foramen magnum to exit the left jugular foramen. The forceps have transected the attached edge of dura mater forming the roof of the left Meckel's cave

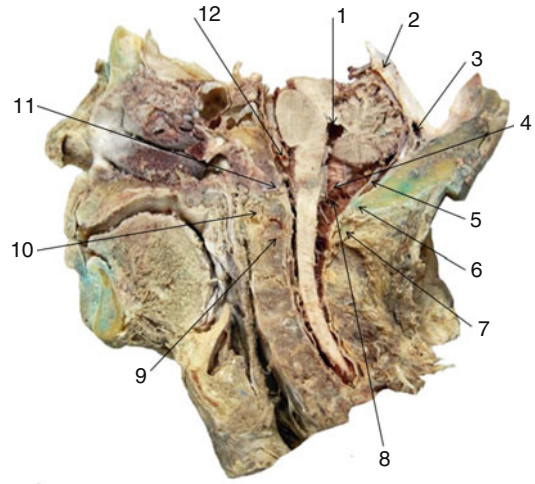

Fig. 5.4 Midsagittal transection through the head of an adult male cadaver. Note the (1) fourth ventricle, (2) tentorium cerebelli, (3) torcular Herophili, (4) right cerebellar tonsil, (5) dura mater underlying the occipital bone, (6) opisthion, (7) posterior arch of C1, (8) arachnoid trabeculae of the cisterna magna, (9) odontoid process, (10) anterior arch of C1, (11) basion, and (12) left vertebral artery in cross section and just prior to contributing to the basilar artery

The paired transverse sinuses connect venous blood flowing into the torcular Herophilus from, for example, the superior sagittal and straight sinuses to the sigmoid sinuses, which after a short course, drain into the superior jugular bulb.

Dural Innervation

The innervation of the dura mater of the posterior fossa is important as many pain symptoms found in patients with Chiari malformations can be explained due to irritation of such nerves. The dura mater of the cranium is a two-layered membrane that is derived from neural crest cells. However, the spinal dura mater is a single layer and is derived from paraxial mesoderm. This difference in derivation helps one understand the varied innervation pattern seen between posterior fossa and cervical dura mater. In the cervical spine as well as the remaining spinal dura, the recurrent nerve of Luschka (recurrent meningeal or sinuvertebral nerve) segmentally innervates the dura mater. These meningeal branches arise from the spinal nerves and enter the intervertebral foramen to innervate the dura as well as the adjacent annulus fibrosis, periosteum, and posterior longitudinal ligament.

The dura mater of the posterior cranial fossa receives multiple nerves that contribute to its innervation. Branches have been found to arise from the facial, glossopharyngeal, vagus, and hypoglossal nerves. The majority of fibers from the hypoglossal nerve are thought to arise from the upper cervical nerves.

Once overlying muscles have been dissected away, the posterior atlanto-occipital membrane can be observed. This structure is often thickened in the Chiari malformation and travels between the posterior arch of C1 to the posterior aspect of the occiput. A venous plexus may be found within this membrane and the third part of the vertebral artery will pierce it prior to traversing the dura mater to enter the posterior fossa.

Posterior Aspect of the Atlas

The posterior arch of the atlas is easily seen with its midline posterior tubercle for the attachment of the rectus capitis posterior minor (Figs. 5.2 and 5.4). The posterior arch may be bifid or assimilated to the occiput (atlanto-occipital fusion). Lateral on the posterior arch, the horizontal segment of the vertebral artery, following leaving the transverse foramen of the atlas, courses around the superior articular process to pierce the posterior atlanto-occipital membrane. A bony foramen (arcuate foramen) may be found at this location. The periosteum along the anterior surface of the posterior arch of the atlas may be thickened in the Chiari malformations.

Intradural Anatomy of the Craniocervical Junction

First Denticulate Ligament

Intradurally at the craniocervical junction and from a posterior perspective, some of the lower cranial nerves and upper cervical nerves are observed. A good landmark for these structures is the first denticulate ligament, which is a pial extension from the C1 segment of the spinal cord to the inner aspect of the intracranial dura mater. Superiorly, this ligament attaches near the entrance of the third part of the vertebral artery, and inferiorly, it separates the vertebral artery and ventral rootlets of the upper cervical spinal nerves anteriorly from the dorsal rootlets of the upper cervical spinal nerves and spinal accessory nerve posteriorly. Of note, the dorsal roots are not always present nor are the dorsal root ganglia of C1. The ventral root of the C1 spinal nerve is often connected to the spinal accessory nerve via a communicating branch (nerve of McKenzie).

Accessory Nerve

Although variation exists, the spinal accessory nerve arises from the upper five or so cervical spinal cord segments, and connections between the nerve and especially the dorsal rootlets of the upper cervical spinal cord segments are common. The spinal accessory nerve will ascend from its spinal origin to enter the foramen magnum and, near the jugular foramen, unite with its cranial part to exit the skull (Figs. 5.2, 5.3, 5.4, and 5.5).

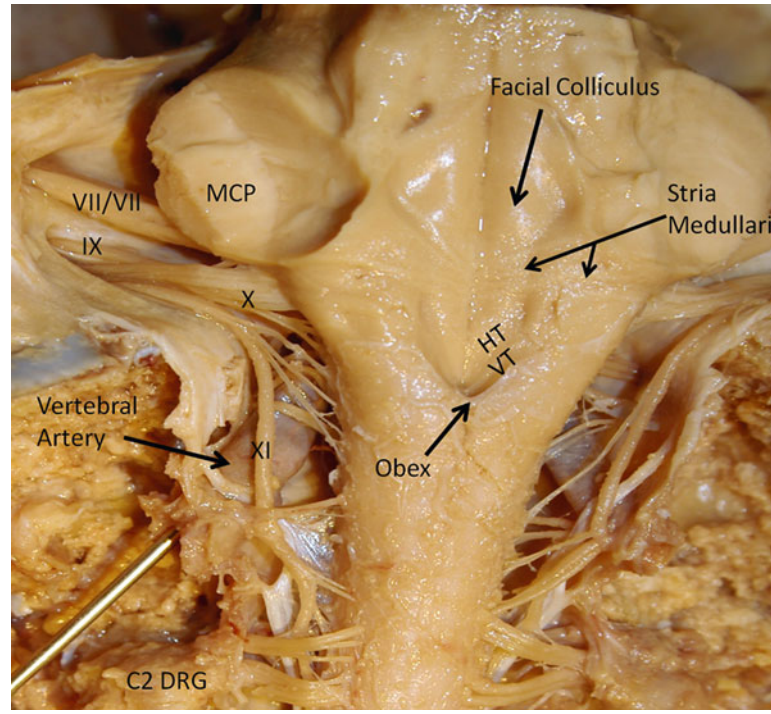

Fig. 5.5 Posterior craniocervcial junction following removal of the cerebellum. Note the floor of the fourth ventricle with the facial colliculus, stria medullaris. In the lower half of the floor, note the hypoglossal trigone (*HT*) and vagal trigone (*VT*). The obex marks the lowest part of the brain stem. On the left side, the middle cerebellar peduncle (*MCP*), cranial nerves VII–XI, and dorsal root ganglion (*DRG*) of C2 are seen

The spinal portion will continue out to innervate the sternocleidomastoid and trapezius muscles. Although controversial, many opine that the cranial roots of the accessory nerve send their fibers to the vagus nerve (internal ramus or pars vagalis) and, specifically, its recurrent laryngeal branch to innervate the laryngeal muscles (less the cricothyroid muscle) and laryngeal mucosa below the vocal cords. Innervation of palatal muscles may also occur via the cranial rootlets of the accessory nerve.

Hypoglossal Nerve

Just superior to the uppermost attachment of the intracranial and first denticulate ligament is the hypoglossal nerve, which will innervate three of the four extrinsic tongue muscles (hyoglossus, styloglossus, and genioglossus). Also, as mentioned above, fibers from the upper cervical nerves will travel along the hypoglossal nerve to terminate on posterior fossa dura mater and thus provide some of its innervation.

First Spinal Nerve

The C1 nerve (Fig. 5.2), as mentioned above, travels posteriorly to innervate the muscles of the suboccipital triangle including the rectus capitis posterior minor and overlying semispinalis capitis muscle. This nerve, in general, does not have a cutaneous distribution. Anteriorly, the ventral ramus of the C1 spinal nerve contributes to the cervical plexus and travels along the hypoglossal nerve to terminate on the thyrohyoid and geniohyoid muscles.

Posterior Spinal Artery

The posterior spinal arteries arise from the vertebral arteries and travel around the brainstem and then inferiorly along the posterolateral surface of the cervical spinal cord. They are distinct single vessels only at their origin and distally become irregular anastomosing channels, retaining, to a large degree, their embryonic plexiform pattern. The posterior spinal arteries are largest in the cervical and lumbar regions.

Posterior Inferior Cerebellar Artery

An important artery of the posterior fossa, especially in regard to the Chiari malformation, is the posterior inferior cerebellar artery (PICA), which arises from the vertebral artery near the vertebrobasilar junction and travels inferiorly toward the foramen magnum (Figs. 5.6 and 5.7). Occasionally, PICA may extend extracranially, especially in the hindbrain hernias. Once it reaches its lowest point, PICA recurs (caudal loop) around the cerebellar tonsil. PICA then ascends to its superior most point (cranial loop) and travels inferolateral to course over the convexity of the cerebellar hemisphere. Along its course, PICA supplies the lower medulla oblongata, choroid plexus, posterior fossa dura, fourth ventricle, cerebellar tonsils, vermis, and inferolateral hemisphere. PICA can be divided into five segments:

1. An anterior medullary segment, which is often absent (i.e., PICA does not originate anterior to the medulla oblongata), extends from the origin of PICA to the inferior olive.
2. A lateral medullary segment that extends from the inferior olive to the origins of the lower cranial nerves.
3. A posterior medullary segment (tonsillomedullary segment) begins where the PICA passes posterior to the lower cranial nerves and ends where the ascending vessel reaches the midlevel of the medial surface of the tonsil. It passes immediately posterior to the roof of the lower half of the fourth ventricle. All medullary segments give rise to perforating branches, which, if injured, are the reason nuclear dysfunction occurs (e.g., Wallenberg syndrome).
4. A supratonsillar segment (telovelotonsillar segment) begins at the midportion of the tonsil, includes the cranial loop, and ends where the PICA exits the fissures between the vermis, tonsil, and cerebellar hemisphere to reach the suboccipital surface. This is the most complex of the PICA segments.
5. Cortical segments (hemispheric segment) supply such areas as the midline vermis and tonsils. The PICA often bifurcates into medial and lateral trunks where the vessel emerges onto the inferior cortical surface. The medial trunk gives rise to vermian and tonsillar branches, and the lateral trunk gives rise to hemispheric branches.

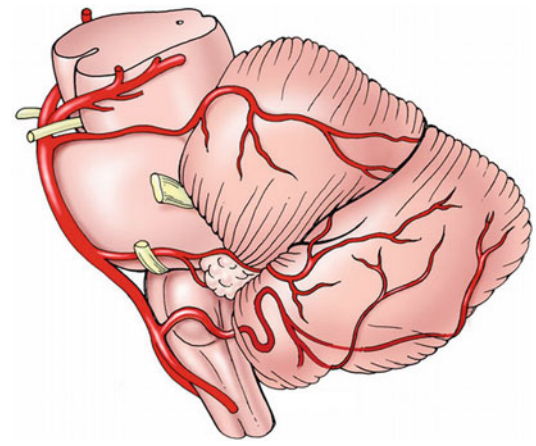

Fig. 5.6 Schematic drawing of the lateral brain stem and cerebellum. Note the course of the posterior inferior cerebellar artery (PICA) from the vertebral artery at its confluence into the basilar artery. The various segments of PICA are shown as it passes by the brain stem and then along the cerebellar hemisphere

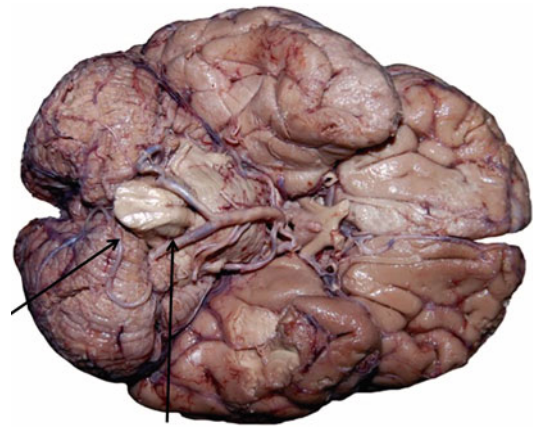

Fig. 5.7 The basilar surface of the brain illustrating the left vertebral artery (*right arrow*) and the tonsillar segment of PICA (*left arrow*)

Variations of PICA are common such as it arising from the basilar artery. For example, PICA may be found to arise extradurally in up to 20 % of cases and may be duplicated in up to 5 %. The vertebral artery may terminate (approximately

0.2 %) as PICA and PICA may be absent or hypoplastic and may share a common origin with the anterior inferior cerebellar artery.

Cerebellar Tonsils

The cerebellar tonsils (Fig. 5.8) are normally found several millimeters above the foramen magnum and are often asymmetric between left and right sides. These structures are connected to the cerebellum along their upper lateral surface by the so-called tonsillar peduncle. Laterally, the cerebellar tonsils are covered by the biventral lobule. The cerebellomedullary fissure separates the tonsil from the posterior surface of the medulla oblongata. The space that separates the left and right tonsils across the midline is referred to as the vallecula. At its superior pole, each tonsil's anterior surface faces the nodule, inferior medullary velum, and tela choroidea. This superior pole of the tonsil, which faces the uvula medially, is separated from the aforementioned structures by an extension of the cerebellomedullary fissure known as the telovelotonsillar cleft.

Retrotonsillar Veins

The superior retrotonsillar vein originates from the superior pole of the cerebellar tonsil and travels posteriorly to unite with the inferior retrotonsillar vein, which arises near the inferior pole of the tonsil to course superiorly. Together, these vessels form the inferior vermian vein, which therefore drains the medial and lateral surfaces of the tonsils. The inferior vermian vein may drain into the tentorial or transverse sinuses or into the torcular Herophilus.

Fourth Ventricle

Communicating superiorly with the cerebral aqueduct and inferiorly with the subarachnoid space, the fourth ventricle lies just posterior to the pons and medulla oblongata. The fourth ventricle

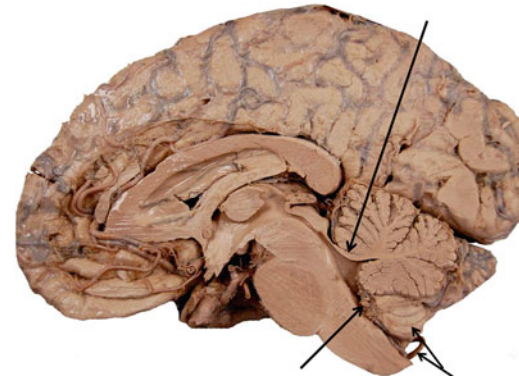

Fig. 5.8 Midsagittal section of the brain noting the superior medullary velum (*upper arrow*), choroid plexus of the fourth ventricle and attached to the inferior medullary velum (*left lower arrow*), and the right cerebellar tonsil and PICA (*right lower arrows*)

can be described as a gable-roofed chamber with a diamond-shaped floor. The gables are directed lateralward and are prolonged in tunnellike extensions around the restiform body. The long axis of the ventricular floor is parallel with the spinal cord and extends from the superior extremity of the pons to the middle of the medulla. The fourth ventricle (Figs. 5.5 and 5.9) is lined with ependyma, which is complete throughout, except in the roof of the inferior part, where below the inferior medullary velum only the epithelial layer is present. The choroid plexus of the fourth ventricle invaginates the roof epithelium and hangs from the roof into the lateral recesses and the inferior part of the ventricular cavity. Its roof is composed of the superior and inferior medullary vela, which come into contact at the fastigium (Fig. 5.8). The superior medullary velum is partially concealed by the lingula of the cerebellum, and its proximal portion acts as a bridge for the crossing of the fibers from the contralateral trochlear nerve nucleus. The inferior medullary velum is smaller and gives rise to the tuft of choroid plexus found within the fourth ventricle. Specifically, the tela choroidea, which is a fold of pia mater and related ependyma related to the inferior medullary velum, gives rise to the choroid plexus here and is the basis for the so-called telovelar approach to the fourth ventricle. The tela choroidea turns inferiorly from the telovelar

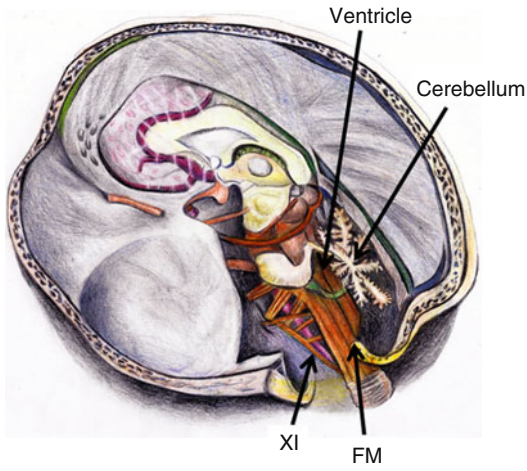

Fig. 5.9 Schematic view of the posterolateral posterior fossa demonstrating the posterior edge of the foramen magnum (*FM*) and the nearby spinal accessory nerve (*XI*), cerebellum (*arrow*)

junction around the superior pole of the tonsils to attach to the inferolateral edges of the fourth ventricular floor termed the taeniae. Superiorly, the taeniae travels lateral over the inferior cerebellar peduncles and travels horizontally along the inferior aspect of the lateral recesses. Branches of PICA supply the choroid plexus of the fourth ventricle. Specifically, these are derived from the telovelotonsillar segment of this vessel.

The floor of the fourth ventricle (rhomboid fossa) contains multiple landmark structures formed due to underlying bulging of various tracts and nuclei. Dividing the fossa into an upper and lower half, the stria medullaris of the fourth ventricle represents fibers connecting arcuate nuclei to the middle cerebellar peduncle. Above this horizontal marker is the facial colliculus, which represents the underlying motor nuclei of the facial and abducens nerves. Vertically, the left and right sides of the rhomboid fossa are divided by the median fissure, and on either side of this fissure and extending cephalad from the facial colliculus is the medial eminence. Lateral to the facial colliculus is the fovea superior that represents the remnant of the sulcus limitans, which, more or less, differentiates medial motor nuclei from lateral sensory nuclei. The sulcus limitans represents the embryologic border between the alar (sensory) and basal (motor) plates. The upper aspect of the fossa above the facial colliculus contains the locus ceruleus and may have a darkened appearance. This nucleus is a site of norepinephrine production. Laterally, at the junction of the upper and lower half of the rhomboid fossa, the dorsal cochlear and vestibular nuclei are found in the so-called acoustic area. The lateral recesses of the acoustic areas (foramina of Luschka) allow for CSF egress and may allow for a tuft of choroid plexus (basket of Luschka) from the fourth ventricle to protrude out into the cerebellopontine angle. In the lower half of the fossa, a collection of underlying nuclei forms two V-shaped trigones, the hypoglossal and vagal, representing the nuclei of the vagus and hypoglossal nerves. The obex (Latin, barrier), which is a small fold of tissue at the lower dorsal fourth ventricular wall, marks the lower level of the fourth ventricle and is found, on average, 12 mm above the foramen magnum. Arachnoid webs have been observed at the level of the obex that occlude the foramen of Magendie. The obex is inferiorly displaced with both the Chiari 0 and 1.5 malformations. The edges of the V-shaped lower half of the rhomboid fossa are termed the calamus scriptorius due their resemblance to a writing pen, and just inside this edge are the nuclei related to the emetic response termed the area postrema. The "closed" (i.e., nonventricular) posterior aspect of the medulla demonstrates additional external landmarks including the clava (gracile tubercle), located just inferior to the obex and off the midline from the dorsal median sulcus, which is formed by the underlying funiculus gracilis carrying proprioceptive fibers. Lateral to the clava and separated by the dorsal intermediate sulcus is the cuneate tubercle, which also carries proprioceptive fibers. Lateral to the cuneate tubercle and marking the position of the spinal tract and nucleus of the trigeminal nerve is the tuberculum trigeminum (cinereum). Ventral to the tuberculum trigeminum and not seen with a direct posterior view of the posterior brain stem is the site of emergence of the rootlets of the cranial part of the accessory, vagus, and glossopharyngeal nerves (Fig. 5.5).

The foramen of Magendie is a median aperture resting at the inferior aspect of the fourth ventricle and, with the laterally positioned foramina of Luschka, allows CSF egress from the fourth ventricle into the cisterna magna and cervical subarachnoid space. The foramen of Magendie may be stenotic or imperforate as it is in other mammals. Interestingly, neither the foramen of Magendie nor the foramina of Luschka are lined with ependyma.

Epidemiology of the Chiari I Malformation

6

John D. Heiss

Abstract

Almost 1 % of normal adults undergoing MRI scanning have cerebellar tonsillar ectopia of 5 mm or more, sufficient for radiographic diagnosis of Chiari I malformation (CM1). Only about 0.01–0.04 % of adults demonstrate symptoms and MRI evidence of CM1. Symptoms of CM1 usually accompany tonsillar ectopia over 12 mm, a narrow CSF space posterior to the cerebellar tonsils, and molded cerebellar tonsils. In CM1, reduced bony development of the posterior fossa creates morphologic changes in the cerebellum and medulla. Factors predisposing to CM1 include an affected close relative, birth injury, trauma, pseudotumor cerebri, hydrocephalus, Pacific island ancestry, female gender in US adults, male gender in Russian Tartar adults, and possibly epigenetic changes. Prospective well-designed studies of large populations will provide better estimates of CM1 prevalence than existing retrospective queries of the databases of private and governmental healthcare organizations.

Introduction

Epidemiology is defined as "the branch of medicine which deals with the incidence, distribution, and possible control of diseases and other factors relating to health" [1]. A determination of the incidence and distribution of Chiari I malformation therefore depends on the criteria one uses to characterize the "disease" of Chiari I malformation. Disease can be defined as "a disorder of structure or function in a human, animal, or plant, especially one that produces specific symptoms or that affects a specific location and is not simply a direct result of physical injury" [2]. Based on that definition, one could describe the disease of Chiari I malformation simply as a disorder of hindbrain structure, as seen on MRI imaging, or could, in addition, require specific symptoms to be manifested. On the other hand, realizing that the epidemiology of Chiari I is not well established at this point, one could look at the epidemiology of Chiari I malformation from the perspective of both (1) prototypical MRI characteristics alone and (2) MRI characteristics that must be accompanied by distinctive clinical criteria. This two-pronged

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approach would not preclude longitudinal evaluation of presently asymptomatic people with MRI findings of Chiari I malformation (incidental Chiari I malformation) who may later develop typical symptoms of Chiari I malformation. In addition, comparison of the determinants that predominate in symptomatic versus asymptomatic people with Chiari I malformation could lead to insights into possible environmental events that could trigger the onset of symptomatic Chiari I malformation. The ultimate goal would be to design interventions to reduce the occurrence of symptomatic Chiari I malformation in the population [3].

Epidemiology of Rare Diseases

There are several ways to measure the frequency of a disease such as Chiari I malformation (CM1) in a population [4]. The *incidence rate* of CM1 is the number of new cases per unit of person-time at risk. The *cumulative incidence* refers to the proportion of people who develop CM1 during a specified period of time. The *period prevalence* is the proportion of individuals in a stable population who have CM1 during a specific period of time. *Point prevalence* is the proportion of individuals in a population who have CM1 at a specific time. *Lifetime prevalence* is a measure of current cases of CM1 and cases of CM1 that have previously occurred, including those that have been treated [4]. The *case fatality rate* for CM1 refers to the proportion of deaths caused by CM1 in a population of patients with CM1.

Symptomatic CM1 appears to be a rare condition [5]. A rare (or orphan) disease is generally considered to have a prevalence of fewer than 200,000 affected individuals in the USA [6]. Research studies of a rare disease do not usually include a population of patients that is sufficiently large to allow determinations of the incidence or prevalence of a disorder [7]. Most rare diseases do not recognize geographical or political borders [7]. Of the more than 7,000 conditions that are considered rare diseases, a majority are inherited, but many others are acquired and are related to environmental factors [7]. Expression of a rare disease often varies from patient to patient [7]. Diagnostic delays occur frequently in patients with CM1 and other rare diseases [8].

Prevalence of Chiari I Malformation

A population-based retrospective cohort study was conducted in northern California by searching for the diagnosis of CM1 in radiology reports over a 2-year period (January 1997 to December 1998) [9]. Clinical follow-up was 6.4 ± 4.1 years. From an overall population of 741,815 children under age 20 within Kaiser Northern California (a medical insurance plan), 5,248 (0.71 %) underwent head and spine magnetic resonance imaging (MRI) scans during the 2-year period. Radiographic diagnosis of CM1 required 5 mm or greater of tonsillar ectopia. Of the 5,248 children scanned, 51 (0.97 %) were identified as having a radiographic diagnosis of CM1, with ectopia ranging from 5 to 32 mm, with a median of 7 mm. Patients who previously had been diagnosed with CM1 were apparently not excluded from evaluation, so the incidence rate (new cases per unit of person-time) of radiographic CM1 in this pediatric population could not be determined. The study instead measured period prevalence, which was 0.0068 % (0.68 per 10,000) over the 2-year period. Of the 51 children with radiographic CM1, 32 (63 %) were symptomatic, with the most common symptoms being headache (55 %), neck pain (12 %), vertigo (8 %), sensory changes (6 %), and ataxia or poor coordination (6 %). The period prevalence of symptomatic CM1 in the pediatric population was therefore 0.0043 % (0.43 per 10,000) over the 2-year period. Of the 51 children with radiographic CM1, 6 had syringomyelia (12 %), giving a period prevalence of CM1-syringomyelia of 0.00081 % (0.81 per 100,000). Of the six patients with syringomyelia, five received surgical decompression with significant reduction in syrinx size after surgery. Only three children with CM1 without syringomyelia underwent suboccipital decompression, which initially relieved their daily intractable headaches, although one patient had recurrence of headaches

beginning 1 year after surgery. In the follow-up period, 4 of the 19 originally asymptomatic patients developed symptoms, with headaches being present in 3 and tremor and poor coordination in 2 [9]. No cases of syringomyelia developed in the follow-up period. Interestingly, of the 19 patients with tonsillar ectopia of 2–4 mm, 14 (74 %) of them had headaches, characterized as severe in 3, occipital in 2, and Valsalva-related in 1. The true period prevalence of radiographic CM1 in the pediatric population is undoubtedly higher than the numbers noted above because the entire population did not undergo MRI scanning but only the subset of the population who experienced symptoms that prompted MRI scanning of the head or neck. In addition, the development of symptoms in previously asymptomatic patients indicates that period prevalence of symptomatic CM1 will increase as the period of observation increases. Finally, prevalence figures in this study did not include patients with CM1 who had previously been treated.

The study reported by Aitken and colleagues confirms the general impression among clinicians that the prevalence of CM1 diagnosed by radiographic criteria is considerably higher than that of CM1 diagnosed by radiographic criteria and accompanied by typical clinical signs and symptoms [9]. The radiographic diagnosis of CM1 in that study was defined as 5 mm or more of tonsillar ectopia [9]. Studies based on the amount of tonsillar ectopia indicate that the normal range (mean ±2 standard deviations) of the cerebellar tonsils ascends with age, so 6 mm of ectopia exceeds the normal range in the first decade, 5 mm is abnormal in the second and third decades, and 4 mm is abnormal in the fourth to eighth decades of life [10]. Using these standards, the period prevalence of CM1 in children would be lower than reported in the Aitken study because children with 5–5.9 mm of ectopia in the first decade of life would be diagnosed as normal rather than as having CM1.

After excluding patients with posterior fossa disease, supratentorial tumors, hydrocephalus, increased intracranial pressure, and diffuse or focal atrophy, Mikulis and colleagues studied a population of 221 randomly selected outpatients in the age range of 5 months to 89 years. The upper limit of normal (greater than 2 standard deviations above the mean) for tonsillar ectopia in this population was slightly greater in younger than older people [10]. If the position of the cerebellar tonsils relative to the foramen magnum assumes a normal distribution, about 2.3 % of these outpatients would exceed a threshold of 2 standard deviations above the mean. In contrast, if an upper threshold of 3 standard deviations above the mean were applied, only 0.14 % of the population would exceed this range. Applying this more rigid standard of 3 standard deviations above the mean to the data reported by Mikulis results in similar values to the 2 standard deviation threshold, with the upper limit of tonsillar ectopia being 8 mm in the first decade and 5 mm in the second to eighth decades [10]. This study did not report if any subject with tonsillar ectopia had symptoms related to CM1. The value of 5 mm of tonsillar ectopia corresponds to a threshold for the diagnosis of CM1 established in a previous study [11].

The proportion of the population that has MRI findings compatible with the diagnosis of CM1 far exceeds the proportion of the population with symptoms of CM1. One study found that 0.9 % of normal adults undergoing MRI studies of the brain had tonsillar herniation extending more than 5 mm below the foramen magnum (Fig. 6.1) [12]. People who have MRI findings of CM1 but are asymptomatic are given the diagnosis of "incidental Chiari I malformation." When symptomatic rather than normal subjects undergo MRI scanning, radiographic findings of CM1 similar to those observed in the study of normal subjects often are cited as the cause of symptoms. In a retrospective review of over 22,000 hospitalized patients, only 14 % of patients with radiographic findings of CM1 were thought to be clinically asymptomatic [13]. In another retrospective series of 68 patients with MRI findings of CM1, 30 % of patients were asymptomatic. However, in this study it was apparent that the amount of tonsillar ectopia correlated with symptom production, as ectopia over 12 mm was always associated with symptoms [14]. Symptomatic CM1 patients in one study had a mean tonsillar ectopia

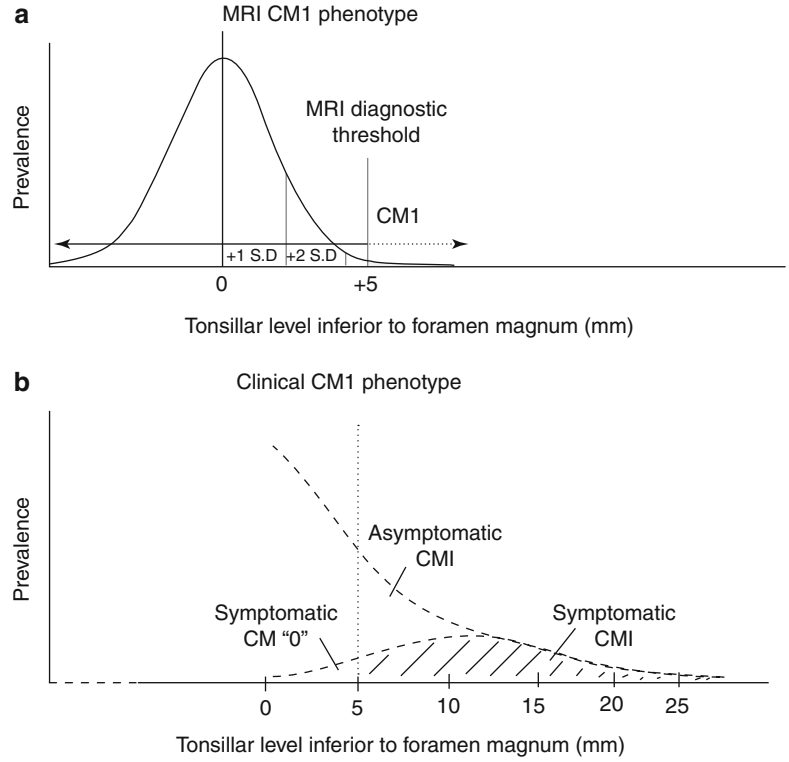

Fig. 6.1 Drawings describe different ways to define Chiari I malformation (*CM1*). In (**a**) the threshold for the diagnosis of Chiari I malformation on MRI scans is usually 5 mm, although this number can be modified slightly to conform to age-based norms. In (**b**) the population of patients with symptomatic CM1 is marked by the angled lines in the area under the curve. The drawing reflects the finding that virtually all subjects with 12 mm or more of tonsillar ectopia are symptomatic [14]. The prevalence of MRI-diagnosed Chiari I malformation in normal adults is 0.009 (0.9 %) [12]. The prevalence of symptomatic CM1 in the population is uncertain. The prevalence of symptomatic Chiari type 0 malformation (CM "0") is probably quite low based on the small number of cases reported in the clinical literature [44]

of 13 mm, although symptoms were reported with as little as 3 mm of ectopia [11]. In patients with lesser degrees of tonsillar ectopia, symptoms can be associated with narrowing of the CSF space posterior to the cerebellar tonsils, molding of the cerebellar tonsils, and/or syringomyelia [15].

The prevalence of CM1 in the general population is uncertain. One can estimate the prevalence of syringomyelia associated with CM1 by multiplying the prevalence of syringomyelia in an English city (8.4 cases per 100,000 people) [16] by the proportion of patients who have syringomyelia due to the CM1 (estimated to be about 70 %) [17]. This calculation would give a prevalence of Chiari I-related syringomyelia (CM1-syringomyelia) of 5.9 cases per 100,000 people. The same method can be applied to a retrospective study of 1.3 million people in northern New Zealand that identified all cases of syringomyelia diagnosed between 1961 and 2003. The prevalence of syringomyelia in 2003 in all ethnic groups was 8.2/100,000 population [18], which is remarkably similar to the figure of 8.4 cases/100,000 population reported for an English city 40 years previously [16]. Syringomyelia in New Zealand was associated with CM1 in 64.3 % of cases, giving a prevalence of CM1-syringomyelia of 5.4 cases per 100,000 people, which is again very similar to the findings of Brewis [16, 18]. These prevalence values that include both the adult and pediatric populations are much greater than the

2-year period prevalence in pediatric patients of 0.8 cases per 100,000 that was reported by Aitken and colleagues [9]. This difference in the prevalence of CM1-syringomyelia in the pediatric and total population is consistent with the observation that symptomatic CM1 and syringomyelia most commonly present in adulthood [19].

Milhorat reported that 65 % of his CM1 patients undergoing surgery had accompanying syringomyelia [15]. The prevalence of all cases of CM1 (CM1-syringomyelia plus CM without syringomyelia) can be calculated by dividing the prevalence of CM1-syringomyelia by 0.65. Assuming a prevalence of CM1 with syringomyelia of 5.9 cases per 100,000 population [16], one would estimate a prevalence of CM1 of 9.1 cases per 100,000 people. However, based on Aitken's study, it is clear that symptomatic patients with CM1-syringomyelia are much more likely to undergo surgery than patients with CM1 without syringomyelia. An estimate of the prevalence of symptomatic CM1 in the general population would be about 36 cases per 100,000 people if one assumed that CM1 with syringomyelia accounts for only 19 % of all cases of symptomatic CM1 [9].

The Role of Nongenetic Factors in the Development of Chiari I Malformation

Nongenetic factors appear to affect the development of CM1. One traditional way to measure the influence of nongenetic factors on the development of CM1 would be to evaluate siblings with identical genomic DNA, i.e., monozygotic twins or monozygotic triplets, to see if they differed in the amount of their tonsillar ectopia and symptomatology. Because these monozygotic siblings had identical genomic DNA sequences, differences in phenotype would presumably be related to nongenetic factors. A first example of differences in phenotype is a report of adult monozygotic triplet sisters in which only the proband met the radiographic criteria for diagnosing CM1 [20]. The amount of tonsillar ectopia in the proband was not given in this report but appeared to be about 15–20 mm in an MRI scan shown in a figure in the article. Tonsillar ectopia of 4 and 2.5 mm in the asymptomatic siblings was considered to be variable expression of tonsillar ectopia. The authors made the case that the triplets demonstrated 100 % concordance for tonsillar ectopia with variable expression. However, if the triplets were evaluated using the accepted threshold of 5 mm of tonsillar ectopia for diagnosing CM1, only one would be diagnosed as being affected by CM1, and the other two would be considered to be unaffected (Fig. 6.2). Despite all three triplets having the same genomic DNA sequence, only one developed CM1! Even acknowledging that each triplet had some degree of tonsillar ectopia, the disparity in the amounts of ectopia among the triplets is striking and cannot be explained in terms of their identical inherited genomic DNA. Compression of the retrocerebellar cerebrospinal fluid space was evident in the MRI scans of the triplets, and it is likely that their common genomic sequences resulted in a smaller than normal posterior fossa in all of them. In this example, pre- and postnatal environmental, nutritional, and epigenetic influences on an identical substrate of genomic DNA led to the development of CM1 in the proband and lesser degrees of tonsillar ectopia in the others [21].

In another report, Stovner and colleagues reported monozygotic twin sisters with 5 and 10 mm of tonsillar ectopia. The twin with 10 mm of tonsillar ectopia also had syringomyelia. Their mother had 8 mm of tonsillar ectopia [22]. In another study, CM1 was diagnosed in monozygotic twin sisters and in the daughter of one of the twins. Although measurements of tonsillar ectopia were not given, imaging suggested that the amount of tonsillar ectopia was similar in the twins [23]. Affected family members had occipital dysplasia and overcrowding of the posterior fossa structures, suggesting that occipital dysplasia was the heritable condition and that CM1 developed in response to reduced posterior fossa volume [23].

The complexity of factors involved in the development of CM1 is apparent in another report describing 11-year-old monozygotic twin boys who had syringomyelia. One twin had CM1 with

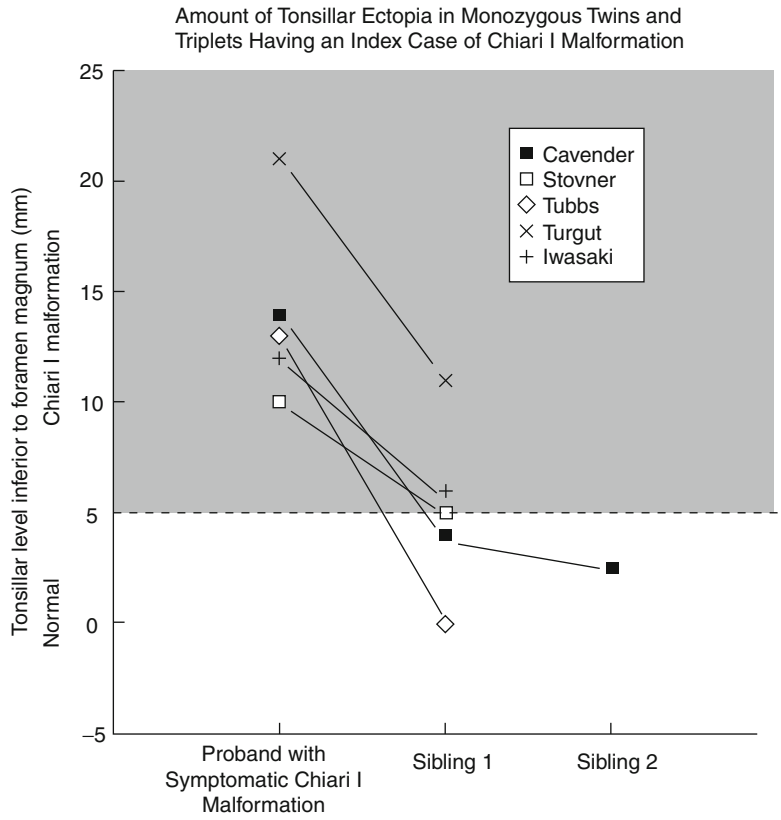

Fig. 6.2 This graph compares the amount of tonsillar ectopia in monozygous twins and triplets from reports in the medical literature in which tonsillar ectopia was measured [20, 22, 24–26]. All probands presented with symptomatic Chiari I malformation. Their monozygous siblings had lesser amounts of tonsillar ectopia and were asymptomatic, with the exception of sibling 1 reported by Tubbs et al. who had symptomatic syringomyelia

13 mm of tonsillar ectopia and associated scoliosis. The other twin did not have any (0 mm) tonsillar ectopia but had findings of lower extremity hyperreflexia, "jumpy legs," syringomyelia, shortening of the basiocciput, and inferior displacement of the obex [24]. Review of the birth history revealed that the twin with CM1 had a cephalic presentation whereas his brother had a breech presentation. Posterior fossa decompression and duraplasty was performed in both twins and resulted in reduction in syrinx diameter and clinical stabilization in both. Both twins shared findings of syringomyelia and abnormal development of the inferior part of the posterior fossa [24]. However, the disparity in the amount of tonsillar ectopia in the two twins cannot be explained on the basis of their common genomic DNA sequence.

A report of 26-year-old, identical twin brothers from Turkey provides further evidence of the amount of variation in tonsillar ectopia and symptoms that can be seen in identical twins. The proband had a 6-year history of headache exacerbated by coughing and the Valsalva maneuver, gait disturbance, and 21 mm of tonsillar ectopia. The other brother was asymptomatic and had 11 mm of tonsillar ectopia [25]. These twins were concordant for having radiographic CM1 but discordant for symptoms.

Iwasaki reported monozygotic twins in which the proband had an uneventful and healthy childhood before developing pain and numbness in the left arm that began at the age of 16 years [26]. Symptoms progressed for 10 years until she was diagnosed by MRI with CM1 (12 mm of tonsillar ectopia) and cervicothoracic syringomyelia at the

age of 26. The asymptomatic twin had 6 mm of tonsillar ectopia. Review of birth records revealed that the affected twin was delivered first and suffered from coiling of the umbilical cord and neonatal asphyxia. In contrast, the unaffected twin was born uneventfully [26]. Neonatal asphyxia is a possible nongenetic factor that could have influenced the development of CM1 and syringomyelia in the proband, although this report stated that she otherwise developed normally [27].

Phenotypic differences in monozygous twins and triplets identified in the studies mentioned above have been used in this chapter and in other studies to make the case that environmental factors play a role in the development of CM1. In most cases, the mechanisms by which environmental factors influence a complex disease such as CM1 have not been obvious. Recently epigenetics has been used to explain how phenotypic differences between monozygous twins become more pronounced with age. Age-related differences in the content and genomic distribution of 5-methylcytosine DNA and histone acetylation are thought to result in gene expression being modulated differently in monozygous twins [21]. Environmental factors such as smoking, physical activity, and diet have been proposed to influence epigenetic modifications, but it has also been suggested that epigenetic changes simply occur as a result of normal aging. Fraga and colleagues reported that one-third of monozygous twins harbored epigenetic differences in DNA methylation and histone modification. Differences in the placenta and amniotic sac between the monozygous twins are also postulated to play a role in creating phenotypic discordance between monozygous twins [21].

Nongenetic Factors Associated with the Development of Chiari I Malformation

Gender

In reports of adult patients with CM1 from the USA and Europe, there is usually a female preponderance. In a cohort of 364 symptomatic patients in the USA with CM1, defined in this series as tonsillar herniation of at least 3 mm below the foramen magnum, there were 275 (76 %) females and 89 (24 %) males. Age of onset of symptoms was 24.9 ± 15.8 years (mean ± standard deviation) [15]. Elster et al. reported 42 females (62 %) and 26 males (38 %) in a series of 68 pediatric and adult patients with CM1 [14]. In a surgical series of 157 patients with CM1-syringomyelia conducted in France, 53 % were female and 47 % were male [28]. However, in the Tartar Republic in the Russian Federation, males are affected more often than females (see below). The prevalence of CM1 in the pediatric population does not appear to be related to gender. In a surgical series of 130 pediatric patients in the USA with CM1, 53 % were males and 47 % were females [29].

Birth Injury

Williams reported that there was an association between difficult birth and the later development of CM1-related syringomyelia. Syringomyelia was more likely to develop in a first-born child, heavy birth-weight babies, and those in whom forceps were used. Williams believed that a difficult birth causes the cerebellar tonsils to engage in the foramen magnum and could also cause basal arachnoiditis [30]. Hida supported the view that adverse events during delivery were associated with CM1-related syringomyelia. In his study, abnormal presentation, the use of forceps, neonatal asphyxia, and birth injury were much more frequently reported in patients with CM1-related syringomyelia compared to normal subjects [27].

History of Trauma

In Milhorat's report, 89 patients (24 %) cited trauma as the precipitating event [15]. In a retrospective Canadian study of 85 patients with symptomatic CM1, 12.9 % reported a history of minor head or neck trauma preceding the onset of symptoms [31].

Ethnic Factors

The prevalence of syringomyelia, including CM1-related syringomyelia, was evaluated in the population of northern New Zealand, which consisted of 1.3 million people in 2001. The ethnic makeup of the population was 11.7 % Pacific people, 12.5 % Maori, and 75.5 % Caucasians or others. Pacific people (18.4/100,000) and Maori (15.4/100,000) had a higher prevalence of syringomyelia than Caucasians (5.4/100,000) [18]. In addition, Pacific people were more likely to have syringomyelia associated with CM1 (87.5 %), than Maori (53.6 %) and Caucasians (58.8 %). The prevalence of CM1-syringomyelia in Pacific people was 16.1/100,000, in Maori was 8.2/100,000, and in Caucasians was 3.2/100,000. In northern New Zealand, CM1-syringomyelia was therefore found to be 5 times more prevalent in Pacific people and more than 2 1/2 times more prevalent in the Maori than in Caucasians. Female-to-male ratios were similar in the Pacific people (55:45) and Maori (50:50), but females (69:31) predominated in the Caucasians. The authors of this study speculated that ethnic variations in the size of the posterior fossa and of cerebrospinal fluid flow in the foramen magnum may underlie the differences in the prevalence of syringomyelia among the ethnic groups [18].

The prevalence of syringomyelia in the Russian Federation, especially in the Republic of Tatarstan, is estimated to be 130 per 100,000 inhabitants, which is approximately 24 times that of Caucasians in New Zealand and over 8 times that of Pacific people in New Zealand. Tartars are the predominant ethnic group in that region and make up 82 % of affected patients. Unlike in the adult population of the USA, males in that population were affected (88 %) much more often than females (12 %). The affected males are predominantly manual laborers who perform agricultural work [32]. Patients in that population usually develop syringomyelia associated with reduced volume of the posterior fossa, which in about one-half of cases is also associated with CM1 [33, 34]. A study of the genetics of CM1 in Tatarstan is currently being conducted [35].

Reduced Intracranial Volume

CM1 is not associated with an underlying disease and is considered primary in most patients, although a majority of patients have underdevelopment of the posterior fossa of unknown etiology [36]. Processes that reduce the volume of the inferior part of the posterior fossa will result in deformation of the hindbrain and the development of idiopathic CM1 [36–38]. Factors that reduce the supratentorial intracranial volume can also influence the development of CM1. For example, the incidence of CM1 by MRI criteria in children diagnosed with non-syndromic, single-suture craniosynostosis was 5.6 % in Finland [39].

Increased Brain Volume or Intracranial Pressure

Hydrocephalus was included in Chiari's original description of his type 1 malformation [40] and in Milhorat's series was present in 9 % of patients with CM1-syringomyelia and 3 % of patients with CM1 alone [15]. Treatment of associated hydrocephalus usually reduces the amount of cerebellar ectopia [41]. In the Netherlands, the prevalence of CM1 by MRI criteria in patients with pseudotumor cerebri was found to be 10 % (7/68) [42]. All patients with idiopathic intracranial hypertension and Chiari I malformation were overweight or obese women.

Summary

Epidemiological studies are sorely needed in most rare diseases, and Chiari I malformation is no exception. The prevalence of CM1 in the general population of the USA or any other country has not been determined with any certainty. The uncertain clinical implication of tonsillar ectopia that lies just outside the normal range reinforces the need for better criteria for the radiographic diagnosis of CM1. The development of symptoms of CM1 generally correlates with the amount of tonsillar ectopia, but lesser degrees of tonsillar ectopia can sometimes create symptomatic CM1

(or CM zero) and syringomyelia by critically narrowing the posterior CSF space, especially if accompanied by arachnoidal scarring [43, 44]. A retrospective study of the prevalence of CM1 in children has been conducted in northern California. The prevalence of CM1 associated with syringomyelia has also been evaluated in the entire population of northern New Zealand. These studies provide some insight into the prevalence of CM1 in those populations. The vast difference in the degree of tonsillar ectopia among monozygotic twins and triplets suggests that factors other than genomic DNA play a large role in the development of CM1. Several factors that influence the development of CM1 and the onset of symptoms have been described, including female gender in American and European adults and a history of trauma. The reports of ethnic differences in the prevalence of CM1 suggest the need for additional studies to discover if differences arise from genetic or environment factors or a combination of both. Better understanding of the prevalence of Chiari I malformation and factors that influence its development or symptomatology may lead to interventions that could reduce the disease burden of Chiari I malformation.

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Genetics of the Chiari I and II Malformations

7

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Abstract

Chiari malformations are considered to have a multifactorial etiology, likely influenced by environmental and genetic factors. This chapter will detail the evidence that supports a genetic contribution to the disorder, including discussions of twin studies, familial aggregation, co-occurrence with known genetic syndromes, and previous genetic studies. While no susceptibility genes have been identified to date, gene identification efforts are continuing. It is expected that researchers will have a more complete understanding of the specific genes and biological pathways that contribute to disease development in the coming years. The future benefits from genetic research of Chiari I and II may include the development of genetic tests that result in more accurate and faster diagnoses as well as new targeted treatment options for patients.

Introduction

Chiari malformations are considered to be genetically complex with multiple genetic and environmental factors potentially contributing to disease development. As a result, the genetic dissection of Chiari malformations is expected to be challenging. The substantial genetic heterogeneity is likely reflected in the observed phenotypic heterogeneity. Therefore, an important first step is to accurately define the phenotype. Misclassification of patients can result in inclusion of unknown disease subtypes with distinct genetic etiologies, as well as individuals with different diseases or even without disease, all of which will negatively impact the ability to localize "Chiari genes." Identification of subgroups of patients with similar clinical characteristics

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should reduce the phenotypic heterogeneity and ultimately genetic heterogeneity, as well. This approach may lead to improved power to identify Chiari genes. Often the next step to genetic dissection of a complex disorder is to determine if sufficient evidence exists to support a genetic component for the disease. Researchers often look for familial aggregation of the disease, disease concordance between twins, animal models of the disease where a gene has been identified, as well as co-occurrence of the disease with known genetic syndromes. Importantly, it is the preponderance of evidence from multiple well-designed studies that provide the strongest support.

Once sufficient genetic evidence exits, experimental design follows and depends on a variety of factors, including the main goal of the study, disease prevalence, proportion of sporadic versus familial cases, age of disease onset, disease-specific mortality, and practical considerations such as personnel and financial resources. Population ascertainment is a key component of study design that demands a great deal of time and planning to ensure enrollment criteria are met (e.g., disease phenotype criteria and clinical exclusion criteria at the personal and family history level). Once study participants are enrolled, data generation, analysis, and validation (test findings using another method or technique), replication (test findings in a separate study population), and interpretation of findings usually follow. This entire process can take even a large research team many years to complete and can cost anywhere from tens of thousands to millions of dollars.

Given that genetic studies expend tremendous financial and personnel resources, much of what is currently known about the genetics of Chiari relates to the collection of data supporting a genetic contribution to the disease as this is one of the first steps to complete before embarking on more costly genetic studies. There are several lines of evidence including twin studies, familial aggregation, co-occurrence with known genetic syndromes, as well as previous genetic studies that suggest a genetic component in at least a subset of Chiari I malformation cases, while our understanding of the genetic causes of Chiari II malformation is more limited. As such, the focus of this chapter will be primarily on the genetics of Chiari I malformation but will conclude with a brief discussion of Chiari II malformation genetics at the end of the chapter.

Chiari I Malformation

Twin Studies

Twin studies allow researchers to identify the genetic contribution for a disease by comparing the concordance of disease between monozygotic twins (share 100 % of their genome) to dizygotic twins (share on average 50 % of their genome). This approach helps establish if a disease is at least due in part to genetic causes. However, there are several important factors to consider in terms of the design and interpretation of twin studies, especially in the context of complex disease; these include (1) whether a common pre- and postnatal environment was shared between the twins, (2) what additional factors might explain discordance between monozygotic twins (e.g., epigenetic factors or modifications to the genome that do not change the underlying DNA sequence but may affect things such as gene expression), and (3) if the dizygotic twins are of the same sex. The latter point is particularly important in the context of Chiari malformation, as females appear to be three times more likely to be affected with Chiari I malformation than males [1].

The largest Chiari I malformation twin study to date compared three sets of monozygotic twins (two sets of sisters, one set of brothers) to three sets of dizygotic twins (three sets of sisters) and found a higher concordance between monozygotic twins compared to dizygotic twins [2]. Multiple reports have also described concordance between single sets of monozygotic twins [3–9] and one set of monozygotic triplets [10]. In general, twins were concordant with respect to the Chiari I malformation diagnosis, although they were sometimes discordant in terms of other factors, including the presence of syringomyelia, age of onset, extent of tonsillar herniation, and symptom severity. Discordance with respect to

the Chiari I malformation diagnosis between monozygotic twins was noted in at least three studies; [3, 8, 10] however, these differences can likely be attributed to the absence of standardized classification of Chiari malformation patients and our current poor understanding on how best to define the disorder, for example, (1) Iwasaki and colleagues [8] described one twin sister as having Chiari I malformation and the other as having mild tonsillar ectopia (6 mm herniation); (2) Tubbs and colleagues [3] reported a set of twin brothers, one diagnosed with Chiari I malformation and the other with Chiari 0 malformation; and (3) Cavender and colleagues [10] described monozygotic female triplets, one of which was diagnosed with Chiari I malformation and the other two were diagnosed with varying degrees of tonsillar ectopia (4 and 2.5 mm herniation).

Familial Aggregation

Familial aggregation or clustering refers to the identification of families where multiple members are affected with the disease of interest. It is important to keep in mind that the observation of multiple affected individuals in a family does not mean that the disease is genetic. One must also consider that this observation is due to chance or environmental causes. In the case of Chiari I malformation, there are an overwhelming number of reports of familial clustering [1, 5, 6, 9, 11–23] that in combination with other observations (e.g., results from the twin studies, frequent observations that multiple family generations are affected with the disease, many families contain even more than two affected family members, and many families appear to be spread out geographically) makes it less likely to be observed by chance or solely due to an environmental factor(s). There have also been multiple reports of familial syringomyelia, some of which have Chiari I malformation (reviewed in reference [20]).

In addition to family studies, several studies have provided estimates of the proportion of patients with a positive family history for Chiari I malformation. In a seminal paper by Milhorat and colleagues, it was reported that out of a cohort of 364 symptomatic patients, 43 (12 %) had at least one close relative with Chiari I malformation with or without syringomyelia or idiopathic syringomyelia [1]. Additionally, 72 patients (20 %) were reported as having at least one close relative with a similar symptomology without an official Chiari I malformation diagnosis [1]. In a large retrospective review of 500 Chiari I pediatric surgical patients, only 3 % of patients had a positive family history for Chiari I malformation [24]. When interpreting these results, it is important to note that these studies are based on highly selected samples of patients and, in the absence of neuroimaging on all family members, it is difficult to obtain accurate diagnoses.

Although a proper segregation analysis has not been conducted previously for Chiari malformation, the mode of inheritance has been suggested to be either autosomal dominant (vertical inheritance, with male-to-male transmission) with reduced penetrance (disease appears to be transmitted through "unaffected" relatives) or autosomal recessive (horizontal inheritance); [1] however, Chiari malformation is likely to be more complex and influenced by multiple genetic, epigenetic, and environmental factors.

Heritability

Heritability refers to the proportion of phenotypic variation in a population that is attributable to genetic variation among individuals. In other words, if something is found to be significantly heritable, it is likely to have a genetic component. Heritability estimates of the posterior fossa are especially important to the genetics of Chiari malformation as the posterior fossa is compromised in many Chiari I malformation patients and is likely to play an important role in the development of the malformation in at least some patients [25].

Heritability has been previously estimated for various components of the posterior fossa using 99 individuals from 35 Chiari I malformation families [23]. In this study, posterior fossa measurements were taken from presurgical MRIs from both affected as well as unaffected family

members. Out of the 11 measurements examined, the posterior fossa volume ($H^2r = 0.96$, $p = 0.0035$) and basal angle ($H^2r = 0.51$, $p = 0.0144$) were significantly heritable in the families. The clivus ($H^2r = 0.39$, $p = 0.0542$) and the supraoccipital bone ($H^2r = 0.28$, $p = 0.0685$) were also nearing significance. These results were based on a small sample size, so additional heritability studies are needed to try and separate the various genetic and environmental components contributing to the observed trait variation.

Co-occurrence with Known Genetic Syndromes

Another important tool that geneticists use to determine that a disease has a genetic component is to determine if a disease co-occurs with another syndrome with a known genetic basis. If the two diseases co-occur more often than would be expected by chance, then this would suggest that the diseases may be related and perhaps share an underlying genetic risk. For example, if two diseases are independent and both occur at a population frequency of 0.10, one would expect the diseases to co-occur at a frequency of 0.01 (0.10×0.10) in the population. In selected populations, such as a cohort of Chiari patients, the prevalence of another disease in that cohort therefore needs to be higher than that observed in the general population for it to represent a potentially meaningful association.

Although over 20 genetic syndromes have been previously described as co-occurring with Chiari I malformation [2], many of these are based on single case reports in the literature, and more data are needed in order to rule out spurious associations. Examples of the more commonly associated genetic syndromes include Ehlers-Danlos syndrome [26–29], Marfan syndrome [26, 30–32], Klippel-Feil syndrome [1, 24, 33–43], growth hormone deficiency [24, 40, 44–50], Paget's disease [51–53], craniosynostosis [54, 55], Goldenhar syndrome [56–58], Williams syndrome [59–61], Kabuki syndrome [62, 63], hypophosphatemic rickets [64, 65], and neurofibromatosis type I [66, 67]. In some of these reports, authors hypothesize that the Chiari I malformation is "acquired," occurring secondarily to the primary genetic syndrome [30, 36, 52]. In addition, there have also been multiple reports of Chiari I malformation co-occurring with other diseases or syndromes in patients where chromosomal aberrations or genetic defects have been identified. These include a 16p11.2 rearrangement [68], 17p13.3 deletion distal to PAFAH1B1 [69], FOXP1 haploinsufficiency [70], 5p13.3-13.2 deletion [71], germline-activating mutation in TSHR [72], and pentasomy 49,XXXXY [73], among others.

Genetic Studies

Genetic studies can encompass a wide range of study designs depending on the research goal. These may vary by scale (e.g., candidate gene versus whole-genome studies), the type of data generated (e.g., genotype versus gene expression data), as well as the analysis conducted (e.g., association versus linkage). As the development of new genetic techniques and technologies has increased over the years, it has become increasingly feasible to conduct large-scale genetic screens within reasonable time frames and financial constraints. However, regardless of time and money, a separate barrier to genetic research is the ability to ascertain a large enough study population that meets enrollment criteria. Consequently, very few genetic screens have been conducted for Chiari malformations to date, but data from ongoing studies, including our own, will improve this number in the coming years.

As mentioned above, there are multiple varieties of genetic studies that can be employed to detect a genetic component for a disease. One of the first reported genetic studies for Chiari was conducted in 1982 and was a candidate gene association analysis of the human leukocyte antigen (HLA) locus [74]. HLA-ABC antigen frequencies were compared between 53 patients with syringomyelia, 40 of which had a Chiari anomaly (type not specified), and 500 pooled controls. After correction for multiple testing, a significant increase of HLA-A9 was observed in

patients with syringomyelia (corrected $p = 0.007$). When restricted to the Chiari cases, an increased frequency was still observed but did not remain significant after correction (uncorrected $p = 0.0038$; corrected $p = 0.11$). Authors suggested that perhaps there is an association between the HLA locus and the development of syringomyelia or Chiari malformation.

Another type of genetic screen that can be carried out is a candidate gene sequencing study. In this type of study, investigators select a gene based on biological relevance perhaps in combination with positional information and then sequence that gene in a number of cases and controls to identify DNA sequence changes (mutations and/or polymorphisms) that may be associated with the disease. The first candidate gene sequencing study for Chiari I malformation was published in 2003 [2]. Speer and colleagues investigated an excellent biological candidate gene, Noggin, which is known to play an important role in development. Thirty-three cases of nonsyndromic Chiari I were screened for mutations in the coding region and part of the 3′ and 5′ untranslated region by first using pooled samples and denaturing high-performance liquid chromatography, followed by Sanger sequencing to validate potential mutations. No mutations were identified in the 33 Chiari I cases, leading researchers to conclude that Noggin mutations are unlikely to represent a common etiology of Chiari I malformation.

A whole-genome linkage study is another type of genetic screen. The goal of this analysis is to identify regions of the genome that segregate with the disease in families or show excess sharing across affected family members. The only whole-genome linkage screen published to date for Chiari malformation consisted of 23 Caucasian multiplex (two or more affected individuals) families containing 67 sampled individuals affected with Chiari I malformation with or without syringomyelia [23]. Individuals were genotyped using the whole-genome Affymetrix 10K SNP Chip (TGen, Phoenix, AZ). Both parametric and nonparametric two-point and multipoint linkage analyses were conducted. Significant evidence for linkage was identified on regions of chromosome 9 and 15. Biologically plausible candidate genes within these intervals were explored, and in particular the authors discussed the gene, fibrillin-1, located on chromosome 15 due to its role in Marfan syndrome, ectopia lentis, and Shprintzen-Goldberg syndrome; however, sequencing studies to identify causal DNA mutations were not performed.

Chiari II Malformation

While little is known about the genetics of Chiari I malformation, even less is known about the genetics of Chiari II malformation. To our knowledge, there have been no reports of twin studies and only one possible report of familial Arnold-Chiari malformation (unspecified type) occurring in sisters [75]. The sisters were both described as having Arnold-Chiari malformation, myelomeningocele, and hydrocephalus, among other findings [75]. There have been multiple reports of Chiari II malformation co-occurring with known genetic syndromes, including trisomy 18 [76], Kousseff syndrome [77], lathosterolosis [78], Klippel-Feil syndrome [79–81], Duchenne muscular dystrophy [82], spondyloepiphyseal dysplasia tarda [83], velocardiofacial syndrome [84], and osteogenesis imperfecta [85]. While this may lend some limited support to a genetic etiology, with the exception of Klippel-Feil syndrome, these all appear to be single case reports; thus, we are unable to rule out the fact that these diseases co-occurred due to chance or that the association is due to another nongenetic reason.

It is widely believed that all patients with myelomeningocele have a Chiari II malformation [86, 87]. Neural tube defects (NTDs), such as myelomeningocele, are thought to be influenced by genetic as well as environmental factors. While multiple studies have published on the genetics of NTDs [88], one study reported that while screening patients with NTDs for mutations in the candidate gene, VANGL1, a missense mutation was identified in a sporadic case with myelomeningocele, Chiari II malformation, hydrocephalus, tethered cord, clubfeet, scoliosis, and kyphosis [89]. Kibar and colleagues also identified two additional VANGL1 missense

mutations in familial cases, one of which was also described as having myelomeningocele, but there was no mention of a Chiari II malformation diagnosis [89].

There have been no genetic screens conducted to date for Chiari II malformation specifically; however, there have been a few reports focusing on the expression of candidate genes in the ependyma of Chiari II patients, two of which focused primarily on hydrocephalus [84, 90, 91]. One study in particular found that ependymal vimentin was overexpressed only in regions of dysgenesis in Chiari II malformation fetuses and young infants [84]. Vimentin is a cytoskeletal protein that forms intermediate filaments in multiple cells belonging to the immature nervous system [92]. It was suggested that the upregulation of vimentin occurred secondarily in response to aberrant expression of another gene [84]. Although many theories have been proposed regarding the pathogenesis of Chiari II malformation [87, 93], some genetic hypotheses exist including William's hypothesis that both genetics and environment play a role in the underdeveloped posterior fossa or vertebral dysgenesis which results in altered CSF pressure and Chiari II malformation and spina bifida [94], as well as Sarnet's hypothesis that a genetic mutation perhaps in the HOX, WNT, or PAX gene families may be responsible for the rhombomeric segmentation defect as well as the underdevelopment of the posterior fossa [84].

Discussion

The accumulation of data over the years has established that there is a preponderance of evidence supporting a genetic contribution to at least a subset of Chiari I malformation patients, and the field is at a point where significant progress is being made in this area of research. Although there is strong evidence that genetics plays an important role in the development of at least certain forms of Chiari malformation, Chiari malformation is likely to have a multifactorial etiology, influenced by genetic, epigenetic, as well as environmental factors. While it is important not to discount these other nongenetic contributions to disease, there are many potential benefits of genetics research. Future genetic analyses will likely result in the identification of a gene or genes that increase susceptibility to Chiari malformation that may later be translated into a genetic test resulting in more accurate and quicker diagnoses. This can be especially useful for complex diseases, such as Chiari malformation, where the symptoms are vague and not unique to a disorder, resulting in slow diagnoses and even misdiagnoses [1]. Understanding the genetics of a disease can provide more information on the underlying disease mechanism and can also indicate which specific biological processes play a role in disease development. There is also the exciting potential for the development of new therapies and treatments targeting identified genes or pathways that are dysregulated, which may ultimately provide patients with alternative treatment options to surgery.

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Pathology of Chiari I and II Malformations

8

Lucy B. Rorke-Adams

Abstract

Chiari I and Chiari II malformations are generally categorized as primary cerebellar anomalies although critical review of their morphological features indicates that the cerebellar component more often is a secondary abnormality rather than a primary developmental defect. The basic malformation involves that portion of basicranium which comprises the posterior fossa; essentially it is too small. With a few exceptions, the non-bony abnormalities associated with Chiari I are secondary. In contrast the constellation of lesions that form Chiari II are complex and affect all levels of the neuraxis to a greater or lesser degree and consist of a combination of primary malformation and acquired lesions. Ironically, the cerebellar abnormalities more often fall into the acquired category.

More than 100 years ago, Hans Chiari wrote two papers describing four types of cerebellar malformations, all of which currently bear his name [1, 2]. He was primarily interested in the relationship between hydrocephalus and abnormalities of the cerebellum, although only type II is most consistently associated with ventricular enlargement.

This chapter will focus on pathological features of Chiari I and II, as these are relevant to neurosurgeons. Types III and IV are rare, and while some features of type III may be ameliorated by surgery [3], type IV, which is partial or complete aplasia of the cerebellum, is not a treatable condition.

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Chiari I

What is currently referred to as Chiari I malformation consists of clinical and pathological features that do not match Chiari's original description [4]. In the 1891 paper, he basically described chronic herniation of the cerebellar tonsils in a 17-year-old girl who also had mild enlargement of the third and lateral ventricles, unassociated with a large head. Viewed from a distance, it would appear that this case was simply an example of chronic tonsillar herniation secondary to increased intracranial pressure, a concept unknown at that time but only discerned 6–8 years later by Cushing [5] and Collier [6].

In view of that Chiari described no other abnormalities beyond tonsillar herniation and hydrocephalus, it is clear that association of these coexisting conditions as a specific malformation is incorrect.

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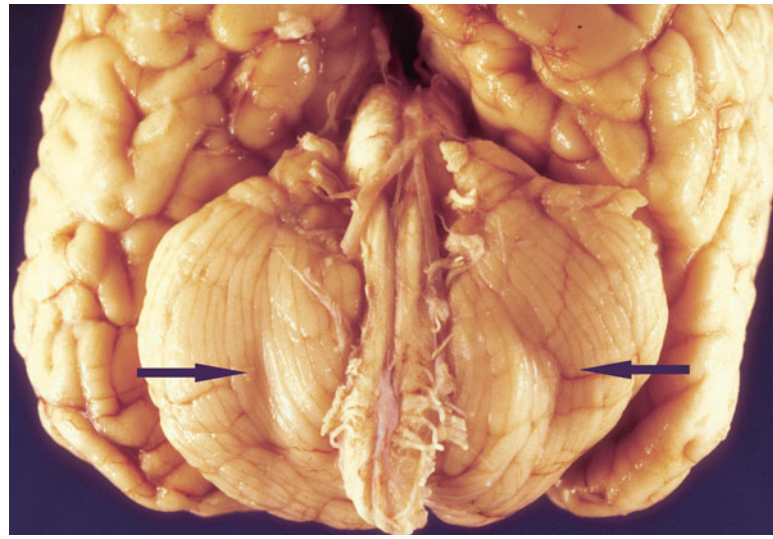

Fig. 8.1 Chiari I defect characterized by striking herniation of cerebellar tonsils into upper cervical canal. Note ridges separating tonsils and adjacent cerebellar tissue produced by bony rim of the foramen magnum (*arrows*)

Nevertheless, there is a clinical-pathological condition most common among older children and young adults currently called Chiari I malformation. Tonsillar herniation is one component, but it does not include ventricular dilatation (Fig. 8.1). However, it is associated with a variety of clinical symptoms and anatomical abnormalities, such as platybasia [7], basilar impression [8], or simply a posterior fossa that is smaller than normal [9, 10]. Occasionally, the foramen magnum is larger than normal, or there are other anomalies of the occipital bone or rostral cervical vertebrae [11].

Additionally, aside from the tonsillar herniation, there may be syringomyelia, especially in older individuals [12, 13], or aberrant dorsal angulation of rostral cervical roots [14]. The chronically herniated tonsils may be sclerotic [4] or be composed of frankly malformed tissue [14]. Among the cerebellar malformations, which may be confined to the tonsils or more widespread, are nonspecific foliar (cortical) dysplasia (Fig. 8.2) and hypertrophy of cerebellar cortex of the type described by Lhermitte and Duclos [15]. This rare condition straddles the divide between malformation and neoplasia. Pathological features are those of a malformation primarily affecting the granule cell layer, whereas clinically, it may present as a space-occupying lesion [16].

It should be emphasized that the clinical and pathological features of what is currently called Chiari I malformation do not match Chiari's original description but are instead a more complex combination of posterior fossa, cerebellar, and spinal cord abnormalities.

Chiari II

Of the four entities bearing Chiari's name, type II is the most severe and complex. There is a vast literature dealing with all aspects of this disorder, including who described what and when, along with issues of nomenclature. A detailed, scholarly review of the historical evolution of Chiari II malformation may be found elsewhere [17, 18]. Here, only key aspects will be noted before focusing upon the pathological features.

The central nervous system (CNS) components of Chiari II malformation were actually described first by Cleland in 1883 [19]. As noted above, Chiari's detailed observations appeared in two papers published in 1891 and 1896 [1, 2], respectively. Subsequently, the name of Arnold was united with Chiari's, even though he (Arnold) made no substantial contribution to either clinical or pathological features of the disorder [20], and Cleland's contribution was lost to the vicissitudes of history.

Currently, Chiari II malformation is often diagnosed on ultrasound monitoring of a pregnancy; otherwise, it is known to be present due to the patient's myelomeningocele. This diagnosis carries with it a substantial number of abnormalities involving all parts of the nervous system, including skull, spine, and dura mater as well. Contributions to this wealth

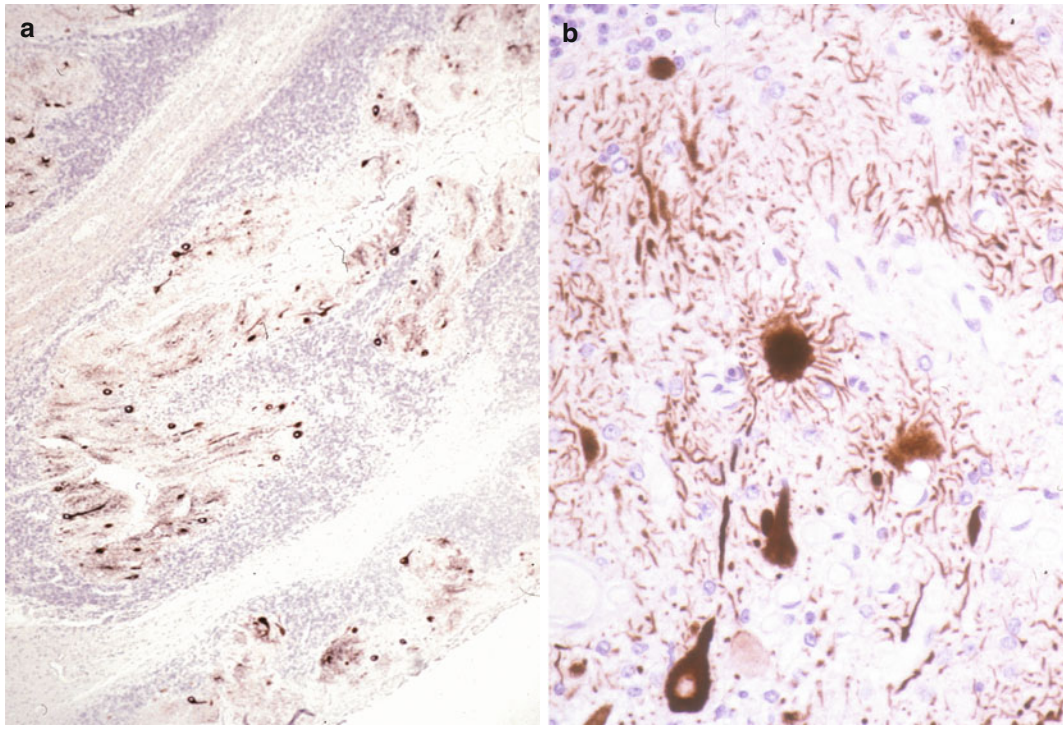

Fig. 8.2 (**a**) Photomicrographs of dysplastic cerebellar tonsils from surgical specimen of child with Chiari I defect. Immunoperoxidase preparation for NFP ×250. (**b**) Higher magnification of **a** showing dysplastic anatomy and bizarre Purkinje cells. Immunoperoxidase preparation for NFP ×400

of information have come from neurosurgeons, radiologists, pathologists, and embryologists.

Presentation of the major pathological features will be separated by structures affected, although this is artificial and, in some instances, cannot be done with precision.

Bone

Skull

Squamous Bones (Membranous)

Aside from sutural separation in infants whose hydrocephalus is not treated, the major abnormality is a condition in which bone is irregularly thinned, the thinned areas being separated by ridges (Fig. 8.3). Originally, named Lückenschädel, i.e., lacunar skull, it was suggested that pulsation of underlying gyri was responsible for the defect, but it is now clear that this is a primary bone lesion and present in at least 80 % of affected babies at birth [21]. It is a consequence of lack of ossification of the inner table of the skull [22].

Basicranium (Endochondral Bones)

Of the bony components of the skull base, those forming the posterior fossa are primarily affected. In general, the volume is reduced, but additional deformities include a short and dorsal concave clivus, scalloping of the petrosal bone with a foreshortened internal acoustic meatus, and an enlarged foramen magnum ([22], p. 500) (Fig. 8.4).

Vertebral Column

The vertebral column is always dysraphic in individuals with Chiari II anomaly. Dysraphism refers to imperfect midline closure of the spinolaminar arch, extent of the defect varying considerably in severity. Least severe is a simple bony defect, generally at the caudal end, spinal bifida occulta, unassociated with neural or mesenchymal components and, hence, not relevant here (Fig. 8.5).

Of major clinical concern is spina bifida aperta, in which the bone anomaly is associated with a wide range of mesenchymal and neural malformations (Fig. 8.6). Although the dysraphic defect may occur at any level, it is most common in the lumbosacral region. In general, there is a correlation between the

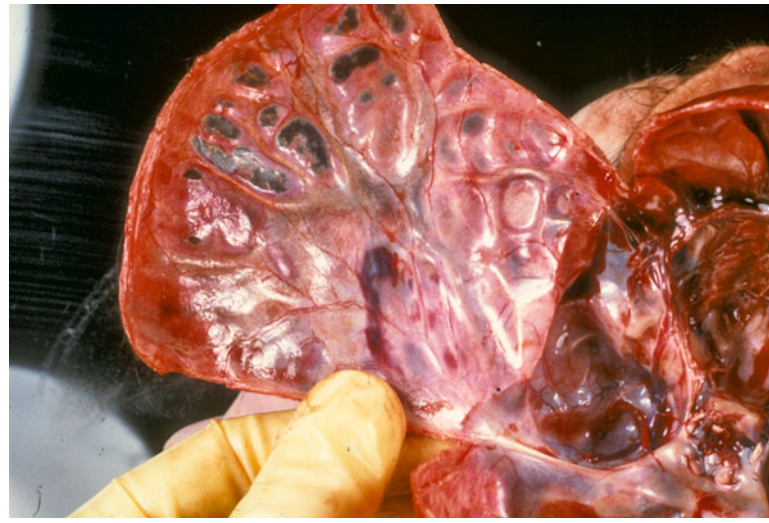

Fig. 8.3 Left parietal bone displaying ridges separating multiple patches of thinned bone characteristic of "Lückenschädel"

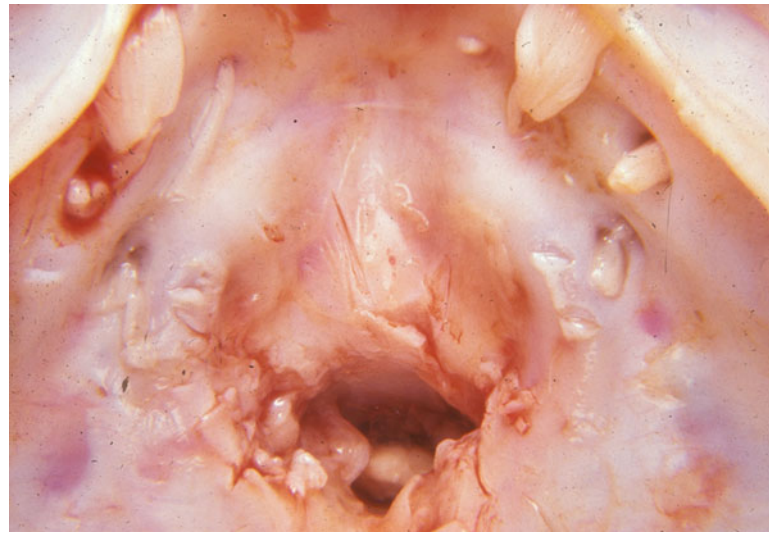

Fig. 8.4 Hypoplastic posterior fossa. Note steep angle of the clivus and overgrowth of bone forming the foramen magnum

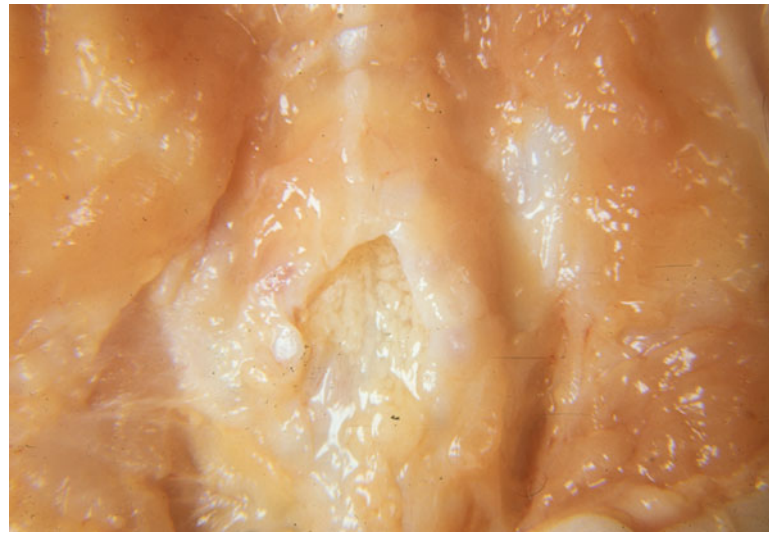

Fig. 8.5 Spina bifida occulta. Note absence of fusion of sacral laminae

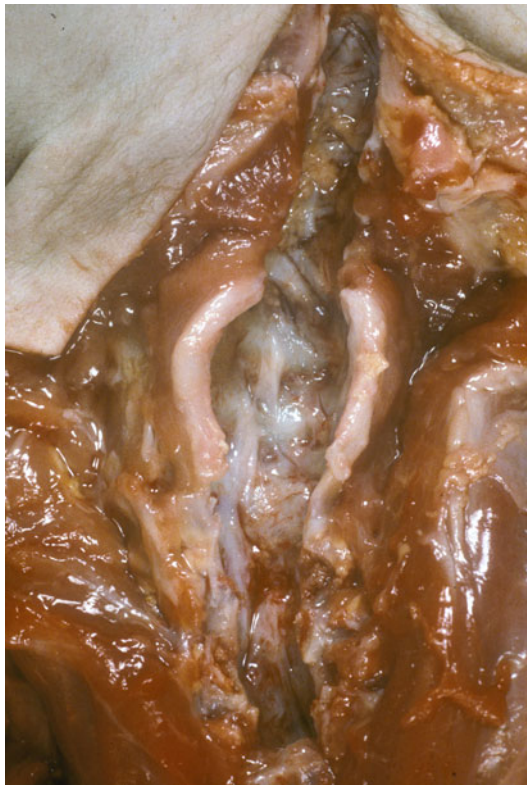

Fig. 8.6 Spina bifida aperta. Note total absence of laminae and round edges of bone allowing exposure of intraspinal contents

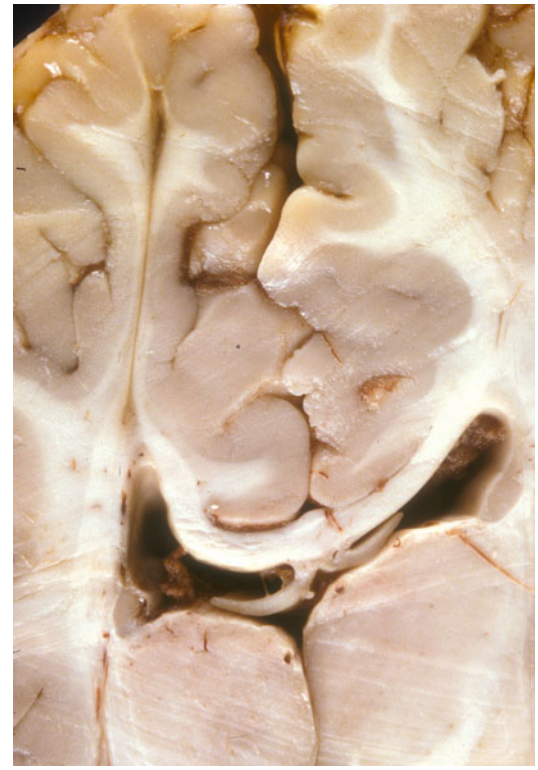

Fig. 8.7 Interdigitation of medially placed cerebral hemispheric gyri in partial agenesis of falx cerebri

vertebral level affected and the extent of neurological deficit; more rostral defects, e.g., involving thoracic vertebrae, are associated with more severe neurological deficits than sacral dysraphism.

Most frequently, the bony defect consists of lack of formation/fusion of laminar processes, but occasionally, a hypoplastic laminar process (spur) may curve inward to separate neural tissue, i.e., split cord malformation.

Mesodermal Component

Dura Mater

Cranial

Dural abnormalities of the cranium largely involve the falx cerebri, tentorium cerebelli, and venous sinuses of the posterior fossa. The tentorium may be absent or hypoplastic, leading to a lateral-low insertion causing vertical orientation of the straight sinuses and a low position of the torcular [22].

In individuals with hypoplasia or aplasia of the falx cerebri, there is interdigitation of medial cerebral gyri (Fig. 8.7).

Spinal

Dural abnormalities are a constant feature in the region of spina bifida aperta. It may be absent altogether, allowing exposure of neural elements, but more often, there is a complete or incomplete dural sac which, along with overlying epithelium, plus or minus dermis, protects the neural elements (Figs. 8.8 and 8.9). Dura and arachnoid herniated through the bony defect and with or without a covering of intact or ulcerated skin form the sac, which is a hallmark of the condition. A placode of neural tissue is attached to the undersurface. See below (Fig. 8.10).

Mesenchymal Tissue

Closure of head and tail ends of the neural tube requires involvement of epithelial, neural, and mes-

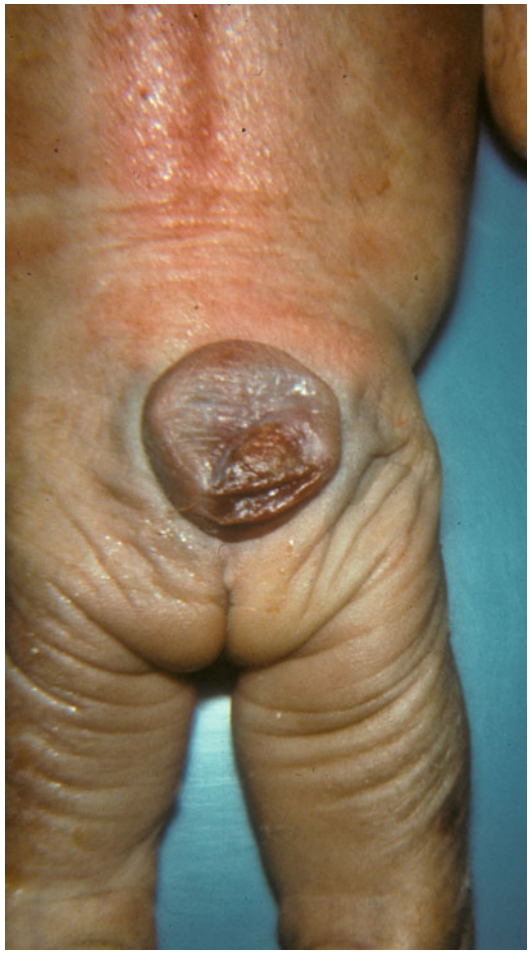

Fig. 8.8 Back of infant with lumbosacral meningomyelocele showing characteristic partially redundant sac

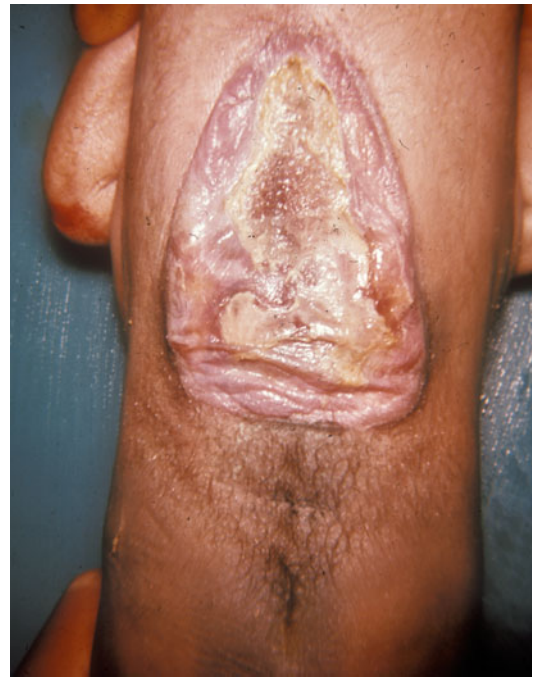

Fig. 8.9 Large thoracolumbar complex meningomyelocele with incomplete formation of sac. Note abnormal hirsutism of skin caudal to the defect

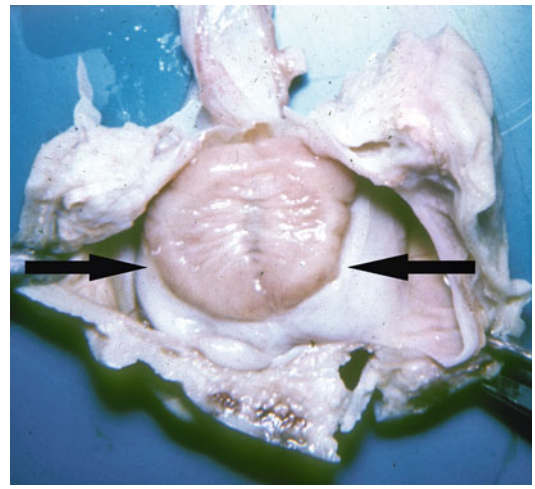

Fig. 8.10 Sac has been opened to expose large neural placode (*arrows*) at caudal end of the cord

enchymal tissue; hence, if the process does not proceed normally, the resulting defect contains a disordered combination of all of these elements. A primary mesenchymal component consists of an excessive number of blood vessels, the structure of which, for the most part, is normal, but because of their abundance, the lesion as a whole is referred to as the "area cerebrovasculosa" if at the head end or the "area medullovasculosa" if at the caudal end. Aside from dysplastic neural tissue and a prominent vascular component, there are disordered fibrous or fibrofatty tissue and often hamartomatous nests/bundles of smooth muscle.

Pathology of the Sac

Pathological features of the spinal defect are variable, ranging from total exposure of neural tissue, i.e., no covering sac, to one that is covered by apparently normal skin (Figs. 8.8 and 8.9). In most instances, however, there is a balloon-like protuberance continuous with normal adjacent skin but which consists of an attenuated layer of intact or ulcerated epithelium. This generally has a reddish color and a somewhat folded redundant character. When the sac

is opened, the bony defect is exposed, along with the herniated neural contents. These include spinal roots (including filum terminale) and dysplastic neural tissue plastered on the undersurface of the sac, the so-called neural placode (Figs. 8.10 and 8.11). This varies in size and complexity. There may also be excessive fatty tissue, i.e., a lipoma.

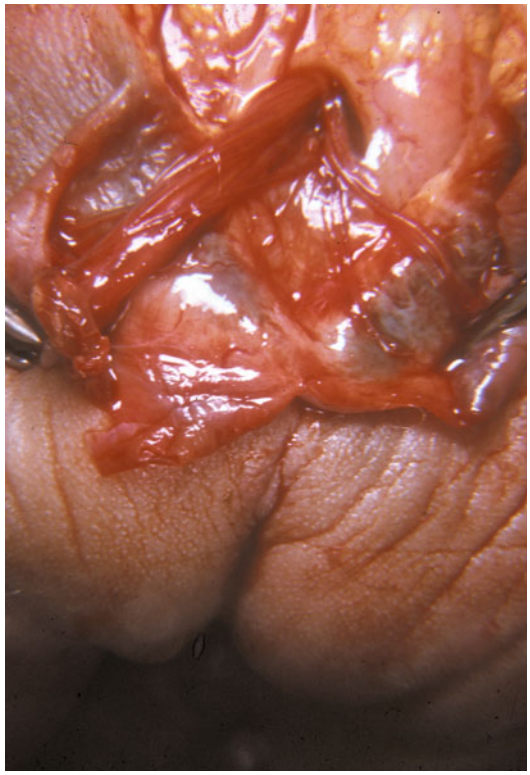

Fig. 8.11 Sac of infant pictured in Fig. 8.8 has been opened to display roots of cauda equina and filum, which are attached to the undersurface of the sac

Microscopic features that are most characteristic display a transition from normal skin to the sac consisting of attenuated, intact, or ulcerated and/or inflamed squamous epithelium. Underlying dermis may/may not be present, but dermal appendages are almost always absent (Figs. 8.12 and 8.13). Heterotopic, dysplastic neural tissue consisting of glia, with or without neurons, may be located superficially or in deeper layers (Figs. 8.14, 8.15, and 8.16). Ependymal cells are a common component and are typically arranged in strips similar to a ventricular lining (Fig. 8.17). Small nerve roots or twiglets are often present as well. These are located within the sac and in deeper tissues. The sac is lined by arachnoid and fibrous tissue, presumably dura, although it does not look like normal spinal dura. Occasionally, abortive dorsal root ganglia are found as well. Associated and generally intermixed with these tissues is an excessive number of blood vessels, typically of small to medium diameter; vascular walls are usually normal although occasionally, they may exhibit structural defects (Fig. 8.18).

A curious component of the dysplastic tissues in these specimens is a scattering of irregular bundles or strands of smooth muscle (Fig. 8.19). Dysplastic striated muscle is much less frequently observed.

Size and complexity of the neural placode is variable. It may be large and consist of dysplastic

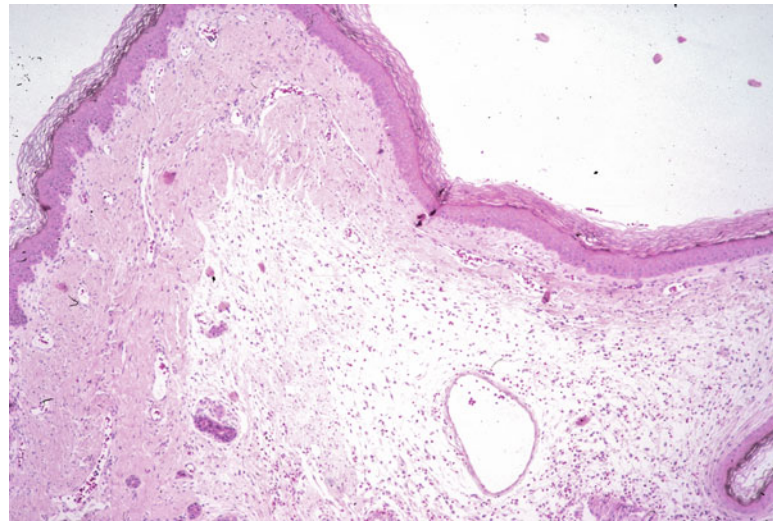

Fig. 8.12 Photomicrograph of intact epithelial covering of sac. Note underlying loose mesenchymal tissue and absence of dermal appendages. H&E ×100

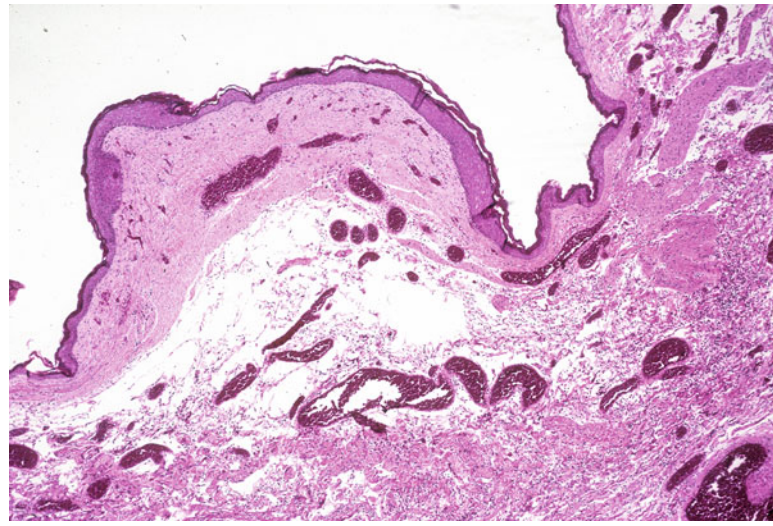

Fig. 8.13 Photomicrograph of sac and contents containing dense and loose connective tissue and abundant blood vessels. H&E ×100

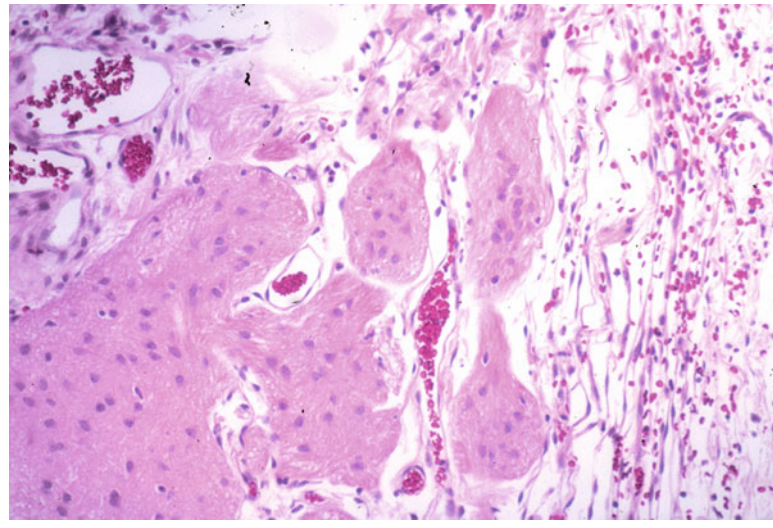

Fig. 8.14 Nests of dysplastic glial islands within sac. H&E ×250

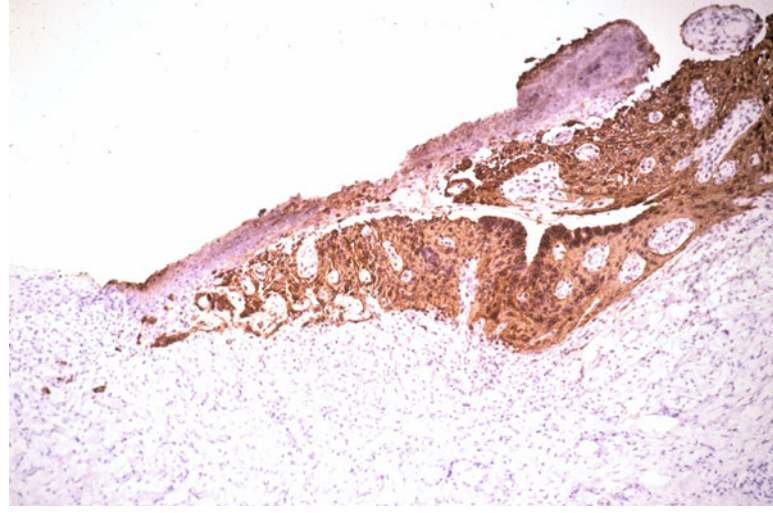

Fig. 8.15 Large strips of glial tissue along surface of myelocele sac. Immunoperoxidase preparation for GFAP ×100

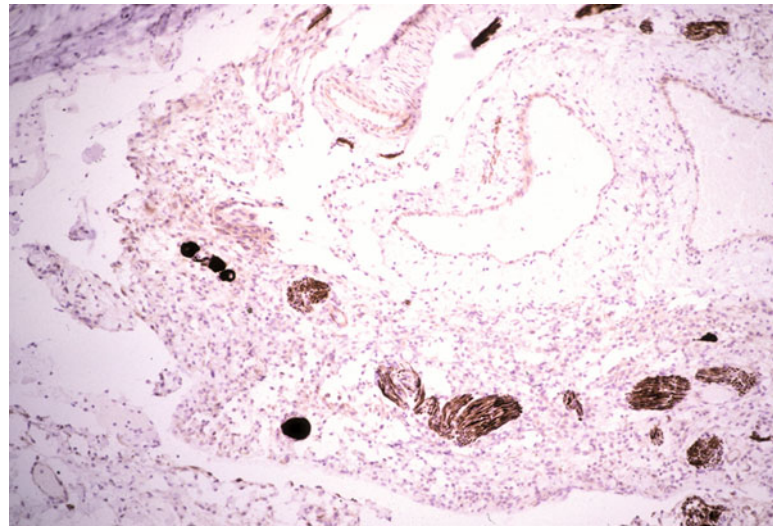

Fig. 8.16 Scattered nests of neuropil containing neurons within myelocele sac. Immunoperoxidase preparation for NFP ×100

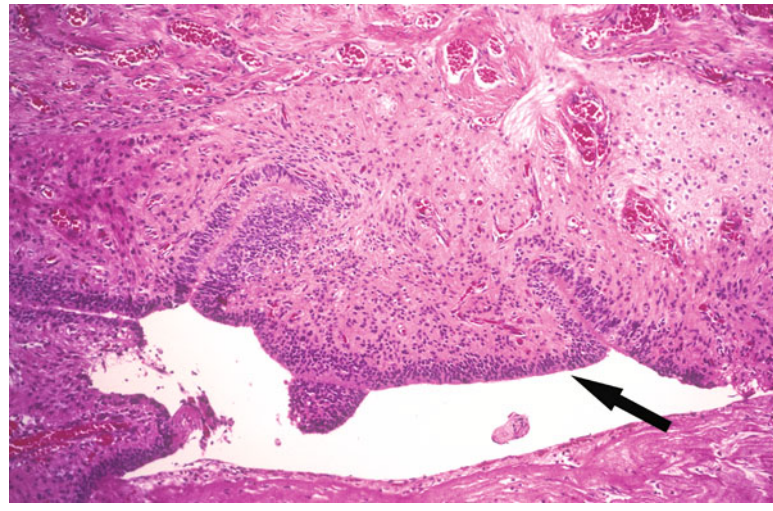

Fig. 8.17 Cavity in myelocele sac lined by ependyma (*arrow*) below which is glial tissue. H&E ×250

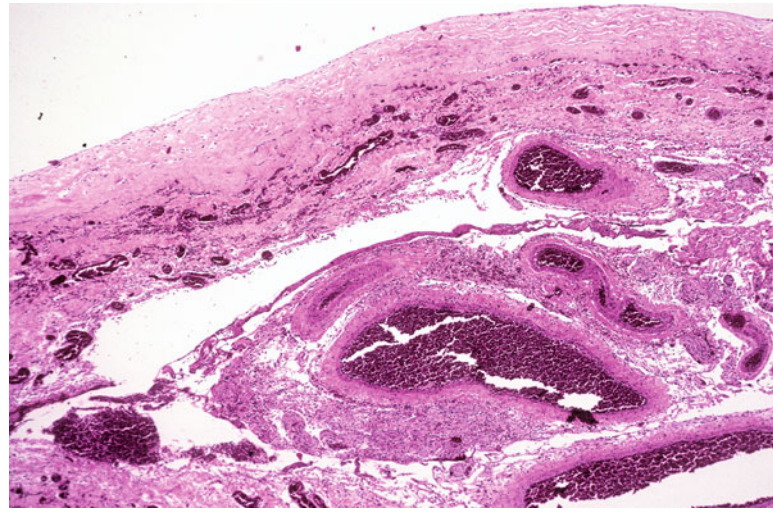

Fig. 8.18 Portion of myelocele sac containing many blood vessels of variable size. H&E ×250

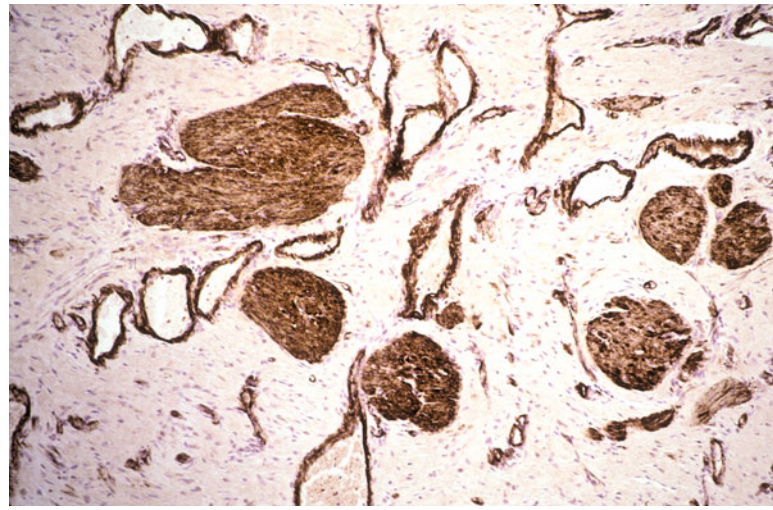

Fig. 8.19 Nests of smooth muscle in myelocele sac. Immunoperoxidase preparation for SMA ×250

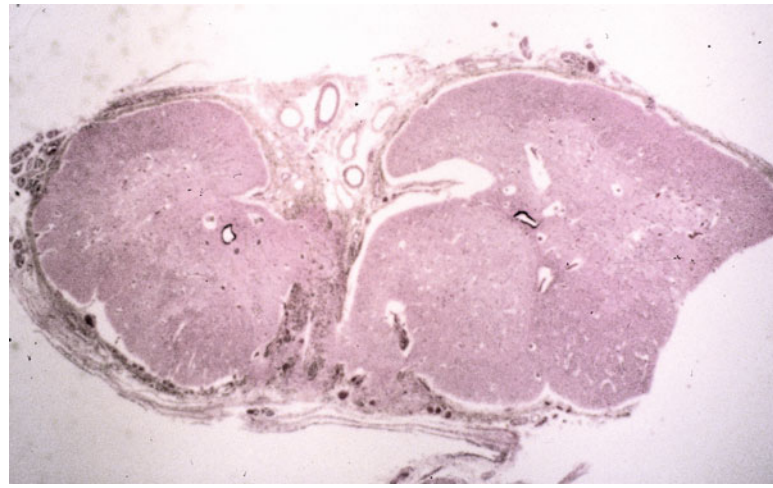

Fig. 8.20 Split cord associated with split cord malformation. Note central incomplete cleft and small central canal in each hemisection. H&E ×40

neuronal and glial tissue that includes ependyma. Recognizable spinal cord, well-formed or dysplastic, a split cord (Fig. 8.20), and duplication or even triplication of the cord are also possibilities. Excessive fat may be associated with the abnormal spinal cord (Fig. 8.21).

An uncommon lesion consists of a dilated sac lined by ependyma, i.e., myelocystocele. This represents distension of an extreme hydromyelic condition; hence, nerve roots are present in the outer walls of the cyst. This lesion may be associated with a defect in one or more vertebral bodies ([22], p. 1274).

Brain Abnormalities Associated with Chiari II Defect

A staggering number of lesions comprise the pathologic spectrum of Chiari II and involve all levels of the neuraxis. Thus, although attention has been focused on the cerebellar and brain stem defects, dysplastic development of the CNS is wide-ranging. One textbook account lists 10 involving the cerebrum, 12 in brain stem, 7 cerebellar, and 10 spinal, aside from those involving the dura (5) and skull and spine (11). Associated abnormalities of other organs are also described [17].

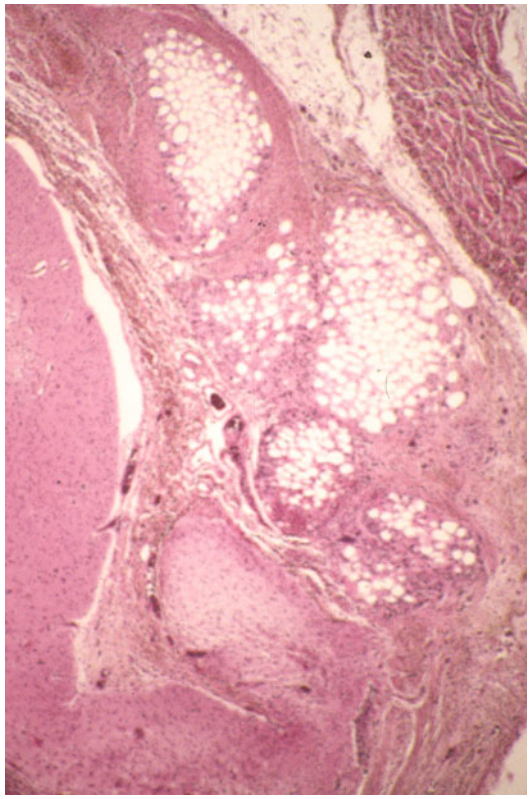

Fig. 8.21 Prominent fat deposits in mesenchymal tissue adjacent to dysplastic spinal cord in left field. Dura is located on right side. H&E ×100

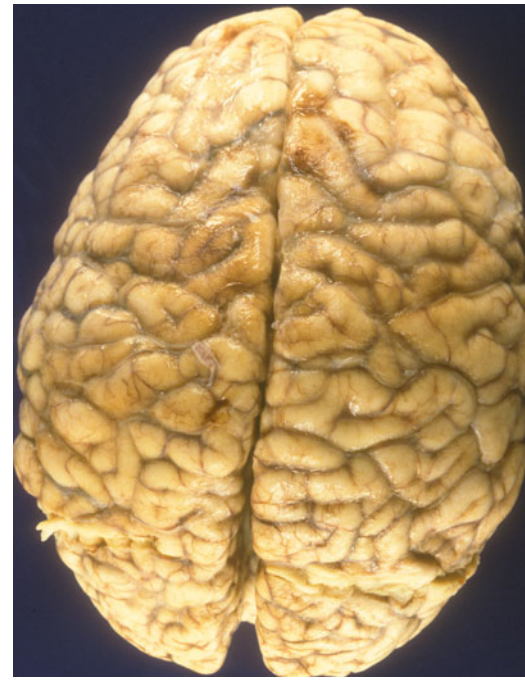

Fig. 8.22 Cerebrum of child with Chiari II malformation displaying polygyria. In this situation there appear to be an excessive number of gyri, but the cortex has a normal six-layered architecture

Clearly, all possible defects do not simultaneously affect all infants, but a sufficient number are found in combination in any given child to lead to significant clinical neurological deficit, only some of which can be treated surgically.

Gross abnormalities found in the cerebrum include polygyria, polymicrogyria, subependymal heterotopic nodules, maldevelopment of basal ganglia, and agenesis of the corpus callosum; rarely, the olfactory bulbs and tracts are agenetic (Figs. 8.22, 8.23, and 8.24). Aside from these, a host of associated abnormalities have been described in individual cases.

In contrast, most defects of the cerebellum and brain stem, which initially captured the attention of Cleland and Chiari, are not primary malformations but are consequent to the bony defects of the posterior fossa, foramen magnum, and tentorial hypoplasia.

Those involving the cerebellum consist of both caudal and rostral herniation of the vermis often in combination with overall hypoplasia. Cerebellar tissue which descends into the spinal canal is vermian but in some instances may also include tonsils. The herniated cerebellum forms a peg on the surface of the spinal cord (Fig. 8.25a, b). It is sometimes difficult to separate the cerebellar from the spinal tissues, as fibrotic leptomeninges may bind them together. In rare cases, a frank cerebellar malformation, rhombencephalosynapsis, may be present. In this defect, the cerebellar hemispheres and dentate nuclei are fused, as the entire vermis is absent.

As the posterior fossa is hypoplastic, herniation of superior vermis rostrally encroaches into the cranial cavity, especially if the tentorium is ill-formed.

Herniated cerebellar folia are often necrotic/sclerotic as the blood supply is compromised secondary to the corking effect caused by herniation of the soft tissue through the bony ring of the

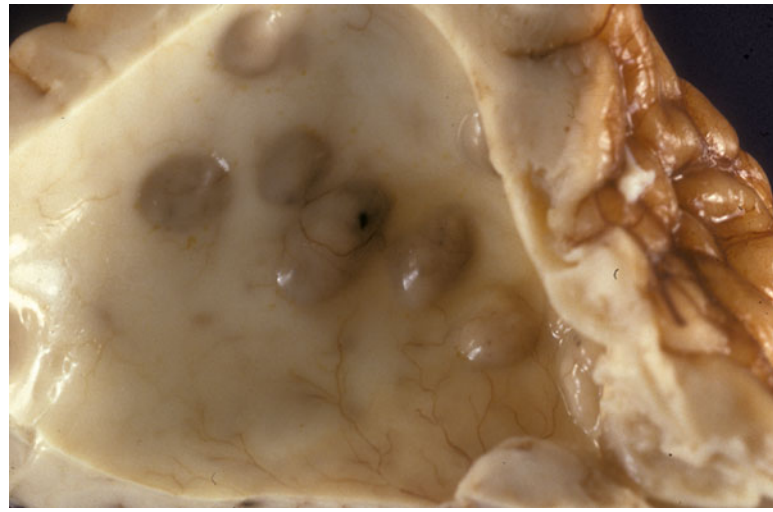

Fig. 8.23 Dilated ventricle containing multiple subependymal heterotopias

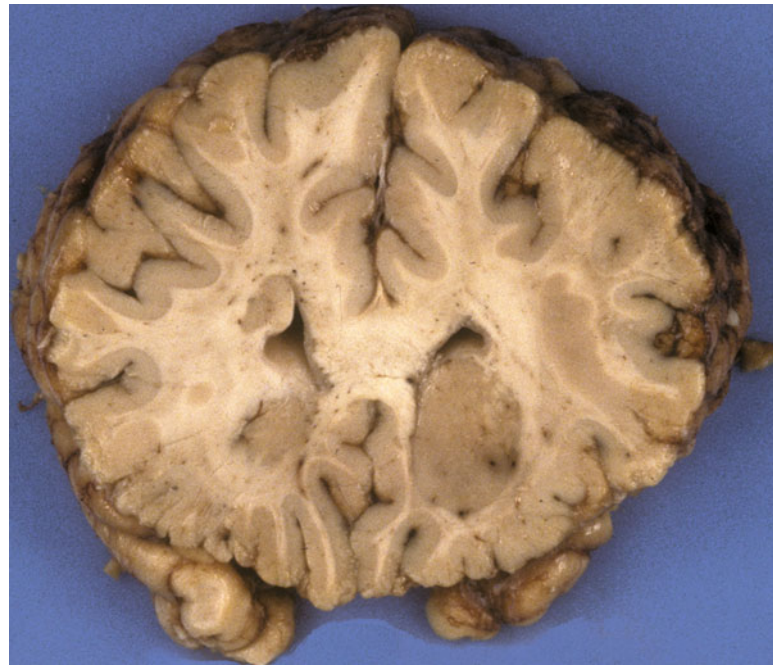

Fig. 8.24 Coronal section of cerebrum at level of corpus striatum. Note dysplasia of striatal nuclei on left and periventricular heterotopia on same side

foramen magnum or, if rostral, by the rigid leaves of the tentorium (Fig. 8.26).

The majority of brain stem defects are also secondary to inadequate space in the posterior fossa. The brain stem is elongated hence has a smaller transverse diameter than normal. A beak-shaped deformity of the quadrigeminal plate is often present (Fig. 8.27). The displaced brain stem structures carry with them the aqueduct, fourth ventricle, and outlet foramina of the fourth ventricle, namely, the foramina of Luschka and Magendie.

Displacement of brain stem into cervical spinal canal also leads to elongation and rostral orientation of cranial and cervical spinal nerve roots (Fig. 8.25b).

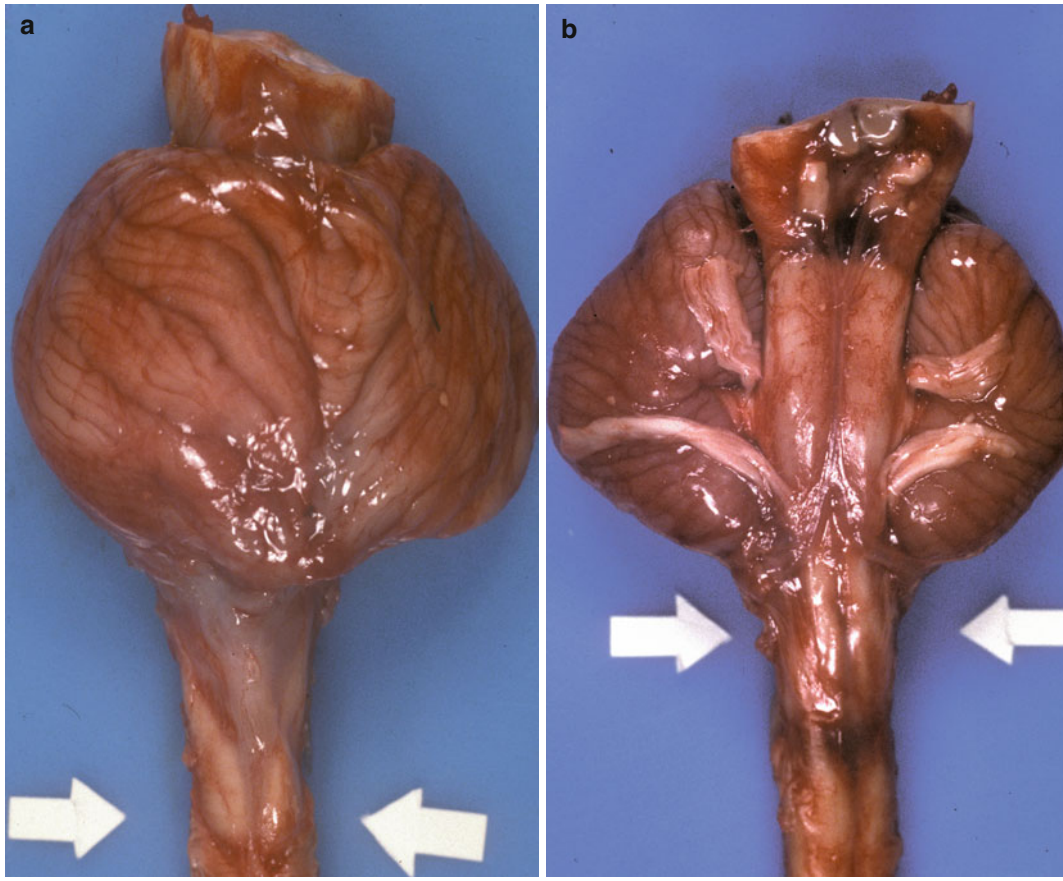

Fig. 8.25 (**a**) Dorsal view of cerebellum and spinal cord of infant with Chiari II malformation. Note tongue of vermis that obscures several levels of cervical cord (*arrows*). (**b**) Ventral view of same specimen displaying elongated, compressed brain stem which exhibits a redundant fold over the ventral aspect of the cervical cord (*arrows*). Note cephalad orientation of nerve roots

Microscopic abnormalities are found at all levels. Aside from those in spinal cord associated with the meningomyelocele, there may be hydromyelia and/or syringomyelia at levels rostral to the sac and its anomalous contents.

Brain stem lesions include syringobulbia, hypo/aplasia of olivary nuclei, hypoplasia of cranial nerve nuclei, and hypoplasia of tegmental or basal pontine nuclei [23]. Microscopic dysplasias are commonly found in cerebella of individuals of any age but are most abundant in infants [24] and have also been identified in these cases, but they have no established clinical significance.

On the other hand, remarkable are relatively common dysplasias of cerebral cortex with or without subependymal or white matter heterotopias [23]. These fall into the general category of migration disorders about which there is a wealth of information relating these to a variety of gene defects [25].

In view of the common association of hydrocephalus with Chiari II, it is of importance to examine the morphological foundation for this phenomenon. One obvious explanation is obstruction of the fourth ventricular outlet foramina consequent to the corking effects caused by herniation of brain stem and cerebellum into the upper cervical canal.

However, flow of cerebrospinal fluid may be impeded rostral to these foramina. For example, crowding of posterior fossa structures may be sufficiently severe to produce stenosis of the fourth ventricle.

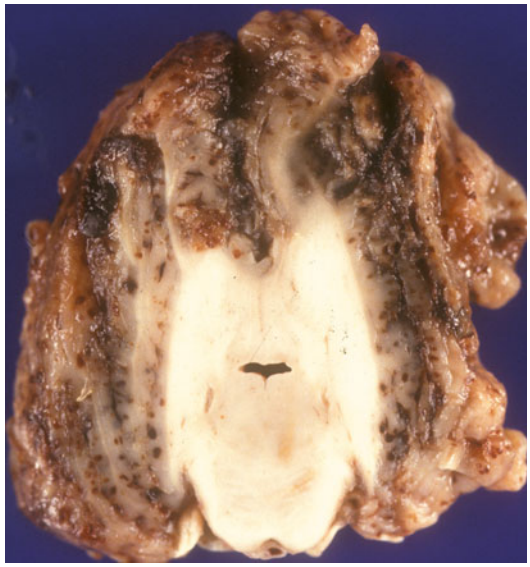

Fig. 8.26 Transverse section through midpons and cerebellum showing compression of pons and fourth ventricle, and hemorrhagic necrosis of cerebellum consequent to compromise of vascular flow

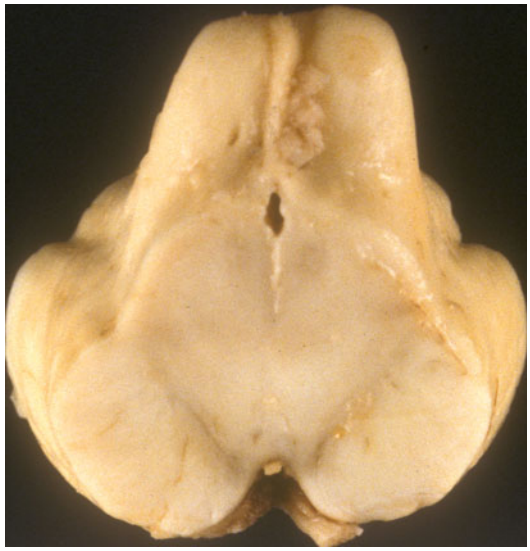

Fig. 8.27 Beaking of collicular plate of infant with Chiari II defect

The most common problematic region, however, is the aqueduct of Sylvius in the midbrain. Major contributions to elucidation of the pathoanatomy have been made by Russell [26] and Alvord [27], in particular, and much of this discussion is based upon their studies.

The aqueduct is not a straight tube but is slightly curved along its path from the posterior third ventricle to the iter at the level of the rostral pons. Its length and transverse diameter naturally change from infancy to adulthood. Suffice it to say that even a small deviation from normal may produce impedance to flow. Aqueductal abnormalities associated with inadequate flow have been separated into hypoplasia, forking, and stenosis.

Stenosis is basically an acquired condition consequent to inflammation.

The other two, namely, hypoplasia and forking, however, are commonly found in this condition and regarded as malformations, although Williams has suggested that they are produced by compression of enlarged ventricles [28]. Hypoplasia refers to a mean diameter below the lower limit of normal range. In practice, it is a qualitative judgment on the part of a radiologist evaluating this region by MRI or a pathologist who examines the midbrain tissue postmortem (Fig. 8.28a, b).

The forking defect consists of two or more ependymal canals in the midline (of the midbrain) separated by normal neural tissue. The dorsal channel tends to be larger and may be branched whereas the ventral channel is simply a slit-like opening. One or the other of these channels communicates with the ventricle, whereas the others have blind pouches (Fig. 8.29).

Rarely, obstruction of CSF flow is caused by atresia of the foramina of Monro (Fig. 8.30) or hypoplasia of the third ventricle (Fig. 8.31). In these defects, the thalami are fused and ventricular dilatation is confined to the lateral ventricles.

Reflections on the Basic Nature of Chiari I and II

This brief review of the pathological features of Chiari I and II forces the conclusion that the cerebellar component of each is, in most cases, not a primary malformation of this part of the brain but is secondary to a malformation of bones forming the posterior fossa.

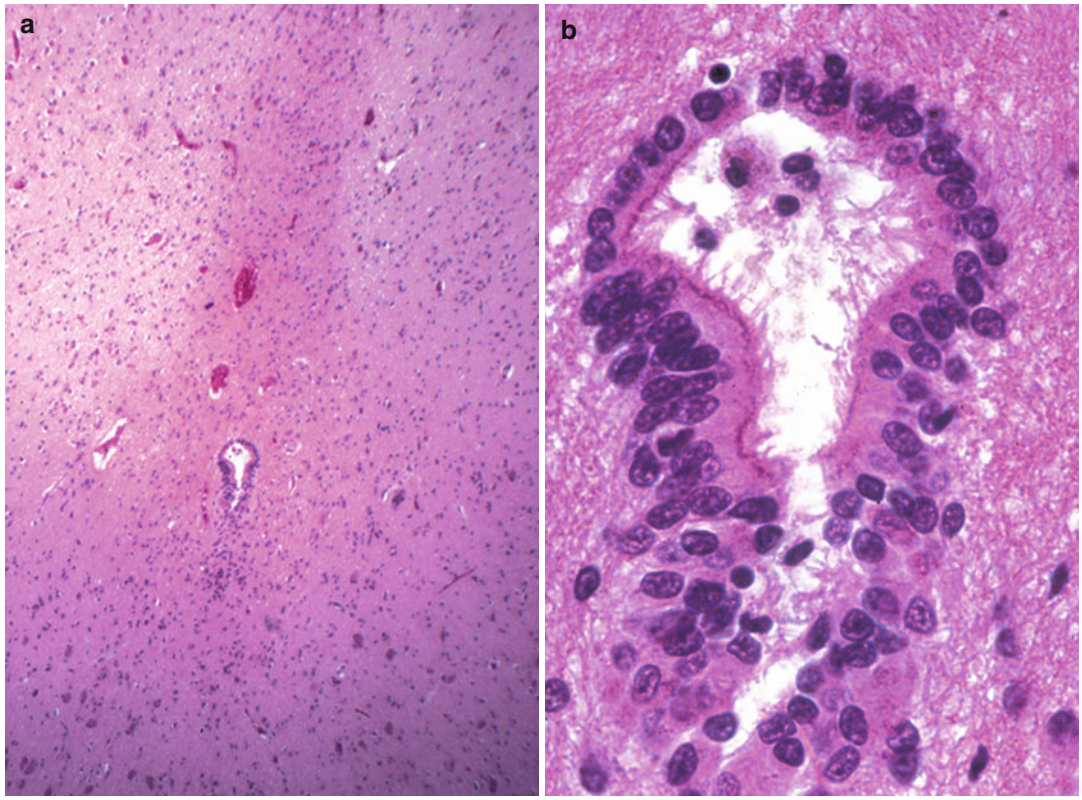

Fig. 8.28 (**a**) Transverse section of midbrain through level of aqueduct. Note isolated tiny channel in center of field. H&E ×40. (**b**) High magnification of hypoplastic aqueduct shown in Fig. 8.28a. Note normally formed structure with tiny lumen. H&E ×400

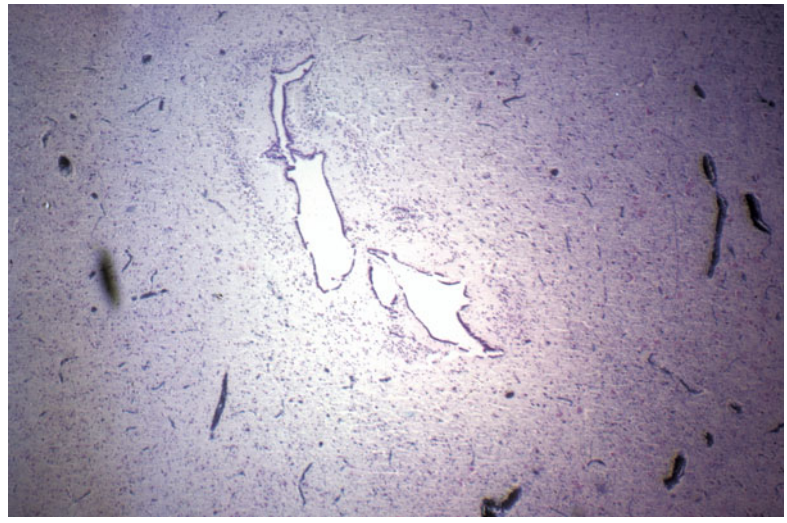

Fig. 8.29 Transverse section through midbrain showing forking defect. Note two separate channels separated by normal neural tissue. H&E ×250

With the exception of cases in which there is cerebellar hypoplasia or rhombencephalosynapsis, frankly dysplastic cerebellar tonsils, or Lhermitte-Duclos malformation, the herniation and associated foliar sclerosis are clearly a consequence of inadequate space and other abnormalities of the posterior fossa. Specifically, the malformation in Chiari I in most cases is not a primary cerebellar defect but a consequence of the bone abnormalities of the posterior fossa.

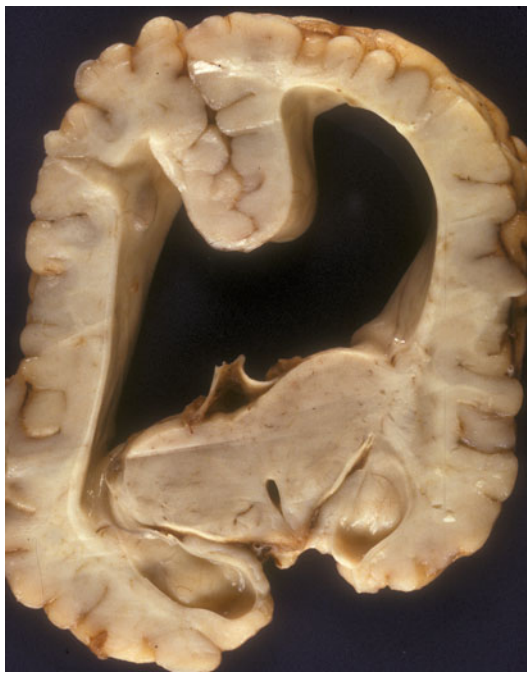

Fig. 8.30 Coronal section through cerebrum of infant with Chiari II defect in which foramina of Monro are absent, the third ventricle is hypoplastic, thalami are almost totally fused, and lateral ventricles are massively enlarged

The constellation of abnormalities at all levels of the neuraxis associated with Chiari II present a more complex problem. Critical consideration of the diverse lesions allows separation into those which qualify as primary developmental defects and a second group of lesions that arise consequent to those malformations.

Primary malformations include the following: (1) skull defects of both membranous and endochondral bones, (2) spinal dysraphism involving bone and other mesenchymal and neural tissues, (3) brain stem neuronal aplasia/hypoplasia, (4) agenesis of corpus callosum, and (5) cerebral migration disorders. Whether aqueductal/third ventricular hypoplasia/atresia is developmental or acquired abnormalities is unclear.

Acquired abnormalities include the following: (1) rostral and caudal herniation of brain stem and cerebellum, (2) syringobulbia/myelia, (3) cerebellar sclerosis, (4) infarction of cerebellum and/or brain stem, and (5) hydrocephalus.

Under the circumstances, it seems that the essential basis for Chiari I consists of abnormalities of skull not cerebellar development. Many of the cerebellar defects associated with Chiari II are also consequent to hypoplasia of the posterior

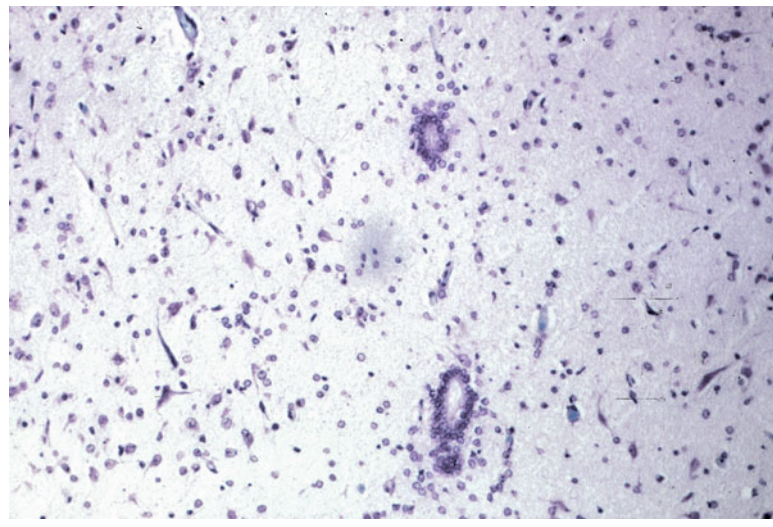

Fig. 8.31 Two small ependymal canals are the only evidence of the third ventricle in infant with Chiari II defect

fossa, but this is a considerably more complex developmental disorder that affects all levels of the neuraxis. Thus, to focus strictly on the cerebellar component is misleading.

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Pathology of Syringomyelia Due to Chiari Malformations

9

Daniel Keith Harrison

Abstract

Since the early nineteenth century, some authors have used the term syringomyelia to describe any tubular cavity within the spinal cord. More recently, classification systems have evolved to describe syringomyelia subtypes as well as distinguish other entities such as hydromyelia, syringobulbia, and myelomalacia. Our current understanding of the etiology of syringomyelia, although more advanced, is still incomplete. Syringomyelia occurs in many different clinical settings with variable clinical symptomatology and different cavitary patterns. Anatomic and pathologic criteria are helpful in establishing basic classification of syringes as well as understanding syringomyelia in the setting of Chiari malformation. The pathophysiological hypotheses for syringomyelia are numerous, controversial, and variable according to the proximate cause. The gross pathology and histology are similar irrespective of cause, and competing theories continue to evolve on the pathogenesis of syrinx formation.

Introduction

In classical mythology, Syrinx was a virtuous water nymph. To escape the importunities of Pan, god of the wild, she sought help from her sisters, the river nymphs, who changed her into a hollow reed. Unrequited and still infatuated, Pan fashioned a flute bearing her name from the river reeds. Since the early nineteenth century, some authors have used the term syringomyelia to describe any tubular cavity within the spinal cord. More recently, classification systems have evolved to describe syringomyelia subtypes as well as distinguish other entities such as hydromyelia, syringobulbia, and myelomalacia. Our current understanding of the etiology of syringomyelia, although more advanced, is still incomplete. Syringomyelia occurs in many different clinical settings with variable clinical symptomatology and different cavitary patterns. The gross pathology and histology are similar irrespective of cause, and competing theories continue to evolve on the pathogenesis of syrinx formation.

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Syringomyelia is characterized by tubular cavitation of the spinal cord that may extend over many segments. The cavity is typically filled with clear fluid [12] that closely resembles cerebrospinal fluid (CSF) or extracellular fluid (ECF) [5]. Occasionally, depending on the cause of the syrinx, the fluid may be yellow with high protein content [30]. It may be lined by ependymal cells or gliotic tissue and may expand over time. The cervical region is most frequently involved although the first cervical segment is often spared and cavitation may extend cranially or caudally. Syringes may demonstrate simple cystic or complex multiloculated morphology with strict, variable, or no involvement by the central canal. Hydromyelia is defined as dilatation by fluid of the central canal of the spinal cord. It is frequently seen in association with some forms of syrinx and can be indistinguishable, even at autopsy, from syringomyelia [14]. To accommodate this reality, some authors use the term "syringohydromyelia" or "hydrosyringomyelia," although the distinction may have etiological implications. Syringobulbia is rare but strongly associated with syringomyelia [17] and connotes fluid-filled or slit-like cavities in the brainstem, most commonly the medulla [20]. Cavitary extension can rarely involve the pons and in exceptional cases reach the midbrain and supratentorial compartment [14].

Classification

Anatomic and pathologic criteria are helpful in establishing basic classification of syringes as well as understanding syringomyelia in the setting of Chiari malformation. Syringomyelia is most frequently associated with a lesion that obstructs CSF flow at the level of the foramen magnum, usually a Chiari malformation. Specifically, Chiari type I malformation is most commonly associated with syringomyelia [8, 12, 21, 27]. Lesions at the foramen magnum invariably produce a cervical syrinx that progresses caudally. Syringomyelia is also seen in patients with Chiari type 0 (syringomyelia development in the absence of cerebellar tonsillar displacement) [4, 31] and Chiari type II malformations. Classification systems vary but most divide syringomyelia into two broad categories, communicating and noncommunicating. Communicating (hydromyelic) syringomyelia is often associated with Chiari type II malformations and is an ependyma-lined expansion of the central canal that is contiguous with the fourth ventricle [23, 24, 26]. Other complex hindbrain malformations such as encephalocele, Dandy-Walker variants, hydrocephalus secondary to hemorrhage or meningitis, or other conditions that increase intracranial pressure can fall within this category. Acquired forms are typically bound caudally by central canal stenosis, a normal age-related phenomenon in humans [23]. Noncommunicating (syringomyelic) syringomyelia is more common and characterized by complex cavitation that does not communicate rostrally with the fourth ventricle. These syringes may involve both the ependyma-lined central canal and paracentral spinal cord parenchyma where the syrinx demonstrates a gliotic lining. Chiari malformations (type I and type 0) are commonly characterized by syringes of this type. Other etiologies in this category could include syrinx secondary to spinal arachnoiditis (postmeningitic or posttraumatic), subarachnoid hemorrhage, extramedullary compressions (cyst, tumor, or spondylosis), and other skeletal abnormalities such as basilar impression. Noncommunicating syringomyelia can also include primary parenchymal cavitations such as trauma, intramedullary hemorrhage, or infarction. In these cases syringomyelia occurs in proximity to the lesion. Spinal cord tethering may also produce caudal noncommunicating syringomyelia. Neoplastic cavitations or cysts and atrophic cavitations secondary to myelomalacia are two other categories that could be considered in the differential diagnosis of syrinx.

Neuropathology

The gross neuropathology and histology of syringomyelia are universal irrespective of the pathogenetic mechanism. Exposure of the spinal cord during surgery or at autopsy demonstrates an expanded taut cord in the region of syrinx, usually

the cervical region, almost filling the spinal canal in some cases. The leptomeninges and the surface of the spinal cord are usually unremarkable. Grossly, the distinction between syringomyelic and hydromyelic cavitation is not reliably possible, although whole mount transverse sections reveal cavitation patterns more clearly. Pure hydromyelic syringomyelia is less common than the syringomyelic form, which may demonstrate involvement of the central canal and paracentral spinal cord parenchyma. In this more common and more complex cavitation pattern, a large syrinx may destroy most of the gray matter structures, also markedly compressing lateral and posterior white columns. Syrinx fluid is most often clear and colorless and when drained at autopsy often collapses the spinal cord in the ventral-dorsal plane [14]. This is likely due to the typical transverse orientation of the syringomyelic cavity that can extend across the dorsal gray commissure and involve bilateral anterior and posterior horns. The walls of syringes vary in thickness and composition depending on multiple factors including etiology, chronicity, and tension within the cavity. Histologically, communicating syringomyelia is represented by simple dilatation of the central canal that may be completely or partially lined by stretched or denuded ependyma. Requisite rostral communication with the fourth ventricle is present, and in acquired lesions, the syrinx may be limited caudally by central canal stenosis. In congenital lesions, holocord syrinx may be seen, and in the setting of Chiari II malformations, the syrinx cavity may communicate caudally with myelomeningocele [24, 26]. Paracentral rupture is much less common in hydromyelic cavitations even when the syrinx is large, a quality that has symptomatic implications. Noncommunicating syringomyelia demonstrates variable histology complicit with its typical complex architecture. These are isolated and anastomosing cavitations that frequently demonstrate intracanalicular septae and erosion of lining ependyma in areas of central canal involvement. Paracentral dissection into the substance of the spinal cord is common and favors the dorsolateral quadrant [24, 26]. Dissections into the cord in general produce clinical symptoms based on the anatomical structures affected. Communication with the subarachnoid space is often recognized and occurs preferentially at dorsal root entry zones [16, 23, 24]. The lining of the syrinx in these cases is variable even within the same patient and can show ependyma or reactive astrogliosis with some collagen deposition. Evidence of chronic edema secondary to tissue damage is common with rarefaction of neuropil, gliosis, and loss of myelin around the syrinx [14]. This histologic appearance suggests chronic mechanical stress with transudation of serous fluid into the parenchyma. Degenerative changes are also recognized and include pyknotic nuclei and Rosenthal fibers associated with the syrinx [1, 22]. Dilated hyalinized blood vessels are also commonly seen in and around the wall of the syrinx with primarily adventitial thickening [7, 28].

Pathogenesis

The pathophysiological hypotheses for syringomyelia are numerous, controversial, and variable according to the proximate cause. In the case of communicating syringomyelia (hydromyelia), resistance to the normal flow of CSF is thought to drive both hydrocephalus and hydromyelia by causing a greater CSF pressure in the ventricle than the subarachnoid space [6, 9, 19, 20, 32]. In the setting of Chiari malformation, most modern theories on noncommunicating syringomyelia focus on disruption of cerebrospinal fluid flow at the craniocervical junction. Investigators differ on exactly how this flow disruption causes syrinx formation. Gardner and Angel [9–11], Williams [36], and Oldfield et al. [28] all proposed different hydrodynamical theories suggesting basic pressure disassociations between the intracranial subarachnoid space, the spinal subarachnoid space, and the central canal or various combinations thereof. These theories all postulate CSF as the source of syrinx fluid and differ as to the driving mechanism of the fluid into the syrinx and whether CSF is driven from the fourth ventricle or spinal subarachnoid space. More specifically, Gardner [12] was the first to recognize syringomyelia in the setting of Chiari I malformations and

proposed a hydrodynamic theory whereby an embryologic delay in perforation of the roof of the rhombencephalon led to inadequate development of the foramina of Magendie and Luschka. The functional closure of these outlets produced a "water-hammer" pulse effect driven by CSF production through the obex into the central canal of the spinal cord [12]. This theory required at least intermittent hydrocephalus whether it occurred prenatally or postnatally. Williams [32–35] championed a CSF pressure disassociation theory that focused more on the relative obstruction of the subarachnoid space at the foramen magnum and pointed out that relatively few patients with Chiari I malformation and syringomyelia had hydrocephalus. The obstruction of CSF flow at the foramen magnum caused an increase in intracranial CSF pressure relative to spinal CSF pressure by impeding CSF flow caudally but not rostrally. This valve effect, exacerbated by activities that increased intrathoracic pressure such as coughing or Valsalva maneuver, could cause sustained elevations in intracranial CSF pressure by filling spinal epidural veins and increasing CSF flow into the cranial compartment. This pressure differential could effectively "suck" CSF from the fourth ventricle into the central canal via the obex [35]. Another series of investigators led by Oldfield et al. [28] suggested spinal subarachnoid CSF as the source of syrinx fluid noting neuropathologic evidence that syrinx communication with the fourth ventricle only occurs in hydromyelic syringomyelia and that the more common syringomyelic form demonstrates no syrinx communication with the fourth ventricle. Oldfield et al. [28], Heiss et al. [14], and Levy et al. [20] all postulated that brain expansion during cardiac systole created a "piston effect" whereby the cerebellar tonsils were thrust into the subarachnoid space of the foramen magnum. Pressure waves created by this mechanism forced CSF into the substance of the spinal cord via perivascular spaces. Other studies have shown pressure recordings within syringes that are higher than the adjacent subarachnoid space and question the ability of these pressure waves to push fluid from the subarachnoid space into the cord [6, 25].

More recently, theories have emerged that incorporate pressure disassociation and hydrodynamic hypotheses but suggest spinal cord edema and extracellular fluid as the source of syrinx fluid brought about by disturbances in the microcirculation of the cord [13, 17, 18, 20]. One theory suggests mechanical stress on the spinal cord due to pressure differences bordering a subarachnoid space obstruction [2, 3, 13, 20]. In the case of Chiari I malformation, the pressure differential between the cranial and spinal subarachnoid spaces at the foramen magnum corresponds to transmural venous pressure changes that collapse vessels above the obstruction and dilate vessels below it. Pressure differences can occur due to variations in pressure during the cardiac cycle, changes in patient position (recumbent to erect or certain neck movements), or increases in intrathoracic pressure (cough, Valsalva) with pressures always greater caudal to the block. Repeated mechanical stress produced by the change in vessel caliber across the obstruction causes disruption of the blood-spinal cord barrier and tissue destruction affecting the microcirculation of spinal cord. Tissue destruction is characterized by neuropil and myelin disruption with shearing of axonal and cell membranes. Chronic gliosis results from repeated tissue injury, and increased transmural venous pressure leads to dilatation and thickening of spinal cord venules. In this way, extracellular fluid escapes, and an ultrafiltrate of plasma accumulates within the open segments of the central canal or spinal cord parenchyma. Mechanical stress seems to be concentrated at the caudal end of the obstruction where hydrostatic pressure is greatest and preferentially affects anatomically vulnerable areas of the spinal cord where elastic properties of the tissue are weakest (central canal, dorsal and ventral gray commissures, gray matter, and gray-white junction).

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Associated Disorders of Chiari Type I Malformations

10

R. Shane Tubbs and W. Jerry Oakes

Abstract

There exists a plethora of diseases affiliated with CIM and certainly more to be discovered in the future. While the final outcome of CIM may be the same, the strength of the correlation and pathophysiological mechanisms of each differs greatly, and some may be spurious associations. Thus, the need for additional genetic research and investigation of CIM continues. This chapter will discuss the conditions associated with CIM in order to potentially shed light on how the pathophysiological mechanism of one condition, no matter how remote, might lead to the development of CIM. It should be noted that many of these associations may be incidental with an asymptomatic hindbrain hernia being identified due to testing for other pathologic entities, for example, endocrinopathies.

Introduction

Chiari postulated that the cerebellar herniation might have been due to hydrocephalus with the three different types representing various degrees of disease progression [1]. In ensuing years, Chiari's mechanism of pathogenesis would be disproven as the primary cause of CIM. Among the classifications, however, no current consensus exists for the exact pathogenesis or treatment regime for all [2]. Many have formed theories such as the hindbrain dysgenesis and developmental arrest theory, caudal traction theory, small posterior fossa/hindbrain overgrowth theory, hydrocephalus and hydrodynamic theory of Gardner, and the lack of embryological ventricular distention theory, yet no single theory has been able to prove a single pathway in the pathogenesis of CIM [3–15]. This chapter will discuss the conditions associated with CIM in order to potentially shed light on how the pathophysiological mechanism of one condition, no matter how remote, might lead to the development of CIM. Many of these associations are summarized in Table 10.1. It should be noted that many of these associations may be incidental with an asymptomatic hindbrain hernia being identified due to testing for other pathologic entities, for example, endocrinopathies.

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Table 10.1 Disorders associated with Chiari type I malformations

Craniosynostosis
Antley-Bixler syndrome
Apert's syndrome
Crouzon's syndrome
Jackson-Weiss syndrome
Kleeblattschädel syndrome
Loeys-Dietz syndrome type I
Seckel syndrome
Shprintzen-Goldberg syndrome
Endocrinology
Achondroplasia
Acromegaly
Growth hormone deficiency
Hyperostosis
Craniometaphyseal dysplasia
Erythroid hyperplasia
Osteopetrosis
Paget's disease
Bone mineral deficiency
Familial vitamin D-resistant rickets
Cutaneous disorders
Acanthosis nigricans
Blue rubber bleb nevus syndrome
Giant congenital melanocytic nevi
LEOPARD syndrome
Macrocephaly-cutis marmorata telangiectatica congenita
Neurofibromatosis type I
Phacomatosis pigmentovascularis type II
Waardenburg syndrome
Spinal defects
Atlantoaxial assimilation
Basilar impression
Caudal regression syndrome
Klippel-Feil syndrome
Lipomeningomyelocele
Odontoid retroflexion
Spondyloepiphyseal dysplasia
Space-occupying lesions
Other
Beckwith-Wiedemann syndrome
CHERI
Cloacal exstrophy
Costello syndrome
Cystic fibrosis
Ehlers-Danlos syndrome
Fabry disease
Kabuki syndrome
Pierre Robin syndrome
Situs inversus
Williams-Beuren syndrome

Pathophysiology

Small Posterior Cranial Fossa

Morphometric studies by authors such as Schady et al. [16] and Milhorat et al. [8] have provided evidence that the volume of the posterior cranial fossa in CIM patients was less than controls. Furthermore, Badie et al. [3] discovered the ratio of posterior fossa volume to supratentorial space ratio was significantly lower in symptomatic CIM patients compared to control patients. Marin-Padilla and Marin-Padilla [17] added to the understanding of this anatomical pathology by inducing underdevelopment of the basi-occiput and posterior fossa in hamsters through high doses of vitamin A. In doing so, these authors demonstrated how impairing posterior fossa development could induce caudal displacement of the cerebellum. Others, however, have challenged this proposition with studies showing no difference in posterior fossa volume in this group [18]. Additional morphological findings in CIM may include an underdeveloped supraocciput and exocciput, large foramen magnum, short clivus, and longer anterior cranial fossa [19–22]. Therefore, while it may be a common school of thought, a smaller posterior fossa does not necessarily lead to CIM.

Hydrocephalus

Hans Chiari's aforementioned original theory regarding the causative association between hydrocephalus and hindbrain herniation has not allowed for an all-encompassing explanation into the pathophysiology of CIM [79]. Nonetheless, hydrocephalus is seen in approximately 4–18 % of CIM patients [3, 14]. Tubbs et al. in a review of 500 patients treated between 1989 and 2010 demonstrated that 9.8 % of patients had concomitant hydrocephalus [23]. These patients all required CSF diversion in addition to an operative posterior fossa decompression. The association is likely secondary to fourth ventricular outflow tract obstruction or concurrent aqueductal stenosis. As a result, endoscopic third ventriculostomy has been used with success in this patient population.

Craniosynostosis

Craniosynostosis and CIM are a well-documented association first noted by Saldino et al. [24] in which certain cases will have abnormalities in the skull base with subsequent decreased posterior fossa volume and tonsillar herniation. More specifically, this most often occurs when the lambdoid sutures fuse too early in skull development, which is representative of 1 % of all types of craniosynostosis [25]. Synostosis can exist solitarily or as part of a syndrome such as Crouzon's (72.7 %), Apert's (1.9 %), Pfeiffer's (50 %), and Kleeblattschädel syndromes (100 %) [26, 27]. Additional studies estimated the Crouzon's syndrome association to be as high as 70 % [28]. Moreover, CIM is now thought to be associated with Pfeiffer type II [29], Jackson-Weiss [30], Seckel [31], Antley-Bixler [32], and Shprintzen-Goldberg syndromes [33] as well. In each of these associated syndromes, CIM is not present at birth because the lambdoid suture has not yet fused. The incidence and severity, however, has been correlated to the time of closure [34, 35]. Therefore, the higher incidence of CIM in Crouzon's syndrome patients can be explained by the median fusion time of 6 and 21 months as compared to that of Apert's syndrome at 51 and 60 months of age [26]. Normally, the skull continues to expand along with brain growth until the age of 16 years [36].

Although lambdoid synostosis is the most common type of craniosynostosis to be associated with CIM, evidence of additional premature suture closures leading to CIM is growing. In utero synostosis of the sagittal and coronal sutures, for example, can force neural growth posteriorly and inferiorly as is present in the association with Loeys-Dietz syndrome [37]. As a result, the attachment of the tentorium cerebelli is displaced towards the foramen magnum with subsequent reduction in posterior fossa size and development of CIM [27]. Additionally, Tubbs et al. [38] reported a 30 % incidence of CIM associated with simple metopic ridging without signs of trigonocephaly. Tubbs et al. [38] hypothesized this was the result of a decrease in anterior cranial fossa volume and that the incidence of metopic ridging in this population may be overestimated.

Endocrinopathy

Reduced posterior fossa volume is also seen in other medical conditions, including those involved in cell signaling. For example, growth hormone deficiency (GHD) has been linked to CIM with 5–20 % of GHD patients [39, 40]. This endocrine deficiency in children is thought to be a physiological mechanism for insufficient development of the posterior fossa with resultant tonsillar herniation [41]. While the posterior fossa volume of GHD patients has not been found to be significantly smaller, research has shown certain bony structures to be underdeveloped similar to those commonly seen in CIM patients [41]. Additionally, somatotropin replacement therapy in patients with GHD and CIM has resulted in improvement of tonsillar herniation with stabilization in syrinx size in some patients [22]. Conclusive evidence, however, of the pathophysiological mechanism and possible treatments is yet to be determined.

Acromegaly has also been implicated as an endocrine-related disorder causing CIM that also fits in the category of hyperostosis. In this scenario, an excessive amount of growth hormone is thought to thicken the bones of the posterior fossa resulting in CIM. CIM has also been seen in patients with achondroplasia because of the small, shallow posterior cranial fossa present in these patients [42].

Hyperostosis

When hyperostosis affects the posterior fossa, it can lead to CIM. Paget's disease of the skull is one example in which exaggerated bone turnover leads to thickening and deformation of bones. When this process takes place in the skull, it can compromise the posterior fossa and, in a few cases, has been reported to result in CIM. Both Iglesias-Osma et al. [43] and Richards et al. [44] have described cases of this association.

Cases of CIM relating to craniometaphyseal dysplasia is rare but has nonetheless been reported. Craniometaphyseal dysplasia, similar to the other types of hyperostosis, can manifest with CIM due to abnormal bone formation and progressive thickening. Of the few cases, Sewell

et al. [45] documented cervicomedullary compression as well. CIM secondary to osteopetrosis [46] and erythroid hyperplasia [47] have been documented but are also considered to be exceptionally rare.

Bone Mineral Deficiency

In regard to bone mineral deficiencies, familial vitamin D-resistant rickets has also been coupled with CIM at 44 % [48] thought to be due to overcrowding of the posterior fossa. In this condition, bony overgrowths and calvarial thickening as a result of low serum phosphate have been proposed to be the attributing factor. Further studies, however, have not found a difference in rachitic patients' posterior fossa volume, and thus, the pathophysiological mechanism remains unknown [49]. Kuether and Piatt [50] suggested in a case study that CIM development from rickets is due to foramen magnum stenosis. Renier et al. [51], interestingly, discovered that among 129 patients with oxycephaly, 15 % suffered from rickets.

Cutaneous Disorders

Although it may not be considered a traditional association, cutaneous disorders are frequently reported to occur in conjunction with CIM [61]. One such disorder is neurofibromatosis type I, in which a relationship as high as 8 % has been reported [52]. Some investigators have hypothesized that mesodermal deficiency arrests posterior cranial fossa development, which is also proposed to occur in cutaneous disorders such as neurofibromatosis type I [8].

Equally mysterious is CIMs association with macrocephaly-cutis marmorata telangiectatica congenita (M-CMTC) [53]. M-CMTC is characterized by benign spider nevus-like telangiectasias and superficial ulcerations, but little is known about the pathology. Hence, no mechanism has been suggested for the association.

Several other cutaneous disorders have been advocated as being involved in CIM, including LEOPARD syndrome [54], blue rubber bleb nevus syndrome [55], giant congenital melanocytic nevi [56], phacomatosis pigmentovascularis type II [57], acanthosis nigricans [58], and Waardenburg syndrome variants [59]. These are all based on scarce case reports and thus may have occurred coincidentally with CIM.

Spinal Defects

Not all causes of CIM have been shown to be directly related to the posterior fossa and skull base. A few disorders, such as spondyloepiphyseal dysplasia [60], caudal regression syndrome [80], Klippel-Feil syndrome, atlantoaxial assimilation, basilar impression, and odontoid retroflexion in which the vertebral column is the site of deformation, are also associated with CIM. Little is known about the pathophysiology of these spinal deformities, but it is thought that difficulty in equilibrating the dynamic CSF pulse pressure induced by the Valsalva maneuver is responsible for the CIM presentation.

Lipomeningomyelocele has been shown to be coupled with CIM in as many as 3–6 % of patients [62, 63]. It has been postulated that a decrease in intracranial nervous tissue and CSF due to the lipomeningomyelocele removes the expansile pressure of the brain on the skull, thus causing the posterior fossa to be smaller and less developed [64].

Space-Occupying Lesions

To this point, all mentioned associated disorders have been congenital, but acquired methods of CIM manifestation also exist. This category includes both space-occupying lesions and cerebrospinal fluid leaks. Space-occupying lesions within the posterior cranial fossa can be caused by a variety of disorders ranging from brain tumors to hematomas. These can include supratentorial [65] and infratentorial [66] lesions. The multitude of potential space-occupying lesions is vast and will not be discussed further.

Not Otherwise Specified

A case of Beckwith-Wiedemann syndrome in association with CIM has been reported. Tubbs et al. [61] hypothesized the pathological mechanism responsible for the CIM to be hemihypertrophy involvement of the skull. Costello syndrome has also been recognized as presenting with concomitant CIM, although it too is described as having a low-frequency association [66]. Hemihypertrophy [67] and GHD [68] have been reported in both Costello syndrome patients and CIM and thus may be the common factor. Furthermore, an association with Marfan syndrome is commonly recognized due to intracranial hypotension [69]. Additionally, associations with Williams-Beuren syndrome have been found with morphometric analyses suggesting a diminished posterior fossa leading to CIM [70, 71]. Finally, associations with disorders such as cystic fibrosis [72], Pierre Robin syndrome [73, 80], Ehlers-Danlos syndrome [74], Fabry disease [75], Kabuki syndrome [76], situs inversus [77], CHERI [78], and cloacal exstrophy [81] have been made with no clear pathophysiological mechanism yet identified.

Conclusions

There exists a plethora of diseases affiliated with CIM, many of which have been mentioned in this article and certainly more to be discovered in the future. While the final outcome of CIM may be the same, the strength of the correlation and pathophysiological mechanisms of each differs greatly and some may be spurious associations. Thus, the need for additional genetic research and investigation of CIM continues.

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Chiari-Like Malformation in Dogs

11

Dominic J. Marino and Curtis W. Dewey

Abstract

The Chiari I malformation in humans and Chiari-like malformation in dogs (CLM) is a condition in which the cerebellum descends out of the foramen magnum affecting normal cerebral spinal fluid (CSF) flow. It is considered to be a developmental abnormality and is commonly confused with many other conditions. Chiari-like malformation in dogs affected approximately 85 % of Cavalier King Charles Spaniels evaluated, as reported in the most recent studies. The specific cause has not been determined; however, because of an abnormal shape or reduced skull size in the caudal occipital region, part of the cerebellum is forced through the foramen magnum, altering CSF flow patterns. Changes in CSF dynamics result in an abnormal accumulation of fluid within the substance of the spinal cord called a "syrinx." The diagnosis of CLM in dogs and Chiari type I in humans can only be confirmed by MRI which is essential for determining the cause of syringomyelia. Current concepts in the diagnosis and treatment of Chiari-like malformation in dogs will be discussed.

Craniocervical junction abnormalities (CJAs) in small-breed dogs are being increasingly recognized as common and challenging disorders [1–9]. In particular, Chiari-like malformation (CLM), the canine analog of human Chiari type I malformation, has emerged in recent years as the possible cause of major health problems in several small-breed dogs, most notably the Cavalier King Charles Spaniel (CKCS) [5, 6, 8– 11]. The term CJA, as used in human medicine, serves as an "umbrella" term for a variety of malformations that occur in the craniocervical region. The craniocervical junction refers to the occipital bone (primarily the supraoccipital component) that forms the boundaries of the foramen magnum, the atlas (C1), and the axis (C2). In veterinary medicine, the term "Chiari-like malformation" or CLM has been widely

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used to describe constrictive disorders at the cervicomedullary junction that are apparent on MR imaging. Numerous abnormalities of the craniocervical junction in dogs (primarily) and cats (rarely) are presumed to be heritable malformations; all have been associated with the secondary development of syringomyelia (SM) [11, 12]. Syringomyelia refers to the accumulation of fluid within the spinal cord parenchyma [10–20]. Although the features for some of the more newly reported disorders have not been clearly defined, all of the disorders tend to affect young, small-breed dogs. The nomenclature used for these disorders is often confusing and generally assumes that these are all distinctly separate disorders. Included among these diseases is CLM, also termed caudal occipital malformation syndrome or COMS, and occipital hypoplasia [20–22]. Recently, it has been found that many dogs have abnormalities in the craniocervical junction region that do not comply with traditional veterinary nomenclature [23]. These include atlantooccipital overlapping (AOO) and dorsal constriction at the C1–C2 vertebral junction [1–3, 23]. Both of these abnormalities may represent the canine analog of human basilar invagination [24–31]. Finally, it has become apparent that some dogs with suspected "classical" atlantoaxial instability have other concurrent abnormalities at the craniocervical junction. Because the occipital region of the skull and the first two cervical vertebrae develop together embryologically, it makes inherent sense that multiple developmental disorders, as well as combinations of these disorders, should occur in this anatomic region in our patients, as they do in humans [27, 30–32]. For these reasons, we refer to all of these disorders under the general heading of craniocervical junction abnormalities. It has been reported, especially for reasons of surgical planning, that optimal individualized patient descriptions of a craniocervical junction disorder often depend on a combination of MRI and CT scans [23]. Although this section will focus on CLM and SM, it should be emphasized that the morphologic description of a particular patient's craniocervical junction abnormality is far more important than a name for that malformation.

Chiari-like malformation is believed to be the canine analog of Chiari type I malformation in people. Similar to the human disorder, the cranial cavity is too small to accommodate the contents of the caudal fossa (cerebellum and brainstem), resulting in overcrowding of the cerebellomedullary region of the brain (Fig. 11.1) [5, 8, 20]. Increasing evidence suggests that CLM in dogs is a condition in which the entire skull is malformed, although the caudal aspect is the most obvious abnormality on MRI. On MRI, the abnormality of the supraoccipital bone that causes an indentation of the caudal cerebellum is often visible. In addition, an impingement of the dorsal subarachnoid space typically occurs at the level of the cervicomedullary junction. In a recent review of MRI studies of 359 dogs [23] with CLM, 86.9 % had evidence of cerebellar herniation through the foramen magnum (Fig. 11.2). Most of these dogs also have cervical SM evident on MRI (Fig. 11.3) [14, 15, 17]. Multiple mechanisms have been proposed for the formation of SM, all of which are based on the pressure differential between cranial and spinal compartments created by constriction at the cervicomedullary junction [15, 33]. Older, probably incorrect theories assume that fluid that accumulates within the spinal cord is cerebrospinal fluid, while newer theories suggest that the syrinx fluid is actually extracellular fluid [15]. The intramedullary pulse pressure hypothesis theorizes that a pressure wave is transmitted across the foramen magnum during systole that is insufficiently dissipated during diastole and that the fluid that is pushed across the craniocervical junction becomes trapped, resulting in SM. Along with the "intramedullary pulse pressure" theory, a phenomenon called the Venturi effect has been proposed to be involved in syrinx formation. The Venturi effect is based on the phenomenon of a jet of cerebrospinal fluid flowing from higher to lower velocity. Low pressure outside the spinal cord (cerebrospinal fluid) combines with high pressure inside the spinal cord, leading to the spinal cord substance being pulled in an outward direction, facilitating the accumulation of fluid in the syrinx cavity. The Venturi effect has been theorized to be responsible for the formation of syringomyelia in veterinary patients in at least

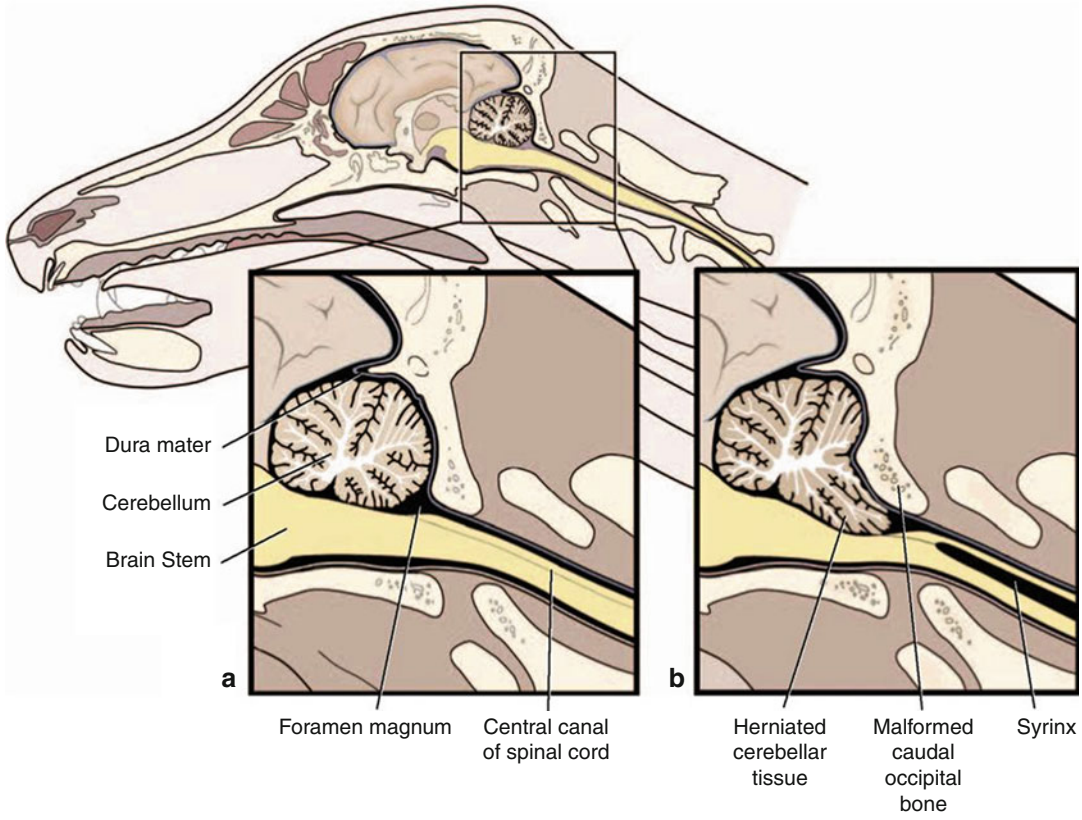


Fig. 11.1 Schematic illustration depicting normal (**a**) versus abnormal (**b**) configurations of the canine occipital/brainstem region (From Dewey et al. [20])

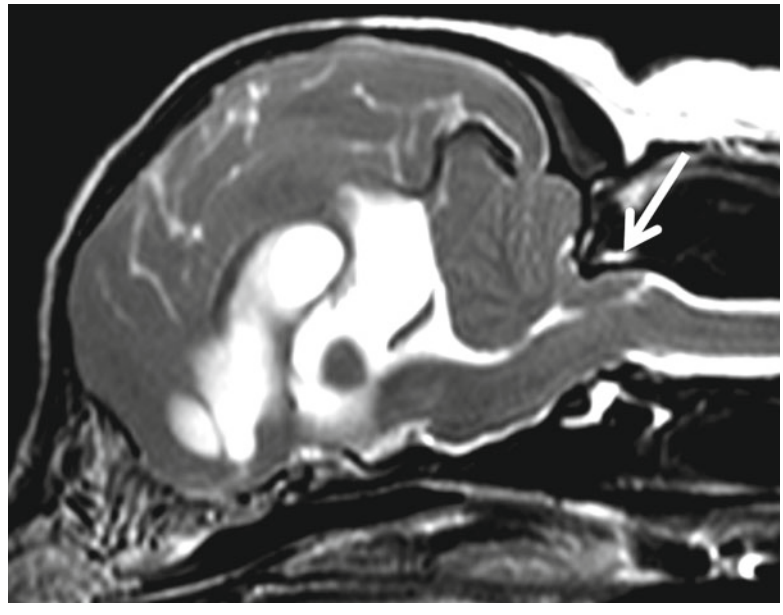


Fig. 11.2 Sagittal T2-weighted magnetic resonance image of a dog with Chiari-like malformation and cerebellar herniation through the foramen magnum (*arrow*). MRI herniation and compression

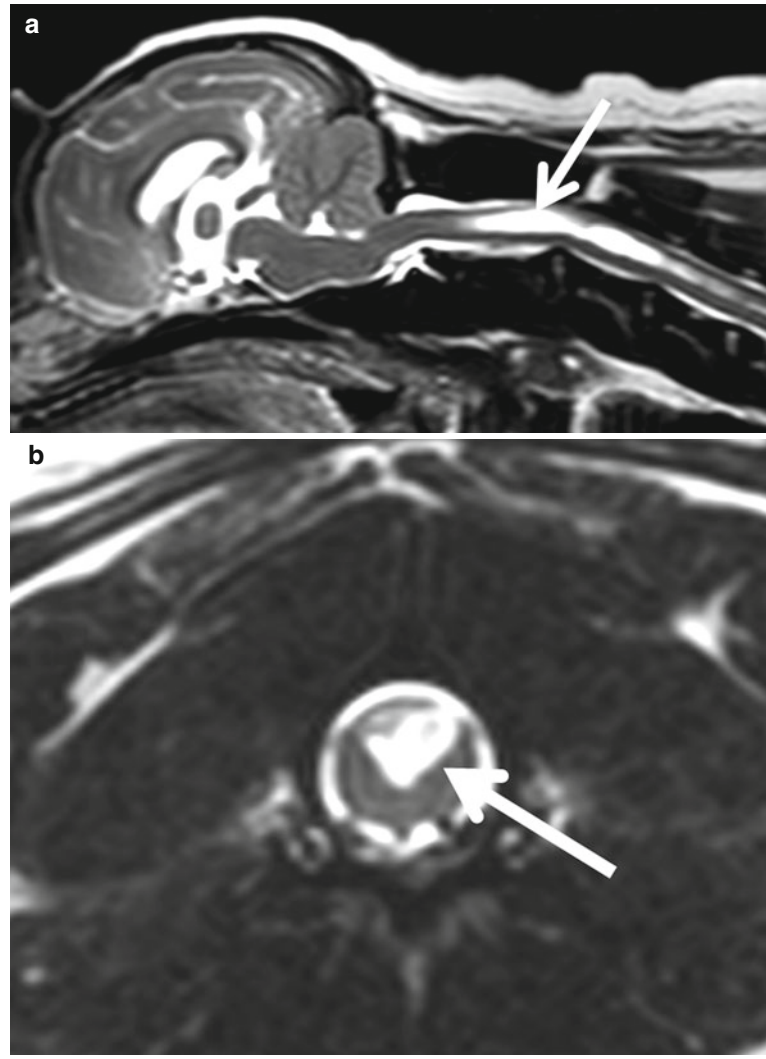


Fig. 11.3 Sagittal (**a**) and axial (**b**) T2-weighted magnetic resonance images of the cervical spine of a Chiari-like malformation depicting syringomyelia. MRI cervical syrinx sag and axial (*single arrow*)

one report [15]. We have found that of dogs that have MRI of their entire spine (i.e., not just the cervical region), most have syrinx cavities in the thoracic and lumbar spinal cord regions, in addition to the cervical region. In a recent review of MRI studies in over 350 dogs, we found that syrinx formation begins in the cervical regions and sequentially progresses to the thoracic region and finally to the lumbar region without skipping over a region [23].

Chiari-like malformation is typically encountered in small-breed dogs, with the Cavalier King Charles Spaniel being the most commonly encountered breed. Other breeds affected by this disorder include Brussels Griffon, miniature poodle, Yorkshire terrier, Maltese, Chihuahua, Bichon Frise, Staffordshire terrier, Pug, Shih Tzu, miniature Dachshund, miniature Pinscher, French bulldog, Pekingese, and Boston terrier [10, 17, 20]. We have observed this disorder in several brachycephalic cats as well. The typical age range at presentation appears to have changed over time, with many dogs developing clinical signs within the first year of life. In general, although the age range at clinical presentation is broad, most dogs present by the time they are 4 years old. Dogs that are presented at younger than 2 years of age often have more severe clinical signs than older

dogs. In recent years, we have seen an increasing number of younger patients (<1 year of age); whether this trend reflects increasing severity of the disorder with subsequent generations, increased awareness of the veterinary community and within the general public and hence earlier diagnosis, or a combination of these factors is unknown [34].

Clinical signs are variable, but the most consistent clinical features are cervical pain and apparent pruritus of the head, neck, and shoulder regions. Clinical signs of CLM and SM include neck pain, back pain, vestibular dysfunction, cervical myelopathy, incessant scratching activity, lameness, diminished hearing, and scoliosis. Cervical myelopathy (with associated neck pain) and cerebellovestibular dysfunction (e.g., strabismus, decreased menace response with normal vision, head tilt, nystagmus) are most commonly encountered [17, 20, 34]. In most cases, cerebellovestibular dysfunction is revealed during a neurologic examination and has not necessarily been observed by the pet owner. Many dogs with CLM will have decreased to absent menace responses with normal vision as well as varying degrees of positional ventrolateral strabismus. An unusual and distinctive feature of the scratching activity associated with CLM in dogs is that these patients typically do not make contact with the skin while scratching at the head and shoulder regions, so-called phantom scratching or "air guitar." Scratching often occurs on only one side. Facial rubbing (pawing at the face and/or rubbing against objects) is also encountered in some dogs and is considered to be a form of pain and/or paresthesia. Spinal hyperpathia (typically cervical), scratching activity, and scoliosis are all generally believed to be related to interference of the syrinx cavity with ascending sensory pathways in the spinal cord. Scratching activity and neck discomfort are often exacerbated by abrupt weather changes, stress, or excitement and by physical contact with the neck/shoulder region [1, 20, 34]. The presence of both pain and scoliosis is correlated with syrinx width in Cavalier King Charles Spaniel dogs with SM secondary to CLM [14]. Some of the neck pain may be directly related to constriction at the cervicomedullary junction or comorbid CJA [23]. Occasionally, dogs with CLM and cervical SM present with a specific variant of cervical myelopathy called central cord syndrome. In this scenario, the outwardly expanding syrinx in the cervicothoracic intumescence causes damage to the lower motor neurons of the thoracic limbs within the regional gray matter, leading to lower motor neuron paresis of the thoracic limbs while sparing the more peripherally located white matter tracts (UMNs to pelvic limbs). Damage to the regional white matter would cause general proprioceptive/upper motor neuron paresis to the pelvic limbs. The result is thoracic limb paresis (lower motor neuron in nature) that is notably worse than pelvic limb paresis. In some dogs with this syndrome, the pelvic limbs may appear normal [1, 14, 17, 18]. It is important to realize that, especially in the Cavalier King Charles Spaniel breed, other conditions may account for some or all of the clinical signs identified. It has recently been reported that more than 40 % of Cavalier King Charles Spaniels with CLM/SM are asymptomatic for the disorder [35]; however, in a recent pilot study we found that 41 % of 227 dogs demonstrated clinical signs that went unrecognized by their owners [36, 37]. Idiopathic epilepsy is also a prevalent disorder in the Cavalier King Charles Spaniel breed. Seizures have been reported to occur in 10–12 % of humans with Chiari type I malformation; in the authors' experience, seizure activity is an infrequent concurrent occurrence in dogs with CLM, and it is not possible to distinguish whether this is due to CLM or concurrent idiopathic epilepsy. Congenital deafness is also well described in the Cavalier King Charles Spaniel breed. The severity and rate of progression of CLM in dogs are variable, ranging from asymptomatic (i.e., finding evidence of CLM while imaging for some other reason) to extreme pain and debilitation with rapid worsening over a short time period. In addition, some dogs with CLM have other unrelated, concurrent disorders (e.g., disc extrusion, inflammatory brain disease) that could explain observed clinical signs [1–3, 34]. In such situations, it may be difficult to discern whether CLM is the main problem, contributory, or an incidental finding. Finally, other CJA can occur concurrently with or be mistaken

for CLM [23]. In the authors' opinion, a complete an accurate diagnosis including identification of all types of CJA is essential for development of an effective treatment plan.

Diagnosis

The diagnosis of CLM can only be made by MRI, which is also the preferred imaging modality for diagnosing SM. Although there has been some acceptance in the veterinary community of the use of "abbreviated" MRI studies utilizing views of the head and neck region with implementation of limited imaging sequences in an effort to reduce costs, the authors believe these "cost-saving efforts" may lead to incomplete assessments of the patients and result in erroneous conclusions. At the Canine Chiari Institute (CCI) at Long Island Veterinary Specialists, all patients are assessed with a whole body (brain and full spine) 3 T MRI, multi-detector CT scan, medical infrared imaging, as well as skull and cervical radiographs. On MRI, the malformation is best visualized on a midsagittal view (preferably T2-weighted), which includes the caudal fossa and the cranial cervical spinal cord. Consistent findings on MRI indicative of CLM are attenuation/obliteration of the dorsal subarachnoid space at the cervicomedullary junction and rostral displacement of the caudal cerebellum by the occipital bone [1, 17, 20, 34]. Other common MRI findings in CLM include syringomyelia (usually C2 level caudally), herniation of the caudal cerebellum through the foramen magnum, and a "kinked" appearance of the caudal medulla [20, 23]. Phase-contrast MRI (cine-MRI) is often used to measure cerebrospinal fluid flow in humans with Chiari type I malformation and has recently been evaluated for use in dogs with CLM. It was found that cerebrospinal fluid flow velocity and flow pattern are useful predictors of CLM/SM in Cavalier King Charles Spaniels [38]. Occasionally, dogs with MRI findings consistent with CLM will have evidence of other congenital disorders such as intracranial arachnoid (quadrigeminal) cyst, malformation/malarticulation of the C1 and/or C2 vertebra, and hydrocephalus. In the authors' opinion, most small-breed dogs normally have large lateral ventricles as a breed characteristic (ventriculomegaly) and are not truly hydrocephalic. In the absence of concurrent disease processes, cerebrospinal fluid analysis is usually normal; occasionally, a mild mononuclear pleocytosis will be apparent, however [1, 20, 34].

Although encroachment on the cerebellomedullary region by portions of the occipital bone has been the focus of many studies, evaluation of the entire skull shape and size utilizing multi-slice computed tomography technology with 3D reconstruction (CT) is currently in progress at the CCI at Long Island Veterinary Specialists to identify additional mechanisms of syrinx formation. Some reports describe a volume mismatch between the caudal fossa volume and its neural contents resulting in compression and herniation as the most common finding, while others failed to identify such a mismatch [39–42]. Patients with "normal" skull volumes may have a loss of the integrity of the brain's collagenous suspensory apparatus allowing for cerebellar "slouching" into the foramen magnum and a state of craniocervical hypermobility as suspected in human patients [43]. Although an association of CLM and syringomyelia with absent or abnormal frontal sinus formation has been reported [44], it has not been determined to be a causal relationship. Although CT imaging is able to define volume or conformational abnormalities in affected patients, the clinical focus is now on correcting the flow of CSF as the malformation affects its normal passage around the brain and spinal cord, leading to the syrinx formation [15, 38, 45–47].

Medical infrared imaging (MII) is a noninvasive imaging technique involving the recording of cutaneous thermal patterns. This imaging modality provides information about the function of the sympathetic nervous system. Because of recent advances in technology and the ability to image patients without the need for sedation, MII has potential use as a screening test for CLM in dogs. Loughin and others recently concluded a study documenting the reproducibility of image generation in normal canine limbs [48]. A current study by the same authors is attempting to establish a thermographic imaging protocol for dogs

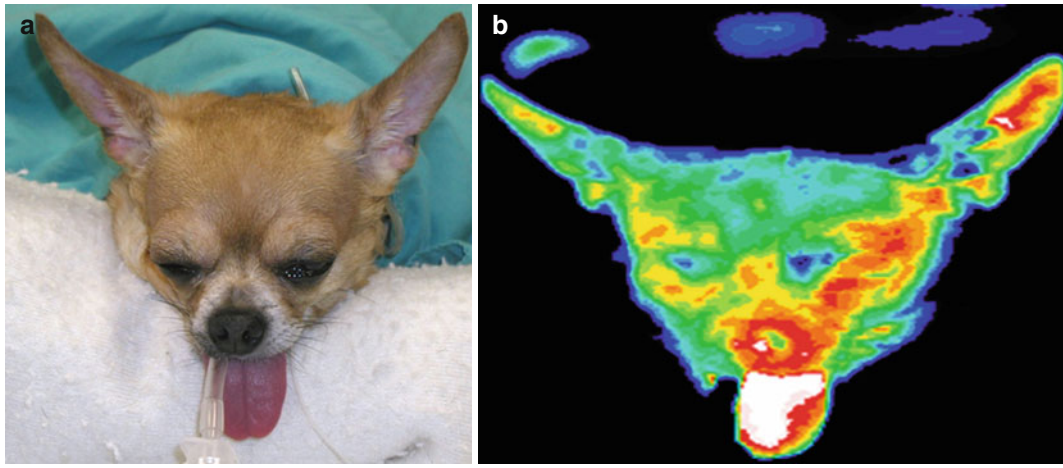


Fig. 11.4 A dog with Chiari-like malformation (**a**) and the corresponding medical infrared imaging depicting an asymmetric thermographic pattern (**b**)

suspected of having CLM, to identify thermal imaging patterns for various regions of interest (ROI), to evaluate changes in thermal pattern, and to compare the results to those of MRI findings, considered the standard for CLM in dogs [49–51]. Preliminary results revealed lower-temperature thermographic patterns in dogs with abnormal MRI findings compared with the dog with a normal MRI (Fig. 11.4). Severity of compression as determined with MRI was classified as mild, moderate, and severe and was found to correlate with thermographic findings, 100, 50, and 0 % of the time, respectively. Based on these preliminary findings, MII may be a viable imaging modality to use as a screening tool to detect CLM in dogs [36, 37, 49, 51].

Medical Therapy

Medical therapy for dogs with CLM generally falls into three categories: (1) analgesic drugs (implies relief of dysesthesia/paresthesia also), (2) drugs that decrease cerebrospinal fluid production, and (3) corticosteroid therapy. Anecdotally, the most useful drug available for relief of scratching activity associated with syringomyelia has been gabapentin (10 mg/kg body weight PO q8h). It has been shown that neuropathic pain is accentuated over time because of upregulation of the alpha 2 delta 1 subunit of voltage-gated calcium channels in dorsal root ganglion neurons and dorsal horn nociceptive neurons of the spinal cord. Gabapentin and the newer gabapentin analog, pregabalin, are believed to exert their antinociceptive effects by selectively binding to the alpha 2 delta 1 subunit and inhibiting calcium influx in these neurons. Side effects of gabapentin are minimal and are usually restricted to mild sedation, pelvic limb ataxia, and weight gain [1, 16, 20, 34]. Our recent experience with pregabalin (2–4 mg/kg q12h) suggests that it is a more effective drug in relieving pain and scratching activity in CLM/SM dogs. Because the half-life of elimination of pregabalin is nearly twice as long as that of gabapentin, twice a day dosing is possible. It is important to start at the low end of the dose range to avoid the side effects of sedation and ataxia. Orally administered opiate drugs are sometimes helpful in alleviating neck and head pain in dogs with CLM/SM. We have had success using oral tramadol (2–4 mg/kg q8–12 h), especially when used in conjunction with either gabapentin or pregabalin.

Several drugs aimed at decreasing cerebrospinal fluid production have been used in dogs with CLM/SM in an effort to diminish cerebrospinal fluid pulse pressure. All information regarding efficacy of these drugs is anecdotal. They include omeprazole (a proton pump inhibitor), acetazolamide (a carbonic anhydrase inhibitor), and furosemide

(a loop diuretic). Omeprazole, a proton pump inhibitor, has been shown to decrease cerebrospinal fluid production by 26 % in experimental studies when administered via the CSF in dogs. The oral dose for dogs is 10 mg (for dogs weighing less than 20 kg) q24h and 20 mg (for dogs weighing more than 20 kg) q24h. Acetazolamide is a carbonic anhydrase inhibitor that is used to treat glaucoma, epileptic seizures, idiopathic intracranial hypertension, altitude sickness, and cystinuria and is also classified as a diuretic. Medically, it may be used to treat conditions of moderate to severe metabolic or respiratory alkalosis. It does this by interfering with bicarbonate (HCO_3^-) resorption in the kidneys, thereby re-acidifying the blood (and thus alkalinizing the urine). Acetazolamide is also used to decrease the production of cerebrospinal fluid in idiopathic intracranial hypertension. Furosemide is a loop diuretic that acts on the distal tubules by abolishing the corticomedullary osmotic gradient and blocking negative as well as positive free water clearance. Its action is independent of any inhibitory effect on carbonic anhydrase or aldosterone. Due to the large NaCl absorptive capacity of the loop of Henle, diuresis is not limited by development of acidosis, as it is with the carbonic anhydrase inhibitors. When treatment decisions are made, the potential side effects of long-term corticosteroid and/or diuretic therapy should be considered, along with the questionable efficacy of this therapy. Electrolyte depletion (especially potassium) and dehydration are concerns when diuretics are used for prolonged periods, particularly when combined with corticosteroids.

Corticosteroids are often used in the medical management of CLM/SM in dogs. Potential benefits include anti-inflammatory effects, decreased cerebrospinal fluid production, and decreased substance P (a nociceptive neurotransmitter) expression in spinal cord dorsal horn neurons. An initial anti-inflammatory dosage of 0.5 mg/kg PO q12h is often effective in controlling clinical signs. This dose should be tapered, if at all possible, to an every other day schedule within the first month of therapy. In most cases of CLM/SM, medical therapy will diminish the severity of clinical signs, but resolution is unlikely [1, 17, 19, 34]. It is the authors' opinion that medical therapy should be viewed as a temporary treatment "bridge" until more definitive therapy like surgical decompression with cranioplasty to restore normal CSF flow can be performed.

Surgical Treatment

We consider CLM/SM to be a surgical disorder. In our opinion, based on more than 300 operated cases, the preferred surgical procedure for treatment of CLM in dogs is foramen magnum decompression with cranioplasty utilizing titanium mesh and polymethyl methacrylate (PMMA). This procedure involves a suboccipital craniotomy, dorsal laminectomy of C1, and removal of the cranial 20 % of the dorsal spinous process of C2, with subsequent placement of a titanium mesh/PMMA plate on titanium screw anchor posts inserted around the circumference of the occipital bone defect. For the foramen magnum decompression procedure, the dog is placed in sternal recumbency with the neck flexed (Fig. 11.5). The dorsal aspect of the head and neck is shaved from the level of the bregma to the level of the third or fourth cervical vertebra, with a width approximately equal to the width of the atlas. A dorsal midline incision is made extending from approximately 1 cm rostral to the external occipital protuberance to the middle of the second cervical vertebra. The superficial dorsal cervical musculature is separated at the median raphe, exposing the underlying biventer cervicis muscles (Fig. 11.6). The paired biventer cervicis muscles are then separated on midline, exposing the rectus capitis dorsalis muscles. The caudal aspects of the rectus capitis dorsalis muscles are removed from the cranial half of C2, using sharp dissection and periosteal elevation; these muscles are then split on midline. The cranial aspects of the rectus capitis dorsalis muscles are sharply incised from the nuchal crest, exposing the caudal portion of the occiput and the arch of the atlas. Hemorrhage is controlled with bipolar electrocautery. A high-speed air drill with a 3–4-mm diameter round drill bit and Lempert rongeurs are used to remove a portion of the occiput and the

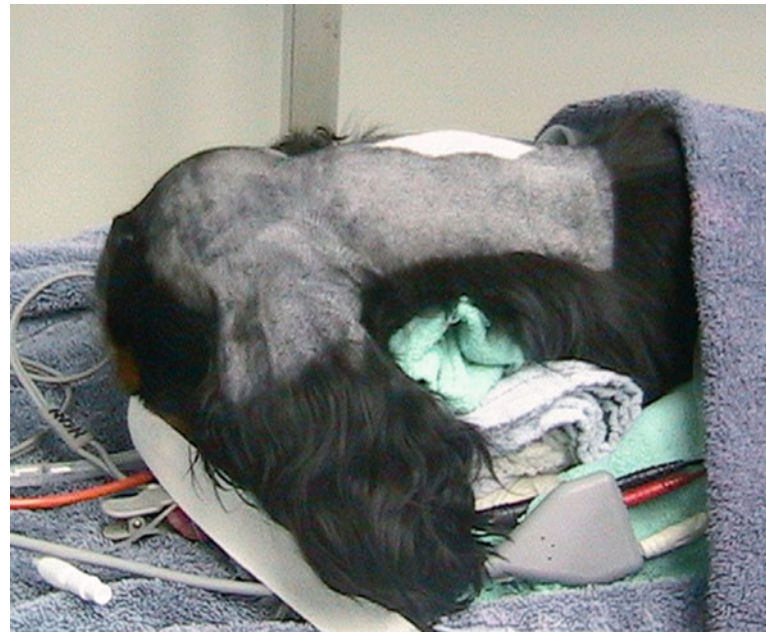


Fig. 11.5 Proper positioning of the head and neck for foramen magnum decompression in a dog with Chiari-like malformation (From Dewey et al. [17])

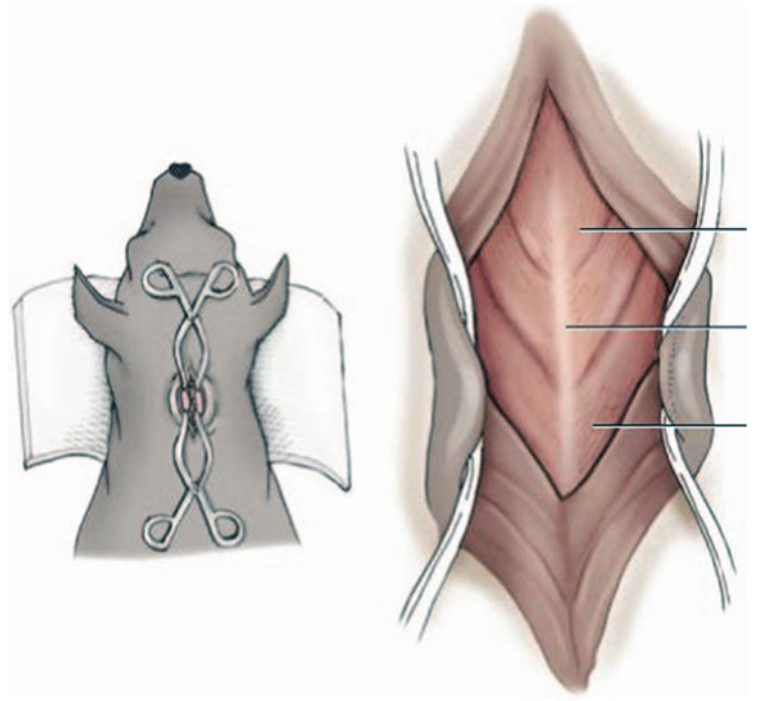


Fig. 11.6 Illustration of the initial surgical approach for foramen magnum decompression in dogs with Chiari-like malformation. *A* occipitalis muscle, *B* median raphe, *C* cervicoscutularis and cervicoauricularis superficialis muscles

dorsal aspect of the first cervical vertebra (Fig. 11.7). The dorsal arch of C1 and the cranial 20 % of the dorsal spinous process of C2 are routinely removed.

The meninges (dura/arachnoid) are incised in the midline, and the meningeal tissue in the region of the foramen magnum decompression is resected. Care is taken to identify and resect the

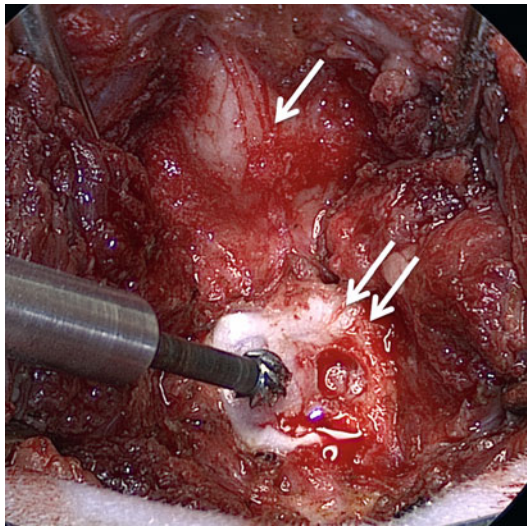


Fig. 11.7 A high-speed air drill with a 3–4-mm diameter round drill bit and Lempert rongeurs are used to remove a portion of the occiput (*single arrow*) and the dorsal aspect of the first cervical vertebra (*double arrow*)

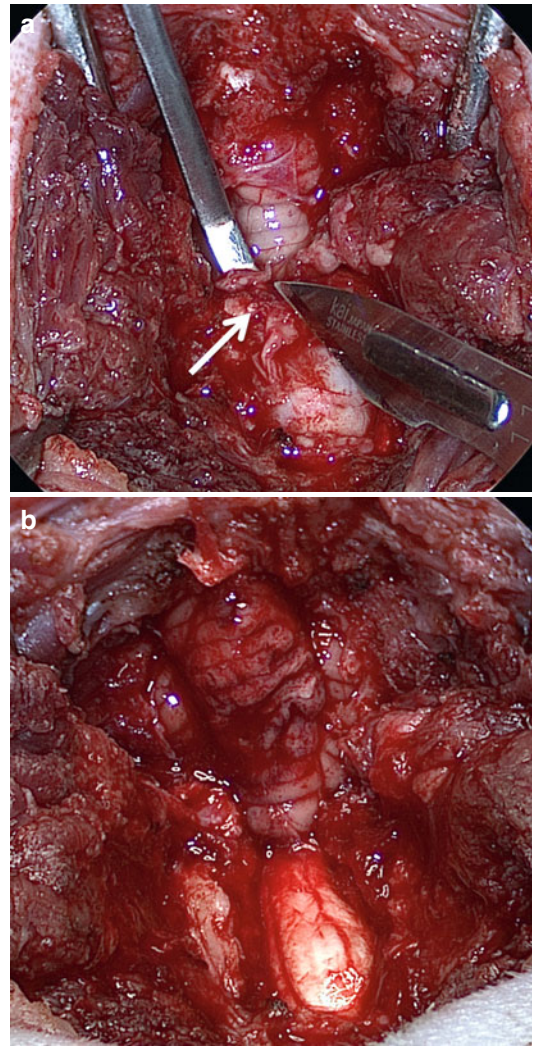


Fig. 11.8 Care is taken to identify (**a**) and resect (**b**) the fibrous constriction (*arrow*) frequently found at the time of the dural resection

fibrous constriction frequently found at the time of the dural resection (Fig. 11.8). Five guide holes are drilled in the occipital bone around the periphery of the skull defect, using a 1.1-mm drill bit. Self-tapping 6-mm length (1.5-mm width) screws are inserted into the guide holes for an approximate depth of 2–3 mm (Fig. 11.9). The dog's head is then released from the flexed position and is repositioned at a normal resting angle. The skull plate is fashioned using titanium mesh and PMMA and is fixed to the back of the skull, using the titanium screw heads as anchor posts for the PMMA (Fig. 11.10). The titanium mesh and PMMA "plate" is shaped somewhat like a guitar pick, with the wide end of the pick toward the occiput (Fig. 11.11). Only a thin layer of PMMA is applied to the outer surface of the titanium mesh to form the plate, with some PMMA extending beyond the edges of the titanium mesh to adhere to the titanium screw heads. The caudal aspect of the plate is made to extend slightly over the dorsal defect of C1; the tail aspect of the plate is curved dorsally to avoid impinging on the medulla or the cranial cervical spinal cord. Closure is routine. Proper plate application is confirmed via radiography or (preferably) CT scan (Fig. 11.12) [17, 18]. The short-term surgical success (sustained improvement in neurologic status and/or pain/scratching relief) rate with foramen magnum decompression in dogs with CLM is approximately 80 %, whether or not adjunctive cranioplasty is performed [10, 17, 18]. One report found an inverse relationship between the length of time clinical signs were present before surgical intervention and the extent of postoperative improvement [17]. Unfortunately, a disease relapse rate ranging from 25 to 47 % has been reported among cases treated with

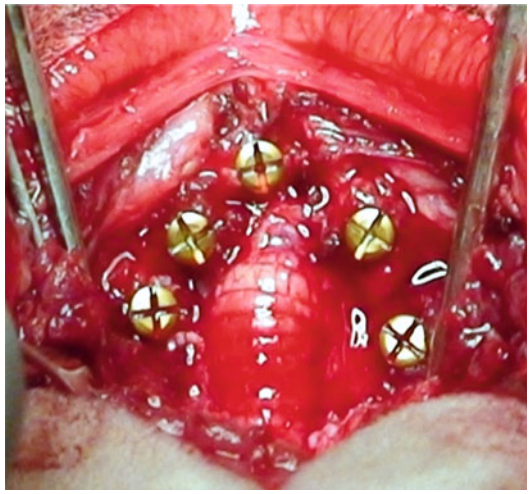


Fig. 11.9 Self-tapping 6-mm length (1.5-mm width) titanium screws are inserted into the guide holes for an approximate depth of 2–3 mm surrounding the decompression site

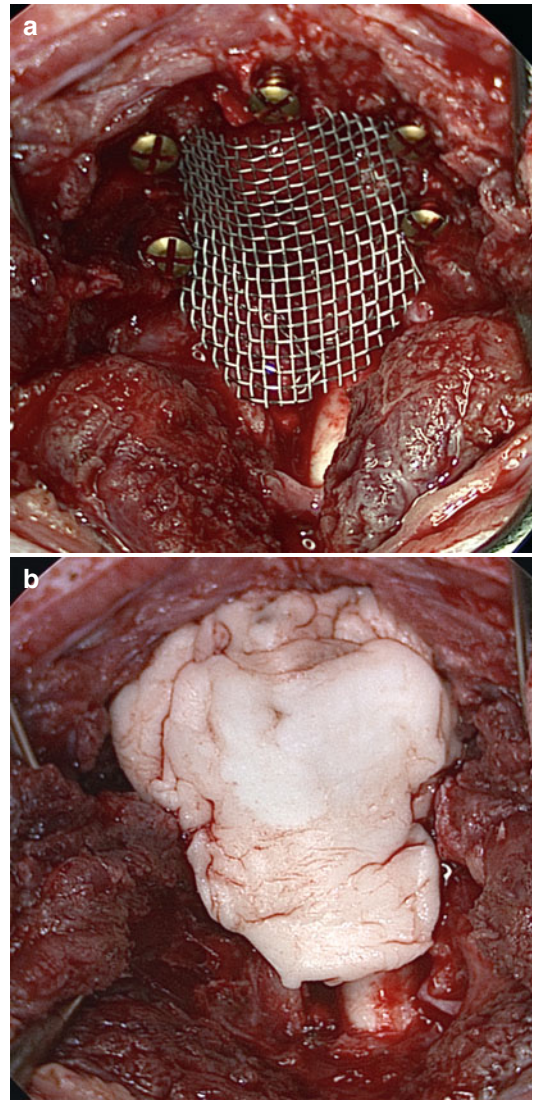


Fig. 11.10 The skull plate is fashioned using titanium mesh (**a**) and PMMA and is fixed to the back of the skull, using the titanium screw heads as anchor posts for the PMMA (**b**)

foramen magnum decompression alone; most of these relapses are suspected to be due to excessive postoperative scar tissue formation at the foramen magnum decompression site [10, 18].

The authors and colleagues developed the cranioplasty procedure (based on a similar procedure used in human foramen magnum decompression surgery) to discourage excessive postoperative scar tissue from recompressing the operative site. Our initial report suggested a dramatic reduction in the reoperative rate due to scar tissue formation after the cranioplasty procedure was instituted, but this was based on only 21 cases, with about a 1-year follow-up period [18]. In our most recent analysis of more than 300 cases of foramen magnum decompression with cranioplasty, the reoperative rate was less than 1 % [23].

Most dogs with CLM/SM will respond favorably to medical therapy, although in many cases this response is temporary. In one group of 10 CLM/SM dogs treated medically, 5 dogs were euthanized within 2 years because of disease progression and diminished responsiveness to therapy [20]. In another study, 36 % of CLM/SM dogs treated medically were euthanized at a mean of 1.7 years from the time of diagnosis because of clinical signs of their disease [34]. Although the surgical success rate is favorable for CLM/SM in dogs, the recurrence rate due to excessive postoperative scar tissue formation has been unacceptably high with foramen magnum decompression without cranioplasty. It appears that cranioplasty has improved the success rate of foramen magnum decompression and is currently the recommended procedure by the authors for dogs with CLM/SM exhibiting clinical signs.

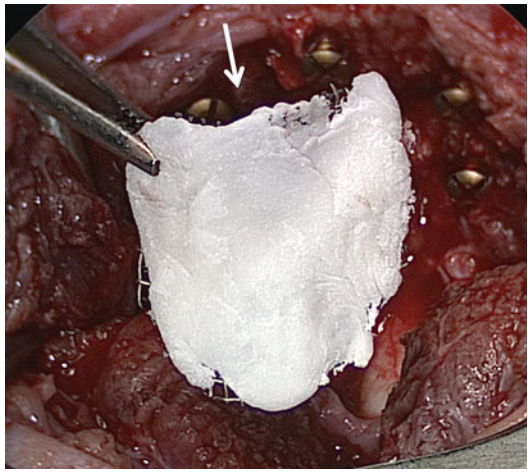


Fig. 11.11 The titanium mesh and PMMA "plate" is shaped somewhat like a guitar pick, with the wide end of the pick toward the occiput (*arrow*)

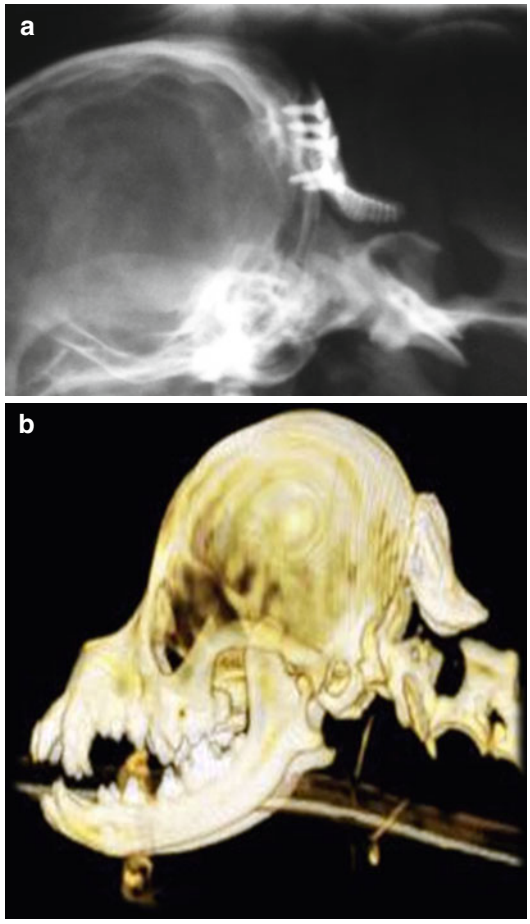


Fig. 11.12 Proper plate application is confirmed via radiography (**a**) or preferably CT scan (**b**)

Primary Secretory Otitis Media (PSOM)

Most dogs with CLM/SM having foramen magnum decompression and cranioplasty are routinely relieved of clinical signs, however, with some, scratching activity tends to persist. Primary secretory otitis media (PSOM), a common cause of scratching, is the canine analog of otitis media with effusion (OME) in human patients. In a recent study of 120 dogs with CLM, 38.7 % of dogs had PSOM [52]. There was a significant difference between the prevalence of PSOM in CKCS (46 %) and non-CKCS (13 %); $p < 0.0001$. Pharyngeal "slouching" associated with brainstem dysfunction in patients with CLM may result in closure or narrowing of the eustachian tube. The resultant pressure gradient between the middle ear and pharynx is theorized to cause the accumulation of mucus in the middle ear. Affected dogs have a mucus plug in the tympanic cavity that causes the tympanic membrane to bulge. Treatment recommendations for dogs with PSOM include myringotomy and flush/aspiration. A 25–30 % recurrence of PSOM has been found within 6 months with the myringotomy and flush/aspiration techniques [52]. Efforts should be made to ascertain whether PSOM is present concurrent with CLM/SM given the prevalence of comorbid disease and appropriate treatment measures instituted. Dogs with recurrent clinical signs after surgery for CLM/SM should be evaluated for PSOM before concluding surgery is deemed a failure.

Atlantooccipital Overlapping (AOO)

An abnormality at the craniocervical junction in small and toy-breed dogs has recently been described, called atlantooccipital overlapping (AOO) [1, 2, 4]. In this malformation, the atlas (C1) is cranially displaced into the foramen magnum, and overlap of the occipital bone and the atlas occurs. This displacement tends to compress the caudal aspect of the cerebellum and to elevate and compress the caudal medulla (medullary kinking). Atlantooccipital overlapping is likely a

form of basilar invagination. Basilar invagination is a human craniocervical junction disorder in which the atlas and/or the axis (C2) telescopes toward the foramen magnum [30, 53]. We have seen this disorder as a sole entity and in combination with CLM and/or atlantoaxial instability. Syringomyelia has been associated with atlantooccipital overlapping, whether as a sole malformation or as part of several craniocervical malformations in the same patient. Because bony detail is difficult to distinguish on MRI, it is likely that AOO has been underdiagnosed in dogs, with most of these patients incorrectly ascribed a diagnosis of CLM. The precise nature of this and other craniocervical malformations is typically apparent on CT imaging (Fig. 11.13). We routinely follow MRI of craniocervical junction abnormalities with CT imaging to fully evaluate the malformation or malformations in the region.

Clinical signs in dogs with atlantooccipital overlapping typically include neck pain and varying degrees of ataxia of all four limbs [1, 2, 4].

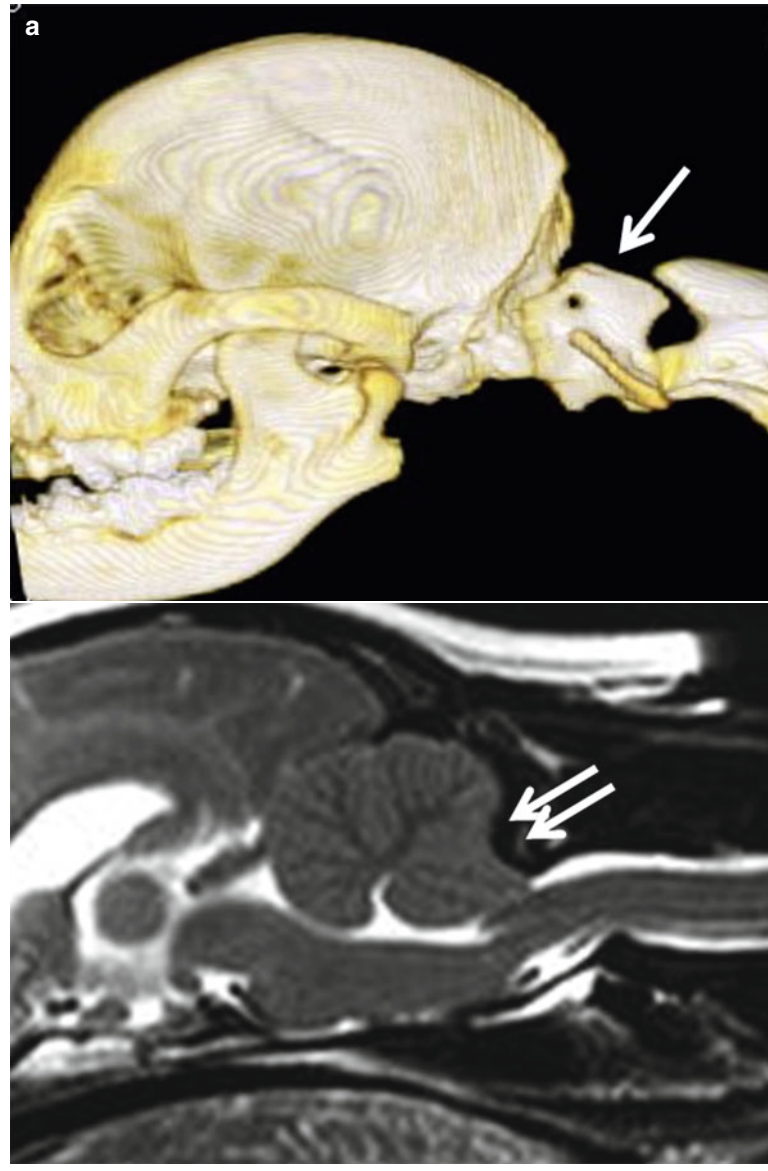
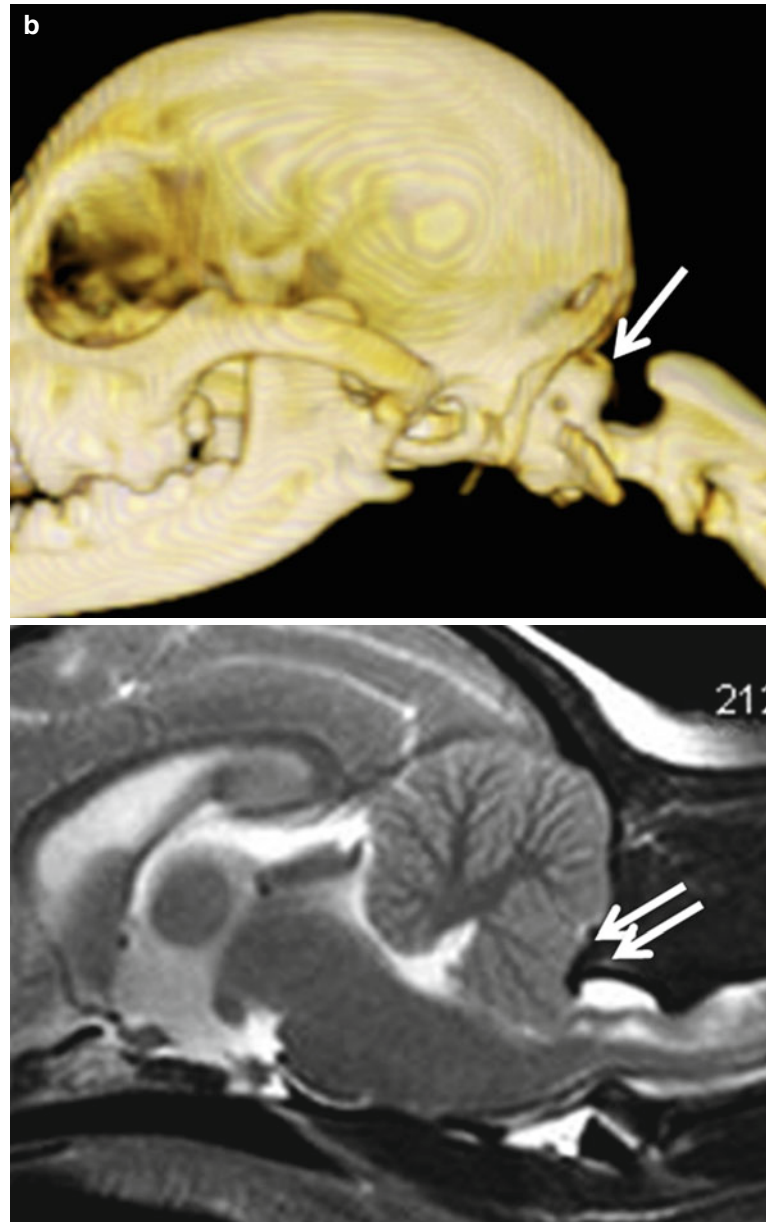


Fig. 11.13 A dog with Chiari-like malformation (**a**) with CT imaging in conjunction with MRI demonstrating a normal position of the C1 vertebra (*single arrow*) and broad cerebellar compression (*double arrow*) compared with a dog with atlantooccipital overlap (**b**) revealing the position of the C1 vertebra within the caudal fossa (*single arrow*) and a linear type compression of the cerebellum (*double arrow*)

Fig. 11.3 (continued)



An insufficient number of cases of atlantooccipital overlapping have been reported in the literature to allow general recommendations concerning therapy. We have found that most dogs with this malformation, similar to dogs with CLM/SM, will respond temporarily to medical management. In a recent review of medical records of 70 dogs with AOO, all dogs have responded to decompression as described in the treatment of CLM [23]. In a recent report, surgical stabilization for relief of clinical signs was reported [4]. At surgery, the compressive mass appears to be soft tis-

sue possibly due compensatory ligamentous hypertrophy secondary to chronic instability. We believe that this disorder is also a manifestation of instability at the C1–C2 junction, possibly a form of basilar invagination similar to the atlantooccipital overlapping problem. This can occur as a sole entity or in combination with CLM and/or atlantoaxial instability. In cases of combined CLM/atlantoaxial instability and C1–C2 dorsal constriction, the authors have pursued combined ventral and dorsal approaches to surgically address both issues (Fig. 11.14). As with atlantooccipital overlapping in dogs, the optimal treatment strategy for dorsal constriction at C1–C2 has not yet been established. However, because of its compressive nature, we believe that this is most likely a surgical disease.

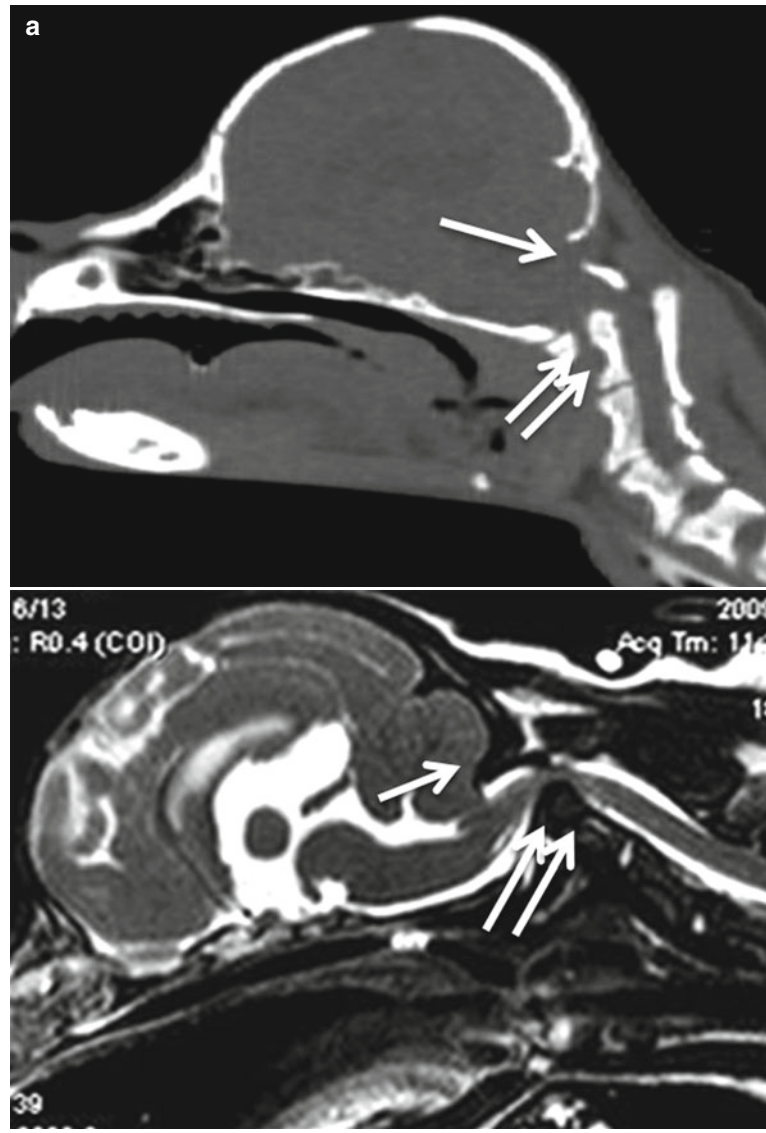
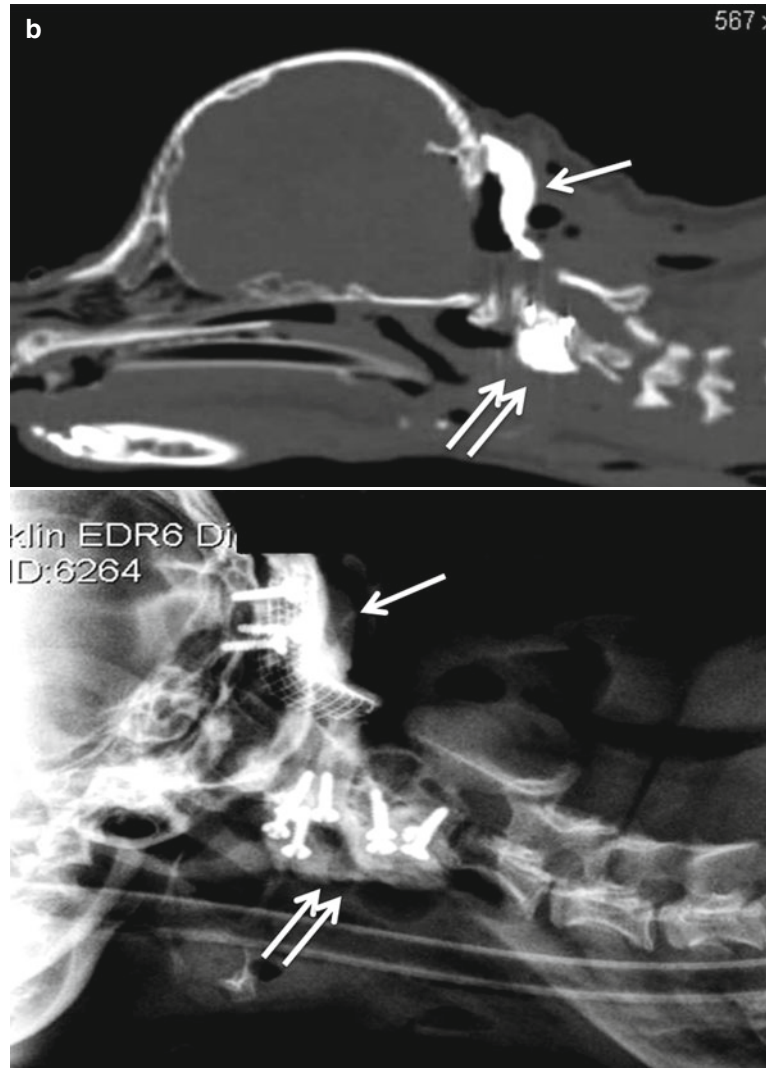


Fig. 11.14 A dog with Chiari-like malformation and atlantooccipital overlap with preoperative CT (*top*) and MRI (*bottom*) imaging depicting cerebellar compression (*single arrow*) and craniocervical instability (*double arrow*) (**a**). Postoperative CT (*top*) and radiographic (*bottom*) imaging depicting cerebellar decompression with cranioplasty (*single arrow*) and craniocervical stabilization (*double arrow*) (**b**)

Fig. 11.4 (continued)



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Radiology of the Chiari Malformations

12

Abby E. Deans and A. James Barkovich

Abstract

Neuroimaging is a key tool in evaluating and diagnosing those disorders of the craniocervical junction known as "Chiari malformations." Although linked by their name, these are very different disorders, linked by a need to image the entire brain and the entire spine for proper evaluation. The Chiari I malformation is a disorder in which a small bony posterior fossa results in the herniation of the cerebellar tonsils through the foramen magnum; as a result, the cerebellar tonsils and cervicomedullary junction are compressed, and CSF flow through the foramen magnum is impeded, putting the patient at risk for syringohydromyelia. Proper imaging evaluation is essential to differentiate this condition from tonsillar herniation due to intracranial hypotension (from CSF leaks) or intracranial hypertension (idiopathic or from masses/hydrocephalus) in which treatment is quite different. The Chiari II malformation results from intracranial hypotension in utero due to chronic CSF leakage at the site of an open neural tube defect (myelomeningocele). The myelomeningocele may be repaired prenatally or soon after birth. The many forebrain and hindbrain malformations that result from the chronic intracranial hypotension in utero are described. The definition of the Chiari III malformation is in transition but is most easily described as herniation of upper cervical spinal cord and hindbrain structures (combined cephalocele and myelocele) through a dorsal low occipital and dorsal upper cervical bony defect. Optimal imaging evaluation for these disorders is discussed.

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MRI is the mainstay of imaging for diagnosis and characterization of the Chiari malformations.

Chiari I

The "Chiari I malformation" is a very misunderstood condition. As illustrated by Chiari's initial paper, it is not a brain malformation; it is a disorder caused by *compression* of neural structures (usually the cerebellar tonsils, upper cervical spinal cord, or medulla oblongata, which have been either pushed or pulled downward) near the craniocervical junction by surrounding bone and consequent alteration of CSF flow through the foramen magnum. The mere presence of low cerebellar tonsils does not constitute the Chiari I disorder; low tonsils are common and usually asymptomatic. When clinical signs and symptoms develop, the responsible compression is caused by a downward push or a downward pull. The push may result from a small posterior fossa as in genetic craniofacial syndromes such as Crouzon syndrome [1–3], from increased pressure due to abnormal CSF flow or resorption [4] or from an intracranial mass (usually in the posterior fossa). The pull is typically from low infratentorial/spinal CSF pressure due to a CSF leak [5, 6] or a lumboperitoneal [7] or even an intracranial [8] shunt. Foramen magnum crowding from either a push or a pull will result in altered CSF flow and craniospinal pressure dissociation; this condition, in turn, can cause intraspinal edema ("presyrinx" [9]) or frank syringohydromyelia.

The imaging study of choice to evaluate patients with cerebellar ectopia is MRI. Sagittal and axial T1- and T2-weighted MRI with images no thicker than 3 mm should be obtained in all patients. The images should include the entire brain and skull, as it is important to look for hydrocephalus, masses, malformations, deformities, or evidence of high or low intracranial pressure. The cervical spine should also be evaluated down to C6–C7 to look for associated spinal cord edema or syringohydromyelia; as it may be difficult to differentiate a syrinx from edema on T2 sagittal images, axial T1 images are useful for confirmation. If the anatomic images are suggestive of cerebellar ectopia, cardiac-gated phase contrast images should be obtained in order to determine the effects of the ectopia upon CSF flow at and around the foramen magnum.

The key anatomic imaging finding on MRI of these malformations is tonsillar ectopia with compressed ("peg-like" or "pointed") cerebellar tonsils and nearly complete effacement of CSF at the foramen magnum or C1 level (Fig. 12.1a). In general, if the tonsils are displaced 5 mm or more below a line drawn from the bottom tip of the basion to the bottom tip of the opisthion (Fig. 12.1b), they are too low and are probably compressed [10]. Children may have slightly greater ectopia of cerebellar tissue without compression and, therefore, without symptoms [11]. However, measurements are less important than the actual appearance of the structures. Notably, most patients with borderline low-lying tonsils are asymptomatic, and the measurement of tonsillar ectopia alone (without tonsil compression or subarachnoid space effacement) should not necessarily instigate further workup. In addition to the pointed appearance of the inferior tonsils and effacement or obliteration of the CSF space in the caudal posterior fossa, foramen magnum, and C1 level, syrinx or presyrinx in the cervical spinal cord (Fig. 12.1a, b) should raise suspicion for compression of the subarachnoid spaces or tumor. Tumor can usually be confidently diagnosed by the finding of an intramedullary mass effect that enhances after administration of paramagnetic contrast. If no tumor is found, cardiac-gated phase contrast CSF flow studies can be used to look for alteration of CSF dynamics. Although described further elsewhere, a brief description of CSF flow studies deserves mention here given the importance of these studies for diagnosis in Chiari I. Normal studies demonstrate craniocaudal CSF flow (white CSF) during cardiac systole, which lasts about 40 % of the cardiac cycle [12]; the lower brain stem and cerebellar tonsils move slightly downward. During cardiac diastole (60 % of cycle), CSF moves rostrally and is black; the brain stem and tonsils move slightly upward [12]. When the CSF flow is impaired by cerebellar tissue in the foramen magnum, the amount of CSF seen in motion ventral and dorsal

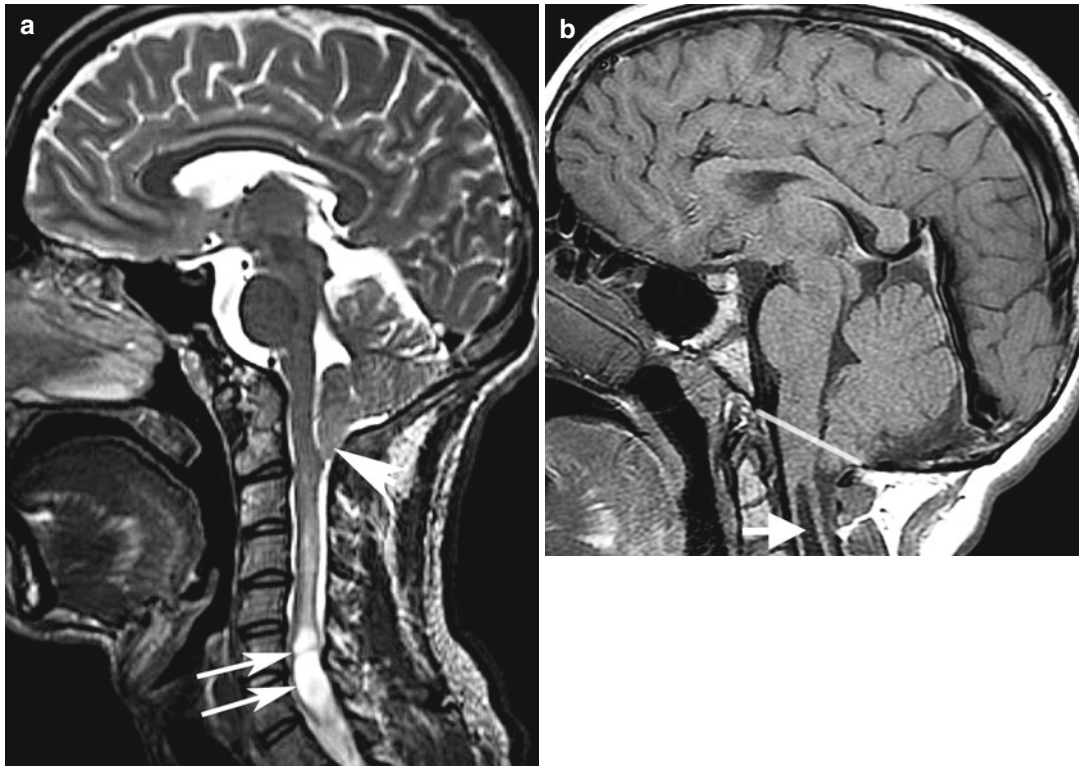


Fig. 12.1 (**a**) Sagittal T2-weighted MRI of the brain and cervical spine demonstrating findings of Chiari I with cervical ectopia of the cerebellar tonsils with compressed, "pointed" or "peg-like," morphology (*arrow*) and effacement of CSF spaces at the level of the foramen magnum and upper cervical spinal canal. This patient was found to have a lower cervical syrinx (*double arrow*) at presentation. (**b**) In another patient, more subtle findings of slightly low position of the cerebellar tonsils, 6 mm below a *line* drawn from the basion to the opisthion, with slightly compressed morphology and effacement of CSF at the foramen magnum. Associated finding of cervical syrinx (*arrow*) suggests narrowing of subarachnoid spaces at the foramen magnum/C1 levels, which could be further evaluated with phase contrast CSF flow imaging to identify region of obstruction to CSF flow

to the brain stem and craniocervical junction is reduced (Fig. 12.2a, b), CSF systole is shortened, diastole is prolonged, and movement of the brain stem and tonsils is increased [13, 14]. When flow studies demonstrate prolonged CSF diastole at the foramen magnum with increased downward motion of the cerebellar tonsils and brain stem, it is strong evidence of impaired CSF flow.

Any cause of restriction of CSF flow at the foramen magnum/C1/C2 levels can cause clinical symptoms or syrinx formation. Imaging is important to differentiate among these different causes, as the treatments might be very different. If a "slumping brain" is seen, with pachymeningeal enhancement (Fig. 12.3b), the brain stem slumping against the clivus, enlarged dural venous sinuses and pituitary gland (Fig. 12.3a), or a low third ventricle floor, intracranial hypotension should be strongly suspected, and a search for the CSF leak should be sought [5, 6]. In the case of primary mesenchymal disorders or premature suture fusion resulting in a small skull base, the head is typically brachycephalic (Fig. 12.4a), and early closure of the sutures can be identified; in this situation, it is useful to perform an MR venogram to look for restriction of venous outflow at the undersized jugular foramina and, more importantly, extensive collateral venous flow via emissary veins in the occipital region [1, 15]. The imaging study might also show hydrocephalus or a posterior fossa mass causing cerebellar herniation through

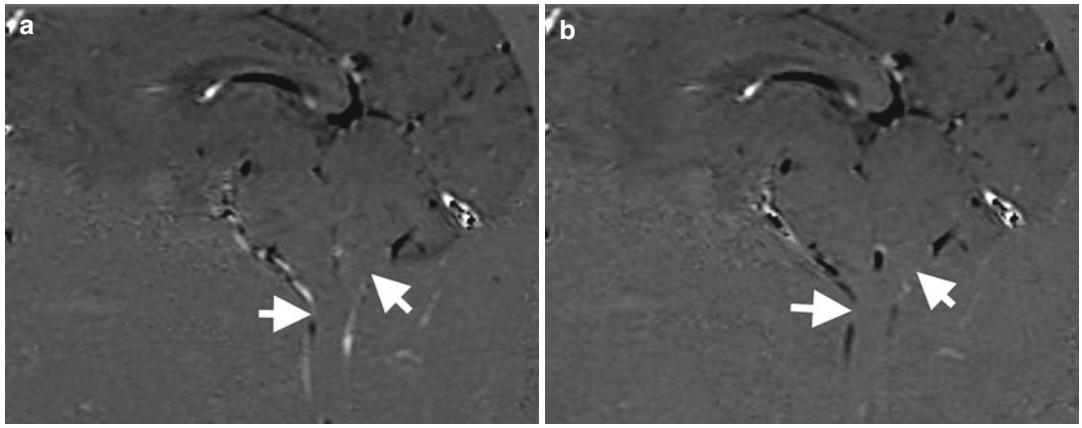


Fig. 12.2 Cardiac-gated phase contrast CSF flow imaging demonstrates obstructed CSF flow at the foramen magnum in a patient with platybasia (same patient as in Fig. 12.4c). (**a**) Decreased CSF flow anterior to the medulla and absent flow posterior to the cerebellar tonsils (*arrows*) in CSF systole (white CSF) and (**b**) absent flow both anteriorly and posteriorly (*arrows*) during CSF diastole (black CSF)

the foramen magnum. In patients with diseases of bone, basilar invagination (Fig. 12.4b) may result in tonsillar herniation. Younger people with mesenchymal abnormalities resulting in a small skull base or a flattened chondrocranium (platybasia) can result in herniation of cerebellar structures (Fig. 12.4c). Any of these conditions can cause occipital headaches and alteration of CSF flow resulting in syringohydromyelia. In fact, even in the absence of tonsillar herniation, patients with clinical history strongly suggestive of CSF obstruction at the level of the foramen magnum or posterior fossa with syringohydromyelia (the "Chiari 0 malformation" [16]) may benefit from evaluation with cardiac-gated phase contrast CSF flow imaging to look for flow or pulsation abnormalities as decompression or targeted shunt placement may provide symptomatic relief.

Chiari II

For assessment of the Chiari II malformation, the complex set of posterior fossa, and supratentorial abnormalities seen in the setting of myelomeningocele, MRI again forms the diagnostic mainstay. However, prenatal screening ultrasound is often where the brain and spine abnormalities in the Chiari II malformation complex are identified initially and deserves discussion in this setting. Subsequent fetal MRI is indicated for further characterization and identification of associated findings. The appearance of myelomeningocele and the Chiari II malformation on prenatal imaging will be commensurate to the relatively early developmental stage, with abnormalities often progressing on follow-up studies.

Fetal Ultrasound

Fetal screening ultrasound protocols [17] include an evaluation of the nuchal translucency late in the first trimester, which includes a limited evaluation of anatomy, followed by a full anatomic evaluation at 18–20 weeks. Therefore, findings suggestive of Chiari II and myelomeningocele are generally first visualized in this period. Maternal serum screening tests or amniocentesis, performed within the same period, revealing elevated alpha-fetoprotein in the setting of open neural tube defect can also be the referring indication for fetal brain and spine MRI.

Screening fetal ultrasound examination [17] includes evaluation of the brain and spine. Evaluation of the brain will include axial view of the fetal head through the level of the thalami and cavum septum pellucidum for measurement of biparietal diameter and head circumference, axial view through the posterior fossa, and axial view

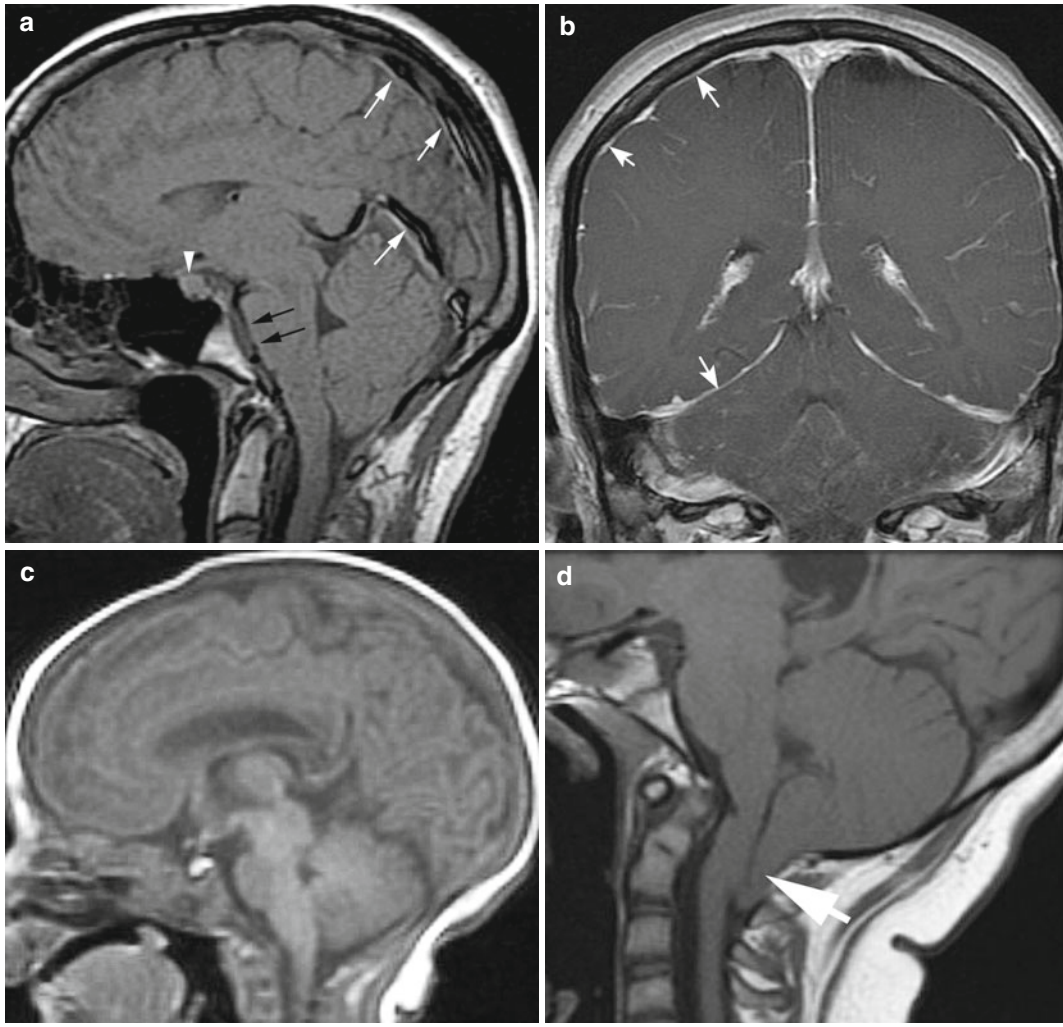


Fig. 12.3 Cervical ectopic location of the cerebellar tonsils can result from a downward pull as in the setting of (**a**) spontaneous intracranial hypotension (SIH) from spinal CSF leak. Findings of SIH on sagittal MRI include tonsillar ectopia, enlarged dural venous sinuses (*arrow*) and pituitary gland (*arrowhead*), compression of pons against clivus (*black arrows*), and (**b**) diffuse pachymeningeal enhancement (*white arrows*) on post-gadolinium T1-weighted MRI sequences. Cerebellar herniation can also result from a downward push from hydrocephalus. (**c**) Normal cerebellar location and morphology in a neonate who later developed hydrocephalus with (**d**) subsequent progressive downward herniation of the cerebellar tonsils (*arrow*) and symptomatic foramen magnum compression by age 11 years

through the cerebral lateral ventricles. Evaluation of the spine includes longitudinal (sagittal) and axial views through the cervical, thoracic, lumbar, and sacral spine. Nearly universally, fetuses with Chiari II malformation will demonstrate bilaterally flattened or slightly collapsed appearance of the frontal calvarium on axial views through the supratentorial brain, the so-called lemon sign (Fig. 12.5a) and effaced cisterna magna with anterior wrapping of the cerebellar hemispheres, the so-called banana sign (Fig. 12.5b) [18], or non-visualization of the cerebellum. Other findings which are suggestive of Chiari II malformation include decreased biparietal diameter [19], with a majority of cases demonstrating measurements below the fifth percentile and ventriculomegaly [20, 21]. Axial views of the normal fetal spine will demonstrate a complete vertebral ring

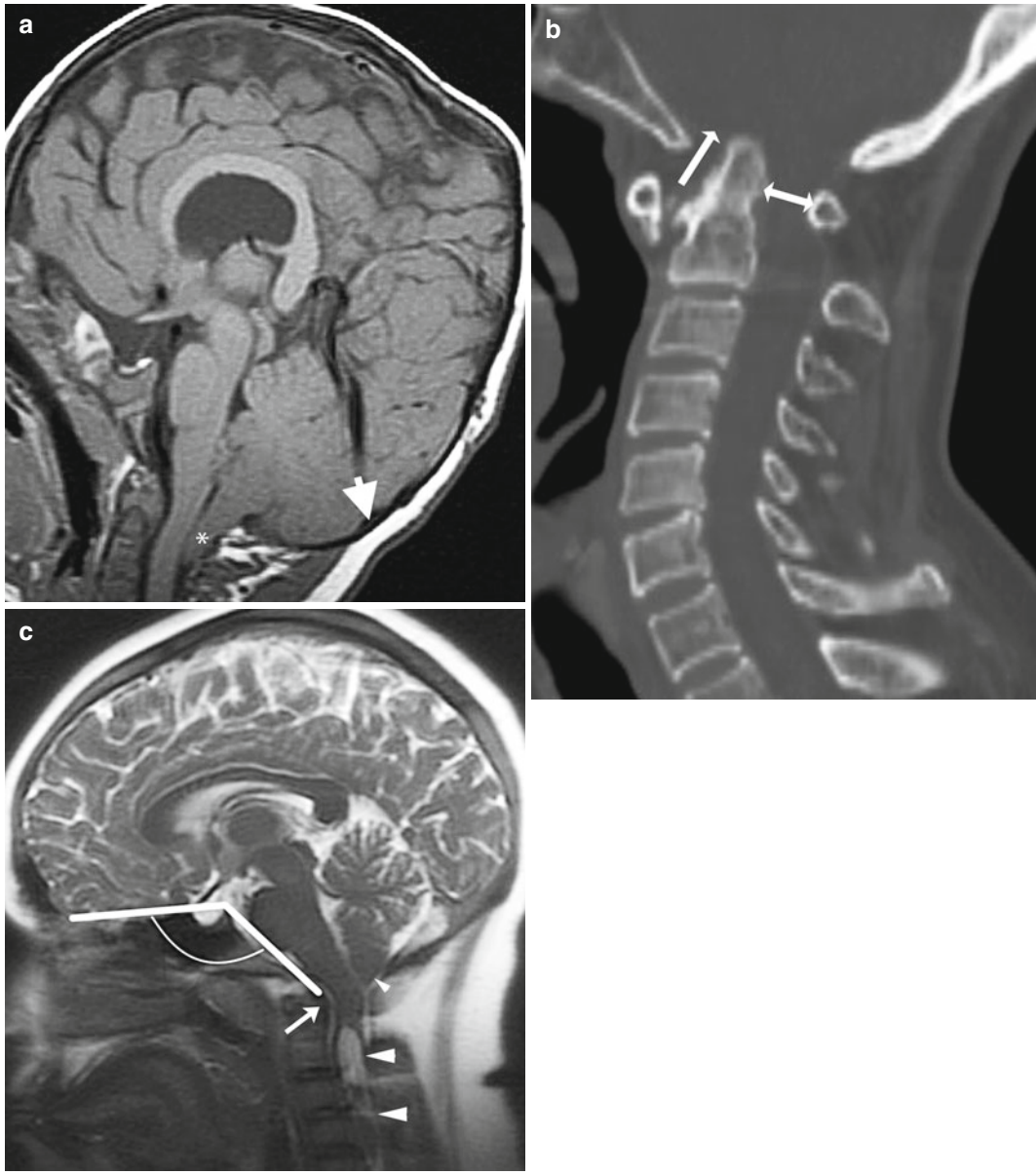


Fig. 12.4 Chiari I malformation can also be seen in the setting of small posterior fossa from other causes. (**a**) Early fusion of cranial sutures in Crouzon syndrome results in brachycephaly, arched morphology of the corpus callosum, and small posterior fossa with low torcular attachment (*arrow*) and cervical ectopia of the cerebellar tonsils (*) to the level of C2. (**b**) Basilar invagination as shown on this sagittal CT of the cervical spine demonstrating upward displacement of C2 (*arrow*) superiorly through the foramen magnum, resulting in foramen magnum and upper cervical stenosis (*double-headed arrow*) with tonsillar compression. (**c**) Platybasia is often seen in association with posterior angulation of the dens (*arrow*) or basilar invagination which exacerbates foramen magnum stenosis. Note pointed morphology of the cerebellar tonsils (*small arrowhead*), effacement of CSF at the foramen magnum, and cervical syringomyelia (*large arrowheads*) suggesting compression at the foramen magnum

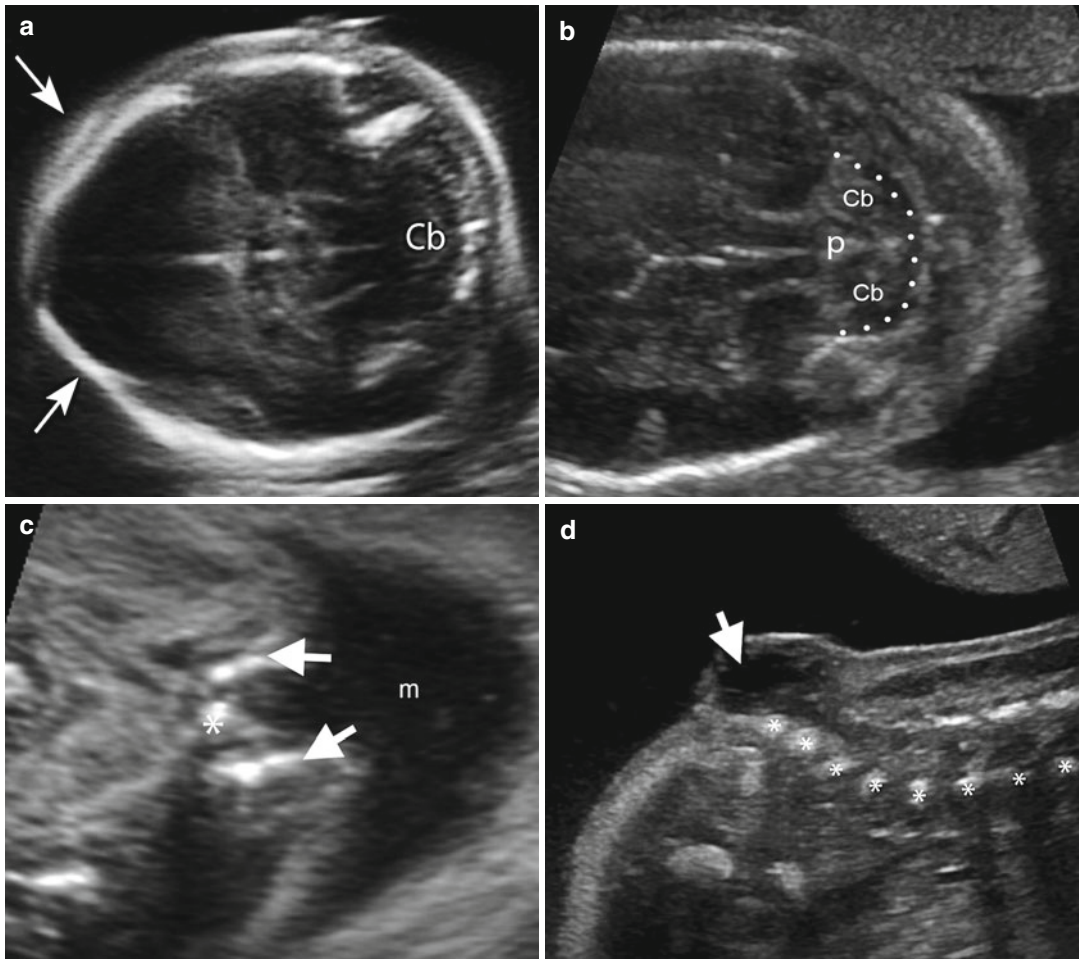


Fig. 12.5 Chiari II malformation and myelomeningocele are often first identified on prenatal ultrasound. (**a**) Flattened or collapsed appearance (*arrows*) of bilateral frontal calvaria at fetal ultrasound at 18-week gestational age, the so-called lemon sign, is thought to be secondary to insufficient distension of the cerebral ventricles due to CSF leakage from the myelomeningocele (*Cb* designates cerebellum). (**b**) Small posterior fossa with obliteration of the cisterna magna and wrapping of the cerebellar hemispheres (*Cb*) laterally around the pons ("p") and midbrain, the so-called banana sign. (**c**) Evaluation of the fetal spine in the transverse (axial) plane demonstrates spina bifida defect in the sacral spine with splaying of the bright vertebral pedicles (*arrows*), absent spinous process, and large anechoic dorsal meningocele (*m*). (**d**) Longitudinal (sagittal) view of the lumbosacral spine (vertebral bodies denoted by * in **c** and **d**) shows dorsal sacral myelomeningocele (*arrow*)

surrounding the spinal canal and intact layer of skin dorsally. In the setting of spina bifida, the posterior vertebrae have a U- or V- shaped configuration with splaying of the vertebral pedicles (Fig. 12.5c), absence of spinous processes, and disruption of the normal overlying integument (Fig. 12.5d), often with associated focal kyphoscoliosis. When any of these findings are identified, referral for fetal brain and spine MRI is appropriate to confirm these abnormalities and to identify any additional abnormalities that may not have been apparent on ultrasound.

Fetal and Postnatal MRI

Although fetal MRI has been performed for more than 20 years, it has become more technically feasible in the past decade through advancements in MRI coil design and development of real-time

imaging using fast T2-weighted MRI sequences, called single-shot fast spin echo (SSFSE) or half-Fourier acquisition single-shot turbo spin echo (HASTE). The subsecond image acquisition minimizes image artifact due to fetal or maternal motion, obviating the need for fetal sedation. MRI at 1.5 T is generally believed to be safe for the fetus throughout gestation, without any risk of teratogenic or developmental consequences [22, 23]. However, second trimester scan acquisition, often after 22 weeks of gestation, yields optimal image quality due to increased fetal size and decreased motion. Standard fetal brain MRI protocol at our institution includes a large field of view localizer to visualize the position of the fetus and location of the placenta in the uterus, followed by sagittal, coronal, and axial sequences with respect to fetal brain with 2–3-mm slice thickness. The images are acquired in at least two sets to guarantee that the entire brain is visualized [24]. Evaluation of the fetal spine includes sagittal and axial T2-weighted sequences with 2-mm slice thickness. Each subsequent sequence is localized based on the most recent prior to adjust for fetal motion.

In the fetus with suspected Chiari II/myelomeningocele, fetal MRI is essential to confirm the level and extent of the myelomeningocele defect (Fig. 12.6b), the severity of posterior fossa abnormalities (Fig. 12.6a), and the presence and extent of associated supratentorial brain abnormalities (Fig. 12.6c), which are often occult on ultrasound. Complete characterization of findings facilitates prognostication for optimal pregnancy and postnatal management, including consideration of termination or planning for fetal myelomeningocele surgical closure where possible.

After delivery, MRI is the study of choice for children with myelomeningocele. Three-dimensional spoiled gradient-echo acquisitions (SPGR, MP-RAGE) in the brain are best acquired in the sagittal plane and reformatted in thin (1–2 mm) coronal and axial sections. Axial and coronal T2-weighted images (either 2D acquisition with thickness of 3 mm or less or 3D volumetric acquisition with reformations in three orthogonal planes) are useful supplemental sequences. For spine imaging, it is essential to acquire sagittal and axial T1- and T2-weighted sequences. If kyphoscoliosis is present, the imaging planes should be angled such that the sagittal images are parallel to and axial images perpendicular to each straight section of spine.

MRI of the brain has identical findings whether performed in the fetus, neonate, infant, or child, although subtle anomalies such as anomalies of the cerebral cortex and smaller commissures are easier to detect in the larger brains [25]. The posterior fossa is small with little or no CSF space. The tentorium cerebelli has a low attachment and steep orientation (Figs. 12.6a and 12.7a), causing the straight sinus to have a nearly vertical course to the torcular Herophili. The cerebellum nearly fills the small posterior fossa with hemispheres wrapping laterally around the brain stem (Fig. 12.7b). As a result of the CSF leakage through the open spina bifida in utero, a rostrocaudal pressure gradient acts upon the posterior fossa structures, resulting in the characteristic downward displacement of portions of the cerebellum, brain stem, and fourth ventricle. The fourth ventricle is small and narrowed in its rostrocaudal dimension (a normal sized or enlarged fourth ventricle should raise the possibility of an isolated ventricle) (Fig. 12.7c). The pons may be pushed against the clivus, and the pressure of the hindbrain structures on the skull base can cause concave erosive changes upon that structure. The foramen magnum and tentorial incisura are enlarged due to the chronic herniation of the cerebellum through these structures. The cerebellar hemispheres and vermis are often very small possibly due to chronic ischemia from compression (Fig. 12.7d). The inferior collicula are often enlarged and stretched in an inferior and dorsal direction, while the superior collicula are small, resulting in the "beaked tectum" appearance (Fig. 12.7a, c, d). The supratentorial vault is small, again, most likely due to inadequate ventricular distension earlier in gestation; however, disproportionate ventricular dilation is common from narrowing of the aqueduct, posterior fossa crowding, or perhaps lack of dampening of CSF pulsations in the spine because the foramen magnum is occluded [26].

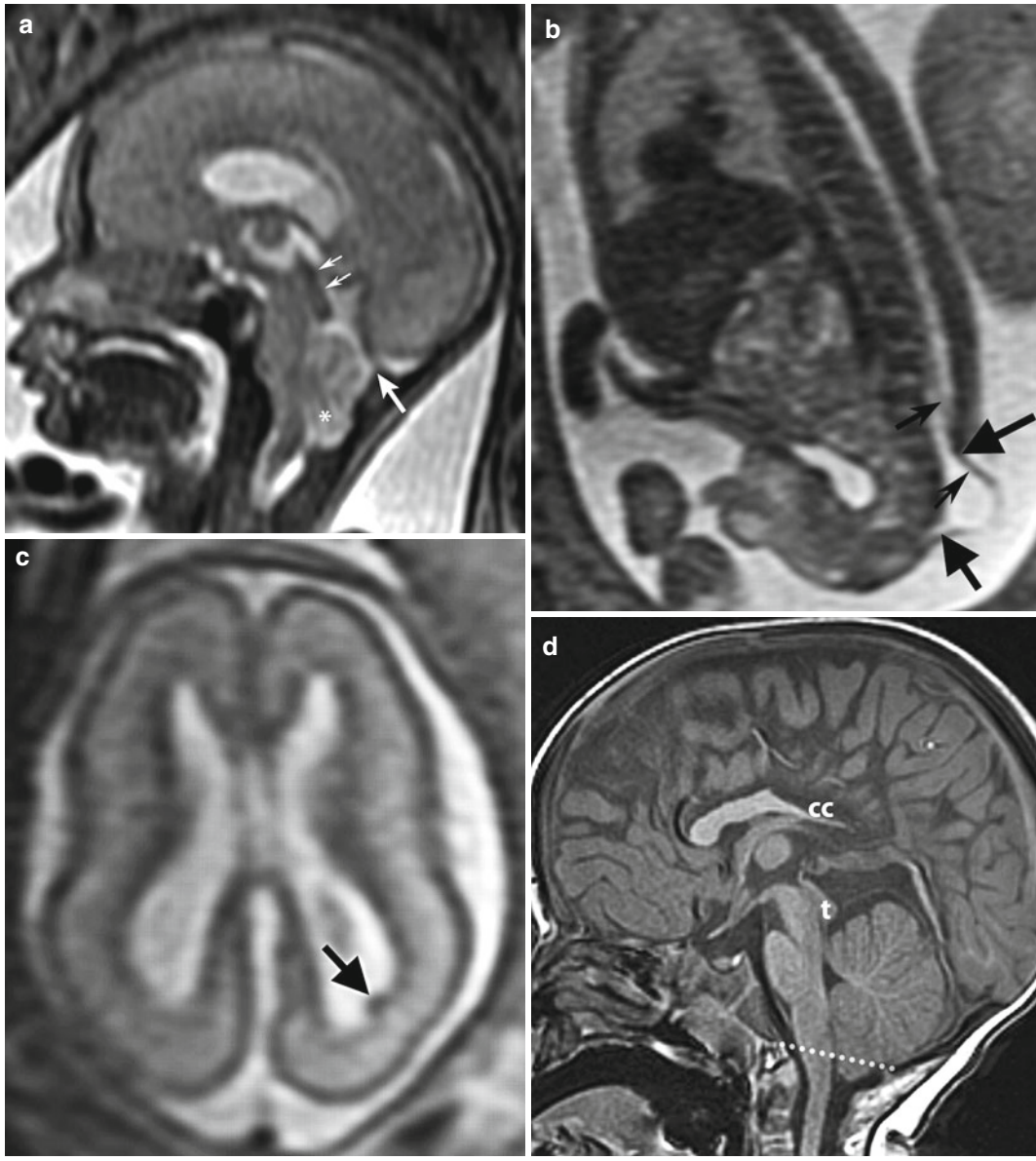


Fig. 12.6 Fetal MRI of Chiari II malformation/myelomeningocele. (**a**) Sagittal T2-weighted fetal MRI at 25 weeks gestation shows small posterior fossa with steep tentorium, narrow and low fourth ventricle, low torcular Herophili (*large arrow*), and elongated midbrain tectum (*small arrows*), with cervical ectopia of the developing inferior cerebellum (*) consistent with severe Chiari II malformation. (**b**) Spine views show lumbosacral myelomeningocele (*large arrows*) and tethered cord (*small arrows*). (**c**) Axial view through the lateral ventricles demonstrates periventricular nodular heterotopia in the atrium (*arrow*). (**d**) Following prenatal myelomeningocele repair, mild findings of Chiari II malformation at 12-month postnatal age include borderline low, rounded cerebellar tonsils, and mild posterior inferior stretching of the tectum (*t*). Note dysgenetic corpus callosum (*cc*)

Supratentorial anomalies are common, although it is not known whether they are genetic, a result of chronic hydrocephalus, or a result of the effects of chronic intracranial hypotension upon the developing brain [27]. Complete evaluation of the supratentorial brain is indicated, therefore, in all affected patients. Anomalies of the cerebral commissures are very

common. The anterior commissure is in a low position (halfway between the optic chiasm and the foramen of Monro) in 40 %. The corpus callosum has a very variable appearance. Most typically, it is thin in the posterior aspects (posterior body and splenium), similar to what is seen associated with other causes of congenital hydrocephalus (Fig. 12.7a). However, ~30 % have frank hypogenesis with absent splenium, absent rostrum, and a small posterior callosal body [28]. The cerebral white matter often has diminished volume posteriorly, particularly in patients with abnormalities of the corpus callosum [28]. It is not known whether this is a result of congenital hydrocephalus, cerebral dysgenesis related to callosal hypogenesis or dysgenesis, or a combination of the two factors. In about 10 %, white matter volume is severely diminished globally. Gray matter heterotopias are identified in 15–20 % of affected individuals (Fig. 12.7e), typically two to three nodules in the periventricular region, with the trigones/occipital horns the most common locations, followed by the frontal horns [28]. Anomalies of sulcation are commonly identified. A condition called "stenogyria (narrow gyri)," in which too

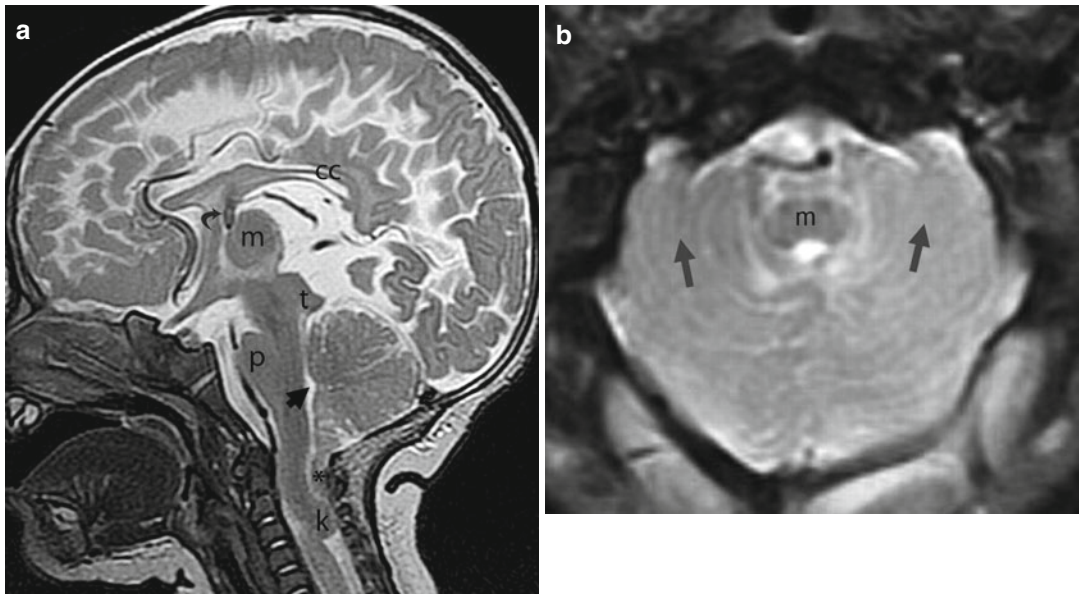


Fig. 12.7 Chiari II malformation. (**a**) Sagittal T2-weighted MRI from an 8-year-old patient born with myelomeningocele demonstrates many of the findings of the Chiari II malformation including small posterior fossa with low tentorial attachment and steep tentorial angle, with downward shift of posterior fossa contents including cerebellum (with herniation * into the cervical canal), pons (*p*), and medulla. The fourth ventricle (*large arrow*) is effaced and low. There is a characteristic cervicomedullary kink (*k*) at the C4 level. The midbrain tectum (*t*) is posteriorly and inferiorly stretched or "beaked." The massa intermedia (*m*) is enlarged. The corpus callosum (*cc*) is thin in the posterior body and splenium. This patient has a ventriculoperitoneal shunt (*curved arrow*) for treatment of hydrocephalus. (**b**) Axial T2-weighted view through the posterior fossa demonstrates wrapping of the cerebellar hemispheres anteriorly (*arrows*) around the medulla (*m*) with effacement of the posterior fossa CSF space. (**c**) In a T1 sagittal image of a different patient, fourth ventricular enlargement (*arrow*) suggests isolated fourth ventricle. This patient has a cervical syrinx (*double arrow*), which resolved after shunting the fourth ventricle. (**d**) Severe Chiari II malformation; sagittal T1 image in a different patient shows very small posterior fossa, near absence of the cerebellum (minimal residual, likely cerebellar, tissue is noted by the *arrow*), and tiny pons. Stenogyria, or increased number of small gyri is apparent in the occipital cortex (*double arrow*) most likely due to shunting of severe hydrocephalus and paucity of subcortical white matter. (**e**) Periventricular nodular heterotopia (*arrow*) and decreased posterior cerebral white matter are common associated supratentorial abnormalities, (**f**) as are dysplastic medial temporal lobes (*arrows*) with herniation across midline (*)

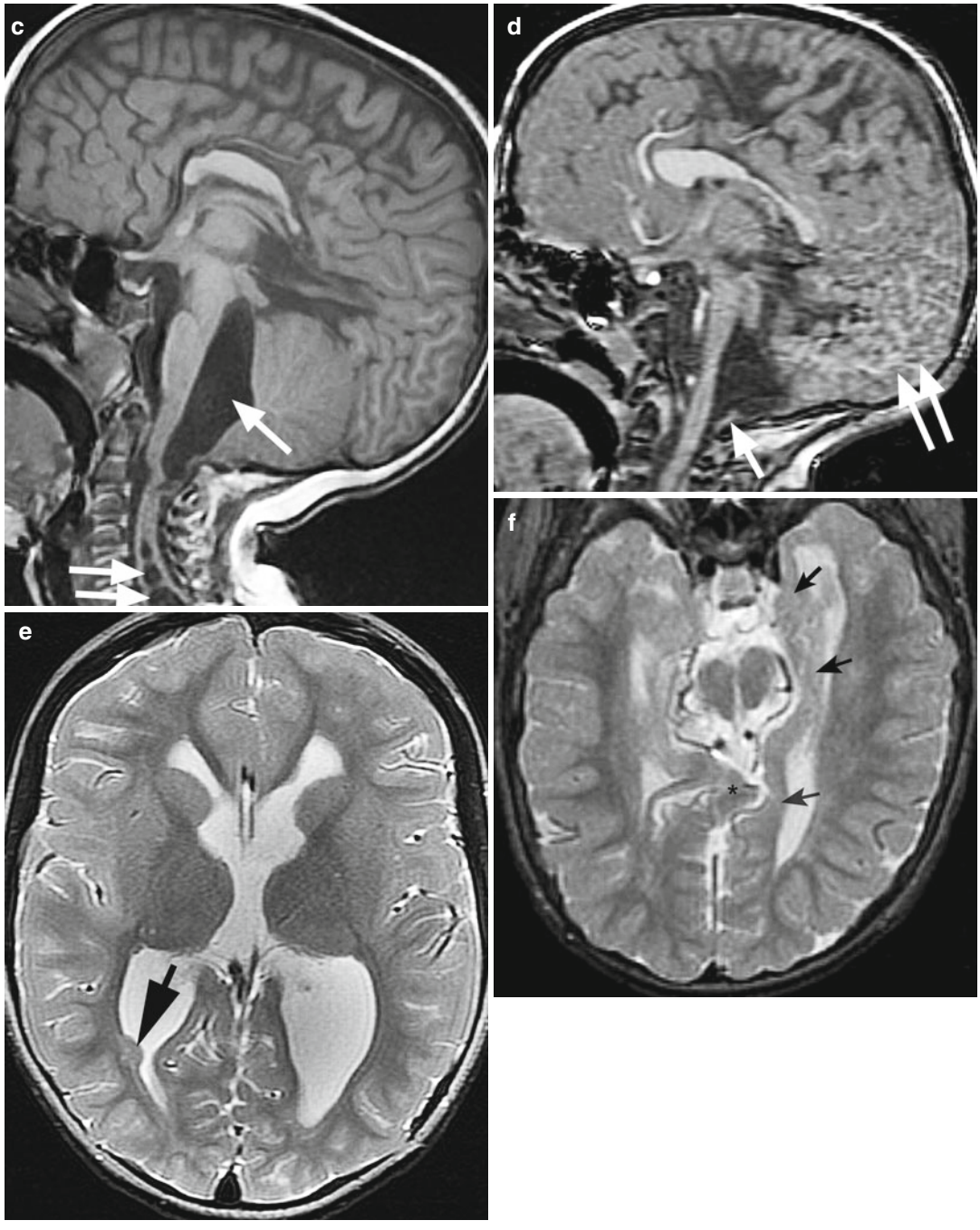


Fig. 12.7 (continued)

many small gyri are seen on the cerebral surface but histology is normal (Fig. 12.7d), is the most common abnormality, seen in about 70 % [28]. It is believed to be the result of cerebral decompression by shunting after the cortex has been stretched by hydrocephalus. Polymicrogyria has been described in humans with MMC [29], but the series was one of very severely affected patients, who died before the age of 2 years; it is very uncommonly detected by neuroimaging. In addition, a sheep model of myelomeningocele showed a "cobblestone-like" cortical malformation, perhaps resulting from disruption of the leptomeninges in utero [27]. The posteromedial temporal lobe, in particular the posterior limbic lobe, is nearly always abnormal (Fig. 12.7f), with cortical thinning, diminution of underlying white matter, and resultant huge supravermian/quadrigeminal plate/interhemispheric cisterns [28, 30]. Occasional aberrant gyri extend into this enlarged cistern, often crossing the midline. Again, the causes of these findings – fetal/neonatal hydrocephalus versus genetic versus compression of the structures in utero versus disruption of meninges during development as a result of the chronic CSF leak – are not known [30], and these abnormalities are not always evident prenatally [25].

Evaluation of the spinal cord differs on the fetal exam as compared to the postnatal (postsurgical) MRI. The purpose of the fetal spine MRI is to identify and characterize the myelomeningocele (MMC) and its levels and to look for associated spine anomalies. The spinal defect is evidenced as splayed pedicles and dorsally open neural tube with variable herniation of the neural plate beyond the spinal canal into the amniotic space (myelocele to myelomeningocele spectrum). Adjacent levels will show lack of mesenchymal tissues, bony posterior elements, and fat, interposed between the spinal canal and the surface. Severity of intracranial abnormalities, necessity of CSF shunting, and clinical prognosis are correlated with more rostral location [31]. The recent multicenter randomized trial comparing prenatal to postnatal surgical closure of myelomeningocele [32] and preceding animal studies [33] demonstrated decreased severity of the Chiari II malformation on follow-up MRI (Fig. 12.6a versus d), decreased necessity of CSF shunting, and improved early functional outcomes following prenatal repair of thoracic and lumbar myelomeningocele. Fetal MRI will likely remain an invaluable tool for characterization of MMC and Chiari II for purposes of pregnancy management and prenatal treatment.

After repair of the myelomeningocele, fetal imaging to assess the state of the hydrocephalus is best performed via ultrasound. After birth, imaging of the spine is usually performed if progressive lower extremity or bladder/bowel function is observed. Potential causes that need to be excluded include hydrocephalus, syringohydromyelia, development of congenital or acquired inclusion masses such as epidermoids, or retethering of the spinal cord at the site of MMC repair. Hydrocephalus and syringohydromyelia are best diagnosed by comparing the MRI to prior studies to look for increasing size of the lateral ventricles or the central canal of the spinal cord. Epidermoids are usually round or lobulated masses that are hyperintense on T2-weighted images (Fig. 12.8a) and hypointense on T1-weighted MRI images (Fig. 12.8b). They do not enhance after contrast administration (Fig. 12.8c). If diffusion-weighted imaging can be performed, the epidermoids will be seen as very hyperintense on diffusion-weighted images (Fig. 12.8d). Retethering of the cord as the cause of symptoms is really a diagnosis of exclusion because all repaired MMCs appear attached to dura or scar tissue at the level of the repair (Fig. 12.8a); the cord does not ascend after MMC repair. A diagnosis of retethering as the cause of symptoms cannot be made, therefore, until all other potential causes have been excluded.

Chiari III

The much more rare Chiari III malformation is also best evaluated with MRI which can characterize the contents of the occipitocervical encephalocele and associated brain and spine abnormalities. Low-dose CT may also helpful to visualize the bony cervical and/or occipital cranial defects. The MRI protocol for evaluation of the Chiari III malformation is the same as for the Chiari II malformation, including multiplanar sequences through the head and spine for evaluation of the Chiari III malformation and associated abnormalities. The purpose of imaging is to define the contents of the encephalocele, including volume of herniated cerebellum and/or brain stem, meninges, and CSF (Fig. 12.9a). MR venography is also indicated to assess the location of the dural venous sinuses with respect to the mass (Fig. 12.9b). These findings are essential for surgical planning and may be helpful for prognostication. Complete evaluation of the supratentorial brain and spinal cord is indicated due to frequent association with callosal abnormalities, gray matter heterotopia, syringohydromyelia, or tethered cord.

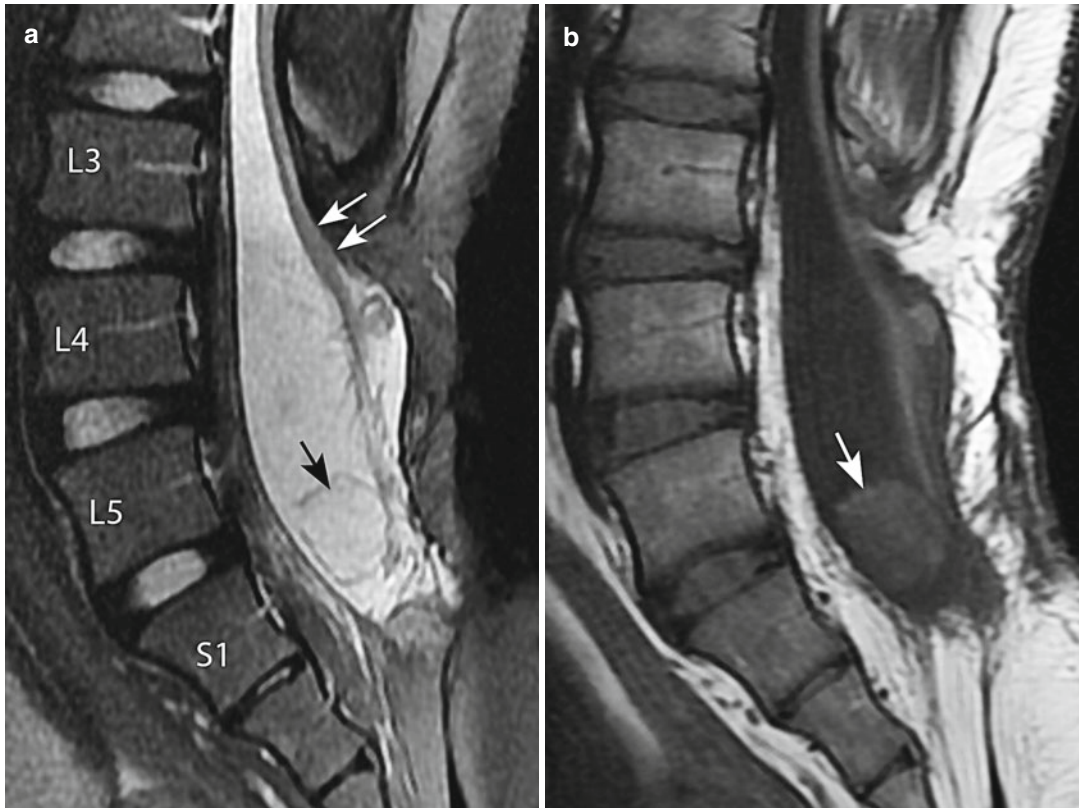
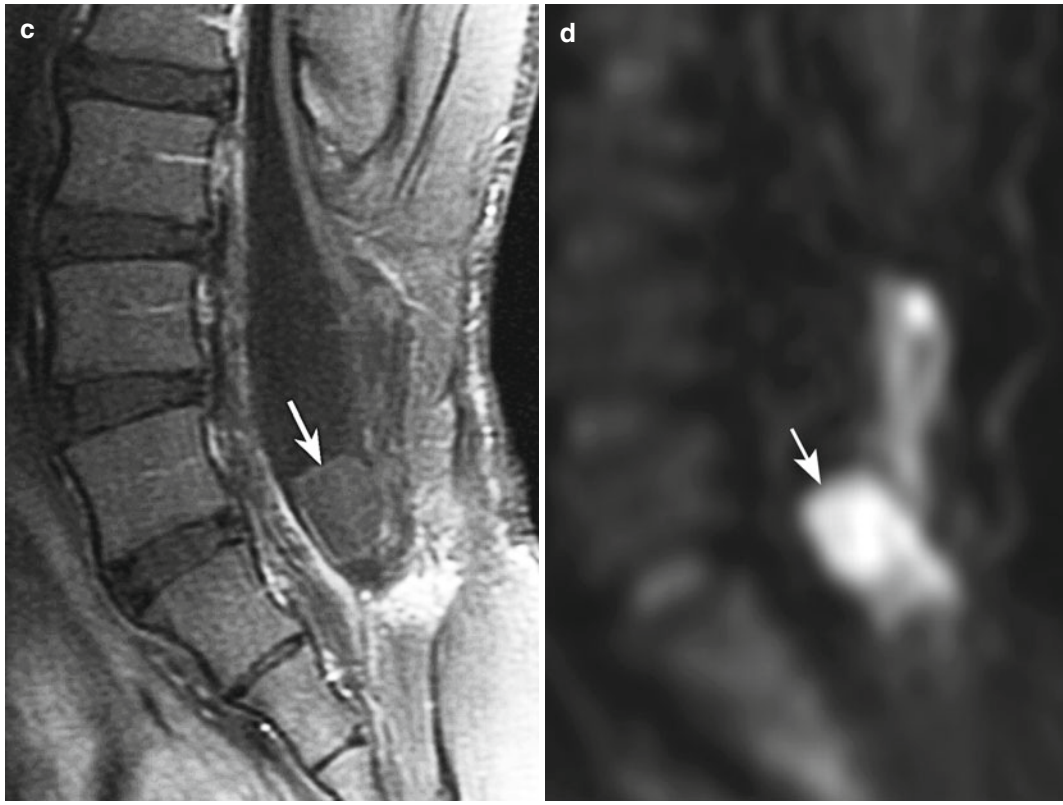


Fig. 12.8 Complications post-myelomeningocele repair. (**a**) Mass (*black arrow* in **a**, *white arrow* in **b**–**d**) within the inferior thecal sac at the S1 level is T2 hyperintense, (**b**) T1 hypointense, (**c**) non-enhancing, and (**d**) demonstrates reduced diffusion (hyperintense on diffusion-weighted image), consistent with epidermoid. Note the persistent low position of the conus medullaris (caudal-most spinal cord, *double arrow* in **a**). The cord does not ascend following repair



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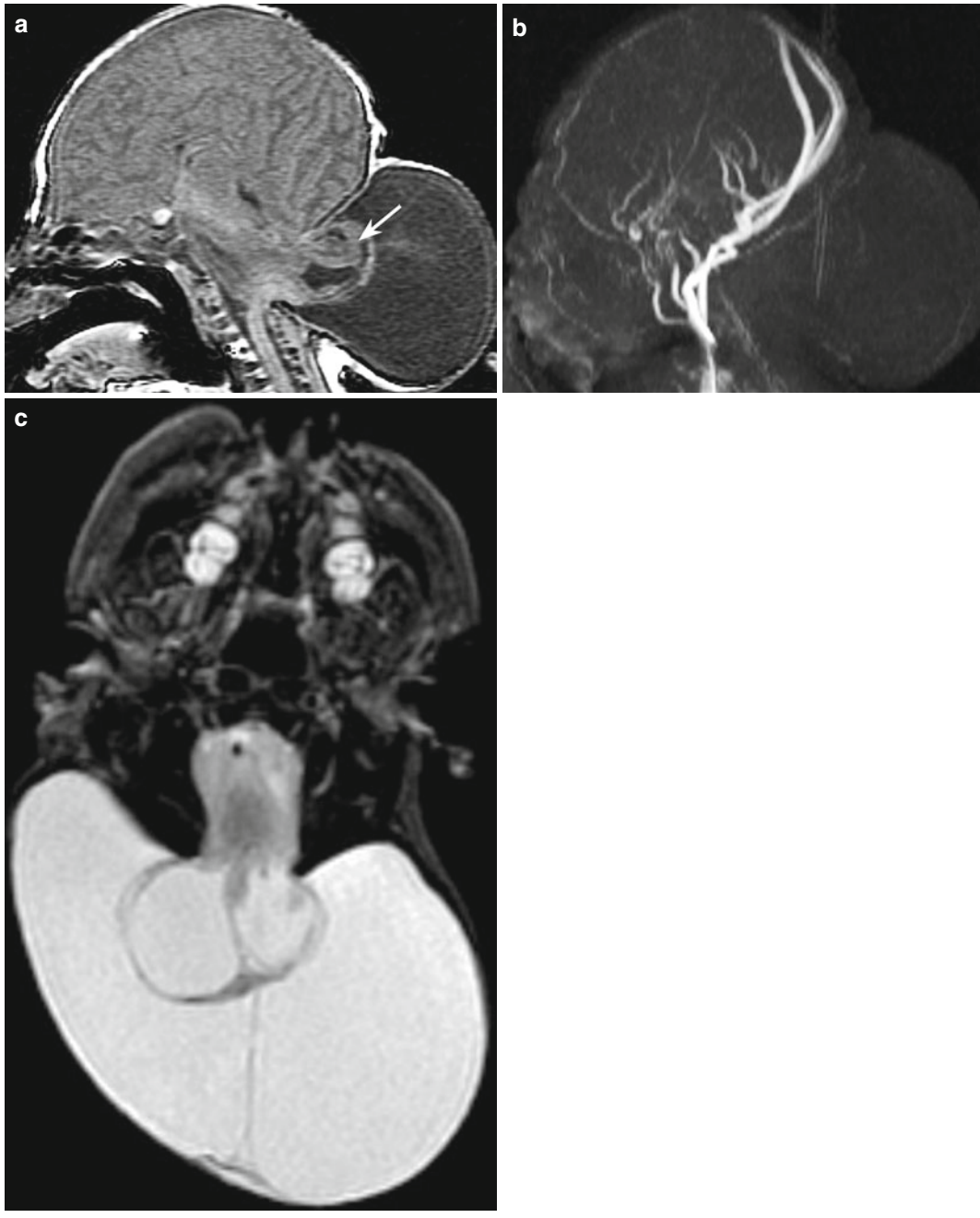

Fig. 12.9 Chiari III malformation. (**a**) Occipital encephalocele with atrophy and herniation of posterior fossa contents as well as part of the occipital lobe (*arrow*). (**b**) MR venography for surgical planning demonstrates that dural venous sinuses are not included in this large mass. (**c**) Axial T2 image shows dysplastic brain stem and cerebellar tissue herniating into larger cystic area

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13 Research on the Pathophysiology of Chiari I-Related Symptoms and Syringomyelia, with Emphasis on Dynamic MRI Techniques

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Abstract

The pathophysiology of Chiari-related symptoms and syringomyelia remains enigmatic. Present-day technology, most notably MR imaging, is providing progressively more sophisticated opportunities to test traditional as well as contemporary theories while adding to conventional animal models a selection of promising mechanical and computational representations of syringomyelia and its etiologies. We will briefly touch on the past and present of Chiari-related syringomyelia research with emphasis on essential questions related to the development of not just the anatomical anomalies but also the constellation of symptoms with which they are associated.

Introduction

Much of the Chiari literature is ridden with questions, but scarcely any answers have emerged since the time of Gardner and Williams. What causes a Chiari I malformation? If it is a mesodermal problem resulting in abnormal bone development, then why do acquired Chiari malformations exist? How important are the tonsils? If the tonsils are considered essential for a diagnosis of a Chiari I malformation, then what explains the Chiari zero? Why do symptoms arise in some patients but not in others, although the MRI images seem identical? And why does syringomyelia exist in some but not in others? Which is the best surgical Chiari decompression technique? How wide should the decompression be? Should the tonsils be reduced? Why are some of the symptoms typical and others "crazy"? Why do children fare better than adults? Why are some Chiari malformations inherited and others not?

Serious multidisciplinary research efforts should be undertaken if any of these questions is to be answered. Research from the Bernard Williams days was limited to clinical observations, basic mechanical modeling, and invasive techniques of cranial and spinal pressure monitoring. The advent of MRI, computer technology, and molecular biology has radically changed both perspective and prospects. Pathophysiological

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theories can now be tested, not just hypothesized. Invasive procedures have been for all practical purposes replaced with noninvasive technology. Probably the most important—certainly the most used—of these technologies is the ability to track CSF flow through dynamic MR imaging, quantitate it, and analyze it using intricate software programs. In this chapter, we will not address research on the embryology or pathophysiology of the Chiari malformation itself as this is covered elsewhere in the text. Instead, we will review research efforts that ask how the Chiari malformation causes clinical problems and syringomyelia. Such efforts have been productive in large part due to collaborative efforts among neurosurgeons, radiologists, engineers, and physicists. The chapter starts with an overview of previously proposed theories of syringomyelia formation and concludes with an examination of present-day tools used to explore the pathogenesis of clinical (symptoms and signs) and imaging (syringomyelia) findings in patients with the Chiari I malformation. This will consist primarily of a review of dynamic MRI flow imaging, followed by a brief overview of other propitious research efforts aimed at understanding this enigmatic anomaly.

Proposed Theories of Syringomyelia Formation

Gardner's Hydrodynamic/ Water-Hammer Theory

In 1959, Gardner and Angel suggested that syringomyelia forms because of a persistent opening of the central canal at the obex, in the setting of closed fourth ventricular outlet foramina [1]. This hypothesis was the basis upon which plugging of the obex was suggested as part of the treatment for syringomyelia. Subsequently, Gardner expanded on his theory to propose that syringomyelia is a result of direct transmission of a CSF pulse through the obex in a "water-hammer" fashion [2, 3]. The theory is based on Bering's assumption that during embryological development, pulsations from the choroid plexus contribute to expansion of the neural tube. Gardner proposed that these pulsations also help with the development of the arachnoid pathways and suggested that a balance exists between the pulsatile flow in the supratentorial and fourth ventricular choroid plexus. When this balance is disturbed, overactive supratentorial pulsations may result in tentorial migration and the development of a Chiari I malformation. In turn, compression by the posterior fossa structures leads to closure of the fourth ventricular outlet foramina, which forces CSF through the opening at the obex and into the central canal. Gardner proposed that the obstruction would first result in distension of the central canal (hydromyelia), after which the fluid would rupture into the substance of the spinal cord (syringomyelia).

Inconsistencies of Gardner's Theory

Gardner's theory could not explain the following observations [4]: First, if one were to assume that the pathophysiology of syringomyelia is invariable regardless of etiology, the hydrodynamic theory cannot explain cyst formation secondary to trauma, arachnoiditis, tethered cord, etc. Second, this single theory of pathogenesis at the foramen magnum does not account for the syrinx septations that are often evident on MRI. Third, West and Williams [5] showed using ventricular contrast studies that the obex is actually patent in only 10 % of patients, thus refuting Gardner's hypothesis. Furthermore, Milhorat and colleagues have suggested that central canal ependymitis can cause an obstruction that results in dilatation of the central canal cephalad to the obstruction. This is based on the observation that CSF can be produced by the ependymal lining of the central canal and the still unproven assumption that CSF normally flows through the central canal [6, 7].

Williams' Modifications of Gardner's Hydrodynamic Theory: The Suck Effect Theory

Based on manometric observations in normal subjects and Chiari I patients, Bernard Williams devised a theory that examined syringomyelia from another perspective [8]. Similar to Gardner, he postulated an obstruction at the foramen magnum. However, he theorized that the Chiari I malformation is an acquired anomaly that results from excessive molding of the head, perhaps

during delivery through the birth canal, which may then cause hindbrain adhesions and related outlet obstruction. In support of this claim, he showed using ventricular contrast that posterior fossa arachnoiditis correlates strongly with a history of difficult birth [5]. Williams hypothesized that hindbrain adhesions can result in transient pressure differentials between the cranial and spinal compartments due to epidural venous congestion, particularly during valsalva maneuvers (coughing, sneezing, straining). This, in turn, may cause a delay of caudad CSF flow while maintaining normal craniad flow, and as a result, fluid is "sucked from the ventricle into the central canal." Williams provided human manometric measurements demonstrating these pressure differentials and showing pressure equilibration postoperatively [8–10]. However, although this theory is more compelling than Gardner's, it fails to provide an adequate explanation of syringomyelia from other etiologies, and as with Gardner's theory, it assumes a patent opening between the fourth ventricle and central canal [11].

Perivascular CSF Dissection Theory

In an attempt to provide a more unified view of syringomyelia regardless of etiology, Ball and Dayan hypothesized that the impact of the tonsils on the posterior fossa structures results in distortion of the subarachnoid space, which then allows CSF to dissect into the perivascular (Virchow-Robin) spaces and subsequently into the spinal cord parenchyma [12]. Aboulker had a similar theory but thought that CSF dissection occurs via the dorsal roots with extension into the spinal cord.

Oldfield et al. expounded on the perivascular CSF dissection theory [13–15] by providing favorable observations using various imaging studies [13–15]. They showed that rostrocaudal movement of the spinal cord results in CSF dissection in the subarachnoid space and documented such movement both intraoperatively using ultrasonography, as well as on dynamic MRI studies. Unlike Williams' theory, in which the CSF dissection is driven by valsalva maneuvers, Oldfield et al. proposed that normal CSF pulsations provides a more or less continuous reason for fluid to enter the spinal cord. They specified that the displaced cerebellar tonsils act like a piston as they are propelled caudally with systole, thus creating a pressure wave within the entrapped subarachnoid space and syrinx. One might consider as supportive evidence of the perivascular CSF dissection mechanism, and specifically Oldfield's piston effect theory, the recent observation of a "presyrinx state," in which spinal cord edema precedes syringomyelia [16, 17]. In addition, animal studies have provided evidence that such fluid flow between the subarachnoid space and the central canal does occur under specific experimental conditions [18, 19], and intraoperative ultrasonic studies have proven the occurrence of cardiac cycle-driven syrinx wall pulsations, which in turn decrease after dural expansion. Furthermore, more recent controversial research emerged, which hypothesizes that resonance between the subarachnoid space and syrinx fluid may be the driving force that causes fluid to enter a syrinx cavity [20]. Yet, the evidence remains incomplete, and others have presented arguments against the piston effect theory, namely, that the mechanism also relies on CSF being forced from the subarachnoid space into the spinal cord, and that the exposure of the spinal cord to an outside force would be expected to crush rather than expand a syrinx [11].

Intramedullary Pulse Pressure Theory

Based on animal experiments, Greitz' group developed a theory that suggests that the fluid within a syrinx derives from extracellular fluid forced into the spinal cord from a high-pressure microcirculation rather than high-pressure CSF from the spinal cord subarachnoid space [11, 21, 22]. Specifically, they state that when the subarachnoid space is obstructed from any cause (Chiari I, tumor, arachnoiditis, etc.), there is significant decrease in pressure transmission to the distal CSF spaces and concomitant increased transmission of the systolic CSF pulse pressure into spinal cord parenchyma close to the obstruction. This imbalance of pressures between the spinal cord and subarachnoid space leads to distention of the spinal cord just below the blockage [11, 21,

22]. Furthermore, part of the systolic CSF pulse pressure is "reflected" into the spinal cord at the site of obstruction, also distending the spinal cord above the blockage [11, 23]. The repeated mechanical distention of the cord results in dilatation of the central canal and accumulation of extracellular fluid (of vascular origin) that ultimately coalesces into cavities [11, 21, 22].

In spite of tremendous advancements in technology and considerable effort by many researchers, no single theory has so far definitively solved the enigma of Chiari-related syringomyelia formation. However, the intramedullary pulse pressure theory seems to best explain the formation of syringomyelia independent of etiology.

CSF Flow Studies of the Foramen Magnum

Chiari Symptoms: A Functional Problem?

It has been suggested that the Chiari I-related symptom onset and syringomyelia formation are related, directly or indirectly, to dynamic processes in foramen magnum physiology that are not reflected on static imaging studies. More specifically, it is becoming evident that the extent of tonsillar herniation and size of the posterior fossa (both quantifiable on standard MRI) are not sufficient criteria for determining the symptomatic state of the Chiari patient. Rather, a more "functional" mechanism is at play. Possibilities include subtle chronic craniocervical instability (detailed in Chap. 14), CSF flow perturbance (central theme of this chapter), and potentially other craniocervical junction stresses that are yet elusive.

Early Work

A variety of methods have been used to study CSF flow abnormalities with no clear anatomical correlates on static MR imaging. Early on, measurements were made using invasive means. Foremost are the studies by Bernard Williams in the late 1970s [24–26], in which he calculated pressure differentials across the foramen magnum by simultaneously measuring intracranial and intraspinal pressures under a variety of clinical conditions. This allowed the study of pressure gradients in that location and showed that correction of the pressure dissociation is often associated with marked clinical improvement. Such techniques were found to support surgical indications while also providing a means of postoperative evaluation. However, with the advent of MRI, noninvasive approaches have been developed to serve the same purpose of measuring flow and pressure dynamics at the foramen magnum and elsewhere in the craniospinal axis.

Cine MRI

The idea that craniocervical hydrodynamics are altered in patients with Chiari I malformation and the possibility that partial CSF flow obstruction via tonsillar herniation and a small posterior fossa plays a role in the pathophysiology of this entity have guided most of the work in dynamic imaging. Initial applications of magnetic resonance imaging to CSF dynamic studies started in the early 1990s. The term *cine* MRI (Fig. 13.1) applies to this modality that evaluates dynamic processes (usually through blood and CSF) rather than the usual static structures (brain, dura, bone, etc.).

Early gated spin-echo MRI sequences were used in healthy volunteers to study the movement of the intracranial components and the pulsatile dynamics inside the cranial vault. Early evidence suggested that brain motion occurs in a funnel-shaped fashion as explained by the following: Blood influx into the cranial cavity during systole causes pulsatile propagation of ventricular compression and CSF displacement to the spinal canal, which leads to a complex interplay between the cranial contents—brain and CSF, both of which are vented through the foramen magnum [27]. When healthy volunteers were studied using cardiac-gated *cine* MRI, a clear relationship between the cardiac cycle and CSF flow termed "flow void sign" was detected, which consists of an area of decreased signal related to CSF flow during systole [28].

Fig. 13.1 Example of a typical qualitative cine MRI. Sagittal PC MRI showing severe flow restriction posterior to the spinal cord and tonsils at the foramen magnum, with craniocaudal flow present anteriorly (*white*). As noted in text, evaluating a severe flow restriction or near-normal flow is straightforward. The difficulties with such qualitative studies arise in patients with moderate flow restriction

Heterogeneity of CSF Flow at the Foramen Magnum

In the early 1990s, Armonda et al. conducted one of the earliest studies, in which *cine* MRI results in healthy control subjects were compared to those of Chiari I patients, before and after surgery. The authors studied CSF velocity and flow direction in four particular regions in the craniocervical junction by examining the CSF velocity profile over the cardiac cycle. They found that normal subjects had a short period of CSF flow in the cranial direction followed by a sustained period of flow in the caudal direction. Conversely, subjects with tonsillar herniation had decreased velocity and obstructed CSF flow pattern with a longer craniad flow phase. In turn, postoperative changes in velocity seemed to mirror those of normal subjects. As the resistance to CSF flow decreased by elimination of the tonsillar herniation, an increase in magnitude and duration of caudad CSF velocity on MRI was observed, accompanied in some cases by syrinx resolution and symptomatic improvement [29].

Combining Invasive and Noninvasive Techniques

Accordingly, it became evident that while static MRI sequences allowed the characterization of anatomical differences between normal controls and Chiari subjects (diameter of the CSF pathways ventral and dorsal to the neural elements at the foramen magnum, syrinx dimensions, size of the lateral ventricles, any evidence of connection between the syrinx and the fourth ventricle, size of the posterior fossa, as well as cerebellar morphology including tonsillar size and displacement), dynamic assessment via phase-contrast imaging provided information that correlates the anatomy with the physiology. This was particularly true with regard to movement of fluid within a syrinx, as well as movement of CSF at the foramen magnum and in the subarachnoid space both ventral and dorsal to the spinal cord [30]. By combining these noninvasive parameters with intraoperative CSF pressure analyses, Heiss et al. were able to experimentally confirm previous hypotheses that tonsillar impaction in a smaller posterior fossa seems to cause partial intermittent occlusion of the subarachnoid space at the foramen magnum. In turn, this occlusion creates a pressure wave that propagates in the spinal subarachnoid space to compress the spinal cord and cause a syrinx to enlarge with every heartbeat. After posterior fossa decompression, craniocervical CSF flow increases while peak CSF pulse pressure decreases [31], correlating with an eventual decrease in syrinx size [30].

Cardiac Gating to Improve MR Signal

Early motion-sensitive MRI techniques (primarily developed for blood flow applications) were plagued by variable signal loss within the cardiac cycle. This was rectified by the addition of cardiac gating. Since CSF flow is pulsatile and synchronous with the cardiac cycle, these technical improvements increased image sensitivity of CSF as well [32].

Cardiac gating was initially applied to routine spin-echo and gradient-echo MRI, which displayed CSF motion as decreased signal intensity resulting from dephasing and washout of moving spins [33].

Cardiac-Gated Phase-Contrast MRI

Phase-contrast MRI (PC MRI) is a dynamic imaging technique in which signal contrast is generated between flowing and stationary nuclei by sensitizing the phase of transverse magnetization to the velocity of motion. Two data sets with opposite sensitization are acquired. For stationary nuclei, the net phase is zero, which eliminates their signal in the final image, leaving only the residual signal from flowing CSF. The resultant signal contains information that can generate velocity data according to an intensity grayscale. Quantitative CSF velocity and qualitative flow information can be obtained by merging information from two series, usually axial and sagittal planes [34]. Further detailed result analysis using complex cardiac gating can be provided to increase sensitivity. Cardiac-gated PC MRI has become a widely used technique in CSF studies, as it allows quantification and is more sensitive to areas of slow flow [33].

CSF Flow Dynamics and Symptoms

Several *cine* MRI investigators have proposed that the added value of flow studies is that symptoms may be related more to the degree of CSF obstruction than the degree of tonsillar herniation, which would potentially aid in the selection of patients who are likely to benefit from surgical correction [34, 35]. Unfortunately, although several attempts have been made to determine the differences in flow parameters between symptomatic and asymptomatic Chiari I patients, flow perturbation at the foramen magnum has been unable to fully account for the significant differences in symptomatic states often observed between patients with nearly identical tonsillar anatomy. Another significant factor is that there may be considerable subjectivity in reading *cine* MRIs. In a 2007 study from our group, in which we asked several neuroradiologists to evaluate the same flow images in a blinded fashion, we found that the readers were more likely to agree on the presence of abnormal foramen magnum flow in symptomatic patients than in asymptomatic patients (76 % vs. 62 %) [36]. However, agreements between pairs of readers were rather low, ranging between 44 and 63 %. Of course, one would expect little disagreement when the tonsillar anatomy is very abnormal or nearly normal, with flow that is either severely restricted or near normal, respectively. In such situations, anatomical images clearly reflect the lack or presence of pathology, making flow analysis a less useful adjunct. Accordingly, most disagreements seem to occur in "gray zone" cases, i.e., in patients with moderate flow perturbation. To date, unfortunately, MRI flow analysis has been unsuccessful at separating symptomatic and asymptomatic patients under these conditions [36]. Similar investigations have been conducted to analyze CSF flow in syringomyelia. Although useful information was obtained with regard to flow velocities around the cyst cavity, these studies had equally negligible impact on understanding the pathophysiology of the anomaly or determining the need for surgery [37, 38].

Measuring Intracranial Compliance on MRI

The utility of PC MRI in the postoperative assessment of the Chiari I patient is illustrated in the work of Alperin et al., who aimed to visualize and quantify pulsatile blood and CSF flow in the craniospinal region in an effort to derive a system that determines both intracranial compliance (ICC) and intracerebral pressure (ICP) before and after posterior fossa decompression. Preliminary data suggested that intracranial compliance, as measured by these investigators, is diminished in Chiari I patients compared to healthy volunteers. Again, more work is required before this effort can result in the identification of an important diagnostic tool for guiding the treatment of patients with the Chiari I malformation [31, 39].

Analyzing Flow Velocity Voxel by Voxel: Bidirectional Flow and Velocity Jets

Analytical techniques using computer algorithms based on cardiac-gated PC MRI images can be used to generate spatial and temporal velocity

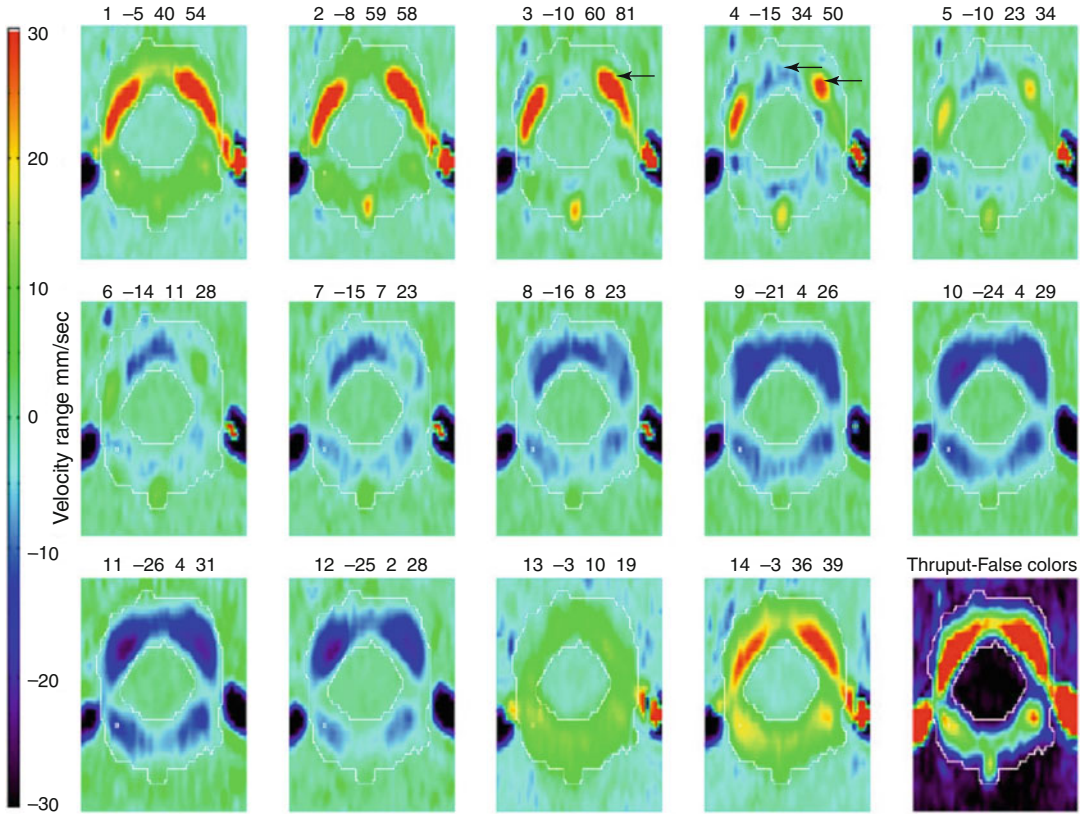

Fig. 13.2 Example of CSF flow velocity plots. Color plot of CSF flow velocity in the foramen magnum of a child with Chiari I malformation. The velocities are color-coded and displayed in consecutive images representing 14 time points during the cardiac cycle (last plot represents the throughput). Note that there is a predominance of cephalad flow in seven of the images and caudad flow in the other seven images. This color plot of velocities displays the cephalad velocities in *green*, *yellow*, and *red*, with *green* being slowest and *red* being fastest; caudad flow is displayed with *light blue*, *deep blue*, and *violet/black*, with *light blue* being slowest and *violet/black* fastest. In children, Chiari I malformation jets (*single arrow*) of elevated velocities occur in the anterior quadrants of the foramen magnum (note the *red* color for velocities nearing 10 cm/s). Finally, note the bidirectional flow evident in some of the images (*double arrows*), in which cephalad and caudad velocities coexist at one time point. Such bidirectionality of flow was not present in healthy (control) subjects

plots that illustrate the qualitative and quantitative characteristics of particular regions. In a 2004 study, our group analyzed voxel by voxel the velocity of CSF throughout the cardiac cycle in both systole and diastole, and corresponding surface contour and time-course color plots were displayed. This work showed that, in Chiari I patients, there was a preponderance of regional flow jets with significant elevations in flow velocity (Fig. 13.2). These jets, which occurred primarily anterior to the spinal cord, comprised only a small percentage of the voxels, which meant that the average flow velocity across the foramen magnum was normal. In addition, select regions within the foramen magnum of Chiari I patients exhibited synchronous bidirectional flow, i.e., CSF that travels simultaneously in the cranial and caudal directions. Such bidirectional flow was obviously absent in volunteer subjects [40, 41]. An excess of 50 qualitative and quantitative parameters was designed to assess the temporal and spatial heterogeneity within the foramen, of which four were found to be particularly useful in separating Chiari patients from control subjects. Still, our studies have not so far been able to identify parameters that specifically distinguished between symptomatic and asymptomatic states within the Chiari I population.

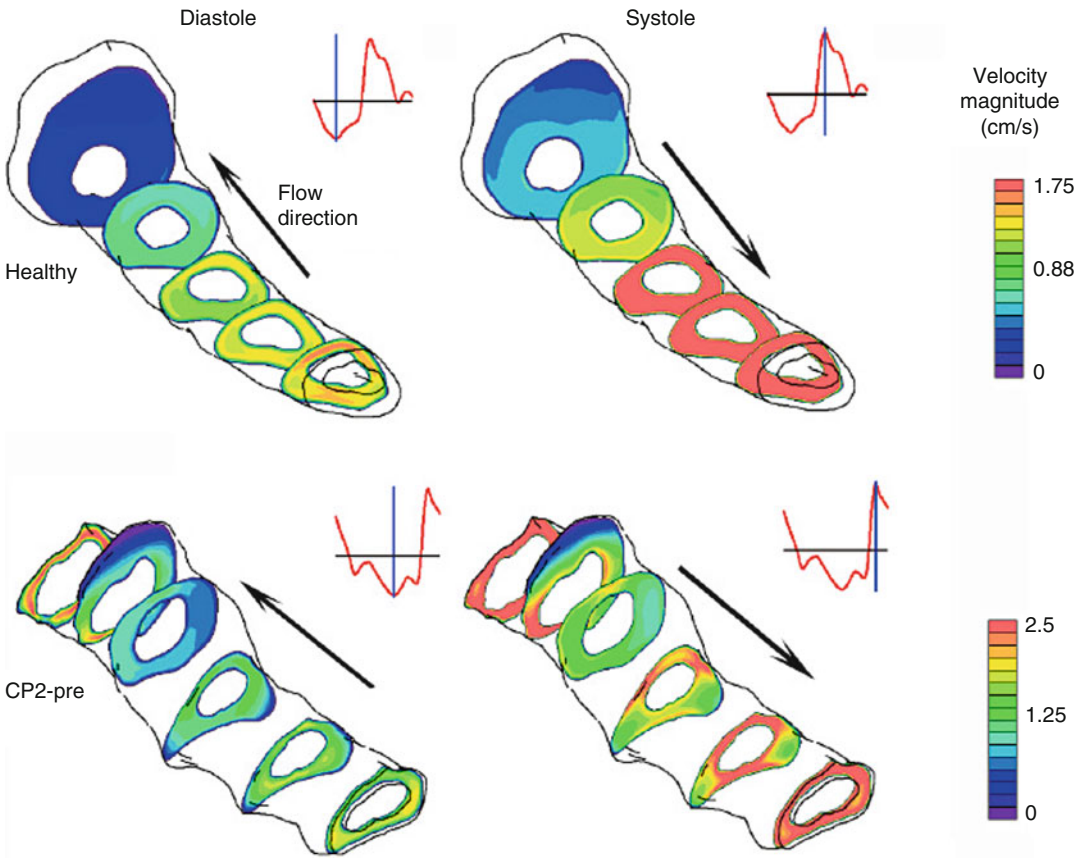

Fig. 13.3 Example of computational fluid dynamics. The spatial distribution of velocity magnitude is shown in the spinal canal below the foramen magnum for a healthy volunteer and a Chiari I patient with significant tonsillar herniation. The velocity distribution is shown at two different time points in the cardiac cycle: peak systolic flow and peak diastolic flow. These distributions of velocity were calculated using the Navier-Stokes equations under the assumption of rigid walls. The geometry and CSF flow waveform were obtained using magnetic resonance imaging data. Note that the velocity is much larger in the Chiari patient due to a reduction in the cross-sectional area of the spinal canal (Courtesy of Frank Loth, PhD [42])

Computational Fluid Dynamics

Over the past decade, a number of physicists and engineers in the fields of biomechanics and fluid dynamics showed interest in developing other modern noninvasive methodologies to study Chiari I and syringomyelia. This recent surge in enthusiasm among non-clinicians seems to have resulted largely from a serious effort by the Chiari and syringomyelia societies (the American Syringomyelia and Chiari Alliance Project, the Chiari and Syringomyelia Foundation, Conquer Chiari, and others) to enlarge the scope of research to specialists outside of neurosurgery by providing grant money and forums for discussion. This culminated in several multidisciplinary research conferences, including the first CSF Hydrodynamics Symposium (Zurich, 2011) organized and attended almost exclusively by engineers and physicists. A major part of this effort was spent on applying principles of computational fluid dynamics (CFD) to the Chiari and syringomyelia pathologies (as well as hydrocephalus). This consists of hydrodynamic modeling of the anatomic region of interest (e.g., foramen magnum) and the prediction of physical interactions between its components (Fig. 13.3). CFD allows characterization of CSF dynamics at a more advanced level as it derives its model from the anatomical and flow data obtained from PC MRI. By applying knowledge and equations from fluid dynamics to simulate CSF flow

under normal and pathologic conditions, the goal is to provide greater temporal and spatial resolution [43, 44]. Such modeling technology can be individualized to the patient's specific parameters and could potentially greatly advance the noninvasive armamentarium aimed at improving treatment and surgical planning for these and other conditions.

Conclusions

It is becoming evident that the simple descent of cerebellar tonsils to the foramen magnum may not be sufficient in creating a pathophysiological disturbance that fully explains Chiari I symptoms and syrinx formation. In fact, syringomyelia can develop as a result of foramen magnum abnormalities without obvious tonsillar herniation [45]. In addition, mere tonsillar descent can create flow alterations at the foramen magnum without the onset of either symptoms or syringomyelia. Meaningful advances in research aimed at improving patient care require close correlation between symptom states and imaging advancements. This requires close collaboration between radiologists, medical physicists/engineers, and neurosurgeons. Novel imaging and simulation tools aimed to improve diagnosis and treatment will derive from these collaborative efforts.

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Associated Bony Malformations and Instability in the Chiari I Malformation

14

Arnold H. Menezes

Abstract

The incidence of craniovertebral junction (CVJ) bony abnormalities in Chiari I malformations is between 7 and 11 %. However, the incidence of CVJ bony abnormalities having a hindbrain herniation is 33–38 %.

There are numerous bony abnormalities with Chiari I malformation in whom instability may be present. The commonest symptom is headache, centered in the base of the skull, often described as "heaviness of the head." Nausea, extreme dizziness, and vasomotor instability are frequently present. This is corrected with stabilization with temporary brace or permanently with decompression and fusion.

Introduction

The morphology of the craniovertebral junction (CVJ) and the explanation of variations in the axis and occipital bone are subjects that have engaged the attention of comparative anatomists and evolutionary biologists for the last two centuries [11]. Improvements in neurodiagnostic imaging have shown the frequent occurrence of patterns of various combinations of both nervous system and osseous abnormalities at the craniocervical junction and have suggested an interrelationship. A database analysis of 2,100 symptomatic patients referred to this author with primary CVJ abnormalities (1977–1994) identified 100 patients with the hindbrain herniation syndrome [10]. Atlas assimilation was the common bony anomaly in these 100 patients with basilar invagination in 92, and 20 showed paramesial invagination. Sixty-six patients of these 100 had cervical C2–C3 vertebral segmentation defects, and syringohydromyelia was evident in 46 individuals. A proatlas segmentation abnormality was present in eight. A common finding of atlas assimilation and Chiari malformation in the 92 patients showed that 70 of them had a shortened clivus with condylar hypoplasia. The posterior fossa was reduced in its vertical height and was further compromised by the basilar invagination, which was present in the majority of individuals.

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Incidence of Bony Anomalies Associated with Chiari I Malformation

In a recent comprehensive review of 364 symptomatic patients with Chiari I malformation, Milhorat et al. found associated syringohydromyelia in 65 % of cases, scoliosis in 42 %, an abnormal retroflexed odontoid process in 26 %, and basilar invagination in 12 % [18]. This is a series which was not skewed to bony abnormalities at the craniocervical junction. In contrast, this author reviewed our Chiari I malformation database, which was different from the craniovertebral junction database, in 2005 [17]. A total of 639 patients had undergone an operative procedure for a Chiari I malformation. Two hundred and seventy-six of these had craniovertebral junction bony abnormalities of which 41 were reducible and 46 % had syringohydromyelia. There were 363 patients who did not have a bony abnormality at the craniocervical junction. The incidence of instability in these patients was 8 %. Sixty-seven percent had syringohydromyelia.

In a study "based on 190 surgically treated patients with basilar invagination," Goel et al. [6] grouped these into those that did have a Chiari I malformation and those that did not have a Chiari malformation. Eighty-eight of the 190 patients with basilar invagination did not have a Chiari malformation. One hundred and two patients had a Chiari I malformation associated with the basilar invagination and 50 % had a syrinx. Perrini et al. reviewed their surgical management of craniovertebral junction malformations and recognized 34 adult patients in a 7-year span who underwent operation [20]. This was for basilar invagination, and 13 of the 34 had an associated Chiari I malformation. Of these, three had a syrinx. In a long-term follow-up of Chiari-related syringomyelia in adults, Aghakhani et al. analyzed 157 surgically treated cases of Chiari-related syrinx and found that only 11 of the 157 (7 %) had basilar invagination or "platybasia" and basilar impression [1]. Thus, the incidence of a Chiari I malformation having craniovertebral junction bony abnormalities is between 7 and 11 % [11, 12]. On the other hand, the incidence of craniovertebral junction bony abnormalities having a hindbrain herniation present is between 33 and 38 % [13]. Table 14.1 refers to the associated bony anomalies with the Chiari I malformation in whom instability may be present at the craniocervical junction. In this author's series, these can be conveniently divided into those of congenital origin, the developmental and the acquired [12, 21].

Instability with the Chiari I Malformation

The preceding chapters have dealt with the symptomatology and the diagnostic imaging recommended for patients with the Chiari malformations. The symptoms of craniovertebral junction instability in patients with the Chiari I malformation with or without syringohydromyelia have headaches as their main symptom. This was present in 82 % of patients whose headaches were worse with exertion or standing [4]. These seem to be relieved by lying down or supporting

Table 14.1 The Chiari malformations: associated bony anomalies/instability

Congenital	Developmental	Acquired
Proatlas segmentation failures (dorsal, ventral, lateral)	Atlas assimilation with segmentation failure C2–3	Basilar impression with bone-softening states
Condylar hypoplasia	Basilar invagination	Os odontoideum
Hypoplastic clivus		Chiari secondary to craniofacial dysostosis and Klippel-Feil
Retroflexed odontoid		Ehlers-Danlos, Marfan's
		Chiari with instability secondary to holocord syrinx and repeated operations
		Morquio's
		Taybi-Rubinstein

their head. The common thread of complaint was a feeling of "heaviness in the head" and "I feel that I have to support my head." This is translated into holding or supporting the head even in a sitting position. The headaches usually are centered in the base of the skull at the junction with the cervical spine. They may project upward but usually are associated with a feeling of nausea unless lying down. Numbness in the scalp or the face was present in 34 % and torticollis in 15 % [4]. Vasomotor instability presented as extreme dizziness and nausea with the headaches and a feeling of impending crisis with exertion. They had relief of these headaches with head support using brace, collar, or cervical traction.

The diagnosis of the craniovertebral bony abnormalities and instability is dependent on complete imaging of the CVJ with preoperative CT and MR studies [14, 23]. A three-dimensional reconstruction of the craniocervical region is made to define the surgical anatomy as well as the bony abnormalities [16]. Also, dynamic MR imaging in both the flexed and extended position is obtained to evaluate the extent of ventral and dorsal cervicomedullary compression, respectively, and is a key component in determining reducibility of the abnormality. Stabilization is of paramount importance for reducible lesions at the craniocervical junction in order to maintain the neural decompression [23]. Irreducible lesions require a decompression at the site of compression. This may be in the form of cervical traction and followed by appropriate decompression and fusion.

Table 14.2 outlines the indications for craniocervical junction fusions in patients with the Chiari I malformation [4]. For ease of recognition, these have been divided into (A) bony abnormalities with reducible compression on the cervicomedullary junction. Into this category would fall the reducible basilar invagination as well as patients in whom cervical traction can be obtained intraoperatively with documentation with intraoperative CT, (B) previous ventral cervicomedullary decompression such as after the resection of clivus-odontoid for bony decompression of the cervicomedullary junction, (C) innate occipitocervical instability in situations such as Noonan's syndrome, and (D) musculoligamentous instability. This category is quite significant and the table is self-explanatory.

Table 14.2 Indications for CCJ fusions in patients with CMI/SHM 1996–2010: 355 (2.5–86 years) – 128 (36 %) <16 years

(A) CCJ abnormalities with reducible compression of CMJ (25 %)
e.g., atlas assimilation with reducible atlantoaxial dislocation. Reducible basilar invagination
(B) Previous ventral cervicomedullary decompression (44 %)
e.g., after transoral resection of bony compression of CMJ
(C) Occipitocervical instability with CMI/SHM with bony abnormalities (26 %)
e.g. Noonan's syndrome
(D) Musculoligamentous instability (15 %)
e.g., 1. Neurogenic: syrinx in upper cervical cord
2. Pathologic states: Ehlers-Danlos, Down syndrome
3. After repeated posterior fossa procedures secondary to muscle dehiscence, fibrotic scar

SHM syringohydromyelia, *CCJ* craniocervical junction, *CMI* Chiari malformation I, *CMJ* cervicomedullary junction

Implications of Bony Abnormalities in the Chiari I Malformation and Craniocervical Instability

Once a bony abnormality is detected at the craniocervical junction, it is important to decide whether this is playing a part in the patient's symptoms within the sphere of the Chiari I malformation. A ventral or lateral compression of the cervicomedullary junction or the medulla that reduces with dynamic positions of the head should be documented with magnetic resonance imaging. If this is a reducible situation whereby the neural compression is relieved off the bony mass, then a dorsal posterior fossa decompression procedure should be completed with an occipitocervical fusion [7, 8, 11]. In individuals below the age of 15, we have performed intraoperative crown halo traction under general anesthesia using muscle relaxation and changing head

position with traction so as to allow for relief of the bony compression [3]. This has to be documented with intraoperative CT. Furthermore, it should be documented both in the supine as well as in the prone position into which the patient would be placed for the definitive procedure. If the lesion is irreducible, then the ventral or lateral compression must first be relieved and followed by a dorsal procedure for the Chiari malformation and fusion. It is critical to differentiate between distraction and reduction [2, 3, 8]. A reducible situation implies relief of neural compression with restoration of anatomical alignment [23]. Mere distraction does not provide reduction. This author has shown that atlas assimilation or "occipitalization of the atlas" is the most common bony abnormality. This, when present, is usually associated with a hypoplastic clivus. In a publication by Gholve et al., 30 children were identified with "occipitalization of the atlas" and were carefully studied [5]. Fifty-seven percent had a C1–C2 instability and "most had congenital C2-C3 fusion." In our series, atlas assimilation was encountered in 550 of 6,000 patients in the craniovertebral junction database [11, 16, 22]. Hindbrain herniation occurred in 38 %. The situation was compounded by failure of segmentation of the second and third cervical vertebrae. In this situation of atlas assimilation, segmentation failure of C2 and C3, atlantoaxial instability occurs as a result of abnormal loads placed on patent motion segments. Initially, the instability is reducible and through a series of events with pannus formation around the odontoid process, the lesion becomes irreducible [10]. This then results into upward migration of the odontoid process by the time the child is between 14 and 15 years of age [11]. The bony abnormality is then an irreducible basilar invagination. Thus, a child who is being evaluated for atlantoaxial dislocation is more likely than a full-grown adult to have a reducible atlantoaxial dislocation or a reducible basilar invagination. It is critical that an operative procedure for "hindbrain herniation" address potential instability also to avoid unfortunate results in the short or long term.

Basilar invagination is commonly associated with an abnormal odontoid process invaginating into the posterior fossa. Of significance is the fact that the body of the axis becomes elongated and the true odontoid process is small. Of greater significance is the abnormal clivus-odontoid articulation. The resultant abnormal clivus-canal angle produces a ventral indentation of the pons, medulla, or cervicomedullary junction. As has been described before, the ability to reduce invagination is related to age in the presence of atlas assimilation. Reduction of the bony abnormality with traction or distraction can result in improvement of the craniocervical relationship and relief of compression on the cervicomedullary junction. This has been documented with postoperative imaging. On the other hand, an irreducible lesion will require decompression first. Restoration of posterior fossa volume by bony decompression, whether by traction or surgical resection, has been shown to produce upward migration of the tonsils and relief of the syrinx when present [15]. This phenomenon in the reverse, with reduction of posterior fossa volume, has led to severe hindbrain herniation in patients with osteogenesis imperfecta and related osteochondrodystrophies [2, 9, 15, 19, 21, 22]. This same mechanism may be present in patients with os odontoideum who develop a secondary "Chiari I malformation."

Craniocervical instability with Chiari I malformation and syringohydromyelia for all the reasons documented in Table 14.2 will require treatment [4]. A properly fitting brace such as the "Aspen or Miami J collar" can be both diagnostic and therapeutic. If the patient has relief of symptoms, it would imply that a fusion would be beneficial in the long term. Below the age of 7, we prefer to use a bony fusion alone. Beyond that age, it is possible to use rigid fixation using plates and screws depending on the size of the bony anatomy.

Illustrative Cases

Case 1

This 3-year-old presented with headaches when he was playing, episodic emesis, and coughing. He was diagnosed as having gastroesophageal reflux. On examination, the main findings were absence of a gag reflex and significantly abnormal hyperactive deep tendon reflexes in the upper and lower extremities. He walked with an extremely broad-based gait. Magnetic resonance imaging revealed atlas assimilation with segmentation failure of C2 and C3 vertebral bodies and gross atlantoaxial instability. The odontoid process indented into the pontomedullary junction (Fig. 14.1). The cervicomedullary buckle was seen at the mid C2–C3 level, and a hindbrain herniation was evident. This was relieved with the patient being in extension and the predental interval became normal. At posterior fossa decompression, the assimilated atlas was resected. A dorsal occipitocervical fusion was made using full-thickness rib grafts between the occiput and C2. He was maintained postoperatively in an occipitocervical molded shell brace for 6 months. His symptoms resolved. This is an example of a reducible craniocervical bony abnormality.

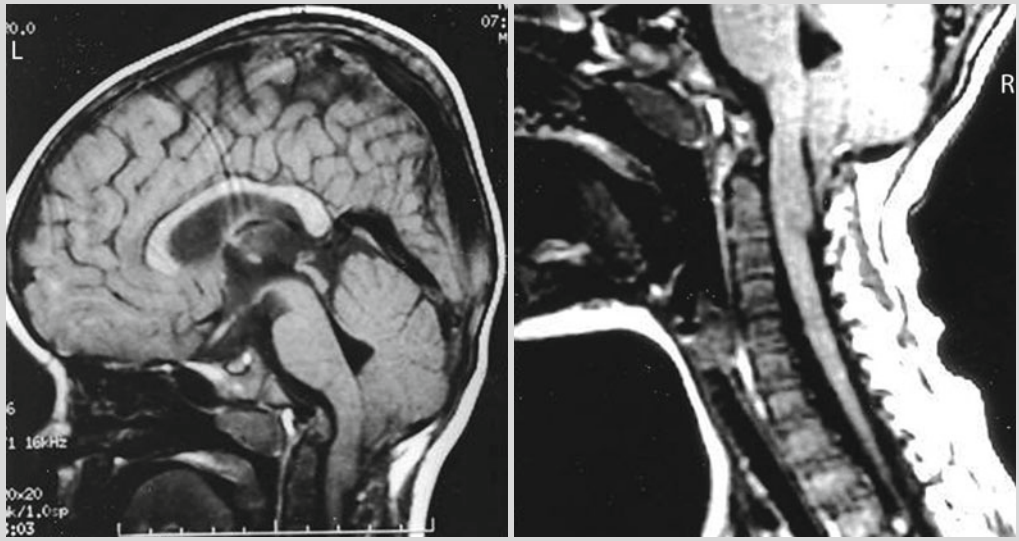

Fig. 14.1 Composite of midsagittal T1-weighted MRI of craniocervical region in flexion (*L*) and extension (*R*). There is atlas assimilation, segmentation failure of C2–C3 vertebral bodies, and gross atlantoaxial instability. The odontoid indentation into the ventral medulla corrects in extension. There is hindbrain herniation

Case 2

This 12-year-old girl presented with occipital and frontal headaches, difficulty swallowing, a lisping speech, and ataxic gait. She had a reduced gag reflex, decreased sensation to the back of the tongue with partial atrophy. The deep tendon reflexes were grossly exaggerated. She was ataxic in neutral position. Magnetic resonance imaging and 3D CT of the craniocervical junction revealed a proatlas segmentation abnormality as visualized in Fig. 14.2a, b. A cervicothoracic syrinx was also indentified. She underwent ventral transpalatopharyngeal decompression of the ventral medulla and a posterior dorsal occipitocervical fusion. Her symptoms resolved. This is an example of an irreducible ventral bony abnormality associated with the Chiari I malformation.

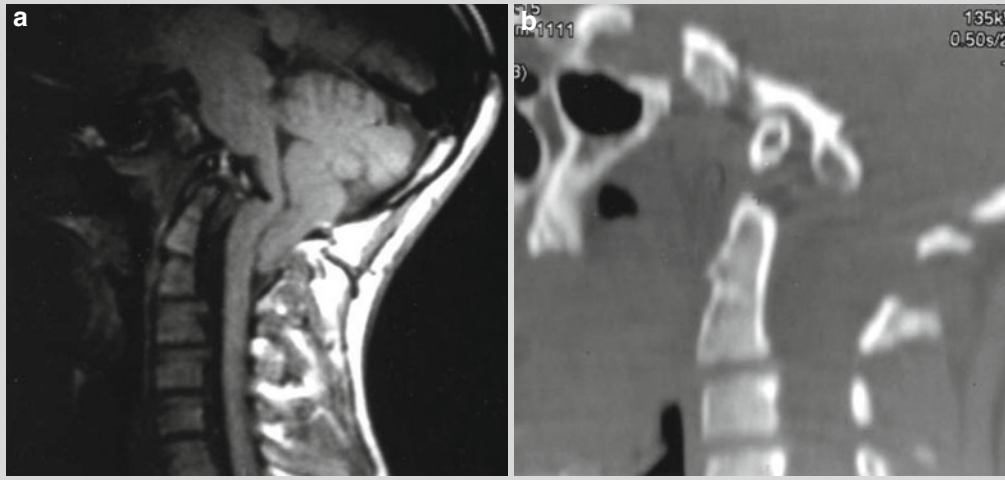

Fig. 14.2 (**a**) Midsagittal T1-weighted MRI of brain and cervical cord. Note the tonsil descent, ventral bony abnormality indenting into the medulla oblongata. (**b**) Midsagittal 2D CT reconstruction of craniovertebral junction reveals the proatlas abnormality as an extension of the clivus

Case 3

This 28-year-old had a history of unrelenting "migraine headaches" and a choking sensation with swallowing. She noticed diminished dexterity in her hands and decreased sensation in her face. On examination, she had a partial glossopharyngeal and vagus nerve palsy with gross hyperreflexia and reduced pain sensation in her face down to the mid neck on the right. Imaging demonstrated atlas assimilation with a short abnormal clivus and an acute angle to the clivus-canal junction (Fig. 14.3). She had basilar invagination, Chiari I malformation, and ventral cervicomedullary compression. The craniovertebral junction abnormality was irreducible and required transpalatopharyngeal resection of the clivus-odontoid process. She was noted to be extremely unstable intraoperatively, and a dorsal occipitocervical fusion was performed.

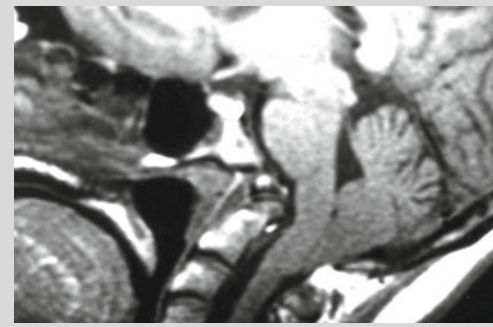

Fig. 14.3 Midsagittal T1-weighted MRI of cervicomedullary junction (CMJ). There is basilar invagination, atlas assimilation, short clivus, reduced clivus-canal angle, ventral CMJ compression with Chiari I abnormality

She recovered the cranial nerve deficits and facial sensation.

Case 4

This 14-year-old boy with osteogenesis imperfecta presented with difficulty swallowing and weakness in his hands. Magnetic resonance imaging confirmed the severe "secondary basilar invagination" or basilar impression with marked crowding of the posterior fossa structures and clivus-canal angle of nearly 90°. There was tonsillar descent and ventral compression of the medulla (Fig. 14.4). He responded to a high transpalatopharyngeal approach with decompression of the medulla and a dorsal posterior fossa decompression with fusion. This is an example of a secondary appearance of the Chiari I malformation as a result of marked reduction in the posterior fossa volume.

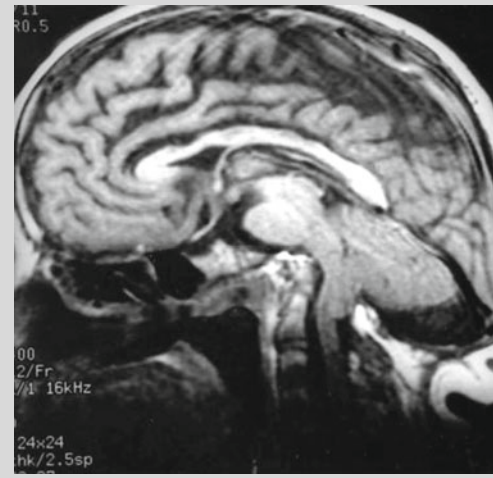

Fig. 14.4 Midsagittal T1-weighted MRI of brain in a 14-year-old with osteogenesis imperfecta. There is severe basilar impression and upward location of the cervical spine with marked reduction in posterior fossa volume and tonsillar herniation

Case 5

This 10-year-old presented with exertional headaches as well as a feeling of being unable to support her head. She had difficulty swallowing solids and had a slow wide-based abnormal gait. Her cervical muscles were weak. Magnetic resonance imaging showed a clivus-canal angle of 92° in flexion, which changed to 127° in extension (which would be considered as being normal) (Fig. 14.5a). She responded to cervical traction, and using an Aspen cervical brace, her headaches were relieved though the rest of the neurological symptoms persisted. The high cervical syrinx was noted. She underwent intraoperative crown halo cervical traction, posterior fossa and foramen magnum decompression with intradural procedure, shrinkage of the cerebellar tonsils, and cervical fascia duraplasty. An occipitocervical fusion completed the operative procedure. Her postoperative MRI shows (Fig. 14.5b) the maintenance of the normal clivus-odontoid angle and disappearance of the cervical syrinx. She is 4 years following her operative procedure and is doing well.

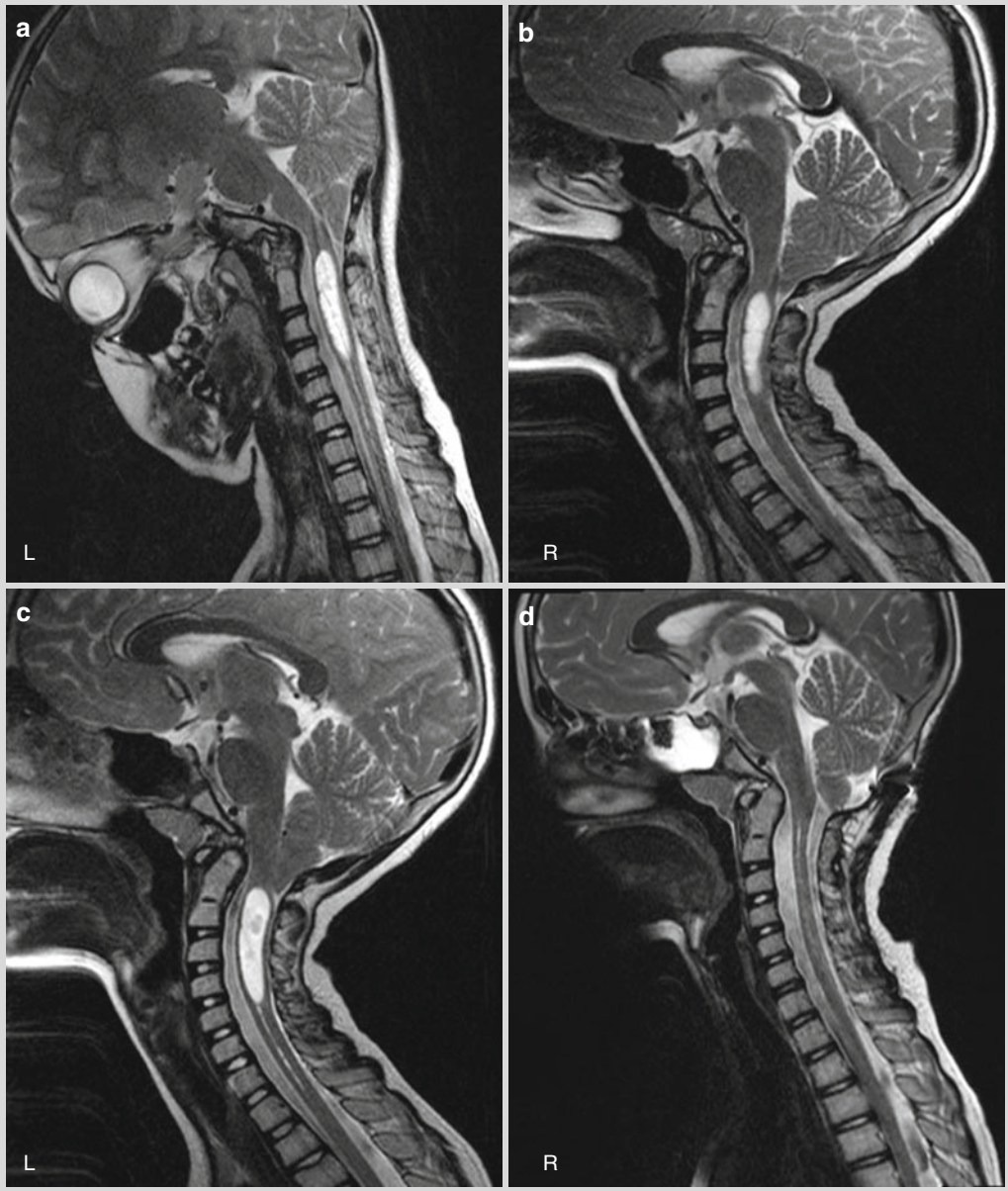

Fig. 14.5 (**a**) Composite of midsagittal T1-weighted MRI in flexion (*L*) and extension (*R*). The clivus-odontoid angle of 92° (*L*) changes to 127° (*R*) in extension. This signifies craniocervical instability. Note the CM1 with high cervical cord syrinx. "Valsalva-type headaches" were present together with a feeling of a "heavy head." She had weak cervical musculature. (**b**) Composite of T2-weighted MRI of brain and cervical cord; preoperative (*L*) and postoperative (*R*). She underwent posterior fossa decompression with duraplasty and occipitocervical (O-C2-C3) fusion. The tonsils have ascended and the syrinx is not seen

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Non-Hindbrain-Related Syringomyelia

15

Jörg Klekamp

Abstract

Syringomyelia is not a disease in its own right but a manifestation of another disease process, which incorporates an obstruction of cerebrospinal fluid (CSF) flow in the spinal canal, tethering of the spinal cord, or an intramedullary tumor. Whenever a syrinx is demonstrated, the clinical examination and the analysis of the patient's history as well as neuroradiological imaging have to concentrate on identifying the underlying cause of the syrinx. If the cause of syringomyelia can be identified and treated successfully, the syrinx will regress and clinical symptoms will improve or remain stable for the future. Whereas diagnosis and treatment of Chiari malformations and intramedullary tumors are well established, the significance of spinal arachnopathies for development and successful treatment of syringomyelia is still not widely recognized. This chapter describes diagnostic and management algorithms as well as results of treatment for patients with syringomyelia related to spinal arachnopathies.

The term syringomyelia was introduced by Ollivier d'Angers in 1827 [1] for cystic cavitations of the spinal cord. Syringomyelia describes a progressive accumulation of fluid inside the spinal cord. Even today, no pathophysiological concept for the development of syringomyelia is generally accepted. However, with the advent of modern imaging techniques in the 1970s and 1980s, it became clear that a syrinx is always associated with other pathologies in the spinal canal or craniocervical junction. This observation has changed treatment concepts for these patients in a fundamental way. If the associated pathology can be treated successfully, no further measures for the syrinx are needed. It is now widely accepted that syringomyelia is related to intramedullary tumors or pathologies that cause a disturbance of cerebrospinal fluid (CSF) flow or spinal cord tethering [2]. Table 15.1 gives an overview on the different pathologies related to syringomyelia in the author's series.

Currently, syringomyelia is considered as an accumulation of extracellular fluid of the spinal cord [2, 3]. In case of intramedullary tumors, it is generally believed that alterations of the blood-spinal cord barrier play a major role [4]. However, this may not be the only mechanism. It is

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Table 15.1 Pathologies associated with syringomyelia

Diagnosis	Total	Syringomyelia
Craniocervical junction		
Chiari I	559	430 (76.9 %)
Chiari II	42	28 (66.7 %)
Foramen magnum arachnoiditis	23	23
Posterior fossa tumors	7	3 (42.9 %)
Posterior fossa arachnoid cysts	10	5 (50 %)
Spinal canal		
Posttraumatic syringomyelia		137
Nontraumatic arachnopathies		280
Intramedullary tumors	301	156 (51.8 %)
Extramedullary tumors	603	74 (12.3 %)
Extradural tumors	467	8 (1.7 %)
Tethered cord syndromes	130	46 (35.4 %)
Degenerative disc disease		63

noteworthy that infiltrating intramedullary tumors rarely produce syringomyelia, whereas a syrinx is a common feature of displacing neoplasms [5]. More information is available on the effects of CSF flow obstructions on the spinal cord from animal [6] as well as computer models [7]. The subarachnoid space pressure is increased above the obstruction inducing changes of extracellular fluid distribution in the spinal cord [6], which may then lead to syringomyelia [2, 3, 8]. Increased flow in the perivascular spaces has been implicated for this effect [2, 6, 9–12]. If flow capacities in the extracellular space are exceeded, there appears to be an evolution from spinal cord edema, that is, the so-called presyrinx state, to syringomyelia [13]. Intramedullary neoplasms and cord tethering may alter extracellular fluid movements to similar effects. Once syringomyelia has developed, the increased intramedullary pressure [14] and fluid movements inside the syrinx [15, 16] may lead to spinal cord damage [17–19] and progressive neurological symptoms.

Diagnosis

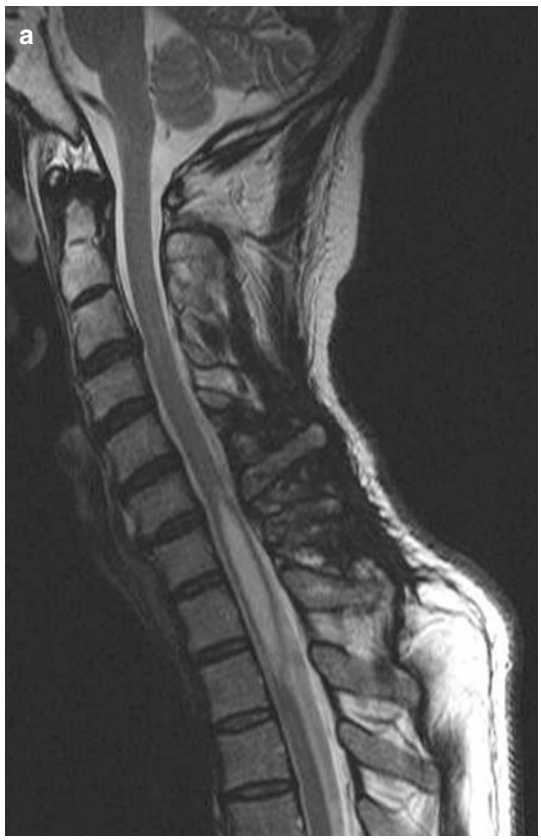
In patients with Chiari malformations, CSF flow can be compromised by cerebellar tonsils filling the space of the cisterna magna, by arachnoid scarring in the foramen magnum area, and by obstruction of the foramen of Magendie. In posttraumatic syringomyelia, CSF flow obstruction may be caused by arachnoid scarring at the trauma level and narrowing of the spinal canal due to posttraumatic stenosis or kyphosis. Furthermore, posttraumatic cord tethering may contribute to syrinx development.

In the absence of a craniocervical malformation, an intramedullary tumor, or a history of spinal trauma, syringomyelia is still considered idiopathic by many physicians. However, these patients have to be evaluated very carefully for radiological and clinical signs of arachnoid pathologies in the spinal canal causing CSF flow obstructions. The syrinx starts at the level of obstruction and expands from there. If the syrinx expands in a rostral direction, the obstruction will be found at the caudal end of the syrinx and vice versa. This also implies that the obstruction will most likely be found close to the largest diameter of the syrinx (Fig. 15.1).

Due to the pulsatile movements of arachnoid septations, webs, or cysts, standard MRIs may not always be able to demonstrate an arachnopathy directly. With a history of spinal meningitis or subarachnoid hemorrhage [20], the often quite extensive arachnopathy is rather easy to diagnose on MRI (Fig. 15.2). Many arachnopathies, however, are quite discrete and extend over a few millimeters only. Cardiac-gated cine MRI should be

employed for such instances to study spinal CSF flow to identify areas of flow obstruction, which may correspond to such circumscribed arachnoid pathologies [16] (Fig. 15.1). Sometimes significant flow signals can also be detected in the syrinx itself. In such cases, the highest flow velocities in the syrinx can be expected adjacent to the arachnoid scarring (Fig. 15.1). The spinal cord should be studied with thin axial slices with T2-weighted imaging over the entire extent of the syrinx to search for areas of cord compression, displacement, or adhesion to the dura [21, 22] (Figs. 15.1, 15.2, and 15.3). In the sagittal plane, the contour of the cord may appear distorted in areas of arachnoid scarring. CISS sequences can be used not only for the demonstration of the syrinx [23] but may also be helpful to detect arachnoid webs, scars, and cysts, because this technique is less susceptible to CSF flow artefacts [23]. Myelography and postmyelographic computer tomography (CT) are alternative methods for demonstrating arachnoid pathologies but have a lower sensitivity.

The sequence of events leading to a syrinx has implications not only for the neuroradiological appearance as just described but also for the



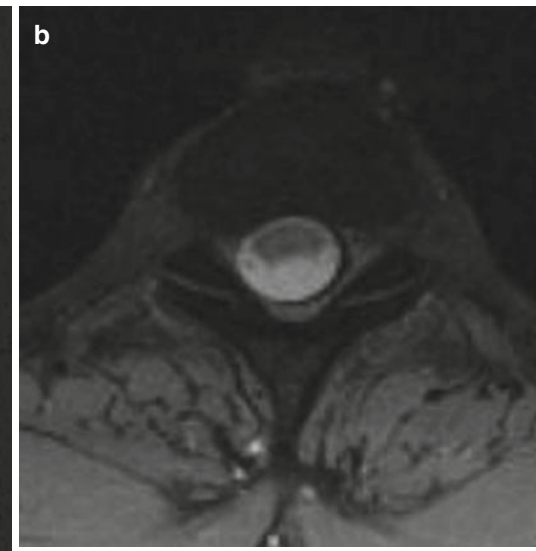


Fig. 15.1 (**a**) This sagittal T2-weighted MRI shows a syrinx extending from C6 to T2 in a 43-year-old neuroradiologist with pain, sensory deficits, and dysesthesias in his left arm. Next to the lower pole, the spinal cord appears slightly indented. (**b**) The axial scan right below the syrinx demonstrates a slight posterior compression of the cord. (**c**) Two years later, the sagittal scan demonstrates the edema extending to C3 with increased diameter of the syrinx C6–T2. (**d**) The cine MRI shows a diminished CSF flow posteriorly across the syrinx and at T2. (**e**) After decompression at Th2, the postoperative MRI demonstrates complete resolution of the syrinx and edema with no further compression of the cord in the axial scan (**f**). Postoperatively, the patient reported no change with 2 years of follow-up

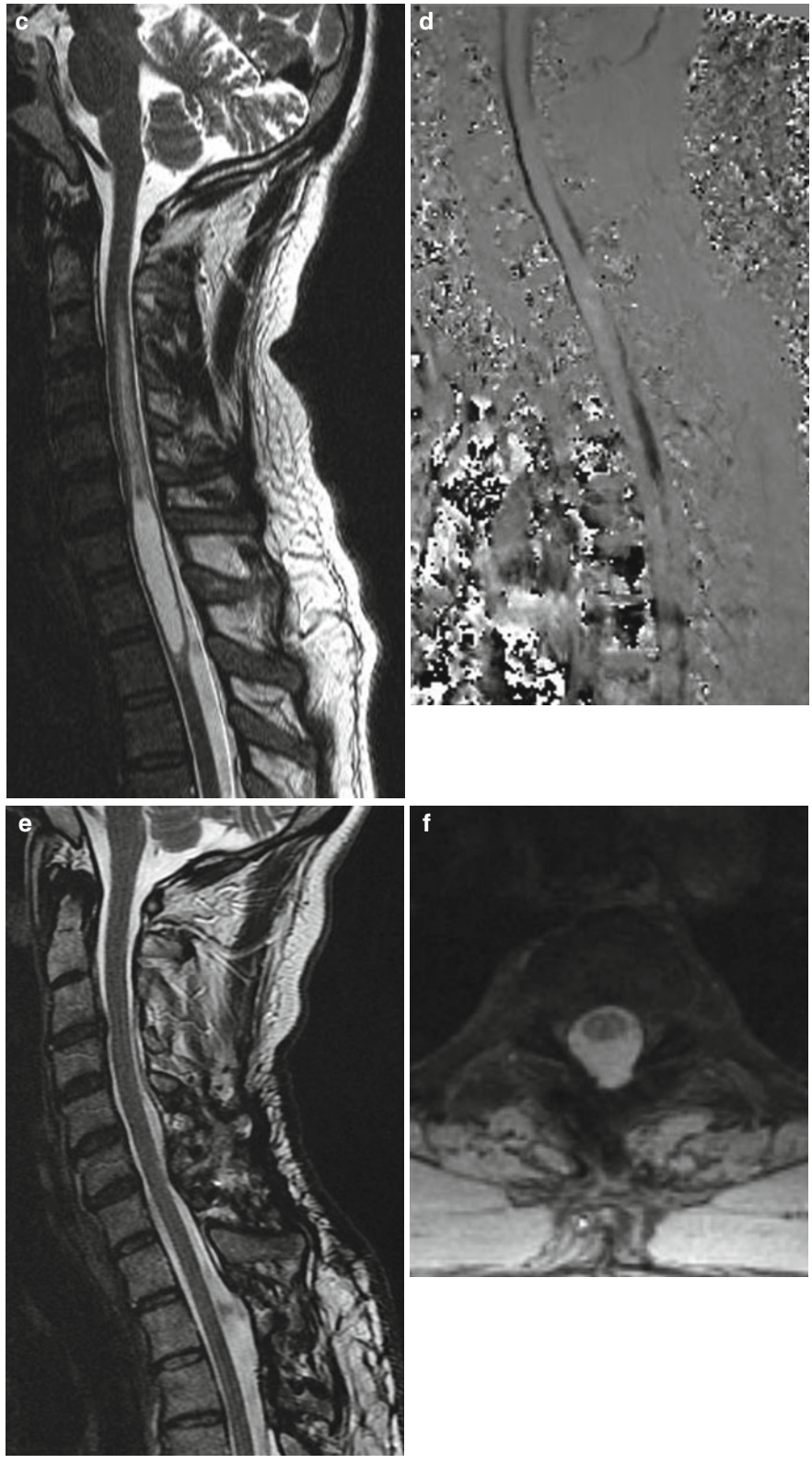


Fig. 15.1 (continued)

evolution of clinical symptoms. The syrinx develops as a consequence of events that are set off by a pathology leading to CSF flow obstruction. Therefore, the first neurological symptoms in the patient's history are generally caused by this underlying pathology rather than the syrinx. In other words, a carefully taken clinical history can provide clues to the underlying pathology. If neurological

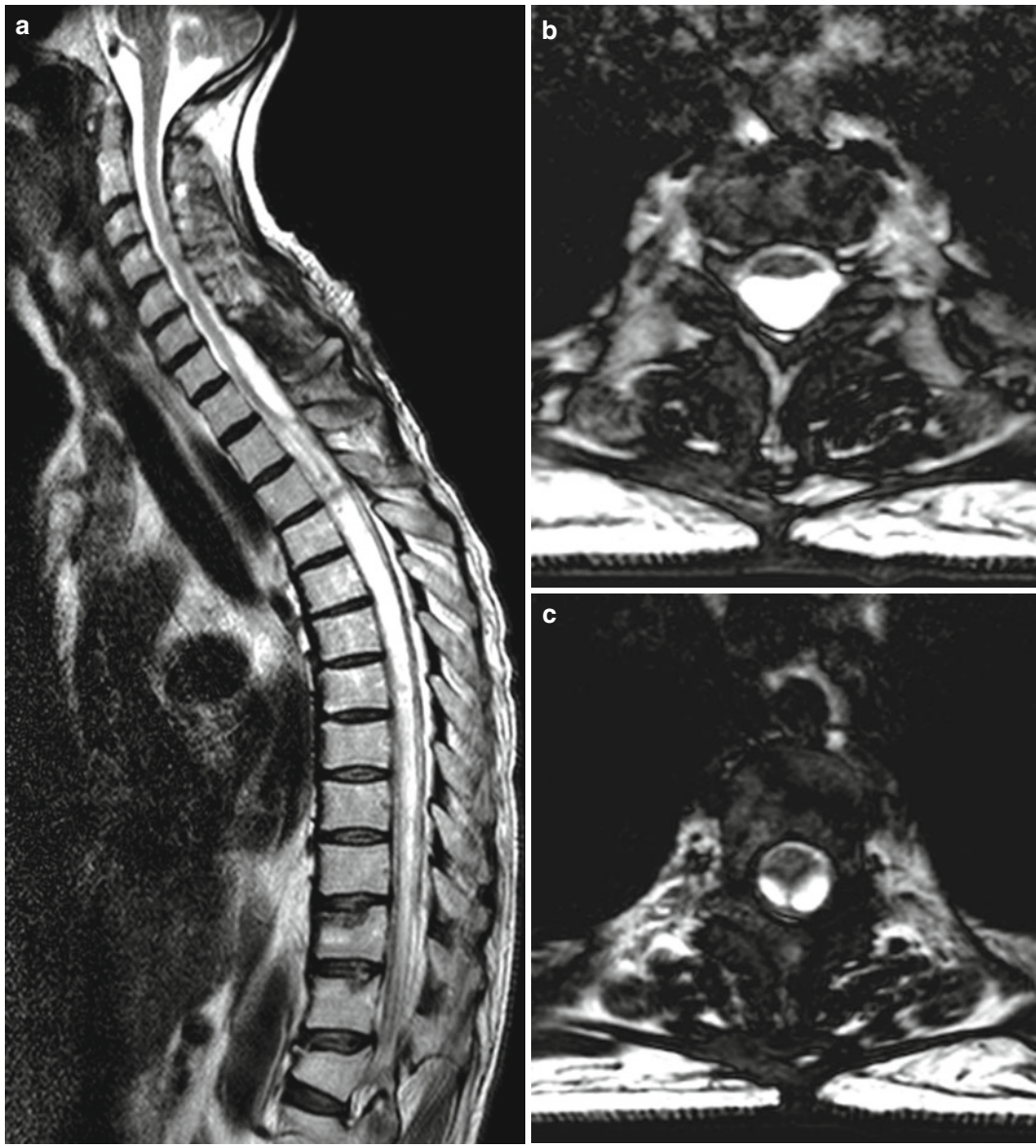


Fig. 15.2 (**a**) The sagittal T2-weighted MRI shows a syrinx T2–T12 related to an extensive postmeningitic arachnopathy extending from C7 downward causing compression of the cervical cord as demonstrated in the axial scan (**b**) in a 67-year-old woman with progressive paraparesis making her wheelchair dependent after unsuccessful fenestration of arachnoid septations in the cervicothoracic region at another institution. The posterior median arachnoid septum appears thickened (**c**). (**d**) Thin sagittal slices in T2 demonstrate arachnoid septations, cysts, and adhesions between cord and dura from C7 downwards throughout the entire thoracic canal. The postoperative sagittal (**e**) and axial (**f**) MRIs show the decompression of the spinal cord after fenestration of arachnoid septations and cysts in the cervicothoracic area. The patient reported postoperative improvement of sensory functions, dysesthesias, pain, and motor weakness but was still left confined to a wheelchair

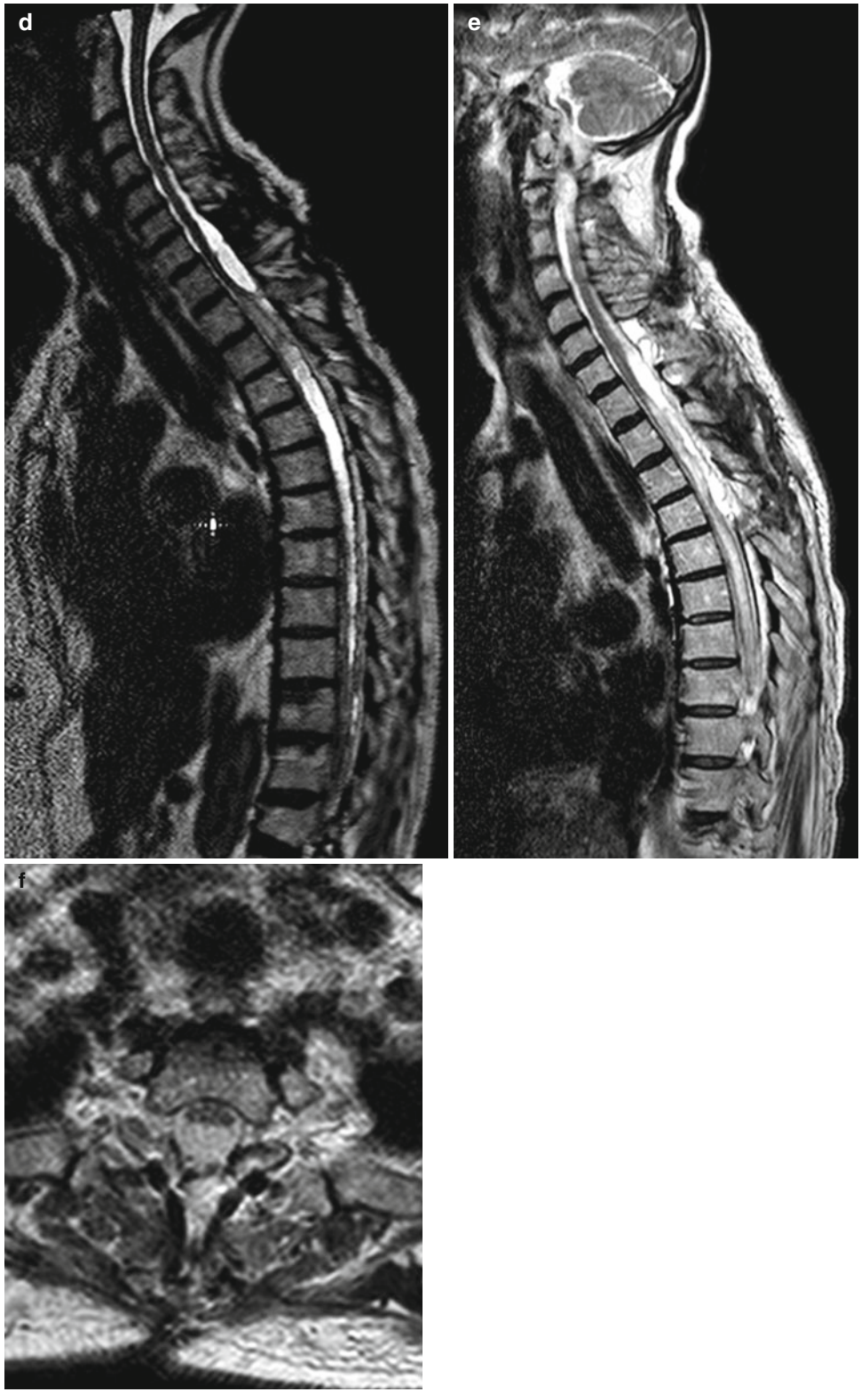


Fig. 15.2 (continued)

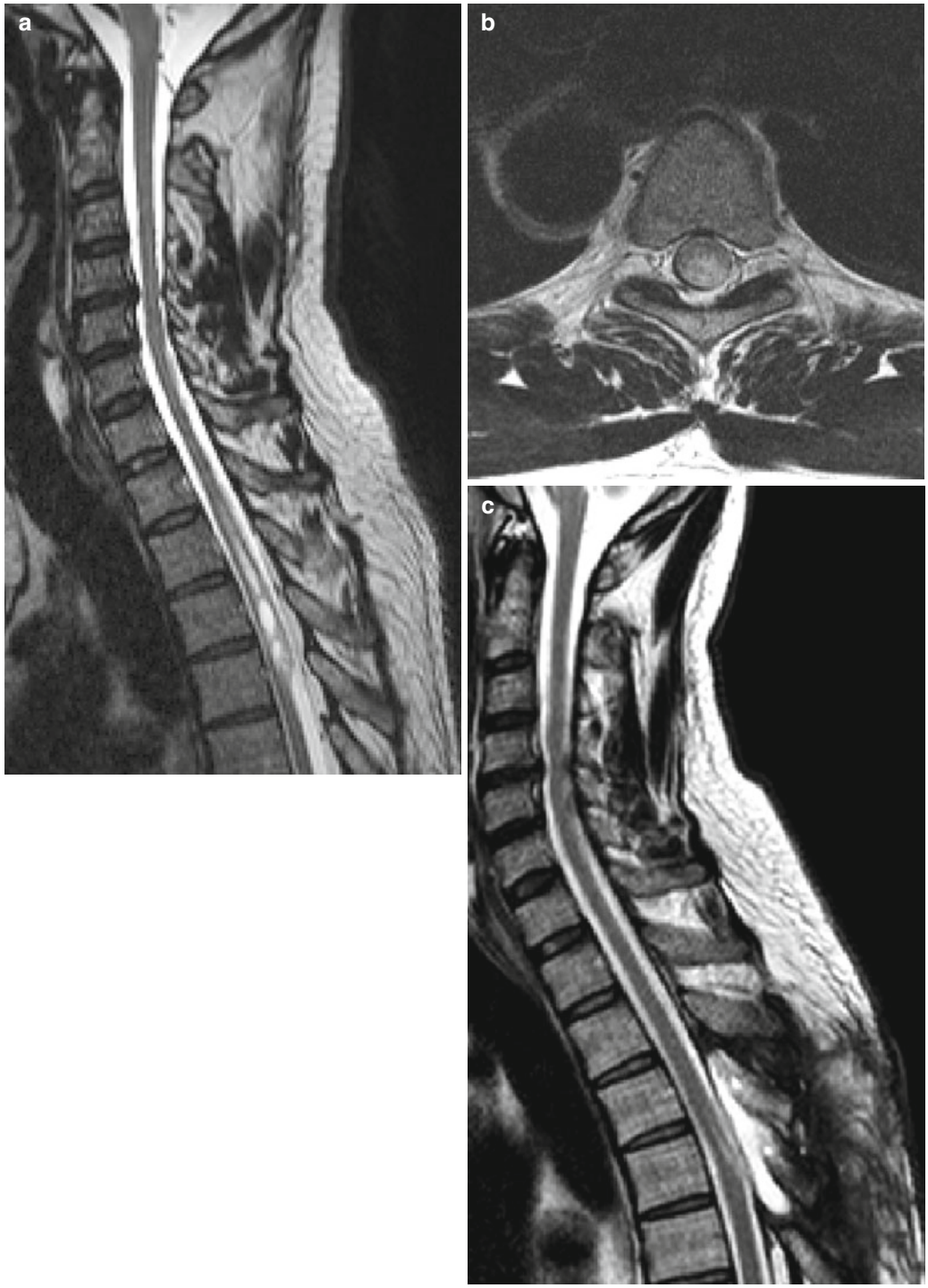


Fig. 15.3 (**a**) The sagittal T2-weighted MRI shows a posttraumatic syrinx T2–T4 in a 46-year-old man 16 months after suffering an incomplete cord injury at T4 with sensory but no motor deficits. The cyst caliber is largest at the lower pole. (**b**) At T4/5 the axial scan reveals an area of cord compression by a cystic posttraumatic arachnopathy at this level. (**c**) After decompression at T3 and T4, the postoperative MRI demonstrates a complete resolution of the syrinx. Postoperatively, symptoms remained unchanged for 14 months

signs spread to other parts of the body in an ascending pattern, the cause of the syrinx will be located at the lower pole of the syrinx and vice versa similar to the radiological evolution. Apart from trauma, arachnoid scarring may be related to infection [24], hemorrhage [20], irritation by old contrast agents such as Pantopaque [25], or surgery, to mention a few.

It is always puzzling that patients may harbor a huge syrinx and yet have just minor symptoms with exactly the opposite observation for some smaller syrinx cavities associated with major neurological deficits. One explanation for this paradox may be that a great deal of the clinical problems are related to the underlying disease process causing the syrinx rather than to the syrinx itself [26].

The classical symptoms of syringomyelia are dissociated sensory loss with loss of sensation for temperature and pain but preserved sensation for light touch. Pain related to syringomyelia is either permanent or aggravated by maneuvers such as coughing and sneezing and perceived in dermatomes corresponding to the syrinx. These symptoms are rarely mentioned as the first clinical manifestations. Late symptoms of syringomyelia are muscle atrophies corresponding to damage of anterior horn cells or trophic changes leading to skin and joint damages, particularly in the shoulder and elbow [26].

Management

In the author's series, about 76.9 % of patients with a Chiari I malformation developed a syrinx. No other pathology causes syringomyelia in such a high proportion (Table 15.1). For syringomyelia associated with intramedullary tumors and Chiari I malformation, the rates for postoperative syrinx resolution are above 80 %, provided the tumor is removed and all components contributing to CSF flow obstruction in Chiari malformations have been surgically addressed, respectively.

Successful treatment of syringomyelia related to spinal rather than craniocervical CSF flow obstruction is much more challenging. The underlying causes are more difficult to identify and to deal with surgically. For this reason, surgery on spinal arachnopathies for treatment of syringomyelia should be reserved for patients with progressive symptoms. Nevertheless, treating the cause of the syrinx with arachnolysis and duraplasty is rewarded by considerably better results compared to syrinx shunting procedures [26–29].

Neuropathic pain and dysesthesias, particularly those of a burning character, may be major clinical problems. Eventhough these may improve with successful treatment of the syrinx, this is never certain. Therefore, the decision for or against surgery should be based on the course of neurological signs and symptoms rather than pain syndromes alone.

In general, surgery can be recommended for patients with arachnoid scarring limited to about 2–3 spinal segments (Figs. 15.1, 15.2, and 15.4). All operations are performed in the prone position. Laminotomies are recommended to reinsert the lamina at the end of the operation with titanium miniplates. After exposure of the dura, the extent of the arachnoid pathology can be visualized with ultrasound. The syrinx can be visualized. Pulsations of syrinx fluid and CSF may become visible. Sometimes, arachnoid septations can be seen. Most importantly, the safest spot for opening of the dura can be chosen with this technique. As contamination of the CSF with blood may cause inflammatory reactions of the arachnoid, great care is taken to achieve good hemostasis. For this purpose, the entire surgical field is covered by moist cottonoids, which keep soft tissues moist and absorb any minor bleeding. Next, the dura is opened under the operating microscope in the midline without opening of the arachnoid. Once the dura is held open with sutures, the arachnoid pathology can be studied, and adequate exposure cranially and caudally is ensured in order to gain access to normal and unaffected subarachnoid space on either end. Obviously, the surgeon should be familiar with the normal anatomy of the spinal subarachnoid space [30]. The posterior subarachnoid space is divided in two halves by a posterior longitudinal arachnoid septum. This septum extends between

the outer arachnoid layer and an intermediate layer on the cord surface. The insertion on the cord surface is related to the midline dorsal vein. Further strands of arachnoid may be encountered in the posterior and – to a lesser degree – anterior subarachnoid space. Another landmark is the dentate ligaments, which originate from the spinal cord pia mater, run between posterior and anterior nerve roots, and insert close to the dural nerve root sleeve. With a microdissector, arachnoid and dura can be separated from each other without any problem in areas without arachnoid scarring, that is, at either end of the exposure. In the area of scarring, sharp dissection with microscissors is usually required to achieve this. At the level of CSF flow obstruction, the arachnoid may become densely adherent to the cord surface. With opening of the rostral and caudal subarachnoid space, CSF rushes into the surgical field and often the cord, which was distended by the syrinx, starts to pulsate, and the syrinx may collapse at this point. The arachnoid scar can be resected layer by layer leaving a last sheath on the cord surface to avoid injury to the cord or surface vessels. This last layer resembles the intermediate arachnoidal layer mentioned above. In this way, a free CSF passage in the posterior subarachnoid space can be created in every

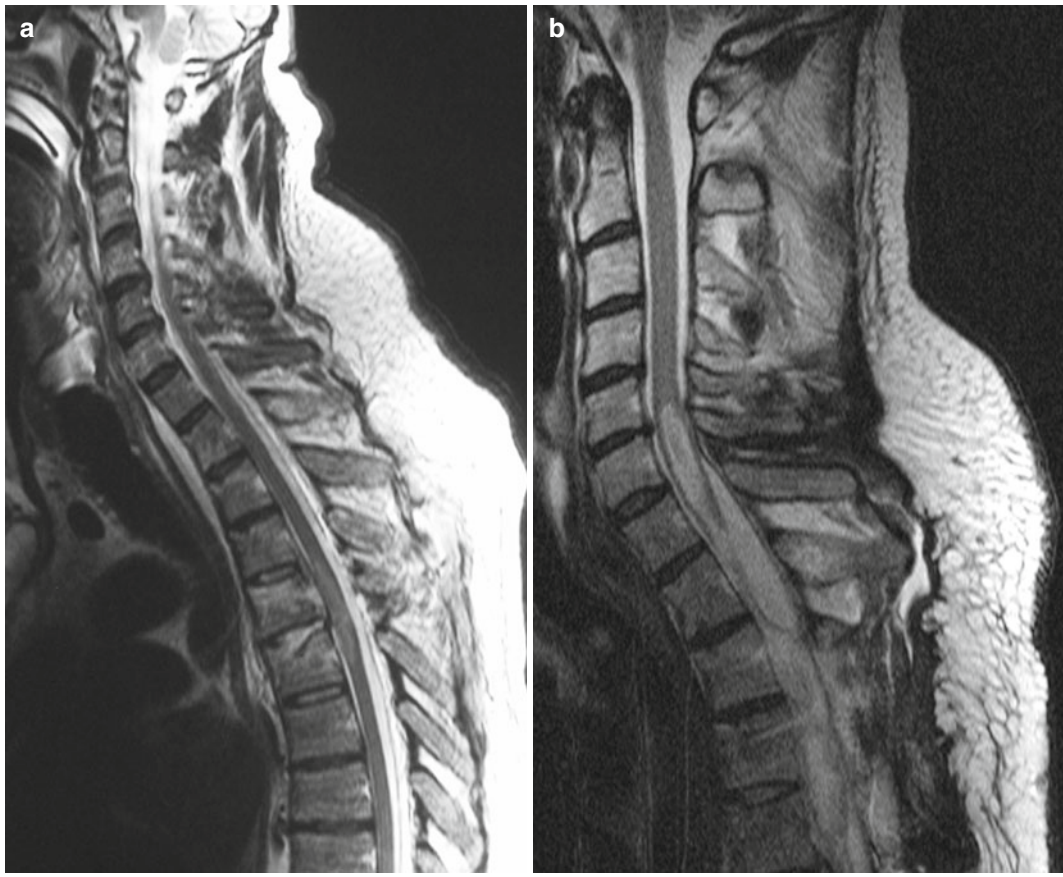


Fig. 15.4 (**a**) The sagittal T2-weighted MRI demonstrates an area of cord edema after a fracture dislocation at T4/5 with complete paraplegia in a 46-year-old patient. (**b**) Five months later the MRI demonstrates profound cystic degeneration of the cord at and below the injury level and an ascending syrinx reaching C5. (**c**) After decompression at T2–T5, the cervical syrinx has collapsed, while the cystic changes in the thoracic cord are still detectable. Postoperatively, the patient experienced improvements of motor function in his hands, sensory function, and pain at 24 months follow-up

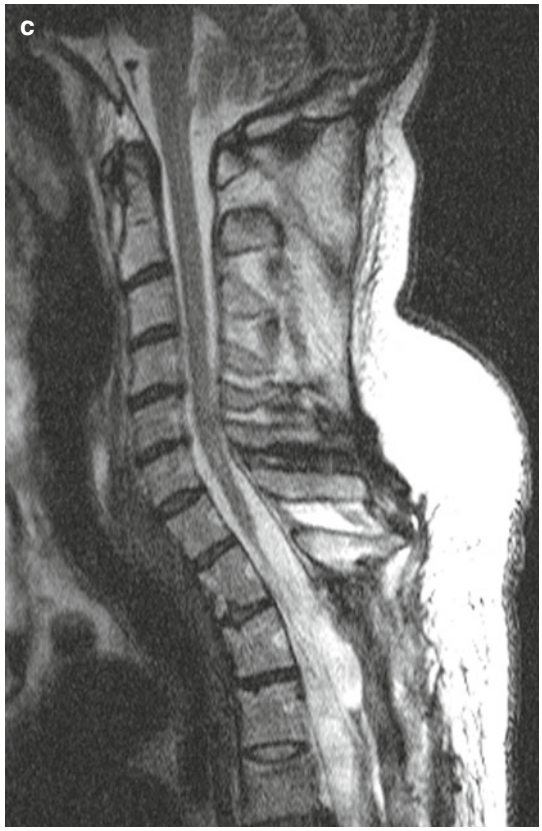


Fig. 15.4 (continued)

patient across the region of the arachnopathy. Dissection is then continued laterally on either side towards the dentate ligaments. This leads to complete untethering of the cord in the majority of cases. No arachnoid dissection should be performed anteriorly of the dentate ligaments to avoid injuries to motor pathways and anterior spinal cord vessels. Closing the microsurgical part of the operation, an expansile duraplasty is inserted with a tight running suture and finally lifted up with tenting sutures on either side. To avoid scar formation and tethering between duraplasty and spinal cord, alloplastic material for duraplasty should be preferred, for example, Gore-Tex® (W.L. Gore & Associates GmbH, 85640 Putzbrunn, Germany). Special attention is finally paid to a good, tight closure of the muscle layer to prevent any CSF from entering the epifascial space. In patients who have been operated before, as in patients with posttraumatic syringomyelia who underwent spinal instrumentation, for instance, a lumbar drain is placed prophylactically if the soft tissue appears scarred and sparsely vascularized.

Considerable experience is needed to be successful with this surgical technique. If unnecessary steps are taken, such as a too extensive dural opening or if the surgical field is contaminated with considerable amounts of blood, postoperative scarring may counterbalance the effect of surgery. On the other hand, if the dural opening is not extensive enough to gain access to the normal subarachnoid space above and below the level of scarring, the procedure is insufficient. As always, it is the right measure that counts and determines whether an operation will be successful or not.

For patients with more extensive arachnopathies after meningitis, multiple intradural surgeries or spinal subarachnoid hemorrhage, for example, surgery cannot provide a normal CSF passage [26]. Axial MRIs taken over the entire area of the arachnopathy should be evaluated in such instances for evidence of cord compression. Quite often, pouches and cysts have formed causing profound cord compression over a few spinal segments. Such compressions can be treated surgically by wide fenestration of the corresponding arachnoid membranes (Fig. 15.2). Such an operation can improve neurological symptoms related to the cord compression, but it will not influence the syrinx.

For this purpose, thecoperitoneal shunts have been introduced, which drain CSF from the subarachnoid space above the level of obstruction to the peritoneal cavity [31–35]. For cavities extending into the cervical cord, ventriculoperitoneal shunts have been used for the same purpose [36, 37]. However, these shunts have their own problems. There is little experience concerning the correct pressure settings other than to set them as low as possible avoiding overdrainage. Programmable shunts are used for this reason, but the shunt systems available are not specifically designed for this purpose. No data exist as to how much tissue coverage may be allowed over the valve in order to still be able to change the setting with the programming device. This leaves the problem as to

Table 15.2 Operations for patients with spinal arachnopathies

Type of surgery	Posttraumatic arachnopathies	Nontraumatic arachnopathies	All
Decompression	56	97	153
Cordectomy	4	1	5
Thecoperitoneal shunt	1	1	2
Ventral fusion	3	3	6
Posterior fusion	1	2	3
Opiate pump	1	–	1

where to position the valve. Low-pressure valves have been used to overcome these problems. Two patients in the author's series were treated this way. In one patient, a low-pressure valve was still not low enough, so that the valve was removed leaving the patient with a valveless drain. This worked for a year after which the catheter became blocked. Another patient does well clinically with a low-pressure valve even though the syrinx did not regress.

For patients with a complete cord lesion, cordectomy is a very effective form of treatment for syringomyelia [38–43]. All patients treated in this manner, in the author's series, improved neurologically with permanent resolution of the syrinx. However, the psychological burden for a patient to accept this operation should not be underestimated. Most patients prefer to undergo a decompression first. After all, this operation does provide good results in the majority of patients [42]. Patients will accept a cordectomy, however, if the ascending neurology cannot be arrested by decompression or shunting procedures and the neurological progress threatens important function such as respiration or hand function.

Results

Concentrating on patients with syringomyelia related to spinal arachnopathies, 137 patients with posttraumatic arachnoid scarring and 280 patients with nontraumatic arachnopathies were encountered in the author's series. Reserving surgery for patients with progressive neurological symptoms and refusal of surgery by some patients led to operations for 61 patients with posttraumatic and 94 patients with nontraumatic arachnopathies (Table 15.2). Overall, 153 decompressions aimed at improving CSF flow and decompressing the spinal cord by resecting arachnoid pathologies were performed, while five patients with complete paraplegias underwent cordectomies and two thecoperitoneal shunts were placed. One patient received an opiate pump for his neuropathic pain syndrome. The remaining operations dealt with degenerative diseases of the cervical spine.

Concentrating on the 153 decompressions with arachnolysis and duraplasty, complications were observed after 23 operations (15.0 %); the commonest were wound infections in seven cases. Permanent surgical morbidity defined as permanent neurological worsening within 1 month after surgery occurred in eight patients (5.2 %). A postoperative decrease in the size of the syrinx was observed in 67 %; 28 % showed no postoperative change, while 6 % increased further despite surgery. After 3 months, 55 % considered their condition improved, 37 % as unchanged, and 8 % as worsened. Looking at individual symptoms revealed postoperative improvements for sensory deficits and pain, whereas motor weakness, gait, and sphincter functions where left unchanged. Long-term results were determined with Kaplan-Meier statistics to determine the rates for progression-free survival after decompression. Overall, 71 % remained in a stable neurological status for 5 years after surgery. This rate was reduced to 52 % after 10 years. Looking at particular subgroups revealed good long-term results for patients with a focal nontraumatic arachnoid pathology not exceeding two spinal segments and for posttraumatic patients who had either conceded no spinal cord injury or a complete cord injury at the time

Table 15.3 Neurological recurrence rates for patients with spinal arachnopathies

Patient group	5 years (%)	10 years (%)	*P*
All	29	48	
Nontraumatic Focal	16	21	0.0006
Nontraumatic Extensive	58	67	
Nontramatic All	29	37	
Posttraumatic No cord injury	6	6	0.07
Posttraumatic Incomplete cord injury	38	74	
Posttraumatic Complete cord injury	14	–	
Posttraumatic All	28	55	

of the accident (Table 15.3). For these subgroups, significantly lower clinical recurrence rates were determined between 6 and 21 % after 10 years. Patients with extensive arachnoid pathologies or those with an incomplete cord injury are the most difficult patients with spinal arachnopathies to treat. For patients with extensive arachnopathies after meningitis or intradural hemorrhage, the surgical concept of arachnolysis and duraplasty is as problematic as any other form of surgical treatment. Treatment of the cause of the neurological deterioration is not possible in a sufficient way. Thecoperitoneal shunts may reduce the ascending syrinx but they hardly influence the myelopathy for which the arachnopathy itself is responsible. The same applies to syrinx shunts. For patients with posttraumatic syringomyelia after an incomplete cord lesion, compromises as to how far the arachnolysis and untethering of the cord should be pursued are unavoidable if surgical morbidity risking the remaining spinal cord functions is kept to a minimum. It remains to be seen whether long-term results will improve with further experience.

Conclusions

The diagnosis of syringomyelia should be reserved for patients with a space-occupying intramedullary cyst of progressive character and differentiated from such entities as a harmless dilatation of the central canal or myelomalacia [26, 44, 45]. Syringomyelia is not a disease in its own right but a manifestation of a disorder of the spinal canal or craniocervical junction that has either resulted in an obstruction of CSF flow or spinal cord tethering or is associated with an intramedullary tumor. Management of patients with syringomyelia requires the correct diagnosis of the underlying disorder and the successful treatment of it. As this can be done in the overwhelming majority of patients, no further surgical measures for the syrinx are required. Shunting the syrinx in particular can and should be avoided as the first line of treatment. The long-term prognosis depends on the treatability of the underlying disorder.

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Secondary Interventions for Chiari I Malformation

16

Jörg Klekamp

Abstract

Patients with Chiari I malformations may present again after a foramen magnum decompression for two reasons: either they are unsatisfied with the result or new neurological symptoms have appeared. This chapter provides a systematic approach to these patients. As a general rule, revision surgery should be reserved for patients with progressive neurological symptoms. Arachnoid scarring causing obstructions of cerebrospinal fluid (CSF) flow was the commonest intraoperative finding in such revisions. Craniocervical instability in patients with basilar invagination or Klippel-Feil syndromes is the other potential mechanism leading to postoperative deterioration after a foramen magnum decompression. In such patients, a revision has to include craniocervical stabilization. Apart from these foramen magnum-related mechanisms, degenerative diseases of the cervical spine may lead to signs of a cervical myelopathy requiring early surgery. With revision surgeries, no major postoperative improvements should be expected. Stabilization of the neurological state is the realistic outlook.

Foramen magnum decompression is widely recognized as the procedure of choice for treatment of patients with Chiari I malformation (CMI) with long-term success rates well above 80 % reported in numerous reports in the literature. On the other hand, few publications deal specifically with treatment concepts for patients who develop new neurological problems after such a decompression. Furthermore, there still exists considerable disagreement, as to what a foramen magnum decompression should include: Is it necessary to open both layers of the dura? Should the arachnoid be opened and dissected? How should we deal with the cerebellar tonsils? Should a duraplasty be performed and if so, what kind of material should be used for grafting? An analysis of patients with new symptoms after a decompression may provide some answers to these questions. Other possible causes for a neurological deterioration have to be evaluated as well.

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Diagnosis

Among a series of 559 patients presenting with CMI, 107 patients had already undergone a foramen magnum decompression. Of these, 27 had also been treated by a syrinx shunt. Fifty-six of these 107 patients were not operated: in 40 patients, a revision was not recommended because the neurological status was stable or considered unlikely to be stabilized by another intervention, while 16 refused another operation. The majority of patients, in whom a revision was not recommended, presented because they were disappointed by the result of their decompression. Burning-type dysesthesias were the commonest complaint of these patients. Although many other symptoms were often improved and a syrinx had decreased, this type of pain persisted and was notoriously difficult to treat with analgesics. It is important to inform a patient before surgery that burning-type dysesthesias may not respond to an otherwise successful decompression. Bernard Williams even observed postoperative aggravations in a few patients despite regression of a syrinx (personal communication). However, this was not observed in this series. Surgery was not recommended for most patients with a history of postoperative meningitis or after multiple procedures at the foramen magnum considering the increased risks of another intervention and the reduced chances for success under such circumstances.

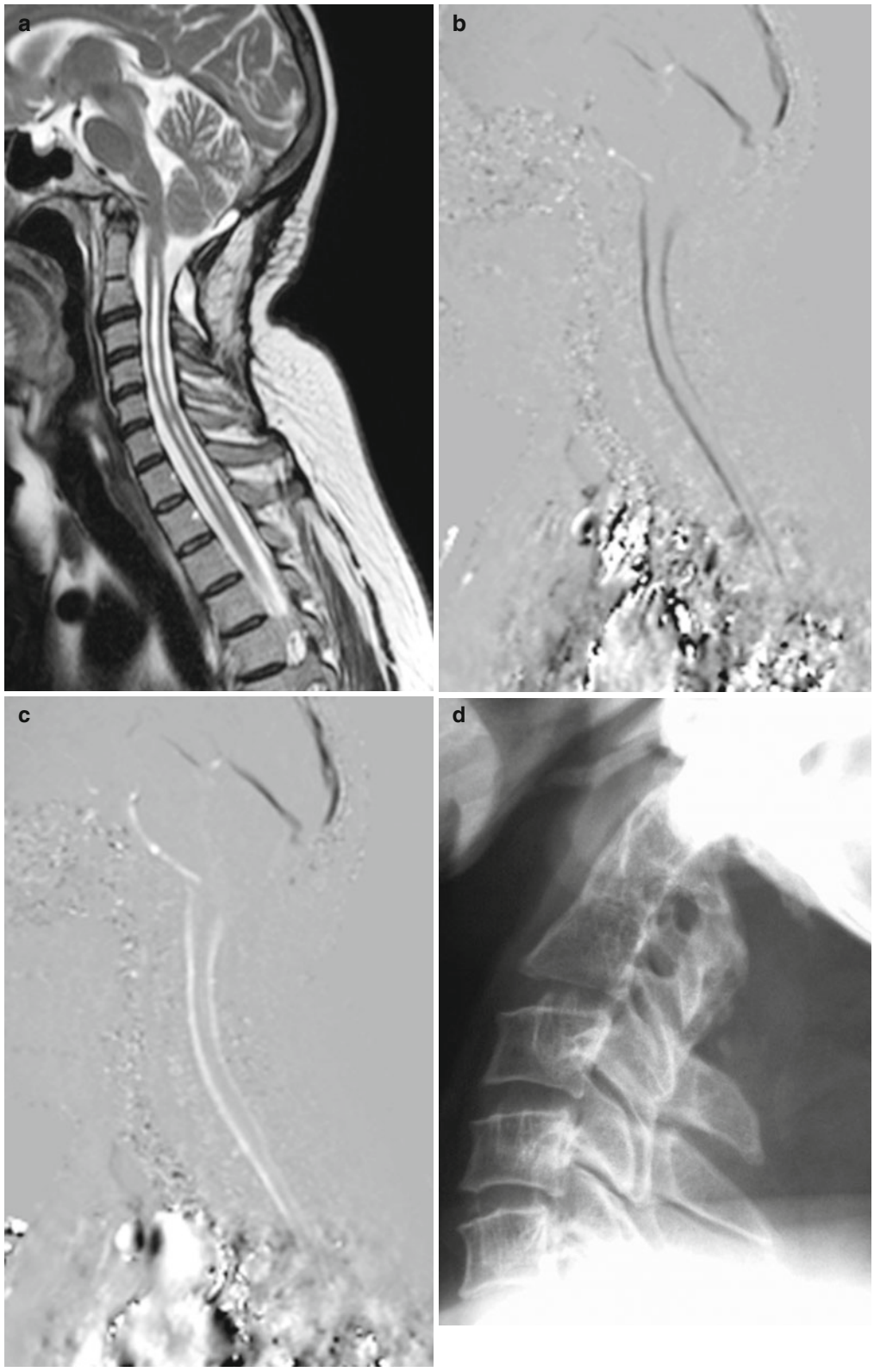
Fifty-one patients underwent another surgical procedure. The decision was based on a detailed clinical and neuroradiological analysis. Once hydrocephalus was ruled out, the evaluation started with the clinical history before the previous decompression and how preoperative symptoms responded to it. Was the neurology unchanged or improved or did symptoms progress further without an interval of stable neurologic function? If symptoms progressed without an interval of clinical stability, such a course suggested an insufficient operation. In most instances, this was related to untreated features of an associated basilar invagination, such as anterior compression by the odontoid or craniocervical instability.

In the majority of patients, however, the clinical history revealed a stable interval after foramen magnum decompression with or without improvement of preoperative symptoms. It should then be noted how and when the deterioration started. The longer the interval of clinical stability before the deterioration began, the less likely the cause was related to the foramen magnum. The only clinical symptoms, which pointed to a foramen magnum problem, were occipital headaches or swallowing dysfunctions. If these did not progress or reappeared, the clinical history often not indicated, whether a foramen magnum-related cause or another pathology, had to be addressed.

Next, a careful neuroradiological assessment was essential for these patients. The area of the previous operation was evaluated comparing pre- and postoperative MRI scans. Was there any evidence for an insufficient decompression or recurrent compression? It has been reported that new bone formation may cause recurrent compression in children [1–3]. This was not observed in this series, however. No example of cerebellar ptosis [4] due to an oversized craniectomy [5] resulting in medullary compression was found either.

Was there a basilar invagination with persistent anterior compression of the odontoid? Was there an indication of craniocervical instability such as an assimilated atlas to the occiput, a Klippel-Feil syndrome of the upper cervical spine, or a pannus formation around the odontoid [6] (Fig. 16.1)?

Fig. 16.1 (**a**) This sagittal T2-weighted MRI was performed 8 years after decompression of the foramen magnum in another institution in a 46-year-old patient with Chiari I malformation, basilar invagination, and syringomyelia. The syrinx appears of small caliber, and a small pseudomeningocele is apparent. C2/C3 is fused, i.e., Klippel-Feil syndrome. The patient complained about severe neck pain, dysesthesias, and a slight gait ataxia. (**b**, **c**) The cine MRI shows no flow signals in the foramen magnum region. (**d**, **e**) Functional X-rays of the cervical spine demonstrate the laminectomy of C2 and C3 and instability at C3/C4. Revision surgery incorporated a revision at the foramen magnum with arachnoid dissection and a new duraplasty followed by occipitocervical fusion C0–C5 with lateral mass screws. (**f**) The postoperative MRI demonstrates a large cisterna magna. (**g**) The control X-ray 7 years later shows the correct positions of all implants with a good sagittal profile. Postoperatively, the patient has remained neurologically stable for 7 years with some improvement of her neck pain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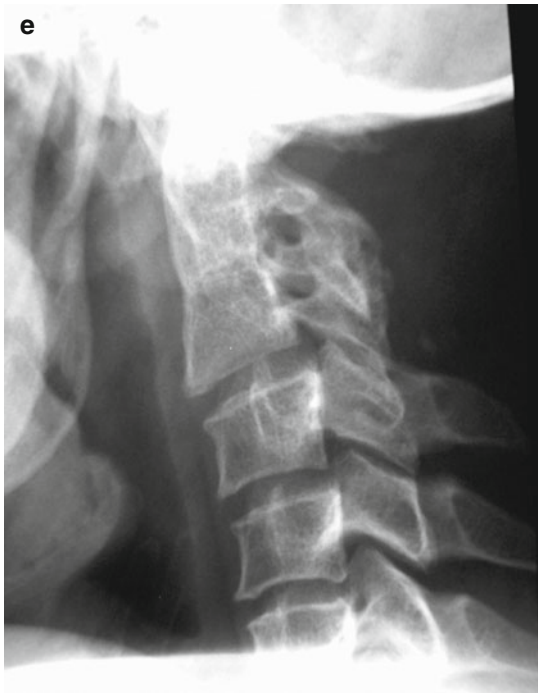
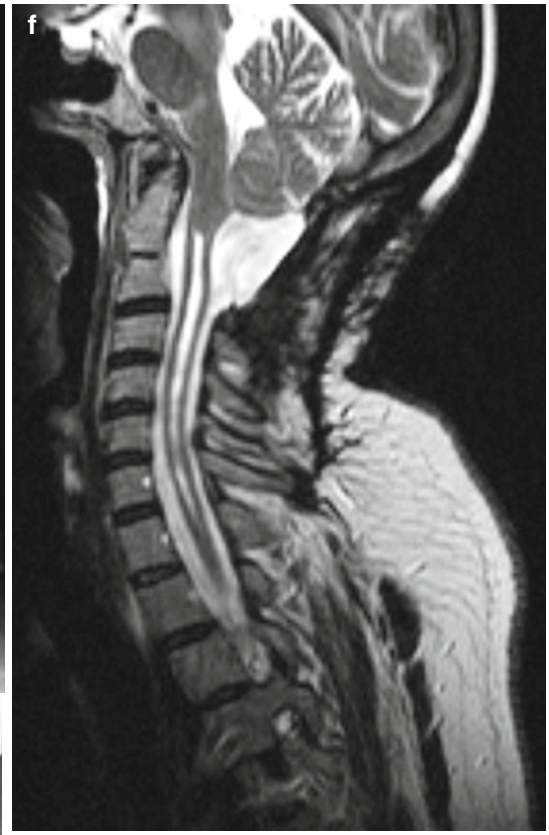




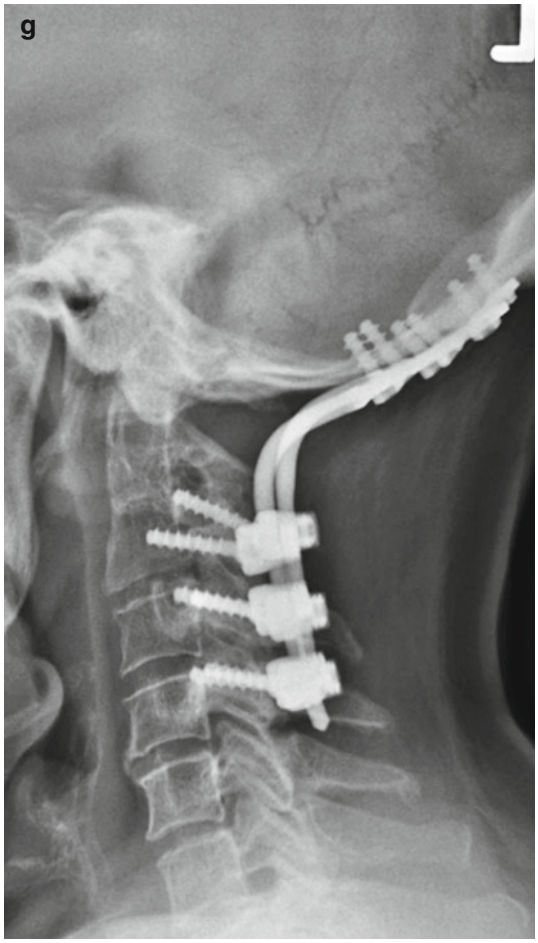


Fig. 16.1 (continued)

Was there a cisterna magna of sufficient size (Figs. 16.1, 16.2, and 16.3)? Was there a pseudomeningocele pushing the dura anteriorly [7] (Figs. 16.1, 16.2, and 16.3)?

Another important aspect was the postoperative course of a syrinx. If the syrinx decreased after surgery and remained so, it was unlikely that new symptoms were related to the foramen

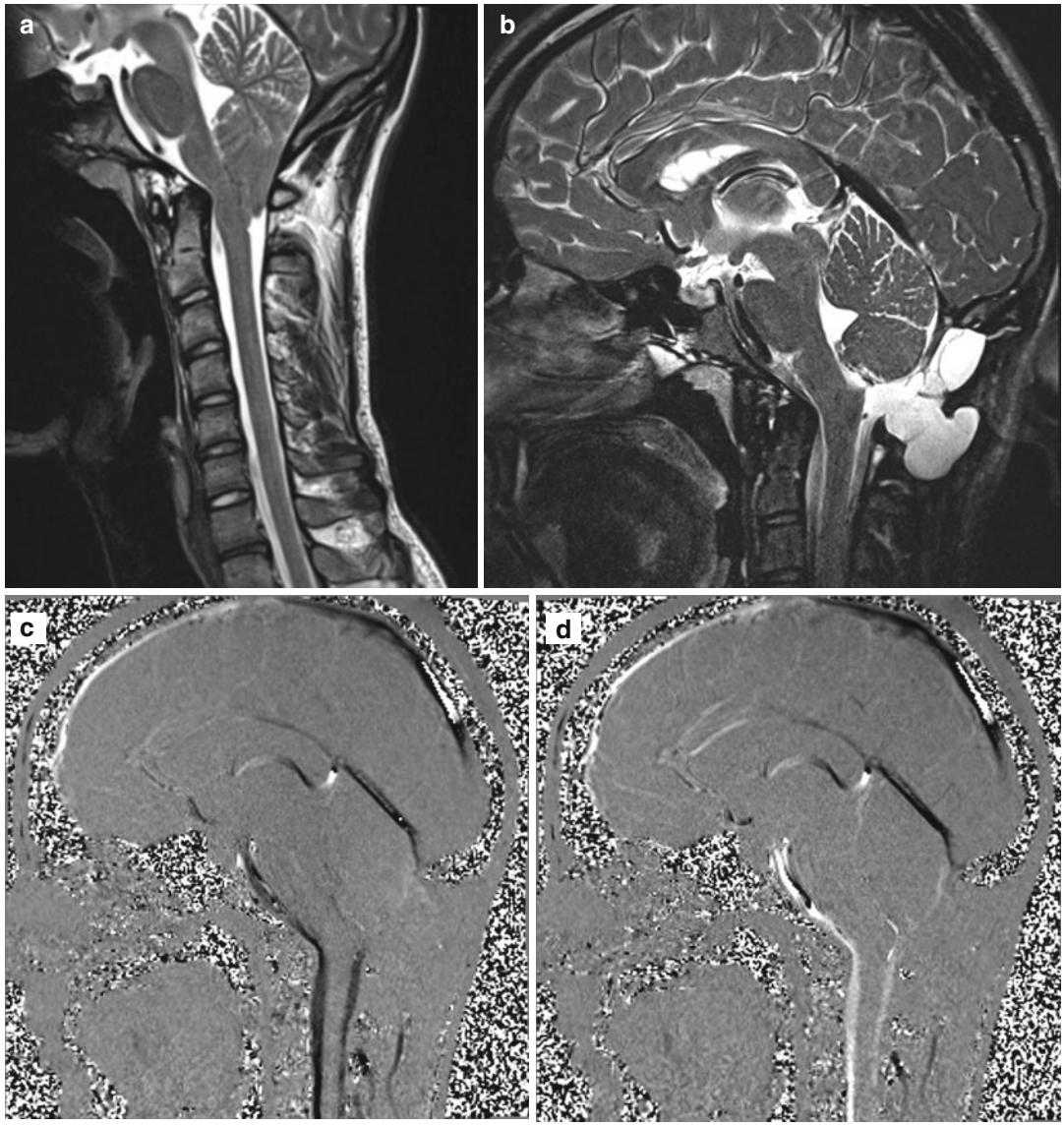


Fig. 16.2 (**a**) This sagittal T2-weighted MRI shows a classical Chiari I malformation without syringomyelia in a 15-year-old boy with occipital headaches. (**b**) After decompression of the foramen magnum with resection of both tonsils in another institution, the postoperative scan demonstrates a large pseudomeningocele. There appears to be a membrane obstructing the foramen of Magendie. (**c**, **d**) The cine MRI shows no flow signals in the area of the foramen magnum. The patient no longer complained about occipital headaches but reported quite severe local discomfort. At reoperation 2 years later, a large defect in the suture line for the duraplasty was evident. After removal of the duraplasty, profound scarring at both tonsillar stumps was detected. Both posterior inferior cerebellar arteries were embedded in this scar tissue which also obstructed the foramen of Magendie. The foramen was not opened to avoid any vascular injuries and a new duraplasty inserted. (**e**) The postoperative scan shows a free CSF passage across the foramen magnum with normal soft tissue healing. The patient made a full recovery

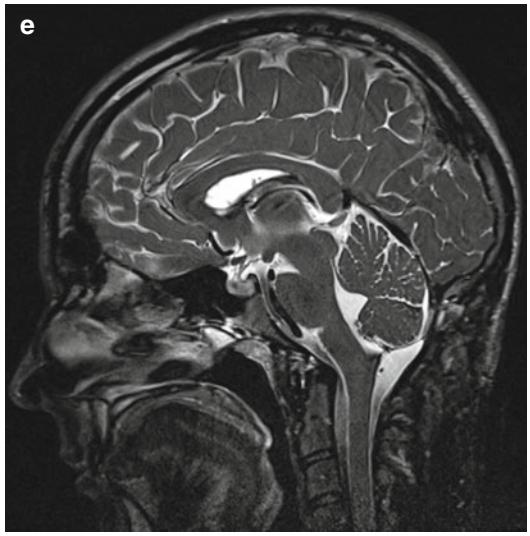
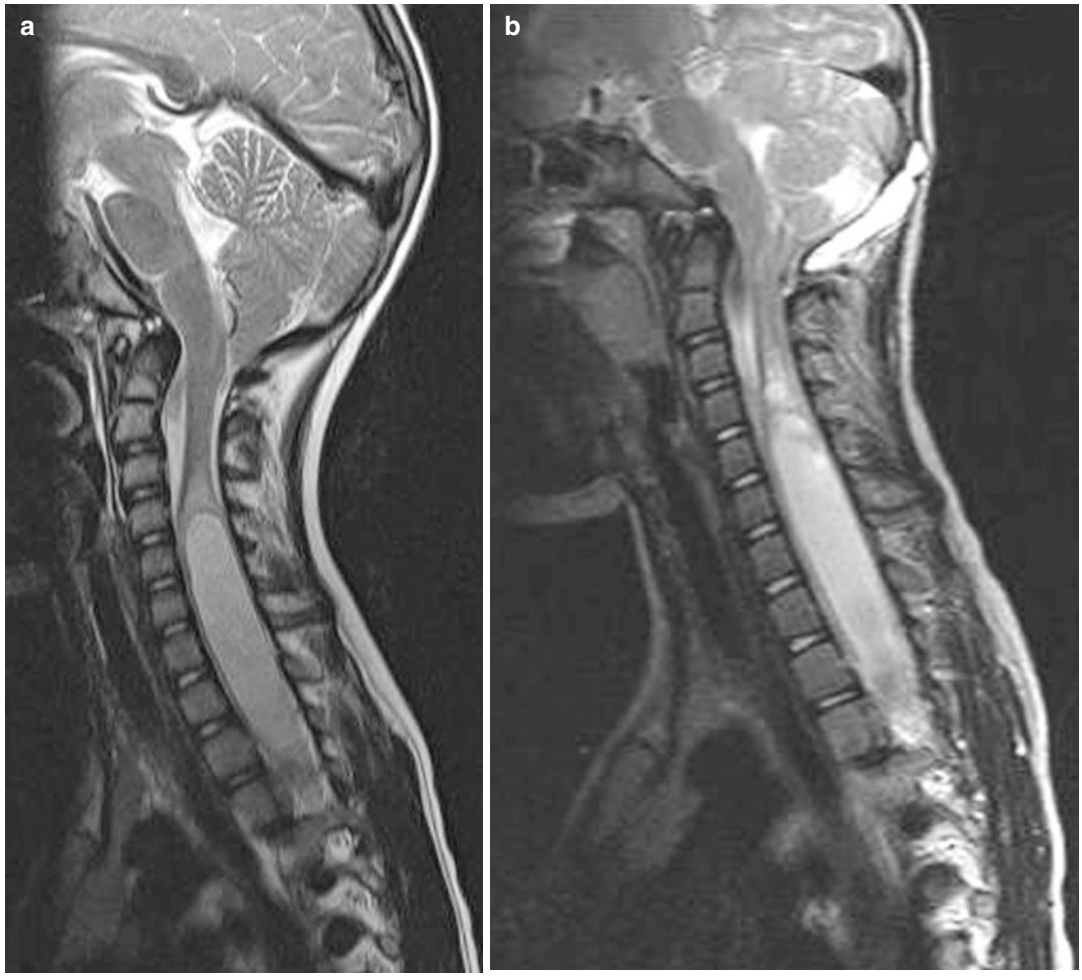


Fig. 16.2 (continued)

magnum with one exception: craniocervical instability still had to be ruled out.

If all these points were excluded by conventional MRI scans, a cardiac-gated cine MRI was performed to evaluate the CSF passage at the foramen magnum. This modality is the most sensitive method to detect or exclude arachnoid scarring and adhesions that may have formed after the first decompression [8–11]. If such a study demonstrated CSF flow at the foramen magnum and the neuroradiological evaluation had excluded all the other above-mentioned possibilities, then the clinical deterioration had to be caused by a process unrelated to the previous decompression.

In patients with syrinx shunts, the shunt catheter might have caused tethering of nerve roots or spinal cord [12] leading to radicular or myelopathic symptoms, which were often provoked by



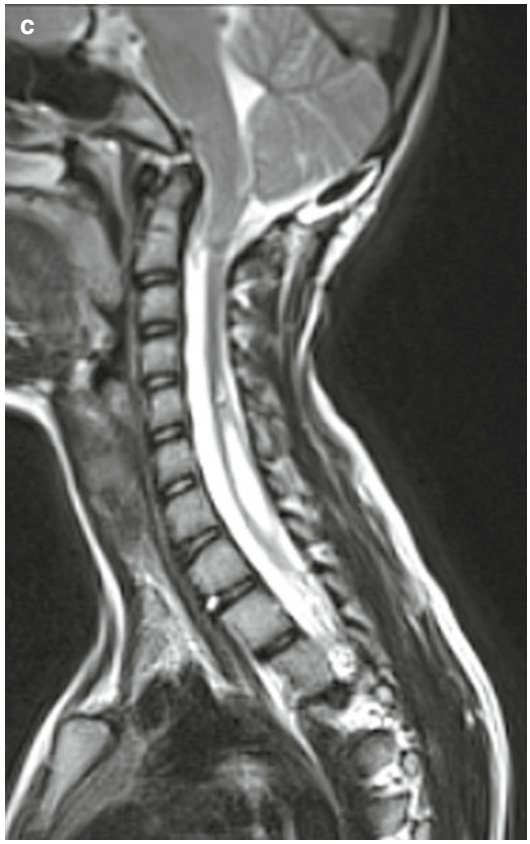


Fig. 16.3 (continued)

neck or arm movements. The MRI in these patients showed adherence of the cord to the dura at the level of the shunt.

If this had been excluded as well, degenerative changes of the cervical spine were evaluated next (Fig. 16.4). Many patients with a well-treated Chiari malformation and a collapsed syrinx demonstrated a considerable amount of spinal cord atrophy as the result of the long-standing syringomyelia. Therefore, MRI scans often gave the impression that a slight or moderate degree of cervical stenosis may not be clinically relevant. However, this is a very dangerous assumption. Such patients had very little functional reserve in their spinal cord as a consequence of their former syringomyelia. Any additional affection – even a minor one – may be enough to cause significant new deficits. It has even been suggested that Chiari patients may be particularly prone to degenerative problems of the cervical spine [13]. Signs of hypermobility of cervical segments should be looked for in particular by X-rays in ante- and retroflexion (Fig. 16.4).

Patients requiring a foramen magnum revision were significantly younger (40 ± 17 years vs. 48 ± 14 years; *t*-test, $p = 0.046$) with trends for a shorter interval between previous decompression and onset of new symptoms (40 ± 34 months vs. 63 ± 49 months; *t*-test, $p = 0.06$) and a longer history before the secondary operation (52 ± 98months vs. 34 ± 65 months; *t*-test, $p = 0.2$). Table 16.1 gives an overview on symptoms at presentation for unoperated patients and patients operated again at the foramen magnum or elsewhere in the spinal canal. The percentage of patients suffering from neuropathic pain was equal in all three groups. For the remaining symptoms, unoperated patients were less severely affected compared to the surgical groups. Patients undergoing a foramen magnum revision presented occipital pain and swallowing problems more commonly, whereas hypesthesia and sphincter disturbances were less common in this group. Otherwise, the neurological courses of patients with either a new foramen magnum problem or a cervical myelopathy were indistinguishable.

Secondary Surgeries in the Cervical Spine

In 15 instances, a mechanism independent from the foramen magnum region had caused a myelopathy (Table 16.2; Fig. 16.4). In all these

Fig. 16.3 (**a**) This sagittal T2-weighted MRI shows a Chiari I malformation with a substantial syrinx and scoliosis in a 5-year-old girl. (**b**) After decompression, a pseudomeningocele had formed pushing the duraplasty anteriorly, obstructing CSF flow. Consequently, the syrinx did not resolve. Seven years after the first operation, the scoliosis deteriorated and the decision was made to revise the foramen magnum. (**c**) After this revision which included arachnoid dissection and insertion of a new duraplasty, the CSF pathway is free and the syrinx has started to decrease. There has been no further progress of her scoliosis

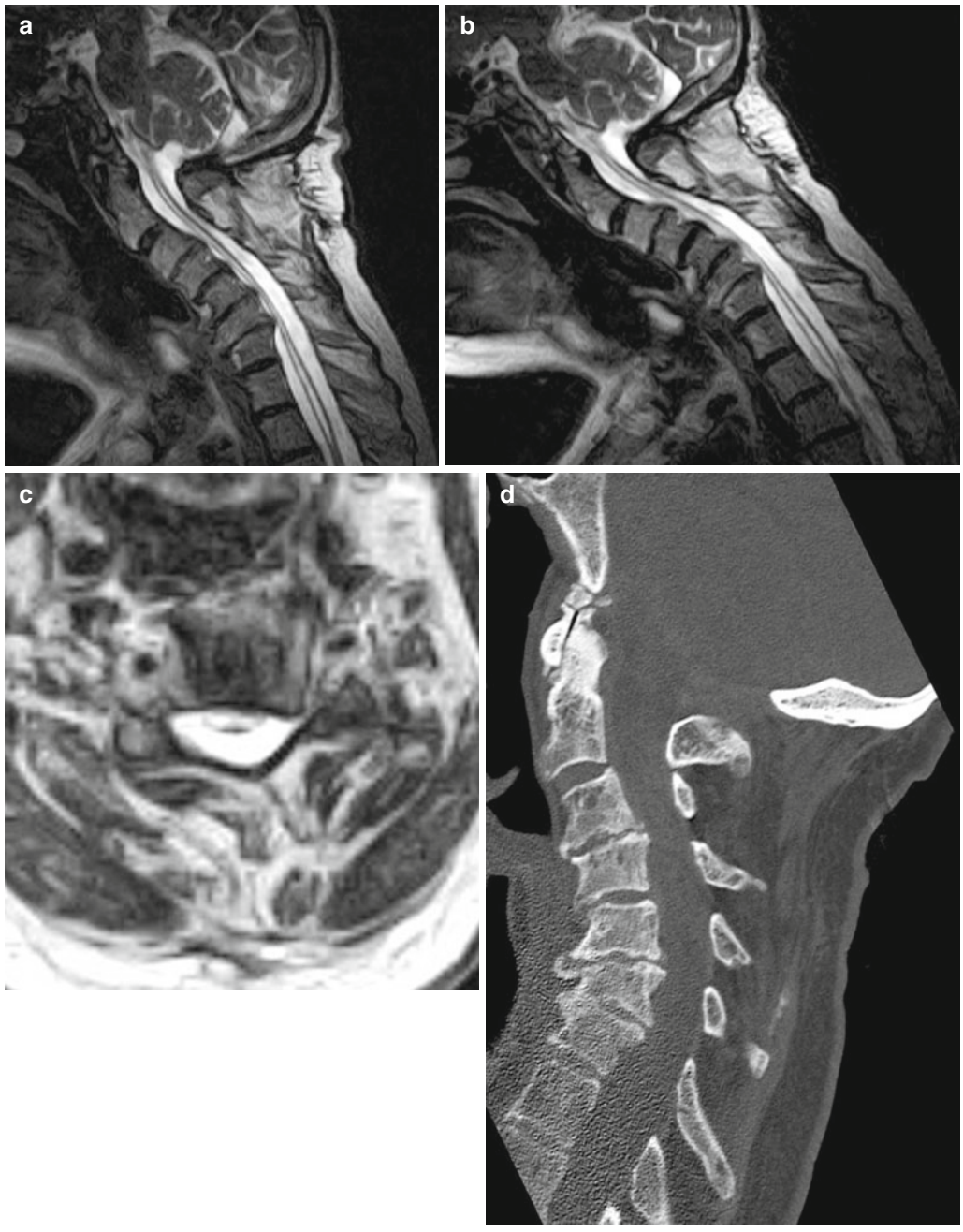
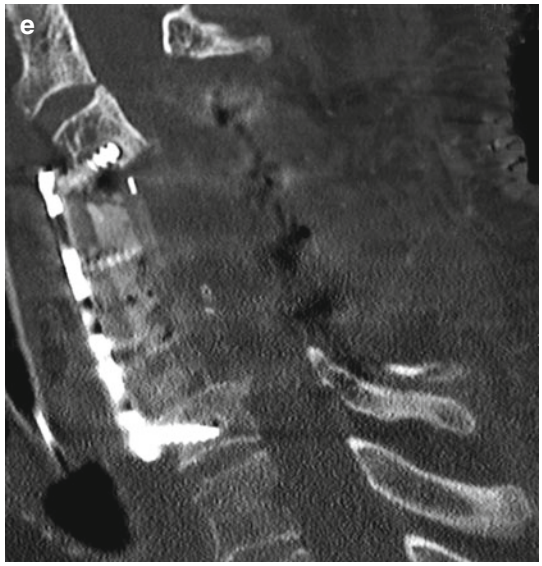


Fig. 16.4 (**a**) This sagittal T2-weighted upright MRI was taken 9 years after decompression of the foramen magnum in neutral position and demonstrates profound spinal cord atrophy, a collapsed syrinx, a free CSF passage at the foramen magnum, and a multilevel osteochondrosis in his cervical spine with a kyphotic deformity in a patient now 74 years of age. He suffered a progressive tetraparesis confining him to a wheelchair with increasing weakness of his respiratory muscles and loss of upper extremity functions. (**b**, **c**) With inclination of his head, the compression of the cord by osteophytes is evident. (**d**) The sagittal CT reconstruction shows the multiple osteochondroses and the swan neck deformity. The patient underwent a combined decompression with corpectomies C4–C6, reconstruction and ventral fusion C3–C7 followed by posterior decompression C3–C6, and fixation with lateral mass screws C3–C7. The postoperative CT reconstruction (**e**) and lateral X-ray (**f**) demonstrate a good sagittal profile with decompression of the cervical cord. Postoperatively, he made a slow recovery. Four months after surgery, he is able to walk again for about 20 m and is gaining strength and coordination skills in his hands. Respiratory functions have improved only slightly



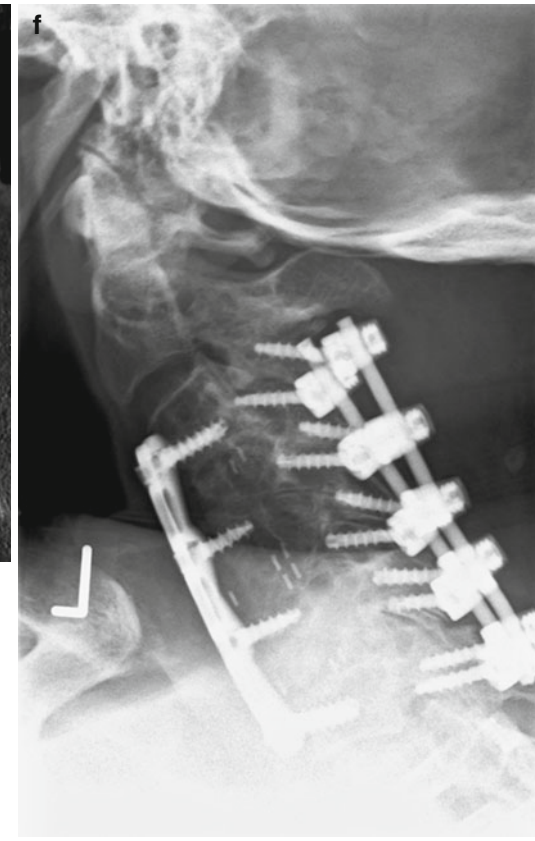


Fig. 16.4 (continued)

Table 16.1 Clinical symptoms for patients presenting after foramen magnum decompression

Group	Occ. pain (%)	Neurop. pain (%)	Hypesthesia (%)	Gait (%)	Motor power (%)	Sphincter function (%)	Swallowing function (%)
No surgery	72	38	58	58	51	5	17
FM group	84	35	73	81	62	19	27
Spinal group	75	38	94	75	69	31	12
Total	77	37	69	69	68	19	20

Abbreviations: *Occ*. occipital, *Neurop*. neuropathic, *FM* foramen magnum

Table 16.2 Operations for patients after foramen magnum decompressions

Group	Ventral fusion	Posterior dec. + fusion	Catheter removal	FM revision	FM revision + fusion	VP shunt
FM group				35	10	1
Spinal group	8	2	5			

Abbreviations: *Dec* decompression, *FM* foramen magnum, *VP shunt* ventriculoperitoneal shunt

patients, the Chiari malformation had been adequately treated with collapse of the syrinx and a free CSF passage at the foramen magnum. Five syrinx shunt catheters were removed to release a postoperative tethering of either nerve roots or spinal cord. In each of these patients, pain and dysesthesias were provoked with certain body movements. The tethering had not caused reappearance of the syrinx in any of them.

For removal of a syrinx catheter, the sharp microsurgical dissection concentrated on untethering nerve roots and spinal cord first. Once this was achieved, the catheter could be removed in most instances. If it was stuck in the cord, it was transected right at the entry point into the spinal cord.

For patients with degenerative disc disease, it was the general policy to restrict one- or two-level ventral fusions to patients with radicular symptoms, whereas multilevel posterior decompressions and fusions were preferred for patients with a progressive myelopathy. This strategy was based on observations that patients with a progressive cervical myelopathy almost always displayed a profound spinal cord atrophy due to the former syringomyelia and often demonstrated multilevel hypermobilities of the cervical spine. The intention was to prevent future deteriorations from adjacent levels in patients with a significantly reduced functional reserve.

Six patients underwent seven ventral fusions for single- or two-level disc disease of the cervical spine. One of these underwent an additional posterior cervical decompression and fusion 10 years later when she developed a progressive myelopathy. One patient underwent a combined anterior and posterior decompression and fusion for a swan neck deformity (Fig. 16.4). Finally, one patient received a posterior decompression and fusion only. Posterior decompressions consisted of laminectomies C3 to C6 with lateral mass fixation (Table 16.2).

There were no surgical morbidity or complications in the spinal group. Looking at individual symptoms, a trend for improvements of pain, sensory disturbances, and dysesthesias was observed. Other neurological signs such as motor weakness or gait problems tended to remain unchanged. At 3 months postoperatively, three of five patients reported improvement after syrinx catheter removals. All but one ventral fusion of the cervical spine resulted in some clinical improvement at that time. Posterior decompressions and fusions were followed by improvement after both operations.

In the long term, two patients developed adjacent-level disease in the cervical spine after ventral fusions and underwent another ventral or posterior operation each, which stabilized the status. After catheter removal, one patient experienced another deterioration due to postoperative scar formation 4 months after surgery. Her past history had been complicated by meningitis after the initial foramen magnum procedure and no further operation was undertaken.

Table 16.3 Pathological findings in 45 foramen magnum revisions

Feature	Number of operations
Pseudomeningocele	8
Adhesion of graft to cerebellum	24
Adhesion of graft to spinal cord	5
Slight arachnoid scarring	7
Severe arachnoid scarring	24
History of meningitis	3
Obstruction of foramen of Magendie	20
Ventricular dilatation	7
Anterior compression by odontoid	1
Craniocervical instability	10

As multiple features were often found in a single operation, the total sum is higher than the number of revisions

Secondary Surgeries at the Foramen Magnum

Apart from one patient in this group requiring a ventriculoperitoneal shunt for late postoperative hydrocephalus, the patients in this subgroup demonstrated either an untreated or new instability of the craniocervical junction, an insufficient decompression, or an obstruction of CSF flow at this level (Figs. 16.1, 16.2, and 16.3). CSF flow obstructions were related to arachnoid scarring or compression of the cisterna magna by a pseudomeningocele. Combinations of these different mechanisms were common (Table 16.3).

In a previous publication, the lack of effect of syrinx shunts in patients with a Chiari I malformation and syringomyelia was demonstrated [14]. Therefore, such shunts were never considered

for patients after a failed decompression. If a syrinx had not regressed or reappeared, the reason had to be looked for and treated at the foramen magnum. This required a revision with opening of the dura exchanging the duraplasty, arachnoid dissection with establishment of a free outflow from the foramen of Magendie, and insertion of a new duraplasty using alloplastic rather than autologous material. Several authors have mentioned the importance of opening this foramen during foramen magnum decompressions [1, 15, 16] and especially in revisions [16, 17].

Forty-five revisions at the foramen magnum were performed (Figs. 16.2 and 16.3), of which ten were combined with a posterior craniocervical fusion (Fig. 16.1), where one revision included transoral resection of the odontoid and posterior decompression and fusion in a second operation. In four instances, the revision was restricted to craniocervical fusion only as no CSF flow obstruction was detectable on preoperative imaging and intraoperatively using ultrasound (Table 16.2).

Severe arachnoid scarring was the commonest feature in patients demonstrating a CSF flow obstruction [18–22] and detected in 31 instances (94 %) in the form of adhesions either between dural graft and cerebellum and spinal cord in 29 operations (88 %) or obstruction of the foramen of Magendie in 20 revisions (61 %) (Table 16.3). Whereas the adherence of the dura graft to underlying nervous tissue was due to either pseudomeningocele formation pushing the dura graft anteriorly [7], the suture material, autologous graft material, or insufficient arachnoid dissection at the first operation, the most severe arachnoid scarring at the foramen of Magendie was encountered after obex plugging, resection of tonsils (Fig. 16.2), or in patients with a history of meningitis [14, 18, 23].

The major problem of preoperative evaluation was the severity of arachnoiditis. The more extensive and dense the arachnoid pathology, the less the probability that a revision may produce a lasting benefit and the higher the risk of surgery. Unless there was a history of meningitis or a clear description of severe arachnoid changes in the operation notes, it was almost impossible to foresee exactly what would be discovered after opening of the dura. Thus, it is difficult to judge the prognosis for a patient before revision surgery. This needs to be discussed with the patient. Reexploration of the foramen magnum is to some degree a diagnostic procedure in order to find out why the first operation did not provide the desired result. Depending on the intraoperative findings, a surgical strategy had to be adopted which improved CSF flow but minimized the risk of postoperative arachnoid scarring, which may again lead to CSF flow obstruction and prevent a long-term benefit. Limiting the arachnoid dissection to the midline with sharp transection of arachnoid adhesions obstructing the foramen of Magendie and the posterior spinal subarachnoid space was all that was required. Blunt dissection or preparation of arachnoid adhesions laterally carries the risk of damage to small perforating arteries and caudal-cranial nerves and should be avoided. Finally, a spacious dura graft using alloplastic material provided reasonable protection against postoperative arachnoid scarring which may otherwise cause another clinical recurrence.

Complications were encountered in 22.2 % of foramen magnum revisions with CSF fistulas being the most common after four operations (8.9 %). Surgical morbidity was observed after four revisions (8.9 %) and encountered exclusively among patients who had undergone their first decompression at other institutions. Compared to patients undergoing a first foramen magnum decompression, the overall complication rate for foramen magnum revisions was similar [24], even though the rate of CSF leaks was higher.

A postoperative improvement after 3 months was reported after 65.1 % of operations, while 23.3 % resulted in no postoperative change and neurological worsening was evident after 11.6 % of revisions. Looking at individual symptoms in the first postoperative year revealed improvements for pain, sensory disturbances, and gait. The remainder of symptoms tended to be left unchanged. Improvements tended to be marginal and of little functional significance. Similar experiences have been made for patients with

severe foramen magnum arachnoiditis of other causes [25]. The realistic outlook for patients undergoing a foramen magnum revision was clinical stabilization of the previously progressive course.

Long-term results determined by Kaplan-Meier statistics revealed a recurrence rate of 34 % within 10 years. Two patients with such a recurrence underwent a third foramen magnum operation without long-term success. Both had been accompanied by severe arachnoid pathology related to obex plugging with muscle or previous meningitis, respectively.

Conclusions

Patients presenting with progressive neurological symptoms after a foramen magnum decompression for Chiari I malformation require a detailed clinical and radiological work-up to identify the responsible mechanism. Not only does the foramen magnum area need a careful analysis, but degenerative diseases of the cervical spine should also be taken into account. Particularly important are signs of instabilities as the often atrophic spinal cords of these patients may be extremely vulnerable to hypermobile segments. Multilevel decompressions and fusions may stabilize the course in such patients. Foramen magnum revisions are indicated in patients with evidence of CSF flow obstruction, cord compression, or instabilities at this level. They carry a higher surgical morbidity and are less likely to produce significant neurological improvements compared to a primary decompression. However, about 66 % can be stabilized with such a revision for at least 10 years.

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Scoliosis and Chiari I Malformations 17

Heather S. Spader and Douglas L. Brockmeyer

Abstract

Scoliosis is a relatively common condition observed in approximately 20 % of patients who have Chiari I malformations. It is most often found in association with syringomyelia. The presence of a Chiari malformation and scoliosis with or without symptoms frequently requires surgical intervention. Patients with scoliosis who have any of the following characteristics should undergo further evaluation: progressive scoliosis in a child less than 11 years old; left thoracic thoracolumbar scoliosis; painful scoliosis; mild painful stiff neck; abnormal deep tendon reflexes; muscle atrophy; minimal sensory loss; minimal weakness of a limb; or absence of abdominal cutaneous reflexes. The initial surgery of choice is a suboccipital decompression. Patients who have the best outcome are younger than 10 years old and have Cobb angles less than 20–30°. It is important to be vigilant about screening patients for Chiari malformations and syrinxes in cases of "idiopathic" scoliosis because early intervention portends the best prognosis for these patients.

Introduction

Scoliosis is a relatively common condition associated with Chiari I malformations. In affected patients, it is most often found in association with syringomyelia, although occasionally patients will present with scoliosis alone. It is important to identify patients with Chiari malformations and scoliosis because they typically require management of their tonsillar ectopia before management of their scoliosis to avoid harmful neurological sequelae. Several studies have shown that identifying these patients early also leads to better outcomes. Here we review the underlying epidemiology, presumed pathophysiology, and clinical

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characteristics of Chiari-related scoliosis and discuss surgical management and patient outcomes.

Epidemiology

Various studies have shown that the incidence of scoliosis in patients with Chiari I malformations ranges from 15 to 50 % [1, 2]. In the largest case series to date, 90 out of 500 (18 %) patients with Chiari I malformations had scoliosis [2]. Between 30 and 85 % of those patients who have both Chiari malformations and scoliosis also have concurrent syringomyelia [3, 4]. Furthermore, most cases of syringomyelia with scoliosis occur in the pediatric population [5]. Although not all Chiari I patients with syringomyelia necessarily require treatment, it is agreed that the occurrence of scoliosis with a Chiari I malformation typically requires a treatment strategy that includes surgical decompression [6].

Pathophysiology

The theories postulating the origins of syringomyelia are described elsewhere in this text and although not all cases of scoliosis and Chiari I malformations are associated with syringomyelia, there is a clear association between syringomyelia and scoliosis [2, 7]. This relationship is still not completely understood.

In a series of experiments in the 1970s, Williams [8] attempted to characterize this relationship through animal models. In these studies, Williams found that injection of cerebrospinal fluid (CSF) into the spinal cords of dogs resulted in the development of a spinal curvature. Another experimental study demonstrated that scoliosis in monkeys with spinal cord damage due to polio was worse when sensory afferents were damaged [9]. Follow-up studies in monkeys examined whether sectioning of the dorsal spinal nerve roots would affect the development of scoliosis. The investigators found that scoliosis developed convex to the damaged side and that the severity was dependent on the number of nerve roots cut. They proposed that the curve was caused by asymmetric paraspinal muscle weakness due to the loss of proprioception [10].

Tachibana et al. used a balloon method to assess the intramedullary pressure dynamics of the spinal cord [11]. This was done by placing intramedullary balloons in 15 dogs and measuring the intramedullary pressure of the spinal cord in different positions and in traction. The authors found that the intramedullary pressure of the cervical spinal cord increased when the neck was flexed, possibly playing a role in syrinx formation. They related this flexion effect to Chiari malformations in that when the neck is flexed, CSF flow is blocked by the cerebellar tonsils, plugging the foramen magnum and collapsing the central canal, causing a syrinx. This pressure also concomitantly causes pressure in the spinal cord parenchyma, which may contribute to the development of scoliosis because of damage to sensory afferents.

If the theory that damage to sensory afferents is caused by increased intramedullary pressure due to syringomyelia is correct, then there seems to be a causal relationship between the damage caused by syringomyelia and scoliosis formation. It does not completely explain, however, how scoliosis develops in patients without syrinxes. The authors of one study that examined a "presyrinx" state hypothesized that even though a syrinx is not seen on imaging, damage to the neurons surrounding the central canal, including, perhaps, sensory afferents, could be responsible for scoliosis formation. This damage was demonstrated by Fischbein et al. through T2 prolongation signals in the spinal cord parenchyma without syrinx formation [12]. This presyrinx state was also associated with a myelopathy that reversed with a restoration of CSF flow without permanent sequelae. In addition to these experimental and imaging studies, there is one case report of a lumboperitoneal shunt that caused a Chiari I malformation, syrinx, and subsequent scoliosis [13].

Signs and Symptoms

Many patients with Chiari malformations and scoliosis initially present with spinal curvature. Among the presenting symptoms (Table 17.1),

Table 17.1 Symptoms and signs of Chiari associated with scoliosis

Symptoms	Signs
Pain in neck, back, limbs, head	Skull defects
Headaches worsened by Valsalva maneuver	Short neck or low hairline
Numbness	Excessive lordosis
	Limb and muscle deformities
	Abnormal abdominal reflexes
	Nystagmus
	Sensory loss
	Spasticity
	Charcot joints
	Sympathetic disturbances

the most common is pain, which may occur in the neck, back, limbs, and head. Headaches, if present, are typically worsened by Valsalva maneuver. The pain may be replaced by numbness if the symptoms persist [8]. Signs include skull defects due to hydrocephalus, short neck or low hairline, excessive lordosis, and limb and muscle deformities. Neurologic findings include abnormal abdominal reflexes, nystagmus, sensory loss, muscle wasting, spasticity of the lower limbs, Charcot joints, and sympathetic disturbances such as Horner's syndrome [8, 14]. Of note, often the only sign of an underlying neurologic pathology is the loss of the superficial abdominal reflex. This spinal reflex is often absent on the same side as the scoliosis [15].

Diagnosis

Spinal magnetic resonance imaging (MRI) studies reveal that between 2 and 26 % of patients with "idiopathic" scoliosis have neuroanatomic abnormalities [16]. The majority of these abnormalities are Chiari I malformations and syringomyelia [17]. Three studies have shown a wide range of diagnostic yields with MRI, depending on the patient's age. Neuroanatomical abnormalities were diagnosed in 22 % of infants and 26 % of juveniles but only 1.2 % of adolescents [16, 18, 19]. The implications of these findings are not clear at the present time.

The spinal curvature of patients diagnosed with scoliosis and Chiari malformation differs from that of patients diagnosed with the idiopathic scoliosis (Fig. 17.1). Scoliosis associated with Chiari malformations and syringomyelia has a higher incidence of left convexities, double thoracic curves, triple curves, and long right thoracic curves with end vertebra caudal to T12 [3, 20]. Some patients also have more typical right thoracic curves but have superior or inferior shift of one or both vertebrae and/or apex [20]. Furthermore, in the experience of the senior author, coronal balance is not maintained and rotational changes are not as frequent.

Based on the above information, children with "idiopathic" scoliosis who have any of the following characteristics should undergo MRI scanning for further evaluation (Table 17.2): progressive scoliosis in a child less than 11 years of age, left thoracic or thoracolumbar scoliosis, painful scoliosis, mild painful stiff neck, abnormal deep tendon reflexes, muscle atrophy, minimal sensory loss, minimal weakness of a limb, or absence of abdominal cutaneous reflexes [3, 21]. Some authors even argue that all patients with "idiopathic" juvenile scoliosis should undergo MRI scanning because juvenile scoliosis is relatively uncommon [16]. Infantile scoliosis (ages less than 3 years) is also unusual, and MRI scanning is recommended for all patients with infantile scoliosis and a curve >20° with no other neurologic findings [19]. Of note, the left thoracic curve alone is also a strong predictor for neuroanatomic deformities [22].

Treatment

Although not all patients with Chiari I malformations and syringomyelia require an operation, there is consensus that if the syrinx also results in scoliosis, then operative intervention is warranted. In a 1998 survey of the members of the Pediatric Section of the American Association of Neurological Surgeons (AANS), there was "substantial agreement" to operate on patients with

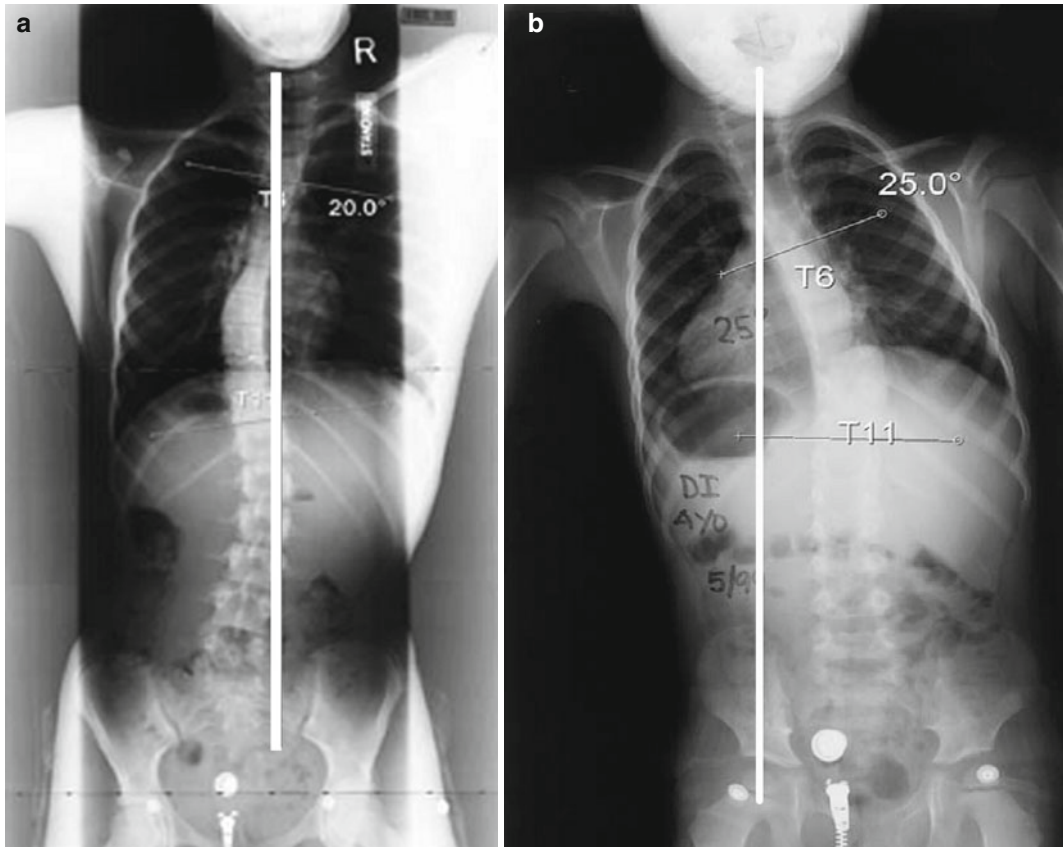

Fig. 17.1 Radiographs showing patients with idiopathic (**a**) and Chiari (**b**) scoliosis curves

Table 17.2 Characteristics of patients with idiopathic scoliosis who should undergo magnetic resonance imaging for evaluation of their potential for Chiari

Progressive scoliosis in a child less than 11 years old
Left thoracic or thoracolumbar scoliosis
Painful scoliosis
Mild painful/stiff neck
Abnormal deep tendon reflexes
Muscle atrophy
Minimal sensory loss or limb weakness
Absence of abdominal cutaneous reflexes

syringomyelia and scoliosis [23]. A survey conducted by the Education Committee of the International Society for Pediatric Neurosurgery in 2003 found that there was a consensus that a Chiari decompression should be performed in patients with scoliosis with syringomyelia, and most surgeons did decompression in patients with scoliosis even without syringomyelia [6].

The most appropriate management of patients who present with Chiari malformations and scoliosis, without syringomyelia, is controversial. There is little data to either support or refute the notion that a prophylactic Chiari decompression in an otherwise asymptomatic patient with scoliosis improves spinal curvature. In the largest series of Chiari/scoliosis patients to date [24], no mention was made of this particular constellation of radiographic findings. Extrapolating from the data available for the Chiari/syringomyelia/scoliosis population, it is reasonable, in the author's opinion, to proceed with a Chiari decompression solely because of scoliosis if the curve is rapidly progressive or if the curve is large and will almost certainly require orthopedic correction. Otherwise, it is reasonable to follow the patient with serial imaging and take appropriate action if spinal curvature worsens.

Earlier reports on the treatment of syringomyelia, Chiari malformations, and scoliosis describe

a Chiari decompression with dural graft as well as syringo-subarachnoid shunts [25, 26]. Other reports also describe aspiration of the syrinx or syringostomy [27]; however, syringo-subarachnoid shunts and syrinx aspiration are no longer widely used in treating these patients because of their limited effectiveness [28].

The authors of larger, more recent case series have employed craniocervical decompression for patients with syringomyelia and scoliosis [24]. Techniques for this procedure vary, but there is consensus that patients benefit from a suboccipital decompression consisting of suboccipital craniectomy, C1 posterior arch removal, dural opening and arachnoid dissection, and a tight dural closure. There is not a complete consensus about the need to reduce the cerebellar tonsils [29]. The decompression eliminates the need for subsequent spinal fusion in 30–60 % of patients [24, 30–34]. The reason for the variable fusion rates lies in the patient characteristics before surgery. Most patients with a scoliosis of greater than 20–40° will require surgery after decompression [7, 24, 31, 32]. Younger patients (less than 8–10 years old) are less likely to require corrective surgery [7, 32, 34]. Patients whose scoliosis crosses the thoracolumbar junction may benefit from earlier orthopedic involvement. In addition, if the syrinx does not abate with posterior suboccipital decompression, these patients are more likely to need orthopedic correction [30].

Of note, treating adult scoliosis and syringomyelia is much more difficult. In one series of 42 patients, adult syringes were found to be larger, the neurologic symptoms were present for much longer, and the surgical outcomes were poor [5].

Results and Long-Term Outcomes

There are many retrospective reviews of the outcomes of pediatric patients with Chiari I malformations and scoliosis. Most studies found that younger age and smaller curves resulted in better outcomes. The largest retrospective review to date, by Krieger et al. [24], included 79 patients with Chiari I malformations, syringomyelia, and scoliosis. Sixty-two percent of these patients had curves less than 20°. The rest of the patients had curves ranging from 25° to 80°. None had neurological symptoms, but 16 % had neurological signs on physical examination. All patients had a craniocervical decompression, which consisted of an occipital craniectomy of 2.5 × 2.5 cm, C1 posterior arch removal and occasional C2 laminectomy, dural opening and lysis of adhesions, and loose dural closure. Eighty-seven percent of these patients had a significant reduction in the syrinx and corresponding ascent of the cerebellar tonsils within 6 months postoperatively. Six (8 %) required reoperation for a persistent large syrinx. Two patients required placement of a shunt for hydrocephalus. Of those patients with curves less than 20°, none had further curve progression after surgery. Of the 30 (38 %) patients with curves 25° or greater, 21 required further scoliosis treatment, with 12 requiring orthotics, 11 needing spinal fusions, and 2 requiring orthoses and fusions [24].

Other case series have shown similar results with some variations. Attenello et al. [30] retrospectively reviewed 21 patients with Chiari I malformations, syringomyelia, and scoliosis that underwent a suboccipital decompression. Of these patients, 38 % had an improvement in scoliosis and 48 % had a progression. Increased risk of progression was associated with thoracolumbar scoliosis and failure of syrinx improvement after surgery. They concluded that patients with a larger Cobb angle or scoliosis that crosses the thoracolumbar junction would probably benefit from earlier orthopedic involvement as these patients are unlikely to improve with posterior fossa decompression alone [30].

In a 10-year experience (1990–2000) at Primary Children's Medical Center [7], a retrospective review of 85 patients who had Chiari I malformations found 22 who also had scoliosis (average age 8.5 years). Of these patients, 20/22 had associated syringes, 15/22 had curves convex to the left, and 7/22 had curves convex to the right. All 22 patients were initially managed with a suboccipital decompression, C1 posterior arch removal, lysis of arachnoid adhesions, and duraplasty with a layered closure of the wound. No patients had shunting. The mean follow-up was 2.1 years, and a change in Cobb angle of greater

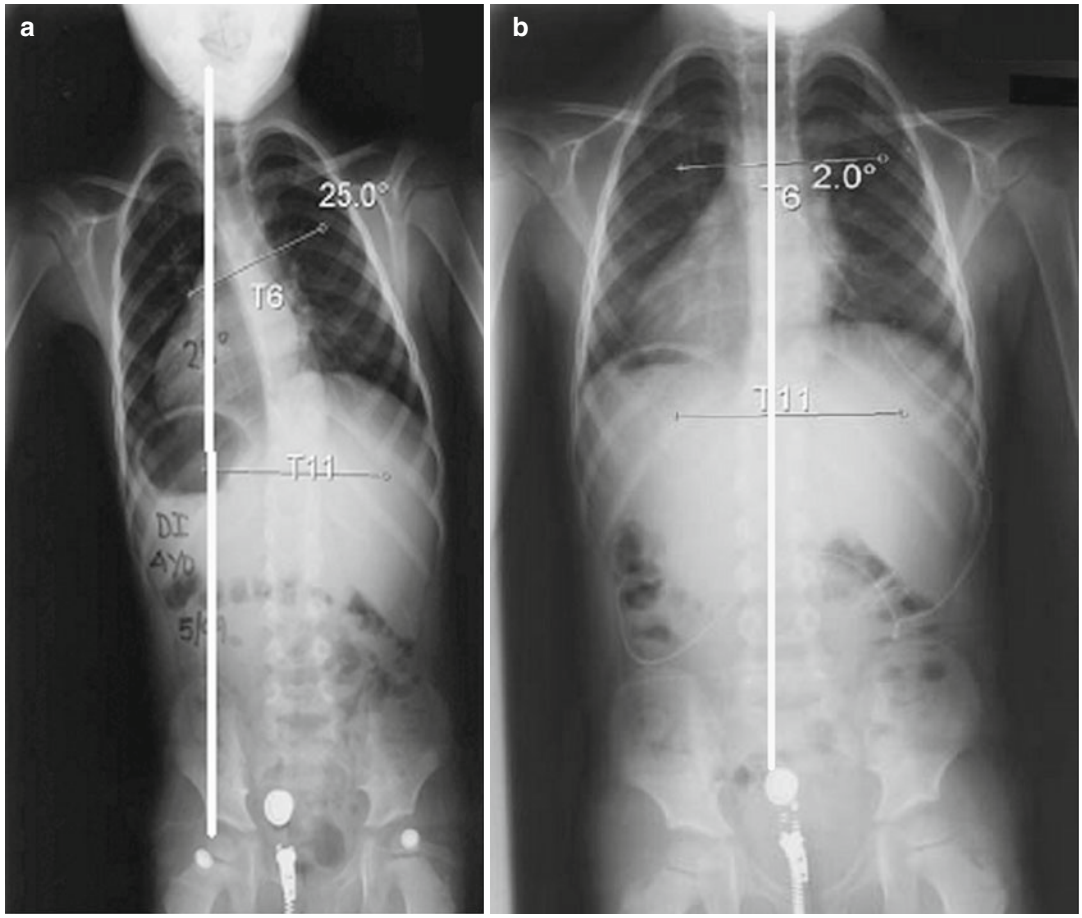

Fig. 17.2 Radiograph showing a patient with Chiari with scoliosis before (**a**) and after (**b**) surgery

than 5° was considered significant for either progression or improvement. Fifty-seven percent of patients had an initial curve of less than 30°, 62 % of curves improved or stabilized after initial decompression, 38 % had a worsening of scoliosis, 19 % required a spinal fusion for curve progression, and three patients were anticipating spinal fusion for worsening curves at the time of publication. All the syringes improved with decompression (Fig. 17.2). Brockmeyer et al. [7] concluded that a majority of patients with scoliosis and a syrinx can be treated with suboccipital decompression and duraplasty alone. They also found that children older than 12 years old and those with curves greater than 30° had a lower chance of improvement. Likewise, patients younger than 10 years old with smaller curves had the greatest chance of curve improvement, since 90 % of the patients of that age had their curves improve or stabilize after suboccipital decompression.

In summary, the procedure of choice in all three of these studies [7, 24, 30] was a suboccipital decompression. The majority of patients also had a duraplasty and coagulation of the tonsils. Between 67 and 100 % of these patients showed an improvement of their syrinxes from this procedure. The rate of persistent scoliosis that needed further treatment was relatively consistent in all three studies and ranged from 38 to 48 %. All three studies also demonstrated that a Cobb angle of less than 20–25° was an indicator of good prognosis. Conversely, curves greater than 25–30° almost always required further intervention, usually

surgically. Lastly, characteristics that suggested a particularly poor prognosis included thoracolumbar disease and age greater than 12 years.

Additional studies support these findings, especially that decompression in patients younger than 10 years of age is far more successful [31, 32, 34]. One retrospective review by Flynn et al. [35] also found that patients who had progressive scoliosis tended to have a double curve, rotation >20°, and thoracic kyphosis.

Conclusion

Patients with Chiari-related scoliosis comprise approximately 20 % of the Chiari population. Most, but not all, of these cases are also associated with syringomyelia. Although the pathophysiology of the relationship between Chiari malformations, scoliosis, and syringomyelia is not completely understood, there is consensus that the presence of scoliosis with or without symptoms requires surgical intervention. The initial surgery of choice is a suboccipital decompression. Patients who have the best outcome are younger than 10 years old, with Cobb angles less than 20–30°. Knowing this, it is important to be aggressive about screening patients for Chiari malformations and syrinxes in cases of "idiopathic" scoliosis because early intervention portends the best prognosis for these patients.

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Natural History of Chiari Malformations

18

Cormac O. Maher

Abstract

Although many aspects of CM-I natural history remain unsolved, some progress is being made. Recently, several groups have reported on CM-I natural history in selected groups of patients that were managed without surgery. Each of these studies followed patients for several years. In general, the natural history for this subgroup of Chiari patients is benign, although cases of clinical progression as well as spontaneous improvement were seen. The available data clarify the natural history of CM-I for the subgroup of CM-I patients that are considered to be asymptomatic or minimally symptomatic and without neurological deficits. Spinal syringes in patients with CM-I follow a varied and unpredictable natural course.

Introduction

For any medical condition or imaging finding, an understanding of the natural history of the condition is a prerequisite to successful clinical decision-making. In order to properly determine the best course for our patients, we must know the relative efficacy of surgical treatment versus "conservative" management. Although patients with Chiari I malformation (CM-I) are frequently referred for evaluation, many aspects of CM-I natural history remain unsolved. As a result, there are no universally accepted criteria for selecting surgical versus nonsurgical management of patients with CM-I. Surveys of pediatric neurosurgeons have consistently found significant differences of opinion regarding surgical indications [29, 31, 62]. In a 2004 survey, Schijman et al. [62] found that 8 % of pediatric neurosurgeons would recommend surgical treatment for an asymptomatic patient with CM-I and 75 % would recommend surgical treatment for an asymptomatic child if a spinal cord syrinx was present [62]. That survey also found that most neurosurgeons (77 %) predicted that an asymptomatic child would likely have symptoms in the future [62].

A principal cause for these uncertain surgical indications is lack of understanding of the fundamentals of this condition, including its prevalence and natural history. Most reported series of CM-I describe outcomes of patients that have been selected for surgery. These reports provide little or no insight into the natural history of this condition. Nevertheless, some progress is being made. In this

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chapter, we discuss our current understanding of this complex topic. The natural history of scoliosis in individuals with CM-I is an important topic covered elsewhere in this volume.

Chiari Prevalence

There are a number of published reports of spontaneous improvement [7, 37, 40, 54, 70–72, 82] and spontaneous worsening [18, 34, 42, 44] in patients with CM-I. In order to place these reports into their proper context, it is necessary to have an accurate estimate of the population prevalence of CM-I.

Most centers use 5 mm of tonsillar descent below the foramen magnum as the imaging criterion for defining CM-I [1, 9, 59, 81]. This relatively arbitrary definition is based on older studies reporting that tonsillar descent more than 3 mm below the foramen magnum was rare in normal adults [1, 9]. Analyses of large numbers of patients undergoing imaging for a variety of indications have estimated that between 0.24 and 3.6 % of the population have at least 5 mm of tonsillar descent below the foramen magnum [3, 19, 45, 67, 81, 86]. Differences in these estimates may have resulted from varying sensitivity in CM-I detection as well as the different populations that were analyzed. Theoretically, true population prevalence of an imaging finding or disease can only be calculated by screening every member of a population of interest with a tool that is both completely sensitive and completely specific. Since such an approach is not practical, prevalence is usually estimated by other means. One technique that has been employed involves reviewing imaging studies obtained from normal volunteers or those screened for reasons other than the disease of interest. This technique is subject to some negative selection bias in that those with disease symptoms may be excluded from such a study. In addition, this technique may be insensitive for discovering common imaging findings that were not an object of the original study. Several groups have reported on various intracranial findings in normal adult volunteers [36, 84, 88]. Although each of these studies was small, a combined meta-analysis by Morris et al. [49]. found CM-I in 71 of 15,559 (0.24 %) MRI studies from combined data of multiple reports in adults. The sensitivity for detecting CM-I in each of these studies and the subsequent meta-analysis is not clear, and in some reports contained in that meta-analysis, no cases of CM-I were found [36]. Given these concerns about the sensitivity of CM-I detection, it is possible that the estimated prevalence of CM-I reported by those studies may be less than the true population prevalence.

Other groups have attempted to estimate CM-I prevalence by reviewing consecutive imaging studies performed for any clinical indication, looking specifically for CM-I. Meadows et al. [45] found CM-I in 0.8 % of those undergoing MRI at a single referral center. All age groups were included in that analysis, but children comprised a relatively small proportion of their subjects. The report by Meadows et al. [45] is remarkable for the relatively few asymptomatic cases of CM-I (14 %) discovered on imaging. More recently, Aiken et al. [3] found CM-I in 1 % of 5,248 children undergoing brain or spine MRI, a prevalence estimate similar to that of Vernooij et al. [81] (0.9 %) in their recent analysis of normal adults over the age of 45. We recently studied a large group of consecutive children undergoing MRI at our institution and found that 3.6 % met imaging criteria for CM-I [67]. In our study, the prevalence of CM-I in those undergoing MRI did not vary significantly by age or gender. The currently available reports on CM-I prevalence vary substantially with respect to the proportion of asymptomatic or incidental CM-I in each group. Aitken et al. [3] reported that only 19 % of findings in their group were thought to be incidental or asymptomatic. By contrast, compared to prior reports, we found a higher percentage of asymptomatic cases (68 %) at the time of CM-I diagnosis, probably reflecting differences in the relative sensitivity of CM-I diagnosis, especially in asymptomatic cases. It is possible that the finding of a larger number of asymptomatic CM-I cases reflects a greater sensitivity for detection of CM-I and is one factor contributing to higher prevalence estimates. If that is the case, then the higher prevalence estimates with a higher

percentage of asymptomatic cases are more likely to reflect the true population prevalence of CM-I than those studies with a greater proportion of asymptomatic cases. Finally, it is worth noting that the largest study in children has found a higher prevalence estimate than the largest study comprised mostly of adults, suggesting a need for age group-specific prevalence analyses in the adult age range [45, 67].

Natural History of Chiari

The degree of cerebellar tonsillar descent is not always stable over time. Gradual ascent of cerebellar tonsils has been associated with normal childhood development [47]. This normal ascent should be considered in any interpretation of the natural history of CM-I. Furthermore, improvement or worsening of tonsillar descent over time may result from changes in the skull or, less likely, cerebellar morphology [43]. There is no convincing evidence to suggest that spinal tethering or caudal traction plays any role in CM-I pathogenesis in most cases [75, 77, 79], although there may be some rare exceptions to this rule [63, 82]. Growth in height during childhood, therefore, does not appear to be an important factor in clinical or imaging progression. Spinal CSF leaks or drainage infrequently cause progressive tonsillar descent, but is not a cause of tonsillar descent in the vast majority of cases [6, 55, 76].

There are several reported cases of CM-I that experienced spontaneous improvement in cerebellar tonsillar descent [7, 27, 35, 37, 54, 70, 71]. Since a finding of CM-I is relatively common on intracranial imaging, case reports or even small case series of spontaneous improvement or worsening do not provide any real insight into CM-I natural history. Any attempt to consider the natural history of CM-I will need to account for selection bias in the decision to pursue surgical treatment. The patients followed in most natural history analyses have been selected for nonsurgical management. Therefore, any conclusions derived from these asymptomatic or minimally symptomatic patients should not be applied to symptomatic patients that are ordinarily considered good surgical candidates. It seems likely that the natural history is worse for more symptomatic patients for whom surgery is more frequently offered. Furthermore, any natural history analyses of patients selected for surgery are biased by a presumed preferential inclusion of those who are presumed to have an unfavorable natural course [23]. Based on results of the best currently available natural history studies, there is no basis for making any assumptions about the natural history of patients that meet our usual surgical criteria [10, 52, 66].

Recently, several groups have reported on CM-I natural history in selected groups of patients that were managed without surgery [10, 44, 51, 52, 66]. Any attempt to analyze changes in CM-I symptoms over time will necessarily require some subjective determinations of CM-I symptoms. CM-I symptoms can be notoriously protean and may overlap with other neurological conditions, making it difficult to precisely identify those patients with symptomatic CM-I [26, 67]. In general, patients with headaches are considered symptomatic if the headaches have at least some of the features considered compatible with CM-I headaches, including a tussive component, short duration, and a lack of migrainous features. Other symptoms typically assigned to CM-I include sleep apnea, swallowing difficulty, scoliosis, and motor or sensory disturbances in the extremities of patients with spinal syrinx. Although there are case reports of sudden symptomatic presentation [4, 13, 22, 30, 39, 58, 64, 73, 74, 85, 87, 89, 91], the onset of symptoms of CM-I is usually gradual [10, 52, 66, 78, 80]. In the series reported by Aitken et al. [3], 4 of 19 patients with incidental CM-I (21 %) developed at least 1 CM-I symptom over an interval of over 6 years. In most cases, the new symptoms were headaches only. They found that no imaging characteristics were predictive of new symptoms. Novegno et al. [52] reported on a series of 22 patients with CM-I for whom nonsurgical management was recommended. Over a mean follow-up interval of almost 6 years, they found that 5 patients had symptomatic worsening and 3 of these required surgery, while 17 of their patients remained asymptomatic or their symptoms improved [52]. They concluded

that a conservative approach to asymptomatic or minimally symptomatic CM-I could be justified based on their data. Benglis et al. [10] recently reported on a larger series of 124 patients with CM-I that were followed without surgery for a mean of 2.8 years. None of the patients in that series had new neurological deficits at follow-up. Finally, in our own series of 147 patients followed after an initial decision for nonsurgical management, 90 % remained asymptomatic or minimally symptomatic over an interval greater than 6 years [66]. In addition, 6 patients who were symptomatic at presentation were not symptomatic at last follow-up. Each of these studies followed patients for several years, but further study will be required before any conclusions can be drawn for determining the need for surgery over the lifetime of a patient.

Gender appears to be an important factor in CM-I presentation. Some groups have reported a female predominance for those undergoing surgical treatment of CM-I, but this has not been a universal finding [19, 28, 45, 48, 52, 90]. There is now evidence that CM-I as an imaging finding has an equal gender distribution [67], but that girls appear more likely to present for medical attention of a CM-I [19, 38, 48, 61]. In our own survey of all symptomatic and asymptomatic children that underwent imaging at our institution, a higher proportion of girls with CM-I (41 %) were considered to be symptomatic compared to boys (22 %), although the prevalence on imaging did not differ according to gender [67]. Girls are also more likely to have an associated spinal syrinx and more likely to have associated scoliosis compared to boys [67]. As a result, girls appear to be more likely to present for neurosurgical treatment, probably explaining the female predominance in some surgical series [19, 38, 48, 61].

In series comprised mostly of children, older age is often associated with symptomatic presentation of CM-I. Aitken et al. [3] found that older age at the time of diagnosis was predictive of having neurological symptoms associated with CM-I. This is also supported by a comparison of pediatric and adult case series with respect to symptomatic presentation. In general, higher rates of symptomatic presentation and syrinx have been reported in series consisting mainly of adults compared to pediatric cases [17, 19, 45, 67, 86]. In our own pediatric series [67], as well as "in several prior reports on CM-I in children [3, 24, 50, 52], patients who were symptomatic at presentation were older at the time of CM-I diagnosis compared to children who were asymptomatic. In contrast to pediatric case series, surgical series that focused on adults have generally reported that symptomatic presentation most often occurs in the third decade or early in the fourth decade of life [2, 8, 48]. This finding, combined with the data from pediatric population studies, implies that patients are most likely to present during late childhood and young adulthood. Symptomatic presentation during late adulthood may occur but is relatively unusual.

The presence of symptoms does not always correlate with the perceived need for surgical treatment. Occasionally, patients and surgeons may elect to manage even a symptomatic CM-I without surgery if the symptoms are mild. In our own series of 147 patients followed after an initial decision for nonsurgical management, 14 (9 %) patients ultimately underwent surgery for CM-I at some point during a 6-year follow-up interval [66]. The most common reasons for surgical treatment during the follow-up interval were medically refractory and persistent headaches, sleep apnea, and changes in a syrinx. For these 14 patients, the mean time to surgery after CM-I diagnosis was 2 years. In some cases, patients were initially recommended for nonsurgical management and then later underwent Chiari decompression despite a lack of any new symptoms or radiological findings. In these cases, the decision to offer surgery was made because symptoms had persisted despite conservative management. There was no significant difference in initial tonsillar herniation in the group that ultimately underwent surgery compared with those individuals who did not undergo surgery. In addition, there were no significant differences in change in CSF flow at the foramen magnum between the group that underwent surgery and the group that did not have surgery. These results are similar to reported rates of surgical treatment in the series by Novegno et al. [52] (14 %) as well as Benglis

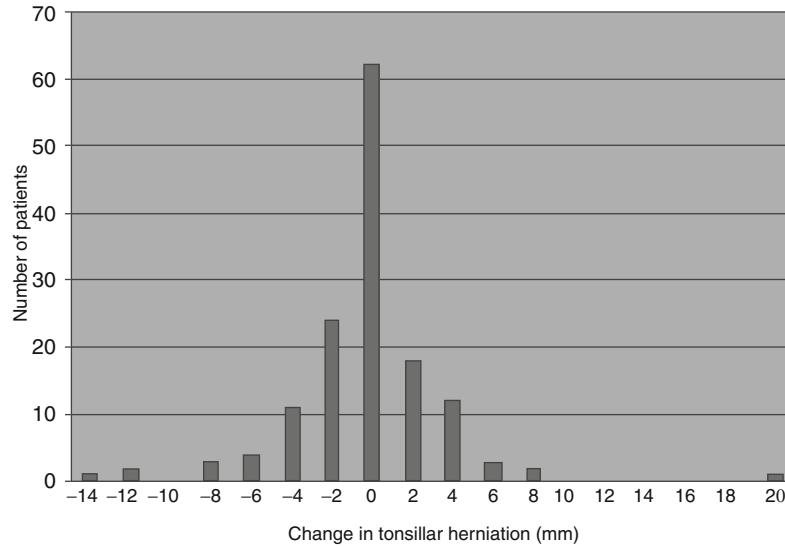

Fig. 18.1 Bar graph illustrating change in tonsillar herniation in 147 patients with CM-I

et al. [10] (4 %). Although the decision to pursue surgical treatment is necessarily based on subjective and difficult-to-quantify criteria, it is clear that surgery is rarely required for patients for whom an initial decision to pursue nonsurgical treatment has been made.

Although changes in patient symptoms or neurological examination have been the primary focus of most efforts at understanding CM-I natural history, changes in tonsillar descent over time have also been noted. In our recent natural history analysis, there was no change in mean cerebellar tonsillar herniation for the group as a whole over a mean imaging follow-up of almost 4 years, although spontaneous worsening and improvement was seen in some cases. Interval improvement in the amount of tonsillar descent was seen in 31 % of patients, and 5 % had a follow-up MRI with less than 5 mm tonsillar descent and were no longer considered to have a CM-I according to the usual definition (Fig. 18.1). An increase in tonsillar herniation of at least 4 mm was seen in 4 % of patients. We attempted to identify factors that were predictive of a change in the degree of tonsillar descent. Gender was not predictive of change in tonsillar descent. Advancing age, however, was associated with a decrease in the amount of tonsillar herniation. Patients between 0 and 6 years of age at the time of CM-I diagnosis had a mean increase in tonsillar herniation of 0.63 mm. In contrast, patients between 6 and 12 years of age at time of CM-I diagnosis had a mean decrease in tonsillar herniation of 0.53 mm, and those between 12 and 18 years of age at time of CM-I diagnosis had a mean decrease in tonsillar herniation of 1.24 mm. Our results, like those of Novegno et al. [52] and Benglis et al. [10], support a generally benign natural history for those patients with CM-I that meet the usual criteria for conservative management.

Natural History of Chiari I-Associated Syrinx

CM-I is known to cause spinal cord syrinx in some patients [5, 11, 12, 15, 20, 33, 42, 51, 53, 57]. Most surgical series report that between 60 and 85 % of CM-I patients have an associated syrinx [46, 48, 80]. Since the presence of a syrinx is an indication for surgery at many centers, reported surgical series tend to overestimate the frequency that syrinx occurs in patients with CM-I [29, 31, 62]. Analyses of imaging databases generally have shown that syringes are less frequently associated with CM-I than have been reported in surgical series. A syrinx was found in 12 % of patients with CM-I in the imaging series reported by Aitken et al. [3] and in 23 % of CM-I patients in our own series [67]. As with CM-I in general,

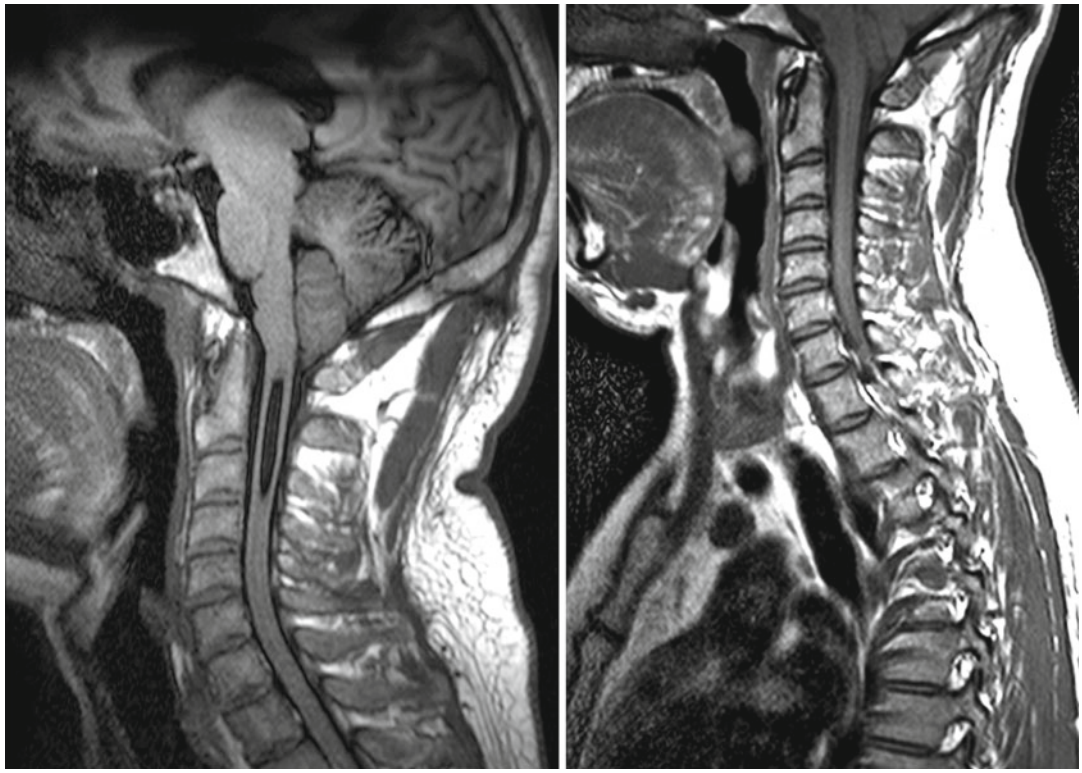

Fig. 18.2 *Left*: Sagittal T1-weighted MRI of a "normal volunteer" for an MRI research study demonstrating a CM-I as well as a cervical spine syrinx. The patient was evaluated by a neurosurgeon but elected follow-up without surgical treatment. *Right*: 6 months later, another sagittal T1-weighted MRI demonstrates substantial resolution of cervical spine syrinx. Such cases illustrate that spontaneous resolution may be rare but is not impossible

the natural history of spinal syrinx associated with CM-I has not been studied until recently. There are several case reports of both spontaneous improvement as well as worsening in individuals with CM-I and spinal syrinx (Figs. 18.2 and 18.3) [40, 54, 70, 71]. The tendency to treat CM-I surgically when a syrinx is present has made any larger natural history analysis of this subgroup particularly challenging [12, 51].

Syrinx formation appears to be a rare event in patients with CM-I over short follow-up intervals. Benglis et al. [10] identified no new syrinx formation among 124 patients with CM-I that were followed for almost 3 years. In our own recent natural history analysis, syrinx formation occurred in 5 % of the 148 patients with CM-I that were followed without surgery over an imaging follow-up duration of nearly 4 years. The mean time interval to syrinx development was 28 months [66]. Of the seven new syringes, two developed from a previously identified pre-syrinx state (T2-hyperintensity on MRI without cavitation) [21, 25, 41], three developed from what had been considered a dilated central canal of less than 3 mm in diameter, and only two patients had previously normal spine MRIs. In patients with CM-I, age appears to be a relevant factor in spinal syrinx formation. In our analysis, although the prevalence of CM-I in those undergoing MRI did not vary significantly by age, spinal syrinx was more commonly found in older children with CM-I [67]. Syringes were much less common during the first years of life but appear to become increasingly common until 5 years of age. It was not unusual for a younger child with CM-I but no syrinx on presentation to develop a syrinx over the follow-up interval. This finding supports our current understanding of the causal relationship between the CM-I and spinal

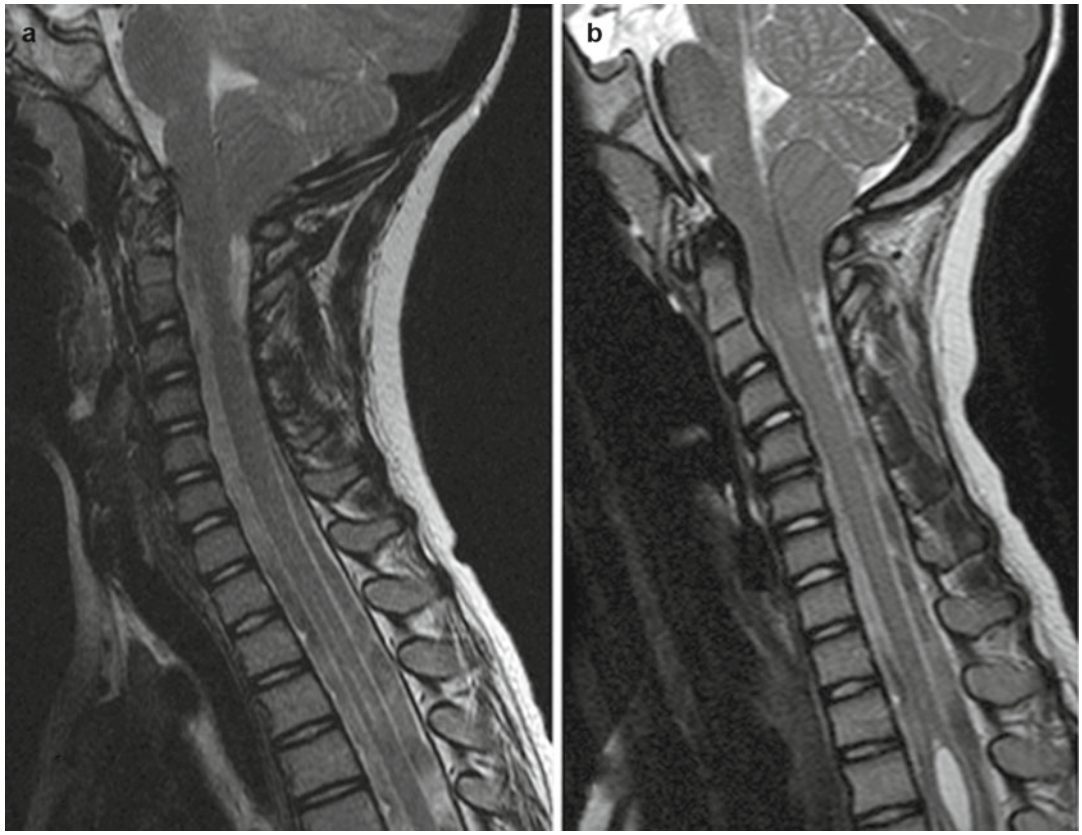

Fig. 18.3 (**a**) Sagittal T2-weighted MRI of a young boy with incidental discovery of CM-I on imaging. The patient was followed without surgery, and MRI obtained 4 years later (**b**) shows formation of a new spinal syrinx

syrinx and suggests some potential utility for spine imaging follow-up in those children diagnosed with CM-I at a very young age. Development of a syrinx later in childhood is certainly possible but was noted less frequently. In contrast to CM-I alone, CM-I with syrinx was more common in girls compared with boys and more common in those with greater degrees of tonsillar descent [67].

Syrinx was more likely to be found in those with more severe CSF flow alterations at the foramen magnum. Over half of patients with significantly abnormal tonsillar pulsations had a syrinx compared with 13 % of patients with normal CSF flow at the foramen magnum. Patients with basilar invagination were also more likely to have an associated syrinx. The relevance of the degree of tonsillar herniation and the likelihood of syrinx formation is controversial. Although some have suggested that an intermediate degree of tonsillar herniation (between 9 and 14 mm) is more likely to be associated with syrinx than lesser or greater degrees of tonsillar descent [65], this proposition is no longer widely supported. Most studies have shown that syrinx is associated with a greater amount of tonsillar herniation (Fig. 18.4) [19, 56, 67]. Taking these known risk factors into account, it is possible to justify following those with abnormal CSF flow, younger age, and more severe degrees of tonsillar descent with more frequent clinical or imaging assessments.

Spinal syringes in patients with CM-I follow a varied and unpredictable natural course. In addition to reports showing stability of syrinx over time, there have been reported cases of regression and complete resolution of syrinx, as well as many instances of symptomatic and imaging progression

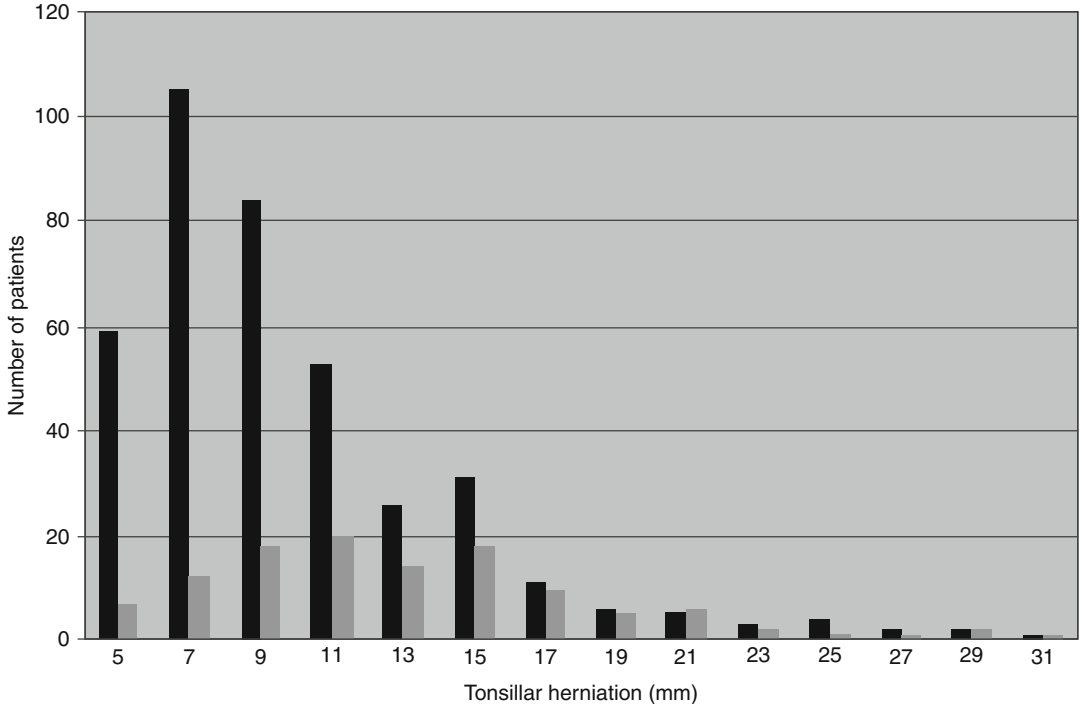

Fig. 18.4 Bar graph illustrating the number of patients with CM-I alone (*black bars*) versus those with both CM-I and syrinx (*gray bars*), according to the measurement (in mm) of tonsillar descent below the foramen magnum. Those with greater amounts of tonsillar decent were more likely to have an associated syrinx

[40, 68–72]. In the report by Benglis et al. [10], seven patients were followed for spinal syrinx in addition to the CM-I. None of these patients had a change in imaging appearance or new neurological deficit over the 3-year follow-up interval. These findings are supported by our recent natural history analysis [66]. Although it has generally been our practice to recommend surgical treatment for a CM-I associated with a spinal syrinx, we identified 13 patients in our series that were known to have a spinal cord syrinx at the time of CM-I diagnosis that were managed without surgery. Of the 13 patients with a syrinx at time of CM-I diagnosis, 6 were unchanged in size, 5 were smaller, and 2 were larger on follow-up MRI after a period of conservative management (Fig. 18.5). Of the five patients with spontaneous improvement in syrinx size, three demonstrated complete syrinx resolution on follow-up MRI. Patients with syrinx progression (mean age, 6.7 years) or regression (mean age, 5.6 years) were younger compared with those whose syrinx remained stable (mean age, 11.6 years). Patients with new syrinx formation over the follow-up interval had a mean initial tonsillar herniation of 13.5 mm. Those patients with larger syringes on follow-up imaging had a greater mean initial tonsillar herniation (14.5 mm) compared with those patients with stable (8.6 mm) or decreased (8.6 mm) syrinx size. In other series, it has been suggested that surgery may not be necessary in all cases of CM-I and syrinx [12, 51]. Nishizawa et al. [51] reported on nine adult patients with incidental CM-I and syrinx, only one of which required surgery over a 10-year follow-up interval. They reported no significant change in the MRI characteristics for eight of their nine patients over the follow-up interval. Although the extant literature suggests an unpredictable course for spinal syrinx in those patients with CM-I, it is worth remembering that in each of the available natural history studies, patients were selected for nonsurgical treatment. It is possible, therefore, that the true natural history for all patients with syrinx and CM-I is worse than

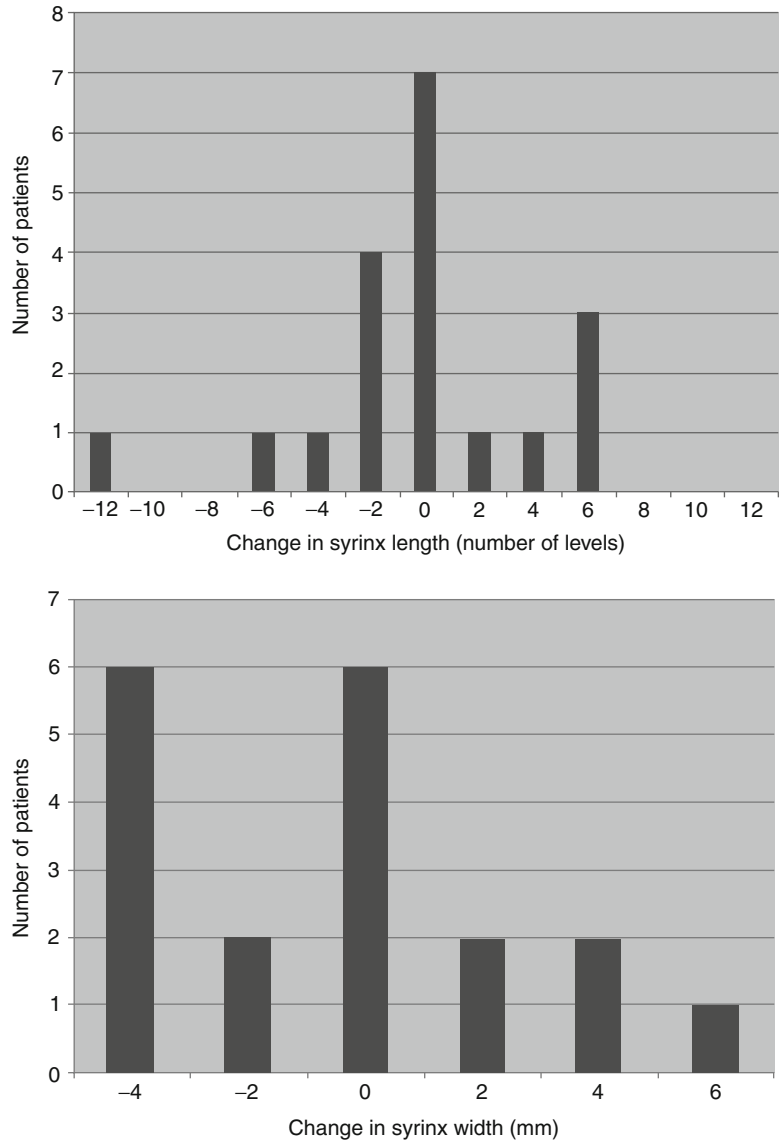

Fig. 18.5 *Left*: Bar graph depicting change in syrinx length by number of levels in patients with spinal cord syrinx at any time over duration of follow-up. *Right*: Bar graph depicting change in syrinx width (mm) in patients with syrinx at any time over duration of follow-up

predicted by outcomes in these series. Future studies will be required before strong recommendations can be made for changing decisions to pursue surgery for patients with spinal syrinx.

Prediction of Injury Related to CM-I

The extent to which physicians should limit sports participation or other activities of patients with CM-I found on imaging has been an area of ongoing debate. In the survey by Schijman and Steinbok [62], only 19 % of neurosurgeons would prohibit contact sport participation for an asymptomatic child with 9 mm of tonsillar descent, and 46 % recommended no restrictions of any kind. Nevertheless, there are many case reports of individual patients with CM-I that presented with acute injury or new neurological symptoms following a traumatic event [14, 16, 32, 39, 60, 83]. In some of these case reports, there was no connection made between the CM-I and the injury, except that the injury occurred in a patient with CM-I found on imaging. It is impossible

to exclude a coincidental co-occurrence in some of these cases. The relative value of these reports in guiding clinical decision-making can only be understood in the context of the prevalence of CM-I in the population. If CM-I is relatively more common than previously believed, then it follows that it also is less likely to present with acute worsening following injury than had been feared in the past. There is now reason to believe that this is the case. In my own practice, I generally do not restrict the activities of children with CM-I found on imaging if a decision for nonsurgical management has been made. Further study of this vexing issue is under way at multiple centers.

Conclusions

Progress has been made in our understanding of the natural history of CM-I. Nevertheless, two significant blind spots remain in our understanding of this issue. Since patients that are normally deemed good surgical candidates are treated surgically, there is very little available information on the true natural history of this subgroup of patients. We may infer certain aspects of their natural history from that of the nonoperative cohort, but this comparison is inexact. Obviously, any analysis of the natural history of a group of patients that are normally considered good surgical candidates will be difficult to perform. The other remaining blind spot results from our need for longer clinical and imaging follow-up in our natural history analyses. The mean duration of clinical follow-up for most studies cited in this chapter is between 3 and 6 years. This follow-up interval may be insufficient to capture all cases of clinical or radiographic deterioration that could be seen over longer follow-up intervals. Further study on patients over longer time intervals will be necessary in order to define the natural history of CM-I over the lifetime of individuals with this diagnosis. Despite these limitations, the available natural history data does help to clarify the natural history of CM-I for that subgroup of CM-I patients that are considered to be asymptomatic or minimally symptomatic and without neurological deficits.

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Newer Subsets: Chiari 0 and Chiari 1.5 Malformations

19

Nitin R. Mariwalla, William R. Boydston, and Joshua J. Chern

Abstract

Morphological components of the craniovertebral junction include bony structures around the foramen magnum, lower brain stem, upper cervical spinal cord, and cerebellar tonsils. Physiological components, which are often overlooked but equally important, consist of cerebrospinal fluid dynamics and motions at the junction. The interplays among these factors may contribute to the pathogenesis of signs and symptoms that are similarly found in Chiari I malformation.

Introduction

In addition to tonsillar ectopia, patients with the Chiari I malformation may also be found to have other morphological findings. These associated findings may include a reduced posterior fossa volume, a change in the degree of inclination of the clivus, posterior tilting of the odontoid, and caudal descent of the brain stem. The term Chiari 1.5 malformation has been used to describe Chiari I malformation patients who also have a caudally displaced brain stem in addition to the cerebellar tonsils.

Another very small cohort who present with syringomyelia without frank tonsillar ectopia but with a syrinx that resolves following craniocervical decompression is the Chiari 0 malformation. The putative mechanism for the formation of the syrinx in this rare group is CSF flow disturbance at the foramen magnum. Chiari 0 malformation may also be associated with a caudally displaced brain stem [1]. In the literature, Chiari 0 malformation, idiopathic cervical syrinx [2], and a tight foramen magnum [3] all describe a similar group of patients.

This chapter will focus on the diagnosis and treatment options of these two subsets of hindbrain-related malformations, the Chiari 0 and Chiari 1.5 malformations.

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Presentation of Chiari 0 and Chiari 1.5 Malformations

Symptoms found in these two malformations are similar to other patients with Chiari I malformation and include headache (Valsalva-induced, occipital in location, prompt resolution with rest), neck pain, paresthesia, dyspnea, swallowing difficulties, and gait changes. Physical finding includes torticollis, opisthotonos, weakness in the extremities, and scoliosis. Lower cranial nerve findings may include an absence of gag reflex, sleep apnea, and hoarseness. In the case of Chiari 0 malformation, a significant proportion of patients presents with scoliosis due to the presence of a syrinx, which all have as part of the definition of this malformation [4]. Dissociated sensory loss, which consists of diminished pain and temperature sensation and a relatively preserved proprioception and light touch, can be elicited in older children. As the syrinx progresses caudally, loss of abdominal reflexes is a frequent finding. Importantly, bowel and bladder symptoms are usually absent (sphincter fibers are located at the periphery not the center of the spinal cord), and the presence of these findings should prompt investigation into other causes for the symptoms.

Taken as a whole, signs and symptoms found in the Chiari 0 and Chiari 1.5 malformations are not significantly different from those found in the Chiari I malformations [5–7]. Despite the presence of brain stem descent, lower cranial nerve dysfunction is usually not present in this group. However, when oropharyngeal dysfunction is present, especially in patients under the age of 3 years, it should always prompt one to consider hindbrain hernia as a possible cause of brain stem compression [8].

Diagnosis

MR imaging of the head is performed in order to exclude intracranial pathology including hydrocephalus and to discern the extent of the hindbrain herniation. In the Chiari 0 malformation (with no tonsillar herniation), the obex will be inferiorly displaced but not to the degree seen in the Chiari 1.5 malformation. Special attention is given to the location of the vertebral artery and its extracranial course for surgical planning purposes. Flexion and extension radiographs should be obtained to rule out craniocervical junction instability. Craniocervical junction instability should be suspected in patients with large pannus formation posterior to the dens, which may represent chronic hypermobility. If instability is present, thin-cut CT of the craniocervical junction is necessary to examine the bony anatomy. CSF flow studies (cine MRI) are an adjunct for documenting CSF flow dynamics around the foramen magnum; however, negative results should not be a contraindication to surgical decompression. Currently, there are no CSF flow studies that are specific to Chiari 0 and 1.5 malformations [9].

When a syrinx is present (required for the definition of Chiari 0 malformation and seen in the majority of patients with Chiari 1.5 malformation), spine MR imaging with contrast enhancement is performed to examine the extent of syringomyelia, to rule out potential intrinsic spinal cord neoplasm, and to exclude a tethered spinal cord. A history of trauma, meningitis, and arachnoiditis or other explanations of the syringes should be determined. Syringes associated with Chiari malformations usually involve the cervicothoracic region and again, where the presence of a syrinx is mandatory for the diagnosis of the Chiari 0 malformation, Chiari 1.5 malformations will most likely have an associated syrinx compared to the Chiari I malformation population. The length of syringes and the cross-sectional area may range from a moderate size involving a few spinal levels to a holocord syrinx. It is also worth noting that sometimes asymptomatic patients are referred for a small cervical syrinx (less than two spinal levels). One should consider following these patients with observation and serial MR imaging instead of posterior fossa decompression.

Both the Chiari 0 and Chiari 1.5 malformations share the features of a compact posterior fossa and caudally displaced brain stem (Figs. 19.1 and 19.2). Several anthropologic measurements have been used to quantify this description. At the level of foramen magnum, the sagittal anteroposterior distance of the spinomedullary

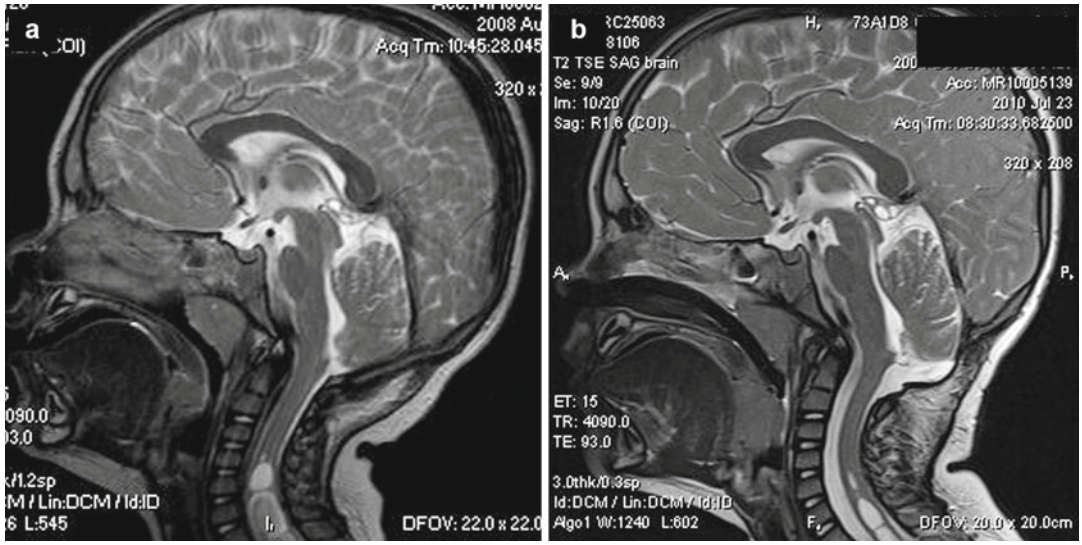

Fig. 19.1 Chiari 0 malformation. (**a**) Before and (**b**) after posterior fossa decompression. Notice the decompression at the cervicomedullary junction and decrease in the size of the syringomyelia

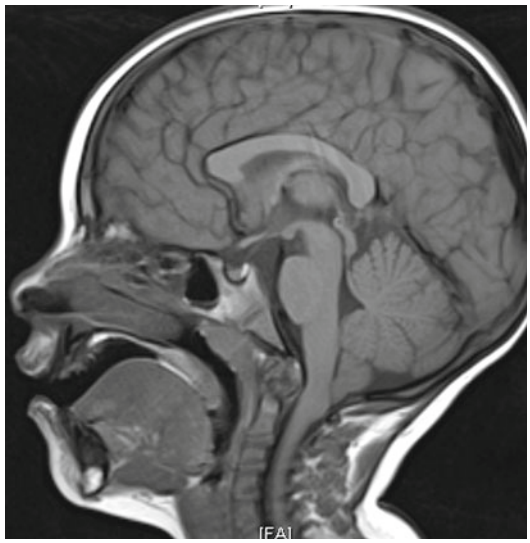

Fig. 19.2 Chiari 1.5 malformation. The position of the obex is below the level of the foramen magnum

junction has been found to be 13 mm versus an average of 11 mm, implying caudal descent of the more rotund medulla oblongata. Correspondingly, the obex is located at or below the level of the foramen magnum, while in controls, the obex was located 8–17 mm above the level of the foramen magnum. Lastly, in the midsagittal plane, there was an increase in the distance between the basion and opisthion (average 37.4 vs. 28–33 mm in age-adjusted controls), indicating a larger than normal foramen magnum as is seen in some patients with Chiari I malformation [1, 6].

While these morphological findings, which have been confirmed by others [2], may help to establish a diagnosis, the decision to operate relies very little on these measurements. Surgery should be considered in patients with credible signs and symptoms that are attributable to tonsillar ectopia and/or syringomyelia. In the case of Chiari 0 malformation, it is essential to stress that this is a diagnosis only given after other etiologies of spinal syrinx are conclusively ruled out and relies on postoperative resolution or improvement of the syrinx. In a group of 500 patients operated between 1989 and 2010, only 15 cases (3 %) fulfilled the criteria of Chiari 0 malformation [5].

Surgical Decompression and Intraoperative Findings

A standard bony foramen magnum decompression with removal of the posterior arch of the atlas is performed for both the Chiari 0 and Chiari 1.5 malformations. Midline dissection of the suboccipital musculature is essential to minimize postoperative

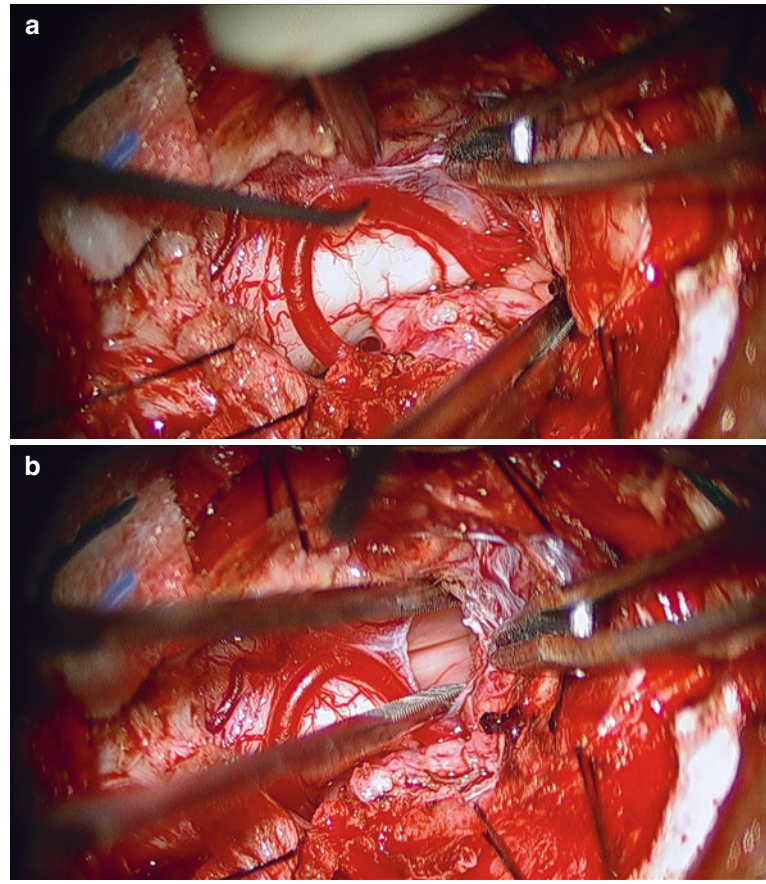

Fig. 19.3 Intraoperative finding of arachnoid veil over the fourth ventricular outlet in a Chiari 0 malformation patient pre- (**a**) and post (**b**) opening

pain and inadvertent vertebral artery injury; however, care has to be taken as one approaches the posterior C1 arch as incomplete formation and C1 assimilation are sometimes present. Thickened bone around the foramen magnum and an upward lipping of the opisthion are also found in some patients. The size of the craniectomy is roughly 2.5 cm in width and height. Too much bony removal may result in cerebellar ptosis.

Since the suspected underlying cause of the Chiari 0 malformation is CSF flow disturbances, intradural inspection of the foramen of Magendie is indicated. Unusual arachnoid adhesions or veils, scar tissue, and exaggerated tonsillar loops of PICA are all potential causes of CSF flow obstruction (Fig. 19.3) but are not found in every case [5]. One possibility is that CSF flow disturbances may be due to extradural compression from a small foramen magnum, thickened lip of the posterior foramen magnum [3], or a "tight" posterior atlantooccipital ligament. This was demonstrated in a case in which the dura was not opened, and the decision of not doing so was facilitated by the use of intraoperative ultrasound (Fig. 19.4). When treating Chiari 0 malformations, both intradural and extradural pathologies should be conclusively ruled out.

It is important to minimize blood spillage into the subarachnoid space, as subarachnoid hemorrhage is an inflammatory agent that will further occlude free CSF flow in this region. All patients undergo duraplasty with autologous pericranium. This last maneuver not only facilitates CSF flow around the craniocervical junction but is also necessary since the dura cannot be primarily closed in a watertight fashion at this location.

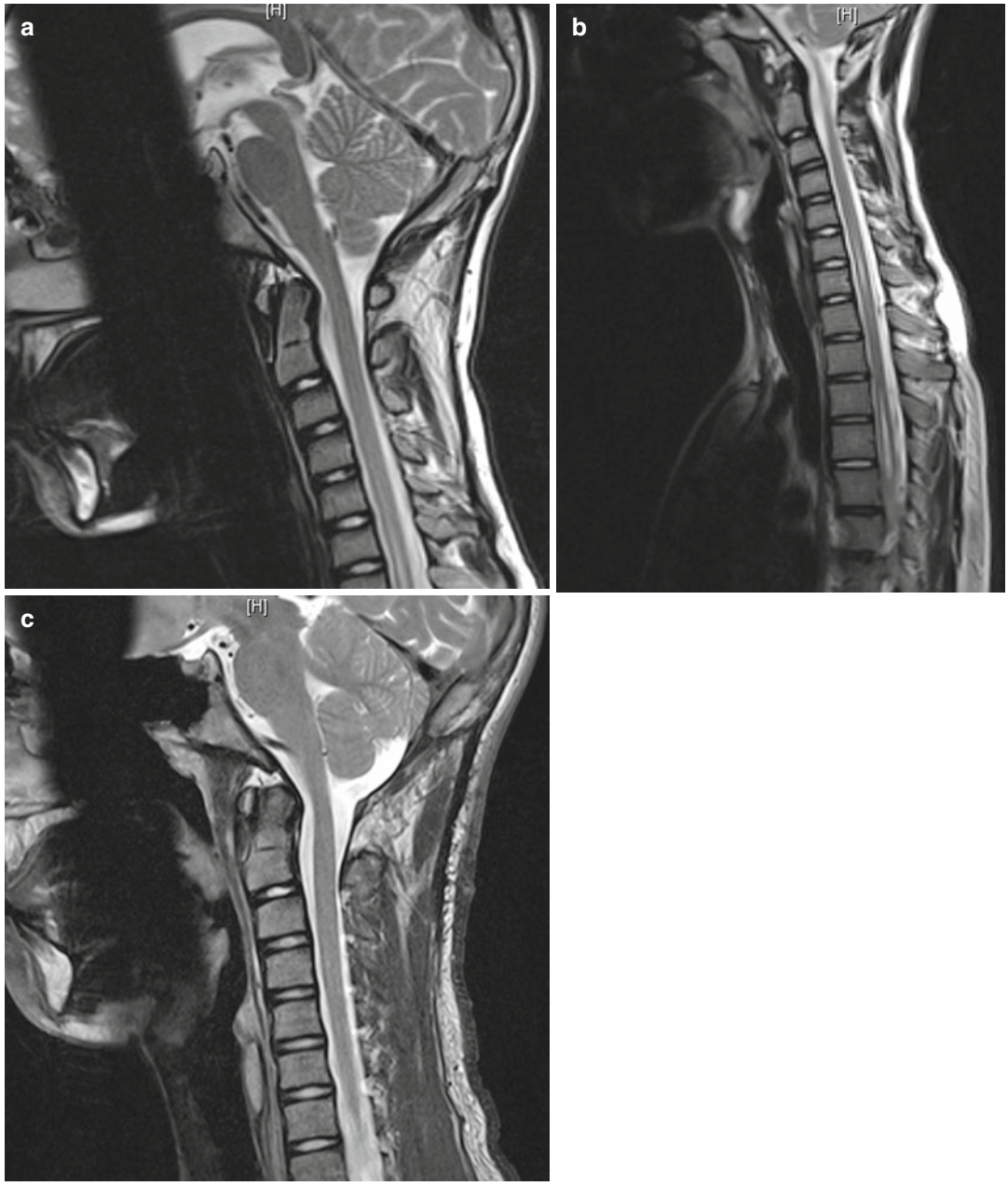

Fig. 19.4 A 12-year-old boy who presented with progressive scoliosis and Chiari 0 malformation. (**a**, **b**) Preoperative MRI showed no tonsillar ectopia and syringomyelia extending from the cervical to lower thoracic spinal cord. (**c**) He was treated with suboccipital bony decompression without opening the dura. Notice the increase of CSF space around the foramen magnum. The scoliotic curve has not progressed over a period of 3 years

Additionally, with a large number of intradural findings resulting in inhibition of CSF egress from the fourth ventricle, especially in the Chiari 0 group, intradural exploration is key.

Results and Follow-Up

With proper patient selection, signs and symptoms of these patients are expected to be greatly

improved or completely resolved postoperatively. Occipital headache and neck pain usually resolve quickly, but other signs and symptoms, such as torticollis, paresthesia, and gait-related complaints, usually take weeks to months to resolve. In the Chiari 0 malformation, with resolution of the syrinx, scoliosis may stabilize and may even improve over a period of months to years. In the Chiari 1.5 malformation, it has been reported that approximately 10 % of patients who presented with syringomyelia required repeated operation [6]. This is probably due to the greater degree of hindbrain herniation.

The relation of the resolution of symptoms caused by syringes and the actual decrease in the size of the syringes is still not clear. Most studies on this topic come from patients with Chiari I malformation, which suggest that about 50–80 % of patients will have a smaller syrinx at 6–12 months follow-up, and symptom resolution usually precedes syrinx resolution [8]. These numbers are a good starting point in patient education, but at least in the case of Chiari 0 malformation, a restoration of CSF dynamics seems to have an even better radiologic outcome [5].

While it is reasonable to expect good surgical outcome with Chiari 0 and 1.5 malformations, there are clinical questions for those patients who remain symptomatic after decompression surgery. Should the observation period be prolonged with the knowledge that the syrinx resolution often lags behind symptoms resolution? Should one proceed with reexploration of the surgical site, suspecting arachnoid scarring due to surgical manipulations? Should one proceed with shunting the syrinx? Our bias is that surgical reexploration is often employed first if the patient fails to improve over a 6-month observational period, but there are others who would choose to shunt the syrinx at this point and accept the significant associated complications [10].

Conclusions

Chiari 1.5 malformation patients present with significant radiologic evidence of brain stem descent but, in general, present similarly as Chiari I malformations and respond well to posterior fossa decompression although they may be more likely to necessitate reoperation compared to the general Chiari I population and, based on our experience, are more likely to have an underlying syrinx.

The mismatch between the posterior fossa neural elements and the surrounding mesodermal derivatives may incite abnormal CSF dynamics at the level of the foramen magnum. The identification of Chiari 0 malformation adds further evidence that this abnormal flow is the main mediator of syrinx formation. Favorable clinical and radiologic responses are possible after restoring normal CSF flow dynamics.

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Clinical Presentation of Pediatric Chiari I Malformations

20

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Abstract

Clinical presentation of the Chiari I malformation varies with patient age, and children typically present with shorter symptom duration than adults. Symptoms and signs of Chiari I malformation in children are most often attributable to impairment of CSF flow, direct neural compression, and/or syringomyelia. Comparison of contemporary and older literature reveals a trend toward earlier diagnosis, prior to manifestation of significant neurologic morbidity. General availability and use of magnetic resonance imaging likely explains this dramatic shift. Occipital and/or cervical pain is the most common presentation, particularly if Valsalva-induced, followed by scoliosis, syringomyelia, and lower cranial nerve dysfunction. Headache not localized to the occipital/cervical region correlates poorly with Chiari I malformation. The natural history of asymptomatic children with Chiari I malformation (absent syringomyelia) appears benign. Surgical treatment should be reserved for patients with localized pain, syringomyelia, or cervicomedullary/cerebellar dysfunction.

Introduction

The clinical presentation of pediatric Chiari I malformations differs somewhat from that of adult patients, especially for those presenting very early in life. Chiari I malformations in childhood typically present with symptoms and signs attributable to CSF flow impairment, compression of neural elements, and/or syringomyelia. Perhaps due to differences in age, children present with a shorter duration of symptoms at diagnosis than adults [1]. This chapter will enumerate the commonly described and generally accepted clinical sequelae of these pathological mechanisms in infancy, childhood, and adolescence. The more esoteric and controversial clinical presentations associated with Chiari I in children are addressed elsewhere in this text. It is also worth noting here that reviewing the literature on this topic reveals a dramatic shift in presentations over time. Prior to the introduction and widespread availability of magnetic resonance image (MRI) scanning, diagnosis was rarely made prior to the onset of significant neurologic morbidity. This chapter

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reflects a greater emphasis on more contemporary literature reports from the MRI era.

Symptoms and Signs

The most common presenting symptom is pain, reported in 60–70 % of patients [2, 3]. It is typically non-dermatomal and localized to the occipital or cervical region. Occipital headache/neck pain is the most common presentation in every contemporary pediatric Chiari I series, accounting for 40–60 % [3–7]. The pain is often precipitated or exacerbated by a Valsalva maneuver, suggesting CSF flow impairment as the pathophysiology. Besides cough, sneeze, or defecation, Valsalva-inducing activities in children may include screaming, running, or repetitive jumping, such as on a trampoline. In nonverbal children, pain may be manifested as irritability, opisthotonos, incessant crying, or failure to thrive. Other symptoms include nonradicular pain in the shoulder, back, chest, and extremities that may be described as deep and burning; weakness and/or altered sensation in the extremities; clumsiness; dysphagia; dysarthria; hiccoughs; severe snoring; and drop attacks. Cerebellovestibular problems have also been cited.

Cephalgia localized beyond the occipital-cervical region and global headache correlate poorly with Chiari I malformation improvement following decompression. Every published series assessing the value of neuroimaging in the evaluation of pediatric headache recommends no imaging for children with common headache syndromes and normal neurological exam findings. The reported incidence of Chiari I malformation requiring a "change in management" in children diagnosed with migraine, tension-type, and/or chronic daily headache and a normal neurological exam ranges from 0 to 1.4 % [8–10]. This incidence range is exceeded by the 3.6 % Chiari I detection rate reported in a review of 14,116 pediatric patients undergoing brain or cervical spine MRI for all indications [11]. Furthermore, a reported series of Chiari I patients analyzing the relationships between headache location, CSF flow dynamics on cine MRI, and headache response to Chiari decompression concluded that non-occipital "headaches are not pathologically or causatively associated with the Chiari I malformation in the vast majority of patients" [12]. Taken together, multiple lines of evidence support a recommendation for medical management of neurologically normal children with Chiari I malformations and "non-Chiari" headache types.

Signs seen in Chiari I malformation are variable but include upper motor neuron changes in the legs, with spasticity, exaggerated deep tendon reflexes, and upgoing toes. The upper extremities may have evidence of lower motor neuron injury, with loss of muscle bulk, diminished or absent reflexes, and fasciculations. Sensory loss is classically described as suspended and dissociated. This non-dermatomal loss involves pain and temperature but spares light touch and proprioception. Ataxia, irregular respirations, and lower cranial nerve dysfunction may also be seen.

Pediatric type I malformations often present with progressive scoliosis attributable to an associated syrinx. Syringomyelia is reportedly present in 5.6–57 % of pediatric Chiari I patients and scoliosis is reported in 18–22 %, although syringomyelia and scoliosis do not always present together [3, 11, 13]. While the typical finding in idiopathic scoliosis is a right curve, the configuration reportedly associated with syringomyelia is levoscoliosis with a single curve [14]. MRI studies of 68 children presenting with left thoracic curves revealed Chiari I in 40 % and syringomyelia in 29 % [15]. Children presenting with scoliosis should be examined carefully for any neurologic abnormalities. The absence of superficial abdominal reflexes ipsilateral to the convexity appears to be a strong indicator of syringomyelia [16]. A relatively high incidence (19 %) of intraspinal pathology, including syringomyelia, is reported in children presenting with idiopathic scoliosis before 11 years of age [17]. MRI screening of idiopathic scoliosis in neurologically normal adolescents, however, yields a low incidence of Chiari I, likely approaching the prevalence in the general population [11, 18]. Pediatric scoliosis associated with syringomyelia and Chiari I often stabilizes or improves following

surgical decompression of the foramen magnum. Significant improvement in the scoliotic curve is reported in 38–73 %, while improvement or stabilization (combined) occurs in 62–91 % [19–21]. Factors reportedly associated with continued scoliosis progression following decompression include age greater than 10 years, female sex, and more severe scoliosis at presentation (e.g., larger curves, double curves, kyphosis, and rotation) [19, 21, 22].

Prior to general availability of MRI, pediatric Chiari I malformations frequently presented with evidence of moderate to severe brain stem/cranial nerve/spinal cord dysfunction. Earlier detection with MRI appears to have significantly reduced the frequency of these presentations. Lower cranial nerve dysfunction may be manifested as vocal cord paralysis, dysarthria, soft palate weakness, glossal atrophy, cricopharyngeal achalasia, absent gag reflex, and facial sensory loss. The most common manifestation of medullary dysfunction in these patients is sleep apnea/vocal cord paralysis [23, 24]. Sleep apnea at presentation is reported in 12.9 % [11] and is seen more frequently in children younger than 6 years compared to older children [25]. Nystagmus is another presenting sign that is classically the downbeat type and increased on lateral gaze [26]. This variety of nystagmus is specific for pathologic conditions involving the cervicomedullary junction. Other less common cranial nerve signs are esotropia, sinus bradycardia, oscillopsia, trigeminal and glossopharyngeal neuralgia, and sensorineural hearing loss [27–32].

Associated Conditions

Syringomyelia and scoliosis, as previously described, are by far the most common conditions associated with pediatric Chiari I malformation. Other associated spinal anomalies frequently reported in surgical series are retroversion of the odontoid process/platybasia/basilar invagination (12–24 %), occipitoatlantal fusion/assimilation of the atlas (8 %), hemivertebra/butterfly vertebra (2.4–4 %), and Klippel-Feil anomaly (2.7–3 %) [1, 3, 5, 11]. The presence of odontoid retroversion, basilar invagination, or platybasia is associated with greater tonsillar descent while only basilar invagination correlates with syringomyelia [11].

Familial incidence of Chiari I malformation ranges from 3 to 12 % with both autosomal dominant and recessive patterns reported [3, 5]. The prevalence of associated hydrocephalus in children diagnosed with Chiari I by MRI criteria is 8.3 % and reportedly ranges from 10 to 31 % in surgically treated series [1, 3, 11, 25, 33]. Neurofibromatosis type I is associated with pediatric Chiari I in up to 5 % [3, 34] and idiopathic growth hormone deficiency in 4.2 % [3].

Natural History

The natural history of pathological (i.e., symptomatic) Chiari I malformation is poorly understood and likely to remain so because surgical intervention is indicated and typically initiated in a timely fashion. However, recent reports have illuminated the natural history of Chiari I presenting with minimal or no symptoms in neurologically normal children. Collectively, these multiyear observational studies suggest that pediatric Chiari I subsequently followed up without surgery remains asymptomatic or improves clinically in 77–94 % [13, 35, 36]. Imaging evidence of progressive tonsillar descent, new syrinx formation, or syrinx enlargement is reported in 4.5–10.2 % [35, 36]. Conversely, resolution of previously diagnosed tonsillar herniation exceeding 5 mm is observed in up to 5 %, and syrinx resolution occurred in up to 15 % of those presenting with syringomyelia [35, 36]. A natural history study of untreated syringomyelia in children with trivial or no symptoms followed with serial MRI found progression in only 2 of 17 individuals (12 %) and diminished syrinx size in eight (47 %) [37]. Nonsurgical management and longitudinal observation of otherwise normal children with asymptomatic or oligosymptomatic Chiari I appears to be a relatively safe treatment option. Repeat MRI is warranted to investigate new or progressive symptoms in this patient population, while serial imaging absent new

complaints or findings appears likely to identify progression prompting a change in treatment for a small minority.

Indications for Treatment

In light of the generally benign natural history of pediatric Chiari I absent syringomyelia, occipitocervical pain, or neurologic compromise attributable to cervicomedullary dysfunction, the malformation's mere presence does not equate to an indication for surgical decompression. Likewise, there is no Chiari I imaging feature, such as extent of tonsillar herniation, which necessitates decompression (although extent of herniation correlates with clinical features that are indications for treatment). Serial observation with or without surveillance imaging is most appropriate for children whose Chiari I malformations do not require treatment.

Widely accepted indications for surgical decompression include (1) occipitocervical pain triggered or aggravated by Valsalva, (2) cervical and/or thoracic syringomyelia with or without scoliosis, or (3) neurologic dysfunction that localizes to the cervicomedullary region, lower cranial nerves, or cerebellum. Because other headache types are not associated with Chiari I malformation, they should not be considered an indication for surgery.

Signs and symptoms of Chiari type I malformations
Impaired CSF pressure/flow dynamic
High cervical or occipital pain or dysesthesia, especially with Valsalva
Hydrocephalus
Syringomyelia
Upper extremity weakness or atrophy
Lower extremity spasticity
Scoliosis, particularly single left thoracic curve
Hemiparesis
Dissociated or suspended sensory loss (pain and temperature)
Absent superficial abdominal reflexes
Direct neural compression
Clumsiness or truncal and appendicular ataxia
Dysphagia
Dysarthria
Hoarseness
Hiccoughs
Apnea
Nystagmus
Recurrent aspiration
Hyper- or hyporeflexia
Babinski response
Oscillopsia
Esotropia
Sinus bradycardia
Trigeminal or glossopharyngeal neuralgia
Opisthotonos
Severe snoring
Drop attacks
Glossal atrophy
Facial sensory loss

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Clinical Presentation of the Adult Chiari I Malformation

21

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Abstract

Adult patients with Chiari malformation, sometimes referred to as hindbrain descent, most frequently present with symptoms in their 20s and 30s.

Symptoms include those which can be attributed to interference with normal CSF flow equalization. Exertionally related headaches, characteristic for Chiari malformation, are due to this mechanism and are also the most common of all Chiari-related symptoms. Symptoms may also be related to brain stem compression and compression of cerebellar connections, reflected in balance problems, visual problems, and autonomic symptoms. Symptoms related to traction on lower cranial nerves may include swallowing and voice problems and may contribute to sleep apnea. Chiari malformation and related symptoms may present as a manifestation of other diseases, including hypophosphatemic rickets, Paget's disease, Crouzon's disease, and achondroplasia. Secondary Chiari malformation may be seen with pseudotumor cerebri (idiopathic intracranial hypertension) and occult cerebrospinal fluid leaks.

Chiari malformations presenting in adults have generally been referred to as Chiari I malformations. They may present in a variety of ways, most probably related to differences in the anatomical abnormalities in the individual patient leading to the clinical diagnosis of Chiari malformation. This may vary from a relatively small posterior fossa to associated bony anomalies such as basilar impression or platybasia. Patients with membrane formation at the outlets of the fourth ventricle similar to those described by Gardner et al. [1], or arachnoid membranes within the cisterna magna, may demonstrate a similar effect on CSF circulation as do impacted

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cerebellar tonsils [2] and may have certain features in common with patients who have tonsillar descent. Some may also develop syringomyelia [2] and these have been subsequently labeled "Chiari 0" malformations. In addressing the symptoms with which patients may present, it is also evident that some symptoms, such as generalized headache or fatigue, are not specific for Chiari malformation and are not uncommon in the general population. One can also surmise that there are individuals with low-lying cerebellar tonsils who remain asymptomatic throughout their lifetime [3].

It is, of course, important to distinguish symptoms due to the Chiari malformation per se from those that are due to coexisting syringomyelia. It is beyond the scope of this chapter to deal in detail with the clinical presentation of syringomyelia. Symptoms of spinal cord dysfunction, notably upper limb atrophy and sensory deficits as well as lower extremity and gait problems, are typical of syringomyelia. Spasticity and leg weakness in patients with syringomyelia, sometimes in combination with sensory impairment, may cause balance problems indistinguishable from those seen with Chiari malformation alone. Postural hypotension may be seen with syringomyelia due to loss of autonomic input and may also be seen in patients with Chiari malformation only. In part, related to limitations in diagnostic imaging, earlier reviews of Chiari malformation tended not to separate symptoms due to Chiari malformation from those due to syringomyelia [4–7].

Age of Onset

Considering that the anatomical variants leading to Chiari malformation are present in early childhood, if not at birth, the reasons for onset of symptoms in adults, often in their 20s or 30s, are not entirely clear. It seems logical to assume that normal activities such as coughing and straining may result in an incremental downward creep of the tonsils and brain stem, until a point is reached at which CSF circulation is compromised. Accidental events such as jarring of the head may play a role in precipitating symptoms in some adults [8–10].

A review of the literature makes it clear that a listing of symptoms and findings in order of frequency of occurrence cannot be made, inasmuch as patient populations differ in different clinics and observations differ for different authors. Overall, the most commonly reported symptoms and findings for patients with Chiari malformation are the following:

Symptoms	Findings
Headache	Nystagmus
Exertional	Impaired spontaneous venous pulsations
Other	Extraocular muscle palsy
Visual symptoms	Papilledema (rare)
Blurred vision	Gag reflex loss
Double vision	Hoarseness
Hearing-related symptoms	Facial sensation impairment
Tinnitus	Tongue atrophy (mostly unilateral)
Hearing impairment	Balance impairment – truncal
Balance difficulties	

Other frequently mentioned symptoms of unclear physiological basis include fatigue, memory impairment, and what has been called "brain fog."

There have been a number of comprehensive analyses of presenting symptoms and findings in patients with Chiari malformation. The most comprehensive is that of Milhorat et al. [10], summarized below:

Ocular disturbances	97/126 patients
Otoneurological disturbances	89/126 patients
Lower cranial nerve, brain stem and cerebellar disturbances	69/126 patients

Dyste et al. [11] reported the glossopharyngeal and vagus nerves to be the most commonly involved cranial nerves, as demonstrated by an abnormal gag reflex (15/50); 13/50 had trigeminal hypesthesia, 9 had unilateral hypoglossal involvement, and a few had facial weakness and abducens weakness on one side.

Pathophysiology of Symptoms and Findings

It is helpful to try to consider symptoms related to Chiari Malformation under the following broad categories:

1. Symptoms due to interference with normal CSF circulation
2. Symptoms due to pontomedullary (brain stem) compression, cerebellar symptoms
3. Symptoms due to downward descent of the cerebellar tonsils and traction on cranial nerves

Symptoms Related to Interference with Normal CSF Circulation

Strain-related headaches are the classical and pathognomonic manifestation of impaired transmission of the normal fluctuations in CSF pulsations at or near the foramen magnum. This may result from descent of the cerebellar tonsils into the foramen magnum or membranous occlusion of the CSF cisterns at or near the level of the foramen magnum. Brief transient increases in intracranial pressure with dural distention are believed to be the cause of these headaches. Occasionally, patients also complain of seemingly strain-related symptoms involving the upper extremities, and it may be relevant to invoke the mechanism suggested by Bell [12, 13]. Coughing, straining, and other similar Valsalva-type activities may be cited by patients. Shouting or even blowing into a wind instrument has also been mentioned by patients as provoking such headaches. These headaches are typically brief in duration, lasting only seconds or minutes, are mostly localized to the suboccipital or upper cervical area, and may occur many times during the day. Such headaches are present in 80–100 % of published cases [8, 10]. The exertional aspect of the headache is characteristic and helps to distinguish this classical symptom from other more common types of headache.

Patients may also complain of less typical headache, such as suboccipital pain, generalized headache, or retro-orbital headache. These are often considerably longer in duration. Other explanations have been offered for these types of headaches, including altered brain tissue compliance [14]. It should be recognized that patients with Chiari malformation may also have other types of headache and it is not uncommon to find patients with unrelated but coexisting migraine headache.

Patients with "Chiari 0" malformation, obstruction of the CSF pathways at the level of the foramen magnum without tonsillar descent, might be expected to show some symptoms of this type, although manifestations of syringomyelia appear to dominate in reports [2].

Changes in CSF dynamics have also been cited as possibly affecting perilymph dynamics, thereby accounting for various otological symptoms, such as tinnitus, hearing impairment, and even dizziness [10].

Findings related to this transient increase in intracranial volume are the obliteration of normal spontaneous venous pulsations on funduscopic examination in the sitting position. Since other factors, including purely technical ones, may affect the identification of such spontaneous venous pulsations, their presence is often considered more significant as a negative finding. Rarely, one may detect papilledema.

Brain Stem and Cerebellar Symptoms

Visual and balance disturbances including blurred vision and occasionally double vision are among the most common presentations of Chiari malformation in adults. Patients may be aware of the nystagmoid motion of their eyes, and nystagmus is reported to be present in up to 70 % of Chiari patients in some series [15], 35 % in others [16]. Downbeat nystagmus is said to be characteristic of abnormalities at the cervical-medullary junction [17]. Special testing may be helpful in defining the type of nystagmus [16]. Double vision is considered to be due to impaired conjugate eye movements [11]. This may result from impaired function of brain stem nuclei or their connections. Traction on cranial nerves, particularly the trochlear, abducens, but also oculomotor, has also been invoked.

Impaired balance may result from traction and distortion of cerebellar pathways due to hindbrain descent and may be seen as frequently as in 40 % of patients [6]. It is usually seen as truncal imbalance, rather than appendicular incoordination, and patients may have difficulty with gait, tandem gait and tandem Romberg stance. Dizziness and balance problems were encountered in almost 60 % of patients in one reported series [10]. "Dizziness" reported by patients may be positionally related, raising questions of positional vertigo in the differential diagnosis. Tinnitus has also been cited by a number of authors [10, 15, 17]. The mechanisms are not entirely clear, inasmuch as tinnitus might result from transmitted alterations in CSF fluid dynamics to the inner ear (see above), or downward traction on the eighth nerve complex.

Swallowing difficulties, particularly of liquids, are a not infrequent complaint, ranging from 6 to 45 % of patients [10, 11, 18]. Impairment of the gag reflex is frequently noted, but can be related to other factors, possibly including the effects of medication, and this finding does not correlate closely with swallowing complaints. Hoarseness is less common but more specifically related to involvement of lower cranial nerve function. Facial pain in trigeminal distribution has been attributed to involvement of the spinal nucleus of the fifth nerve. Trigeminal area pain and findings of sensory loss in trigeminal distribution have been reported by a number of authors [10, 11, 18, 19]. Unilateral tongue atrophy has occasionally been noted [11, 15].

The entire range of autonomic symptoms must also be considered in this category. Up to 10 % of patients have such symptoms, including drop attacks [11, 15, 17], bradycardia [20], dyspnea, syncopal episodes [13, 21, 22], and palpitations. Various forms of sleep disturbances are not uncommonly reported by patients with Chiari malformation. This includes central sleep apnea [23]. These disturbances may be related to brain stem compression involving the respiratory centers or reticular activating system [4]. Other mechanisms to explain sleep disturbances have also been proposed, including stretching of the lower cranial nerves by downward descent of the brain stem and abnormal chemoreceptor sensitivity. Patients with abnormal respiratory response to carbon dioxide have been reported [5]. Vocal cord paralysis and impaired diaphragmatic innervation may contribute to altered sleep patterns in these patients. Sleep studies may be of help in identifying patterns of a specific sleep disorder. Impotence has been reported particularly in patients with Chiari malformation and associated basilar invagination [21].

Syncope may be encountered in relation to coughing or other Valsalva-type maneuvers as well as with head movements and may be due to momentary increased brain stem compression with briefly increased tonsillar descent or possibly to brief vascular compression [13]. Profound sinus bradycardia has been documented in at least one instance and could be the underlying mechanism for a number of symptoms, including transient loss of consciousness and some instances of dizziness [20]. Death, attributed to respiratory distress, syncope, and respiratory arrest, has been cited and there have been isolated reports of sudden death [24, 25].

Symptoms due to Downward Descent of the Cerebellar Tonsils and Traction on the Cranial Nerves

It is difficult to know the precise mechanism by which some "brain stem" symptoms are produced and indeed different mechanisms may interact to produce certain symptoms in any one patient. Thus, hoarseness and swallowing problems might arise either from brain stem compression or from traction on the lower cranial nerves, particularly the glossopharyngeal and vagus nerves. The possible contribution of traction on these nerves to sleep-related problems has been cited above. Involvement of the hypoglossal nerve with tongue fasciculations and atrophy has also been reported [6, 11, 18, 19] as noted above. Penfield and Coburn's [26] autopsy description provides excellent detail of the extent of cranial nerve stretching, as well as stretching of the upper cervical nerve roots.

Frontal or generalized headaches encountered in Chiari malformation patients have been

attributed to a variety of mechanisms (see above), including cervicogenic etiologies. Frontal headaches may also arise from direct compression of the second spinal nerve, as proposed by Kerr [27].

Chiari Malformation as Manifestation of Other Diseases

Crowding of the posterior fossa may result from bony thickening, including the occipital bone, as seen in hypophosphatemic rickets. Caldemeyer et al. [28] reported Chiari malformation in 7 of 16 patients with this metabolic disorder. Flattening of the posterior fossa by thick bone characterized this subtype of patients (5 of 7), and two patients with severe bone thickening also had syringomyelia. Four of 7 had ventriculomegaly. There did not appear to be any specific clinical features of Chiari malformation that distinguished this group of patients. Tubbs et al. [29] established that the posterior fossa volume in children with rickets was significantly smaller than in age-matched controls, presumably also the case in rickets patients who reach adult age.

Bony encroachment of the foramen magnum may also be seen in patients with Paget's disease. Flattening of the foramen magnum with reduction of its anteroposterior diameter in conjunction with basilar invagination has been described [30]. Seen in as many as one third of patients with Paget's disease, it may lead to alterations in CSF flow at the level of the foramen magnum that give rise to symptoms of Chiari malformation and may also be associated with the development of syringomyelia [31].

In both the above conditions, there may be narrowing of the spinal canal due to bony thickening, which may contribute to the development of myelopathy. This includes those patients who also have syringomyelia.

Early closure of the lambdoidal sutures in patients with Crouzon's disease is the likely explanation for a relatively small posterior fossa and the high incidence of tonsillar ectopia (73 %) in these patients [32]. Although the study was performed in children, adults with Crouzon's disease presumably are similarly involved.

Similar bony changes of a small, shallow posterior fossa, leading to symptoms of Chiari malformation, may be seen in achondroplastics [33, 34].

Based on imaging criteria, an association of hereditary connective tissue disorders and Chiari I malformation was reported by one group of investigators [35]. These patients presented with symptoms of Chiari malformation, and evidence for connective tissue disorder was sought subsequently. Royo-Salvador et al. [36] reported an association between Chiari malformation and tethering of the spinal cord at the level of the filum terminale in a small group of adult patients. The concept remains controversial in spite of a larger and more recent study [37]. Some of these patients had symptoms suggesting cauda equina abnormalities. Filum tethering may be verified by comparing prone and supine magnetic resonance imaging studies of the cauda equina.

Secondary Chiari Malformations

At first glance, the fact that cerebellar tonsillar descent may occur with both increased and decreased intracranial pressure may seem contradictory. These patients fall into two main categories: pseudotumor cerebri and undiagnosed or occult cerebrospinal fluid leaks at the spinal level. The importance of this subgroup of patients lies in the fact that both conditions may be easily missed. Patients with pseudotumor cerebri may undergo posterior fossa decompression because of descended cerebellar tonsils, only to have acute or subacute postoperative problems related to their elevated intracranial pressure. Patients with an occult CSF leak may have little or only transient relief of their symptoms following posterior fossa decompressive surgery. This form of secondary tonsillar descent may also be encountered in patients who have undergone lumboperitoneal shunting. Clinically, it is often manifested by headache related to upright posture, relieved when the patient lies down. Although first recognized in children who underwent such shunting [38], it was also observed in adults who had undergone lumboperitoneal shunts and may even

be accompanied by syringomyelia [39]. Secondary Chiari malformation has also been reported in association with cerebrospinal fluid leaks [40]. In our own experience, pseudotumor cerebri was encountered in 2 of 177 patients, occult CSF leak in 1 of 177 patients.

Both problems can be diagnosed preoperatively, provided consideration is given to these diagnoses in the preoperative assessment. Preoperative intracranial pressure measurements [41] are the most conclusive way to make the diagnosis and avoid problems. Consideration should be given to such a study in selected patients with a high level of suspicion, even though it is invasive.

Differential Diagnosis

Other causes of headache, even of strain-related headache, need to be considered in the differential diagnosis. Nystagmus and imbalance have sometimes led to concern about a diagnosis of multiple sclerosis. Syringobulbia may produce many of the brain stem symptoms and signs seen with Chiari malformation [42].

A most difficult situation arises in patients with borderline descent of the cerebellar tonsils who have some symptoms, such as headache and other symptoms not uncommon in the general population. Imaging studies that show somewhat low-lying cerebellar tonsils but without narrowing of the subarachnoid spaces may be interpreted as a borderline Chiari malformation by a radiologist, giving rise to patient concerns. Many patients then also read about this entity, so that it may become difficult to obtain a patient history "uncontaminated" by other input.

In spite of our increased awareness of the disease entity and alertness to a variety of presentations seen in patients with Chiari malformation, it is unfortunately far too common to encounter patients whose symptoms have been passed off, sometimes, for years, before the correct diagnosis is established. This problem may be aggravated by very rigid adherence to imaging-derived measurements, which may also completely overlook patients with membranous occlusion at the foramen magnum without tonsillar descent [2] (Chiari 0 malformation) who present with at least some typical Chiari malformation symptoms.

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Unusual Presentations of the Chiari I Malformation

22

Christopher M. Bonfield and Elizabeth Tyler-Kabara

Abstract

Chiari type I malformations [CM-I] most commonly present with exertional occipital headaches and neck pain. In infants, these headaches may simply present as irritability. Cerebellar tonsil herniation can also cause compression of the medulla and lower cranial nerves leading to neurologic symptoms as well. Syringomyelia, commonly associated with CM-I, also can result in neurologic sequelae. This spectrum of symptoms includes extremity weakness, sensory deficits, and abnormal reflexes. Lower cranial nerves can also be affected resulting in vocal cord paralysis, tongue weakness, aspiration, hoarseness, nystagmus, palatal weakness, and sleep apnea.

Although the vast majority of patients with CM-I present with the symptoms listed above, there have been reports in the literature of more unusual presentations. This chapter will review the less common and more unusual presentations of CM-I, including syncope, hearing loss, cranial nerve neuralgias, respiratory failure, endocrinologic dysfunction, hiccups, esotropia, peripheral nerve syndromes, and acute sensory or motor deficits.

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Chiari first described the Chiari malformations in 1891 after a series of observations in autopsies. These malformations may be associated with a small or shallow posterior fossa, variable skull base dysplasia, and decreased cerebrospinal fluid in the posterior fossa.

Although presenting symptoms are variable, Chiari I malformations [CM-I] most commonly present with exertional occipital headaches and neck pain. This pain can be dull and persistent, but is usually associated with Valsalva maneuvers such as exercise, laughing, sneezing, bearing down, or coughing. In infants, these headaches

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may present simply as irritability. It is thought that the cerebellar tonsils are impacted at the level of the foramen magnum during the Valsalva maneuver, thus causing the headaches.

Cerebellar tonsil herniation can also cause compression of the medulla and lower cranial nerves leading to neurologic symptoms as well. Syringomyelia, which is often associated with CM-I, can result in neurologic sequelae. This spectrum of symptoms includes extremity weakness, sensory deficits, and abnormal reflexes. Lower cranial nerve compression can result in vocal cord paralysis, tongue weakness, aspiration, hoarseness, nystagmus, palatal weakness, and sleep apnea. Scoliosis is also commonly associated with patients who have CM-I and a syrinx.

Although the majority of patients with CM-I present with the symptoms listed above, there have been reports in the literature of more unusual presentations. This chapter will review the less common and more unusual presentations of CM-I.

As mentioned, cranial nerve deficits such as tinnitus can be a presenting symptom of CM-I. However, these are generally limited to the lower cranial nerves and usually follow a subacute to chronic course. In 2008, Heuer et al. reported a case of a 5-year-old female with hearing loss as the only presentation of CM-I [1]. The patient did not have a syrinx. Hearing loss can sometimes be seen in the constellation of CM-I symptoms, but in this case, it was the only symptom of an otherwise asymptomatic CM-I. Also, three adult patients with isolated asymmetric sensorineural hearing loss resulting from CM-I improved after treatment of the CM-I [2]. Cranial nerve neuralgias have also been reported. Papanastassiou et al. described a 63-year-old male with CM-I and a syrinx who presented with chronic face pain and trigeminal neuralgia [3]. The patient failed numerous other treatments, but improved with posterior fossa decompression. Likewise, an 8-year-old with CM-I and syrinx suffered from glossopharyngeal neuralgia [4]. This also improved after CM-I treatment. Another pediatric patient had the acute onset of vocal cord paralysis with a concomitant CM-I [5].

Brain stem and cerebellar dysfunction is due to the compression of the medulla and tonsils at the level of the foramen magnum. Selmi et al. described an adult with CM-I who presented with sinus bradycardia, for which a cardiac etiology was not found [6]. Syncope is another rare presentation of CM-I. In 1982, a report illustrated three cases of CM-I with associated syrinx, all presenting with syncope [7]. These patients varied in age from 20 to 52 years of age. Such "drop attacks" may be secondary to medullary decompression and the resultant dysautonomia. A patient was also reported to have vertigo as the only presenting symptom of CM-I with syrinx, with other causes unable to be found [8]. We treated a 7-year-old with unilateral hearing loss and vertigo associated vomiting and a CM-I without syrinx. At 2-year follow-up, her vertigo was resolved, and her hearing loss has stabilized.

Infants can often have respiratory compromise with severe CM-2. However, it is rare for this to occur in CM-I or older patients. Alvarez et al. and Bokinsky et al. published reports of CM-I resulting in acute respiratory failure [9, 10]. The patients' ages were 38 and 18 years old, respectively, and both had a concomitant syrinx. In 2004, a 22-month-old presented after multiple episodes of apnea. He was found to have a CM-I, and after decompression, he had no further episodes of apnea before being lost to follow-up a year later. Even more devastating, in 1993, Martinot et al. reviewed two pediatric cases (aged 4 and 13) who suffered sudden death, with postmortem evaluation only revealing CM-I as the likely cause of death [11]. One patient had a syrinx, and the other did not.

Although the mechanism is not clear and such an association may be incidental, there have been rare reports of endocrinologic dysfunction as a result of CM-I. A 6-year-old girl was reported to present with profound hypoglycemia and CM-I [12]. Furthermore, a young boy presented with precocious puberty in association with CM-I [13].

Patients with CM-I can also have ophthalmologic symptoms, most commonly nystagmus resulting from cerebellar compression. However, more unusual reports are found in the literature. Gingold and Winfield described a 41-year-old

female with oscillopsia and CM-I [14]. Acute acquired comitant esotropia resulting from CM-I has been reported. These reports describe 11 patients ranging from 5 to 36 years old, both male and female and both with and without an associated syrinx [15–19].

Unusual nonspecific symptoms are also described in case reports. Unrelenting and chronic hiccups were the presenting symptom of a 19-year-old male with CM-I [20]. Eleven patients, with ages ranging from 18 months to 5 years, had their developmental delay (including seizures, motor retardation, and delayed speech) attributed to CM-I [21]. Furthermore, Hudgins reported two children with paroxysmal rage as the presenting symptom of CM-I [22]. The behavior troubles improved after treatment.

Extremity motor and sensory deficits are commonly seen in CM-I. These are mostly caused by an expanding syrinx in the cervical or thoracic spinal cord and follow a progressive and subacute or chronic course. However, acute neurologic deficits may rarely be the presenting symptom of CM-I. Most of these reports involve a traumatic event preceding the onset of symptoms. Yarbrough et al. reported multiple deficits with acute onset in the pediatric population with CM-I and syrinx [5]. A 13-year-old female presented with the acute onset of upper and lower extremity paresthesias. After jumping on a trampoline, a 13-year-old female experienced right-sided hemianesthesia. A 12-year-old female suffered the acute onset of quadriparesis after a fall. Likewise, after a fall, a 10-year-old male had lower extremity paraparesis. A football injury resulted in upper extremity paresthesias in a 14-year-old male with CM-I. Another report of a football injury resulting in transient quadriparesis in an 8-year-old boy with CM-I without a syrinx was reported by Callaway et al. [23].

Peripheral nerve syndromes have also been described as presenting symptoms of CM-I. A 24-year-old male presented with ulnar nerve neuropathy at the elbow from CM-I and syrinx [24]. Similarly, a 26-year-old female had a CM-I with syrinx with carpal tunnel syndrome as the only symptom [25].

In 2008, Laufer et al. reported isolated dorsiflexion weakness in a 5-year-old male and plantar flexion weakness in a 9-year-old girl [26]. In both cases, weakness was the only presenting symptom, and both patients also had an associated syrinx.

Single case reports also exist for the coexistence of CM-I and hypertension [27], hyperhidrosis [28], hemifacial spasm [29], and chronic emesis [30]. Each of these symptoms resolved following posterior fossa decompression leading credence to a cause and effect. Lastly, some have suggested CM-I may be at the root of some patients with autism although this neuroanatomic connection is not clear [31].

With the widespread use of MRI, CM-I is being diagnosed more often and at earlier ages. It is important to remember the more common symptoms that present with CM-I and syrinx. However, if other etiologies are not found, especially in a patient with sensory or motor deficits or brain stem and lower cranial nerve symptoms, one might consider evaluating for CM-I. In the end, unusual presentations may be found in patients with CM-I, but as these may be incidental, the clinical evaluation should be even more stringent.

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Association Between Fibromyalgia, Chronic Fatigue, and the Chiari I Malformation

23

Richard G. Ellenbogen and David F. Bauer

Abstract

Patients with fibromyalgia (FM), chronic fatigue (CF), and Chiari I malformation (CIM) can have overlapping symptoms, including headaches, vertigo, tremors, and gait instability. Authors have proposed that cervical stenosis may be the cause of many of these symptoms in patients with FM, although data is limited on the effectiveness of posterior fossa or cervical decompression in patients with FM or CF. While there are a few retrospective, nonrandomized studies that support an association between FM and CIM, there is one prospective, randomized, high-quality cohort study demonstrating no association between FM and CIM. In this chapter, we will review current evidence on the possible association between FM, CF, and CIM.

Patients with fibromyalgia (FM), chronic fatigue (CF), and Chiari I malformation (CIM) can have overlapping symptoms, including headaches, vertigo, tremors, and gait instability (Fig. 23.1) [30, 37]. Authors have proposed that cervical stenosis may be the cause of many of these symptoms in patients with FM, although data are limited on the effectiveness of posterior fossa or cervical decompression in patients with FM or CF [9, 12, 19, 20, 32]. In this chapter, we will review current evidence on the possible association between FM, CF, and CIM.

Fibromyalgia is characterized by chronic pain with widespread muscle aches and pains, general fatigue, sleep disturbances, and neurological complaints [27, 31]. Often the diagnosis is made using the 1990 American College of Rheumatology classification criteria for the diagnosis of FM [37]. These criteria include chronic, widespread pain for at least 3 months duration, involving the upper and lower body, right and left sides, and axial skeleton. Patients often have allodynia and hyperalgesia arising from muscles and joints. Common pain sites include the neck, back, shoulders, pelvic girdle, and hands, although other sites may be involved [5]. Diagnostic criteria include pain arising from at

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Table 3. Adjusted[a] value for headache characteristics according to fibromyalgia status

Characteristic	Fibromyalgia (*n* = 176)	Healthy (*n* = 67)	*P*
Localized to back of head, %	61	13	<.01
Starts in back of head and radiates, %	55	10	<.01
Temporal/side of head, %	68	19	<.01
Frontal, %	74	33	<.01
Behind eyes, %	76	26	<.01
Lateralized/one side, %	53	11	<.01
Genralized/all over, %	55	22	<.01
Neck pain, %	92	25	<.01
Throbbing and constant, %	70	33	<.01
Nonthrobbing, occasional headache, mean n (SD)/wk	2.1 (2.5)	0.4 (2.8)	<.01
Grade,[b] mean (SD)	5.9 (2.3)	3.6 (2.6)	<.01
Made worse by, %			
Normal activity	59	24	<.01
Lying down	13	3	.09
Standing	48	9	<.01
Head down	46	14	<.01
Coughing	59	22	<.01
Straining	70	25	<.01
Sneezing	52	20	<.01
Playing sports	62	27	<.01
Exercise	74	30	<.01

[a]Adjusted for age, sex, and race.
[b]Range, 1–10: 1 = not bad to 10 = terrible, severe.

Fig. 23.1 Adjusted value for headache characteristics according to fibromyalgia status (Reproduction of Table 3 in Watson et al. [30])

least 11 of 18 tender points on digital examination. These points are digitally palpated with about 4 kg/unit area of force, and bilateral points include under the lower sternocleidomastoid muscles, second costochondral junction, 2 cm distal to the lateral epicondyle, prominence of the greater trochanter, medial fat pad of the knee, insertion of the suboccipital muscle, mid-upper trapezius muscle, origin of the supraspinatus muscle, and upper outer quadrant of the buttock (see Fig. 23.2) [17]. These criteria provide a sensitivity of nearly 88 % and specificity of 81 % in distinguishing FM, and consequently, these criteria are still used by many clinicians to make the diagnosis. In 2010, the American College of Rheumatology created preliminary diagnostic criteria for diagnosis of FM and the measurement of symptom severity. As a screening test, these criteria include the use of a Widespread

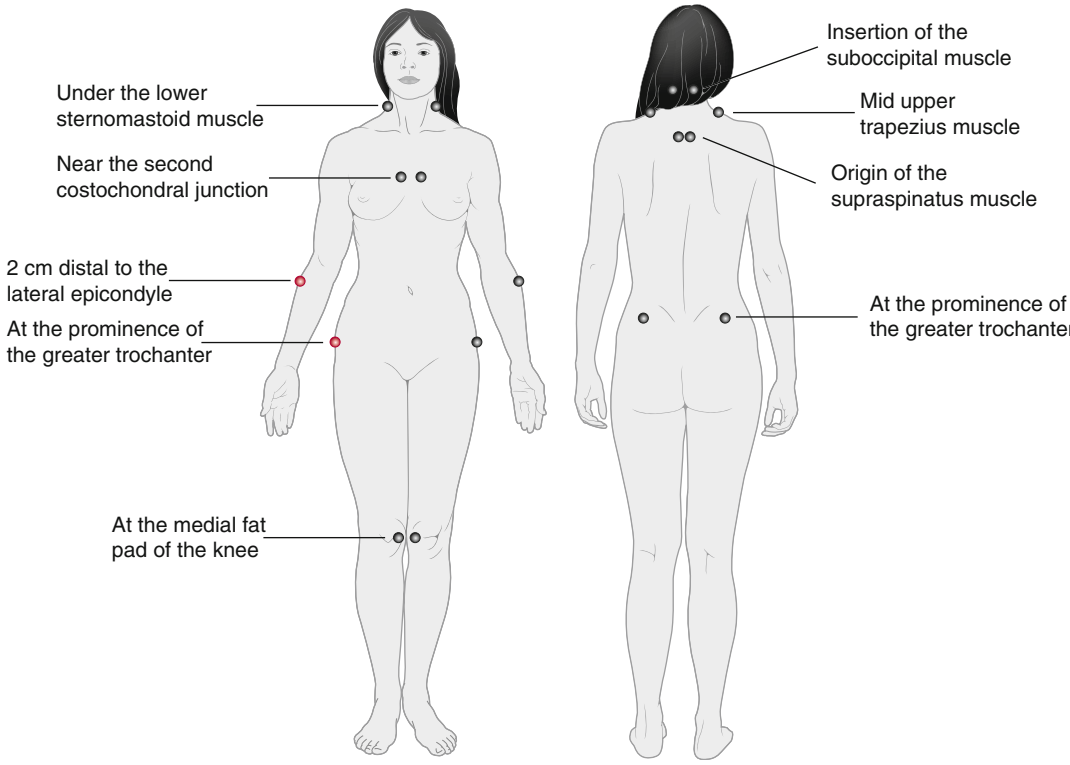

Fig. 23.2 Reproduction of tender/trigger point diagram in Goldenberg [17]

Pain Index and Symptom Severity Scale that can be completed without a patient examination [34]. Fibromyalgia affects 2 % of the US general population, and approximately six million people suffer from FM in the USA alone [33, 35, 36]. Patients are more commonly women, and symptoms usually appear between 20 and 55 years of age. Other common diagnostic features include fatigue, sleep disturbances, stiffness, paresthesias, headaches, Raynaud's-like symptoms, depression, and anxiety. Currently, there is no accepted mechanism for the development of FM, although many possible abnormalities and mechanisms have been proposed [1, 6–8, 13, 23]. There are other systemic diseases that have overlap of symptoms with FM. These diseases include hypothyroidism, systemic lupus erythematosus, and malignancies. Patients diagnosed with FM often report the onset of symptoms after a motor vehicle collision, surgery, or other trauma [10, 11, 28]. Fibromyalgia is 13 times more common after neck injuries than after injures to the lower extremities. Patients with FM also exhibit more neurologic signs and symptoms than control subjects despite lack of imaging abnormalities in these patients. These include greater dysfunction of the glossopharyngeal and vagus nerves; more sensory, motor, and gait abnormalities; and more neurologic symptoms such as photophobia, poor balance, weakness, and tingling [34, 36]. Management of FM can be difficult. Medical therapy includes amitriptyline, cyclobenzaprine, tramadol, serotonin reuptake inhibitors, and pregabalin. Nonmedical therapies include cardiovascular exercise, cognitive behavioral therapy, patient education, biofeedback, and hypnotherapy [18].

CF is a condition characterized by a constellation of symptoms of at least 6 months duration including severe, medically unexplained mental and physical fatigue, sleep disturbances, poor concentration, and flu-like symptoms [24]. It is estimated that between 0.5 and 2.5 % of the general population has CF, and associated physical and psychosocial disability has been thought to lead to high direct and indirect medical and societal costs. Many patients with CF have overlapping symptoms with FM. Patients with CF may

have multiple tender points on examination, and it can often be difficult in these patients to differentiate between a diagnosis of FM or CF. There have been purported links between a diagnosis of CF and chronic Epstein-Barr virus infection, chronic Lyme disease, total allergy syndrome, multiple chemical sensitivity syndrome, and chronic candidiasis, but none of these etiologic agents have been scientifically linked to CF [2]. Current revised CDC criteria for CF include new onset of unexplained, persistent, or relapsing fatigue, not a result of ongoing exertion, and not alleviated by rest, resulting in substantial reduction in occupational, educational, social, or personal activities. In addition, patients must have four or more additional symptoms during a period of at least 6 months of fatigue. These symptoms include impairment in short-term memory or concentration, sore throat, tender cervical or axillary nodes, muscle pain, multijoint pain without redness or swelling, headaches of a new pattern or severity, unrefreshing sleep, and post-exertional malaise lasting >24 h [16]. Treatment options for CF are limited. Meta-analysis has shown that only cognitive behavioral therapy and graded exercise treatment are effective treatments for CF.

Chiari I malformation is a hindbrain malformation characterized by downward extension of the cerebellar tonsils below the foramen magnum [3]. Magnetic resonance imaging often reveals a full posterior fossa, and flow studies often document poor flow of cerebrospinal fluid around the cerebellum and brain stem [4, 14, 15, 21, 25, 38]. Up to 80 % of CIM patients have comorbid syringomyelia, and there is a female predominance with this disorder [26]. Approximately 25 % of patients diagnosed with CIM cite acute head trauma or birth trauma as a precipitating event [14]. While the most reliable symptom in patients with CIM is often a reproducible Valsalva-induced headache, some patients present with complaints similar to FM such as malaise, tremor, and vertigo [30].

Recent uncontrolled case series documented CIM in 4–20 % of FM patients, with 46–71 % exhibiting spinal canal stenosis or cervical compression after flexion/extension of the cervical spine [9, 12, 19, 20, 22, 26, 29, 32]. Nonrandomized studies have shown that posterior fossa decompression with possible cervical laminectomy reduced fatigue and pain in FM patients with presumed CIM; however, a retrospective study has shown no correlation between cervical stenosis and FM [12, 19, 20]. Only one prospective, randomized study has been published looking at the association between FM and CIM [30]. This study, level II medical evidence, demonstrated no correlation between FM and CIM.

For example, Heffez et al. published two studies evaluating FM and CIM [20]. In 2004, they retrospectively evaluated 278 adult patients with a clinical diagnosis of FM. These patients were 87 % female, and they had symptoms predominantly of neck and back pain, fatigue, cognitive impairment, gait instability, grip weakness, paresthesia, vertigo, and numbness. Eighty-eight percent of patients reported worse symptoms with neck extension, 45 % of patients had a cervical canal diameter <10 mm, and 20 % of patients had tonsillar ectopia >5 mm. The authors concluded that FM symptoms may be secondary to CIM and cervical stenosis.

In 2008, Heffez et al. published a nonrandomized, prospective, case–control study comparing outcomes of craniocervical decompression versus nonoperative management of 40 operated and 31 nonoperated patients with FM [19]. They reported an improvement in surgically treated patients at 1 year in physical and mental quality of life, anxiety, and depression. In the study, the authors noted that they chose patients from a larger cohort based on their prompt return of surveys sent to them over a year-long period. They did not describe complications or long-term outcomes.

In 2008, Holman et al. published a retrospective study evaluating "positional cervical cord compression" in patients with FM [22]. Seventy patients seen over a 2-month period in their clinic were evaluated with dynamic MRI, and 52 of 70 patients had cervical cord compression based on this study. The author posed that cervical cord irritation may be the cause of FM in these patients.

Watson et al. published the only prospective, randomized study of the relationship between CIM and FM [30]. This cohort study provides the only level II evidence on this subject. The

Table 4. Adjusted[a] magnetic resonance imaging measurements (means and 95 % confidence intervals) according to fibromyalgia status

Measurement	Fibromyalgia (n = 176)	Healthy (n = 67)	P
Tonsillar position,[b] mm	–0.71 (–1.08, –0.34)	0.00 (–0.66, 0.66)	.09
Posterior fossa volume, cm^3			
Total volume	189 (187–192)	192 (188–197)	.31
Brain volume	163 (160–165)	165 (161–169)	.30
Cerebrospinal fluid volume	27 (26–28)	27 (25–29)	.80
Ratio of brain to cerebrospinal volume	6.5 (6.2–6.7)	6.4 (5.9–6.8)	.72
Cerebrospinal fluid maximum systolic velocity, cm/s			
C2 anterior region	2.63 (2.52–2.73)	2.51 (2.32–2.70)	.33
C2 posterior region	2.29 (2.19–2.39)	2.28 (2.10–2.45)	.91
Foramen magnum anterior region	2.37 (2.23–2.51)	2.17 (1.92–2.42)	.19
Pulsatile tissue veolocity motion, cm/s			
C2 spinal cord pulsatile motion	0.74 (0.72–0.77)	0.67 (0.62–0.72)	<.05
Foramen magnum pulsatile motion	0.76 (0.72–0.81)	0.66 (0.58–0.73)	<.05

[a]Adjusted for age, sex, and race.
[b]Negative values indicate millimeters above the foramen magnum; positive values, position below the foramen magnum.

Fig. 23.3 Adjusted magnetic resonance imaging requirements (Means and 95 % Confidence Intervals) according to fibromyalgia statuses (Reproduction of Table 4 in Watson et al. [30])

authors prospectively obtained MRI studies of 176 participants with FM and 67 pain- and fatigue-free control subjects. Imaging was obtained of the brain and upper cervical spine. Chiari I malformation was defined as inferior extension of cerebellar tonsils greater than or equal to 5 mm below the basion-opisthion line of the foramen magnum or tonsillar ectopia 3–5 mm below the basion-opisthion line plus abnormalities of CSF flow, posterior fossa volume, or hindbrain or cervical spinal cord movement. Morphometric measurements were obtained of posterior fossa volumes, and cerebrospinal fluid flow was evaluated with flow-sensitized phase-contrast gradient echo MRI (Fig. 23.3). The primary outcome was the frequency of CIM in participants with FM compared to healthy controls. The patients with FM were predominantly female (93 % vs. 54 % in the control group). Patients in the FM group had more pain, fatigue, and sleep disturbances than controls. Mean tonsillar position and the prevalence of CIM were similar in the FM and control groups. No association was found between FM and CIM in this study.

In conclusion, the overlap of symptoms between FM, CF, and CIM understandably has led to a search for an association between these entities. While there are a few retrospective, non-randomized studies that support an association

between FM and CIM, there is one prospective, randomized, high-quality cohort study demonstrating no association between FM and CIM. No evidence supports routine use of static MRI to evaluate FM or CF patients. However, despite lack of current evidence, it is likely that future large prospective trials may bring more evidence to this topic.

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The Chiari Malformations and Hydrocephalus

24

James M. Johnston Jr. and John C. Wellons III

Abstract

The association of hydrocephalus and the Chiari malformations has been described from the time of Hans Chiari's initial report in 1891. Whether hydrocephalus is the cause of or the result of hindbrain herniation remains a subject of long-standing controversy, but recent advances in vascular and volumetric imaging may eventually provide definitive information to settle the debate. Though there is a wide range of hindbrain herniations that fall under the Chiari rubric, most authors would agree that coexisting hydrocephalus should be managed with CSF diversion first, either by shunting or endoscopic ventriculostomy, before consideration is given to posterior fossa decompression. It is crucial to keep in mind that pseudotumor cerebri may also present with symptoms that mimic those seen in Chiari malformation, making it critical that the neurosurgeon strive to differentiate these two groups prior to surgical intervention for optimal outcome.

Introduction and Historical Background

The association of hydrocephalus and the Chiari malformations has been described from the time of Hans Chiari's initial report in 1891 [1]. The pathophysiology of Chiari-associated hydrocephalus has nonetheless been controversial, with several hypotheses proposed to explain its pathophysiology. In his original manuscript, Chiari postulated that tonsillar herniation resulted from supratentorial pressure due to concomitant hydrocephalus [1], suggesting that brain herniation was in fact secondary to intrinsic hydrocephalus. This initial explanation was cogent and quite popular and still provides the rationale for CSF diversion as a primary treatment of

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Chiari-associated hydrocephalus. The Dutch surgeon van Houweninge Graftdijk proposed a converse theory in 1932 [2], whereby the foramina of the fourth ventricle, herniated into the upper end of the spinal canal, act as a valvular obstruction and precipitate hydrocephalus. He advocated surgical correction of the hindbrain herniation in order to widen the space and allow for better flow of CSF. More recent advances in cranial imaging and volumetric analysis have provided some detail to this theory, linking tonsillar herniation to a disorder of the paraxial mesoderm with underdevelopment of the occipital somites and secondary hypoplasia of the occipital bone, leading to overcrowding of the vascular and neural structures within the posterior cranial fossa [3, 4]. This combination of factors may lead to impaired CSF absorption and flow due to hindbrain distortion, decreased cisterns, and anomalies of the venous circulation, resulting in hydrocephalus. Whether hydrocephalus is the cause of or the result of hindbrain herniation is quite relevant, as it may dictate the surgeon's approach to a management strategy that is perceived to lead to the best clinical outcome for each individual patient. Given the wide range of hindbrain anomalies that fall under the Chiari rubric, each Chiari subtype will be discussed separately.

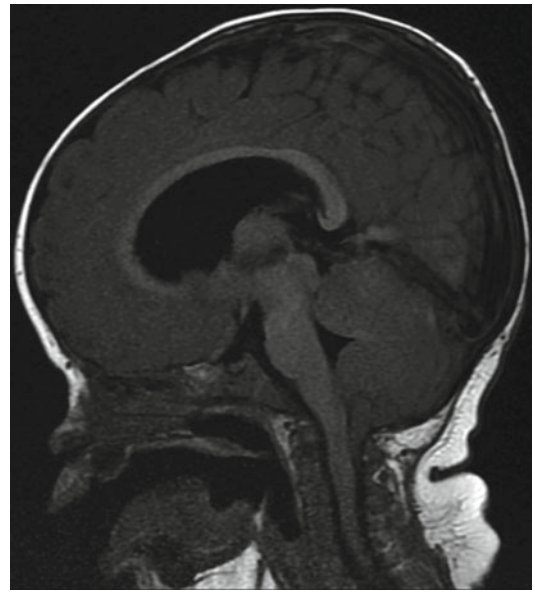

Fig. 24.1 Chiari I malformation with hydrocephalus. Sagittal T1-weighted MR imaging demonstrates caudal displacement of the cerebellar tonsils and ventricular enlargement

Chiari I

Epidemiology and Clinical Presentation

Reported incidence rates of hydrocephalus in cases of Chiari I malformation (CMI) range from 0 to 9.6 % [4–6], and it may often be associated with concomitant syringomyelia [4]. In addition to classic hindbrain symptoms of CMI, symptoms of hydrocephalus and resultant elevated ICP may include headaches, vomiting, papilledema, and enlarging head circumference in infants. Magnetic resonance imaging is the modality of choice for diagnosis of both entities and also allows evaluation of the spinal cord to rule out associated syringomyelia. In patients being considered for ETV, MRI also provides necessary anatomic detail of the third ventricle, basilar artery, and prepontine space (Fig. 24.1). Threshold values of ventricular enlargement necessary for a diagnosis of hydrocephalus are not well defined in the literature, making clinical diagnosis of elevated ICP a crucial component of the decision-making process.

Management and Outcomes

As mentioned before, some controversy exists regarding whether hydrocephalus should be considered the cause of the CMI hindbrain herniation or rather the effect of obstruction at the level of the fourth ventricular outlet or even abnormal CSF absorption at the level of the posterior fossa cisterns [3]. This controversy notwithstanding, it is generally accepted that in cases of CMI, hydrocephalus should be managed by adequate CSF diversion before consideration is given to suboccipital decompression [7–10].

Ventriculoperitoneal shunt placement has long been the mainstay of treatment for CMI-associated hydrocephalus. While there are no published studies looking specifically at the durability of

VPS for CMI-associated hydrocephalus, the complication and infection rates for shunt placement are not insignificant, especially in the pediatric population [11, 12].

Recent studies have reported relative success of ETV in the management of CMI-related HCP [13–24]. The two largest series [22, 23] reported an 87–94 % (28 of 31) early success rate with two failures due to late (>1 year) stoma closure and in one case of a previously shunted patient. Together, the two series reported no mortality or clinically significant complications and syringomyelia resolution or improvement in 8 of 11 patients. Of note, despite similar success rates in management of HCP, the two groups reported very different rates of patients going on to require subsequent posterior fossa decompression for persistent CMI symptomatology (0 vs. 37.5 %). Whether this was due to different mean ages of their populations (15.2 vs. 31.9) or criteria for operative decompression is unclear. Nonetheless, both groups advocate ETV as the procedure of choice in the management of hydrocephalus associated with CMI, both for hydrocephalus control and treatment of hindbrain herniation symptoms, including syringomyelia.

Prospective, randomized studies are required to validate this encouraging preliminary data.

Chiari II Malformation

Epidemiology and Clinical Presentation

The Chiari II malformation (CMII) almost always occurs in patients born with neural tube defects, most commonly myelomeningocele or encephalocele. Criteria for diagnosis include the elongation and caudal migration of the cerebellar vermis, brainstem, and fourth ventricle into the upper cervical canal, as well as a host of other cerebral anomalies (Fig. 24.2). Associated findings may include tectal beaking, basilar invagination, colpocephaly, low-lying torcular, skull anomalies, and syringomyelia (40–95 %) [25]. Incidence of clinical hydrocephalus requiring CSF diversion varies from 40 % in prenatally closed groups [26] to 52–90 % in postnatally closed series [27–33].

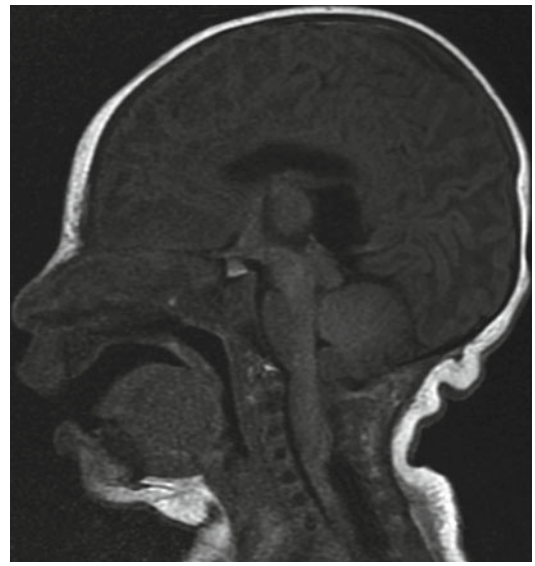

Fig. 24.2 Chiari II malformation with hydrocephalus. Sagittal T1-weighted MR imaging demonstrates elongation and caudal displacement of the cerebellar vermis and brainstem into the upper cervical canal, tectal beaking, and low-lying torcular

This wide variation in reported incidence is likely a reflection of different patient populations, health systems, and criteria for diagnosis and intervention.

Symptoms of hydrocephalus in infants with CMII may include bulging fontanelle, split cranial sutures, and leakage from the myelomeningocele closure site. Of note, hydrocephalus may also worsen symptoms referable to the CMII, including lower cranial neuropathies, swallowing dysfunction, and stridor. Numerous methods exist to quantify ventriculomegaly, including calculation of the ratio of biventricular diameter to biparietal diameter [34], frontal-occipital horn ratio, and ventricular index, though no published studies to date have clearly delineated the best measure.

Management and Outcomes

As in CMI, management of hydrocephalus or verification of a working shunt should always precede suboccipital decompression, even in the setting of brainstem symptomatology (i.e., stridor,

dysphagia, sleep apnea) or worsening syringomyelia. Criteria for CSF diversion have historically been somewhat variable, though efforts have been made to standardize indications to better compare outcomes across multiple institutions [26]. Traditionally, ventriculoperitoneal shunting has been the most common procedure used for treatment of hydrocephalus associated with CMII and myelomeningocele. However, shunt complication rates and death in children with myelomeningocele may be higher than in children requiring shunt for other reasons [35–38]. Some authors have suggested that infective complications of shunting may have a greater impact on cognitive development than the hydrocephalus [39] and that children with myelomeningocele who do not require shunt placement have better survival [40, 41] and higher IQ [42] than those who have undergone shunt placement. These studies are limited by their retrospective nature and potential bias, and prospective studies are required to elucidate the appropriate threshold for intervention given the known risks of shunting. In children with mild ventriculomegaly and no signs or symptoms of increased intracranial pressure, potentially improved brain development must be weighed against the known risks of CSF diversion in this population. Based on preliminary data suggesting improved neuropsychological scores 6 months following shunt insertion [43], prospective studies are under way to evaluate ventricular size and neurocognitive outcome.

More recently, endoscopic third ventriculostomy has been proposed as an acceptable alternative to ventriculoperitoneal shunting in children with myelomeningocele [44–49], with acknowledged lower success rates in infants and children with a previously placed shunt [46–48, 50]. The addition of choroid plexus cauterization to ETV has also been investigated, based on extensive experience with children in developing countries [51–54], where cost and medical access preclude ventriculoperitoneal shunt placement. Long-term follow-up in this cohort demonstrated similar neurocognitive outcomes in the ETV/CPC and VP shunt groups [52]. It remains unclear whether these very promising findings are directly translatable to infants in developed countries.

Chiari III

Chiari malformation type III (CM III) is an extremely rare entity characterized by herniation of the posterior fossa contents through a low occipital and/or upper cervical osseous defect [1, 55, 56], estimated to account for 0.64–4 % of all Chiari malformations [57, 58]. Published series report a high incidence of associated hydrocephalus, syringomyelia, and tethered cord syndrome [25, 55, 56]. Associated hydrocephalus has traditionally been managed with ventriculoperitoneal shunt placement, and the rarity of CM III limits the availability of published data regarding long-term shunt survival or alternative CSF diversion.

Pseudotumor Cerebri and the Chiari Malformation

Tonsillar descent secondary to lumboperitoneal shunting for pseudotumor cerebri (PTC) is quite common, well described in the literature [59], and will not be treated further here. However, there has been much disagreement regarding the nature of the association between PTC and primary Chiari malformation. PTC classically presents with headaches, visual changes, elevated intracranial pressure measured on lumbar puncture in the lateral decubitus position, and no evidence of hydrocephalus or intracranial pathology. It is most often observed in obese women of childbearing age, though it can also be seen secondary to certain medications (tetracycline, minocycline, vitamin A, corticosteroids, lithium, and oral contraceptives) and in the setting of venous sinus thrombosis [60]. The source of the controversy lies in two observations. First, several groups have described an increased prevalence of cerebellar ectopia in patients with PTC. Sinclair described a series of 156 cases of PTC noting an overall incidence of 2.7 %, significantly higher than the 0.77 % rate previously reported in the general population [61]. Banik observed a 24 % rate of inferior tonsillar displacement in patients with PTC, with 10 % fulfilling criteria for Chiari malformation (>5 mm) [62]. Of note, all patients with tonsillar descent were female and obese.

Second, several groups have described the effectiveness of CSF shunting in patients with recurrent Chiari symptoms following posterior fossa decompression. Fagan reported a series of 15 patients with post-Chiari PTC, defined as recurrence of Chiari-like symptoms after decompression, elevated lumbar CSF pressure in the absence of meningitis or ventriculomegaly, and transient resolution of symptoms following lumbar CSF drainage [63]. All patients were evaluated with CSF flow studies at the foramen magnum as well as lumbar puncture to rule out infection/aseptic meningitis and to evaluate intracranial pressure. Those found to have increased ICP underwent lumboperitoneal shunting, with significant symptom resolution in 7/9 (78 %) pediatric patients and in 0/6 adult patients [63]. Bejjani reported a series of six adult patients with similar recurrence of Chiari-like symptoms following posterior fossa decompression and found significant improvement in all following either shunting or repeat LP with acetazolamide [64].

Whether the association is real or coincidental is unclear. Some authors argue that they are two pathophysiologically distinct entities with overlapping clinical presentation, specifically headaches and tonsillar descent [65]. Others suggest that the entities may actually share a similar pathophysiology, namely, increased intracranial contents, engorged brain with venous hypertension, decreased intracranial volume, and mechanical obstruction of CSF outflow at the foramen magnum with a common end result of altered compliance and disturbed neural hydrodynamics [62, 64, 66]. Definitive resolution of the issue will require more detailed imaging and prospective studies of larger populations.

Practically speaking, given the similar demographics, clinical presentation, and increased incidence of tonsillar ectopia in patients with pseudotumor cerebri, it is critical that the neurosurgeon strive to differentiate these two groups during clinical evaluation prior to surgery for optimal outcome. Patients with atypical headaches, obesity, relevant medication exposure, visual changes, and papilledema should be most closely examined to better differentiate between the two diagnoses. Detailed fundoscopic exam, MRI cine studies to visualize CSF flow at the foramen magnum, and lumbar puncture may be considered in these complex patients to evaluate intracranial pressure and also determine if the patient responds symptomatically to CSF drainage. Those patients with evidence of intracranial hypertension and symptomatic improvement following lumbar puncture will benefit from CSF diversion instead of posterior fossa decompression.

A Special Note About Predicting Success of ETV in the Chiari I and II Populations

Major factors that predict the success of ETV include age, etiology of hydrocephalus, and the presence or absence of a shunt preoperatively [48, 67–79]. In 2009, Kulkarni et al. used these factors to develop a model to predict the probability of ETV success in the treatment of childhood hydrocephalus: the Endoscopic Third Ventriculostomy Success Score [48] (Fig. 24.3). By assigning a score to age range, etiology, and shunt history, an overall score is calculated that predicts the likelihood of successful ETV at 6 months post-procedure and was found to closely approximate success. Since that time, there have been several publications using the ETVSS. The Canadian Pediatric Neurosurgery Group evaluated a multicenter cohort of children newly diagnosed with hydrocephalus and evaluated the risk of failure between ETV and VPS for high-, moderate-, and low-ETVSS group [80]. For all groups, the risk of ETV failure became progressively lower compared with shunt failure with increasing time from surgery. In the high-ETVSS group, the risk of ETV failure was lower than shunt failure soon after surgery. For all the rest, the risk of ETV failure only became lower than shunt failure 3–6 months out from surgery. Kulkarni, Riva-Cambrin, and Browd then applied the ETVSS to several well-known published series of patients on whom ETV was performed for various reasons. The overall mean-predicted ETVSS was 58 %, and the actual ETV success rate was 59 %, showing excellent predictive capability of the

Fig. 24.3 The ETV Success Score predicts the likelihood of successful ETV at 6 months after the procedure

ETV success score
= Age score + Etiology score + Previous shunt score
≈ Percentage probability of ETV success

Score	Age	Etiology	Previous shunt
0	<1 month	Post-infectious	Previous shunt
10	<1 month to <6 months		No previous shunt
20		Myelomeningocele Intra-ventricular hemorrhage Non-tectal brain Tumor	
30	6 months to <1 Year	Aqueductal Stenosis Tectal tumor Other etiology	
40	1 Year to <10 Years		
50	≥10 Years		

model [46]. Two articles were published in November of 2011 in Journal of Neurosurgery: Pediatrics intended to further validate the ETVSS [45, 81]. Both single-institution series showed excellent predictive capability of the ETVSS in separate analyses.

As reviewed earlier, hydrocephalus related to the CMI is relatively rare. Therefore, ETVs for hydrocephalus due to CMI make up only a small part of most single-center and multicenter ETV series. Within the etiology portion of the ETVSS, the same predictive capability is apportioned to CMI ("other") as those etiologies that traditionally have a high rate of success: aqueductal stenosis and tectal tumors. Despite the initial success in published series reviewed above, this may very well be an overestimation of the capability of ETV to adequately treat hydrocephalus in patients with CMI, or this may be clinically accurate. Additional series continue to accrue [22, 23], and future adjustments to the model may be necessary.

Performance of an ETV for hydrocephalus related to spina bifida, however, is becoming more common. Based on the current ETVSS model, there is less likelihood of success in patients with this etiology than with CMI. Due to the large number of patients with post-infectious hydrocephalus, Warf, Mugamba, and Kulkarni modified the existing ETVSS in order to apply it to children seen at the CURE Children's Hospital of Uganda (CCHU) [78]. As a result, the CCHU ETVSS for use in the field predicted ETV success to a much higher degree by taking into consideration age, etiology, and the degree of choroid plexus cauterization (CPC). A substantial number of ETVs in this population were performed with choroid plexus cauterization. In a very interesting finding and one that was independent of CPC and age, regression analysis revealed that the odds of ETV success were 2.25 times greater in spina bifida patients compared with other etiologies.

Further validation studies may shed more light on this relationship and again may contribute to a further honing of the model.

Conclusion

The Chiari malformations have long been associated with hydrocephalus. Controversy remains, however, regarding which entity precedes the other, though most authors agree the pathophysiology is multifactorial. Though hydrocephalus is relatively rare in the setting of the CMI, most agree that CSF diversion should be performed prior to suboccipital decompression. In addition to traditional shunting, emerging data suggest that ETV is effective in a large majority of these patients and may improve hindbrain compression symptoms and syringomyelia. Hydrocephalus is much more common in the CMII–myelomeningocele population, though controversy remains regarding the proportion of these patients that will ultimately require CSF diversion. As in the Chiari I population, adequate CSF drainage should be ensured prior to surgical decompression, even in the setting of hindbrain compression symptoms or syringomyelia. Though traditional shunting remains the most common treatment for these patients, ETV has emerged as an acceptable alternative, especially in experienced centers when combined with choroid plexus cauterization. Prospective studies of both entities are ongoing, examining diagnostic criteria, neuropsychological outcomes, and preferred CSF diversion technique in these challenging populations.

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Symptoms of the Chiari II Malformation

25

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Abstract

The symptoms of a Chiari II malformation (CIIM) arise from variable degrees of brain stem compromise and are most commonly manifest as elements of bulbar failure but may involve the long tracts and sensorium as well. Whether this compromise in function arises as a result of inherent brain stem malformation or as a result of physical compression from a malformed posterior fossa remains an active area of debate. Symptoms associated with the CIIM (Table 25.1) are age specific in their presentation and can be subtle or profound. Stridor is the hallmark symptom of symptomatic CIIM in the newborn and represents an urgent neurosurgical need. Impaired airway protection; generalized lethargy, listlessness, and hypotonia; and a variety of gastrointestinal symptoms may also be seen in infants with a symptomatic CIIM. The manifestations of CIIM in the older child and adult are less common, more insidious in onset, and less acutely threatening to survival than in the infant. Progressive dysfunction of the hands (with associated sensory symptoms), sleep abnormalities, and ataxia may be seen in the older child or adult. Symptoms are age related and localize to the dysfunctional bulbar structures of the posterior fossa.

Introduction

The Chiari II malformation (CIIM) is perhaps the single most important component of an open myelomeningocele (MMC). The symptoms of a CIIM arise from variable degrees of brain stem compromise and are most commonly manifest as elements of bulbar failure but may involve the long tracts and sensorium as well. Whether this compromise in function arises as a result of inherent brain stem malformation or as a result of physical compression from a malformed posterior fossa remains an active area of debate. Complications related to the CIIM are protean but remain the most common cause of death for an infant with a MMC. Symptoms associated with the CIIM are variable but are age specific in their presentation. They can be subtle and are rarely intuitive to the uninitiated. Detection of a

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symptomatic CIIM may allow intervention and potentially prevent progression to an irreversible neurologic insult or death. The extent to which an intervention can reverse the course of a symptomatic CIIM appears, but it appears self-evident that early detection and intervention offers a greater likelihood of recovery than an intervention undertaken once severe symptoms or a profound deficit has been observed to occur. As such, it is imperative that those providing care to children with open neural tube defects be aware, watchful, and sensitive to the symptoms of the CIIM.

Symptoms and Signs of the CIIM in the Neonate and Infant

Stridor: Symptomatic CIIM is the most common cause of death in infants less than 2 years who are born with a MMC [2, 3, 5, 19]. Approximately one third of infants born with MMC will develop symptoms of brain stem and lower cranial nerve (CN) failure before the age of 5 years, and up to one third of these patients will expire as a consequence of symptomatic CIIM. The symptoms arising in the neonate arise from progressively severe compromise of brain stem and lower cranial nerve function. This disproportionately impacts the laryngeal muscles, resulting in abductor paralysis of the cords and progressive airway obstruction. Impaired non-laminar airflow across the larynx results in *stridor*, which is the hallmark symptom of symptomatic CIIM in the newborn [2, 3, 5, 6, 9]. Stridor is a high-pitched repetitive sound that can be clearly observed to arise from the throat of an affected infant. It often is worsened with inspiration or crying and may be associated with back arching or opisthotonus [4, 10]. In the child without a neural tube defect, it may be seen as a result of laryngomalacia, epiglottitis, an ingested foreign body, or as a complication of a severe upper respiratory infection/croup. However, in a child with a MMC, it must be considered as pathognomonic of symptomatic CIIM and warrants urgent intervention [3, 14, 16, 19]. The child exhibiting stridor may show a wide range of overall clinical wellness. A newborn is often listless from progressive work of breathing, but occasionally, the child may look well and have stridor as the singular indication of impaired brain stem function and impending peril [4, 5, 10]. Stridor is rarely observed immediately after birth in the child with MMC but rather tends to onset insidiously and often precipitously in the weeks following [4, 10]. Regardless of the associated symptoms, stridor must be interpreted as a neurosurgical emergency in the neonate or infant with hydrocephalus and a MMC [10, 16].

The pathophysiology of stridor associated with the CIIM is incompletely understood, but the preferential impairment of abduction may be related to or potentiated by a rostral-caudal somatotopic organization of the cell bodies that, respectively, serve abduction and adduction within the nucleus ambiguus of the medulla [4, 7]. The nucleus ambiguus provides innervation to laryngeal, pharyngeal, and esophageal skeletal muscle that is branchiomerically derived. The most rostral components serve motor function of the larynx via glossopharyngeal motor fibers. More caudal nuclei serve motor function via vagal special visceral efferent fibers. Volitional control of the larynx is highly complex, but laryngeal function can be summarized to occur via 4 paired and 1 unpaired muscle groups. The paired muscles include the cricothyroids, cricoarytenoids, lateral cricoarytenoids, and thyroarytenoids, and the unpaired muscles are the arytenoids. The most rostral cell bodies within the nucleus ambiguus project to the cricothyroids which provide tensor and adductor function. Cell bodies found slightly more caudally within the nucleus ambiguus project to the posterior cricoarytenoids and provide abductor function to the vocal cords. The most caudal cell bodies project to the arytenoids, which also provide adductor function. Thus, there is a somatotopic organization that may contribute to differential vulnerability to insult or stress in the nuclei that regulate adduction and abduction [4, 7].

There is also some experimental evidence that there is differential susceptibility to injury or stress between fibers supplying adductor and abductor functions of the larynx and that those supplying abduction are more sensitive or vulnerable to injury. This may further contribute to

abduction failure with brain stem shift or compromise. The caudal descent of the brain stem in CIIM may contribute to the overall stretch upon exiting fibers and those subserving abduction may be preferentially compromised [4, 7].

Controversy exists as to whether the primary insult to make the CIIM symptomatic is related primarily to compression, downward traction on the brain stem and lower CN, or is a manifestation of primary dysgenesis [12]. This is an important practical issue as it directs a rational clinical response. If the primary issue is that the congenitally malformed nuclei are vulnerable and sensitive to stress, then the appropriate clinical intervention is normalizing intracranial pressure because impaired shunt function is a great stressor to a compromised nervous system [9, 12, 19]. By contrast, if compression is the primary mediator of the pathophysiology, then the appropriate surgical response would be posterior fossa decompression via suboccipital craniectomy and cervical laminectomy [13, 14]. While both interventions have been shown to have clinical benefit, a convincing propensity of clinical experience over time has supported shunt insertion and exploration as the first clinical intervention [3, 4, 6, 10, 12, 14–18]. Shunt exploration should take place promptly regardless of the CT findings. Absence of ventriculomegaly should not prevent shunt exploration and restoration of normal shunt function [16, 18, 19].

Impaired airway protection is another important symptom of the CIIM in the neonate [3, 6, 11, 14]. Impaired airway protection may not have the striking clinical finding expression as stridor and often requires a keen sensitivity and sense of awareness of risk for these infants. Affected infants will characteristically show pooling of secretions, which are audible when they cry and occasionally visible as they escape the mouth [14]. Nasal regurgitation, coughing, and choking are frequent, and suctioning produces abnormally large volumes of secretions. Most importantly, these children can progress readily to aspiration pneumonia, which can become a ready portal to more generalized infection and sepsis [14, 16].

Generalized lethargy, listlessness, and hypotonia are often seen as a manifestation of a symptomatic CIIM [2, 3, 6, 11]. They are grouped here along with the other respiratory manifestations of CIIM in the infant as they are thought most frequently to arise as a result of progressive fatigue of breathing against an elevated resistance brought about by laryngeal compromise. As such, these are very important comorbidity to stridor that can be a harbinger of impending collapse of the struggling infant. However, there are likely to be other contributors to generalized lethargy in the infant with symptomatic CIIM. Dysautonomias can potentially contribute to alterations and impairments of perfusion contributing to pallor. Impaired descending tract function may contribute to hypotonia. Impaired airway protection leads to a constant exposure to aspiration pneumonia and an elevated metabolic demand of constant low-grade inflammation or infection. The relatively underdeveloped, emaciated muscle mass of the affected infant provides no significant margin of reserve for such stresses and further contributes to overall risk within these young, fragile newborns [2, 3, 14, 16].

A variety of *gastrointestinal symptoms* may also be evident in the infant with symptomatic CIIM. These include impaired swallowing, impaired airway protection, reduced gastric emptying, and impaired bowel motility that is thought to arise from a primary gastrointestinal dysautonomia [3, 6, 11, 17]. Gastrointestinal issues of neurologic origin in MMC affect the upper part of the digestive system early in life (dysphagia, pharyngoesophageal dysmotility, etc.), while issues arising from the lower digestive tract (constipation, incontinence, etc.) plague later in life. Swallowing is frequently impaired by pharyngoesophageal dysmotility and/or an impaired or absent gag reflex. Progressive weight loss may lead to emaciation despite prolonged feeding times. The pathophysiology of these findings is not known in detail but, like respiratory issues, is likely related to impaired medullary and vagus nerve function.

Other symptoms can occur in the infant with a symptomatic CIIM, but those bulbar functions surrounding the respiratory system (airway preservation and protection) and GI system (secretion management, catabolism/emaciation)

predominate. The clinical profiles are variable, but distinct patterns of symptom evolution in newborns can be discerned. The first is that of the progressively and profoundly ill neonate who classically/characteristically has a fairly high (thoracolumbar to high lumbar) spinal defect/placode. These infants classically have nearly immediate hydrocephalus (occasionally with severe intrauterine macrocephaly) and early stridor and poor secretion management with choking, gurgling, and nasal regurgitation. This more involved form of symptomatic CIIM is often modestly or minimally responsive to intervention, and these children often succumb from primary and consumptive brain stem collapse despite aggressive treatment of hydrocephalus and posterior fossa decompression and airway support with tracheostomy. Recognition of this scenario can be helpful as it allows guided counseling of the family and care team toward a more palliative course of comfort, support, and respect for the dignity of the infant rather than a series of invasive and fruitless interventions that hold minimal hope of reversing or impacting the overall situation. In general, the younger the infant and the more severe the hydrocephalus and stridor at the time of prognosis, the more ominous is the scenario.

The second and more common scenario in the symptomatic infant is that of the otherwise adjusted infant with MMC/CIIM who is noted to progressively develop stridor. Stridor often develops insidiously but precipitously in such children. It may be readily overlooked by parents because it is not intuitive that abnormal respiratory sounds may be the harbinger of an important brain stem problem which represents a neurosurgical emergency (Table 25.1).

Table 25.1 Symptoms of Chiari II malformation by age

Neonatal/infant	Older child/teen or adult
Stridor	Neck pain/occipital headache
Weak/absent/silent cry	Upper extremity dysfunction
	Spasticity
	Sensory impairment
Fatigue/lethargy or listlessness	Dysphonia
Poor control of oral secretions	Progressive difficulty with swallowing
Poor feeding	Sleep disorders
	Central sleep apnea
	Obstructive sleep apnea (if obese)
Nasal regurgitation of secretions	Dysconjugate gaze/diplopia
Reduced or absent gag reflex	Facial asymmetry
Poor head control	
Opisthotonus	
Emaciation	
Recurring bouts of aspiration	
Dysconjugate gaze	

Symptoms of CIIM in the Older Child and Adult

The manifestations of CIIM in the older child and adult are less common and differ from those in the newborn and infant. They are more insidious in onset and less acutely threatening to the survival of the affected patient [3, 6, 18, 19]. The most common observed symptom of CIIM in an older child or adult is progressive dysfunction of the hands. Classically, this follows a pattern of cervical myelopathy in which tone in the extremities progressively increases and coordination progressively falters. Associated sensory symptoms may be potentiated by associated syringomyelia. A cervical or thoracic syrinx occurs in up to 40 % of patients who have MMC and CIIM [15]. Its classic manifestation is a suspended sensory loss involving a cape-like distribution over the shoulders and arms. Involvement of the cervical spinal cord impairs the crossing fibers that mediate pain and temperature in the hands and lead to variable but often progressive hand sensory loss. Subtle sensory change can occur, yet what is most commonly observed clinically is a progressive difficulty with delicate hand tasks that has both a sensory and motor component. Such changes often must be actively pursued and directly inquired about by the clinician to be revealed. Practical contemporary tasks such as manipulation of a cell phone, a channel changer,

or recreational digital media devices are good and important screening questions to detect subtle but important decline in upper extremity function [3, 6, 11, 17].

Sleep abnormalities are an important group of symptoms related to CIIM in teens and adults. Central sleep apnea results from impaired neurologic respiratory drive during sleep and may arise from any condition that adversely affects brain stem function such as the CIIM [5, 8]. Central sleep apnea may also be seen in premature infants, patients suffering brain stem strokes or other insults, and as a complication of advanced cardiopulmonary disease. Obstructive sleep apnea occurs when the tongue and muscles of the soft palate, pharynx, and larynx relax and allow physical compromise of the airway. Obesity is a known independent risk factor for obstructive sleep apnea and is a common comorbidity in the MMC community. As such, many patients with MMC are at risk of both central and obstructive sleep apnea. Recent studies have indicated that more than 50 % of patients with CIIM have clinically significant sleep apnea syndrome and that the presence of CIIM is an independent predictor of the severity of the sleep apnea. Typically, a patient suffering from sleep apnea will undergo transient spells of respiratory cessation until the systemic shortage of ventilation and oxygenation elicits an alarm startle arousal response which results in transient wakefulness (for which the patient is usually amnestic) and the restoration of breathing. The most feared complication of this syndrome in the CIIM is the failure of such a startle arousal, which can lead to prolonged respiratory impairment and culminate in respiratory arrest. Mortality in patients with MMC/CIIM is estimated at 1 % per year of which a significant percent are victims are simply found deceased in bed [16, 19]. Symptoms of the CIIM may be at central to the tragic course of events in these unfortunate victims.

A less common but important symptom of CIIM that may be seen in the older child or adult is *ataxia*. Ataxia is widely described in summary chapters and reviews about CIIM, but the underlying evidence and documentation for this finding are relatively sparse. Certainly, there are sufficient abnormalities in the posterior fossa and brain stem to provide an anatomic rationale for these changes. By definition, in CIIM, the vermis is caudally displaced and elongated. Appendicular ataxia may be a component of collective brain stem and cerebellar dysfunction that is seen as upper extremity dysfunction that is common in adults with CIIM. Similarly truncal ataxia has been described but not comprehensively studied nor reviewed.

Impact of Recent Treatment Modalities on CIIM

Results of a randomized multicenter trial comparing prenatal and postnatal closure of MMC were published in March 2011 [1]. This landmark paper was the culmination of the MOMs (Management of Myelomeningocele Study). Women who met strict inclusion criteria and agreed to participate were randomized to either prenatal or postnatal closure of their infant's MMC. Outcomes are better in multiple domains for patients who underwent intrauterine closure of their MMC. Prenatal closure was associated with a decreased need for a CSF shunt (primary outcome measure) and a reduced incidence of radiologically determined CIIM (secondary measure). At 12 months follow-up, approximately two thirds (64 %) of the patients treated with prenatal closure had a radiologically evident CIIM, whereas 96 % of the postnatal group had a CIIM. The extent of brain stem kink and elongation of the fourth ventricle was also reduced in the prenatal group. The infant fatalities in the prenatal group were due to prematurity or stillbirth, while those in the postnatal treatment group died from symptoms and signs of CIIM. Maternal and fetal morbidity was higher in the prenatal group as well [1]. Whether the advantages seemingly conferred by prenatal closure will persist over time remains to be seen. Concern over this, other limitations of the study and concern over other potential morbidities have generated significant controversy around the study results. Yet, the potential improvement in reducing symptomatic CIIM may prove to be the greatest overall contribution of prenatal closure of MMC.

CIIM symptom outcomes should be central in the assessment of other experimental modalities for treating MMC and its associated comorbidities as well. Due to the considerable problems associated with VP shunts, several groups are attempting to decrease the frequency with which shunts are placed. One such approach is to relax the criteria for placement of a VP shunt [3], and another is to treat the hydrocephalus with an endoscopic third ventriculostomy and choroid plexus coagulation (ETV-CPC) [20]. Traditionally, a shunt needs to be placed in approximately 85 % of patients with a MMC, yet these novel approaches have reduced the need for a shunt to 50–60 % and 35 %, respectively [3, 20]. Long-term follow-up with regard to development of symptoms of CIIM will be important in the analysis of these promising results.

Conclusions

The CIIM is a complex anomaly including brain stem displacement and malfunction that is of profound significance to the patient with a neural tube defect. Symptoms are age related and localize to the dysfunctional bulbar structures of the posterior fossa. In the neonate, symptoms of stridor, weak or even silent cry, poor control of oral secretions with nasal regurgitation, and risk for aspiration pneumonia are present and are often progressively associated with fatigue and listlessness that may portend an ominous prognosis. These symptoms are rarely seen before 10–15 days of life and often occur suddenly and insidiously. Recognition and timely intervention (shunt exploration initially followed by consideration for posterior fossa decompression if still symptomatic) provide the best opportunity to stabilize or reverse the findings and optimize outcomes.

Despite maximum treatment, some youngsters (particularly those with high neural tube defects, severe hydrocephalus, and early, pronounced stridor) may not respond to treatment and may succumb to their disease.

Older children and adults usually manifest symptoms of progressive upper extremity dysfunction. Sensory loss is common, and either a myelopathic or ataxia pattern of motor impairment may be observed. Failure to recognize and intervene virtually assures progression of deficit which is likely irreversible. A high index of suspicion and a proactive, assertive surgical approach likely serve the patient and family optimally.

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Treatment of the Adult Chiari I Malformation

26

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This chapter contains video segments that can be viewed at the URL – http://www.springerimages.com/978-1-4614-6368-9

Abstract

Successful surgery for Chiari I malformation in adults requires appropriate patient selection, the identification of the optimal procedure for the specific circumstances of that patient, and careful execution of the surgery. The goal of surgery is to reestablish the unrestricted, pulsatile movement of the cerebrospinal fluid in the subarachnoid space at the craniovertebral junction. This is accomplished almost universally by removing the posterior rim of the foramen magnum and the posterior arch of C1, opening the dura, and placing a pericranial graft to expand the dural space at that level.

History of Treatment of Chiari I Malformation

In clinical practice and in this chapter, Chiari I malformation (CM1) refers to a symptomatic condition associated with caudal location of the cerebellar tonsils and inferior part of the medulla, without displacement of the fourth ventricle [1, 2]. The first posterior fossa decompression for a patient with Chiari II malformation was performed by Van Houweninge Graftdijk in Leiden in 1930 [3]. This was followed by a report of posterior fossa decompression for Chiari I malformation in five patients by McConnell and Parker [4]. Several authors over the following decade reported their experiences using craniocervical decompression to treat the Chiari I malformation [5, 6]. In 1950, James Gardner and associates at the Cleveland Clinic recognized the association of the Chiari I malformation with syringomyelia [7]. They postulated that the outlets of the fourth ventricle were occluded by the Chiari I malformation and that a "water-hammer" pulsation was directed from the fourth ventricle, through the obex, and into the central canal of the spinal cord, leading to pulsatile expansion of the central canal to form a syrinx. To reverse this process, Gardner performed a surgical procedure that (1) removed the bone from the posterior

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Table 26.1 Comparison of outcomes after posterior fossa decompression (PFD) and posterior fossa decompression and duraplasty (PFDD) in patients with CM1

Outcome	PFDD	PFD
Adults[a]		
Clinical improvement	29/33 (88 %)	37/45 (87 %)
Decrease in syrinx size	14/14 (100 %)	21/33 (64 %)
Additional surgery	0/33 (0 %)	1/11 (9 %)
Complications	14/33 (42 %)	4/45 (9 %)
Pediatric[b]		
Clinical improvement	44/56 (79 %)	51/79 (65 %)
Decrease in syrinx size	40/46 (87 %)	9/16 (56 %)
Additional surgery	3/143 (2 %)	15/119 (13 %)
Complications	28/135 (22 %)	3/111 (3 %)

[a]Data are derived by combining the results of the reports by Chauvet et al. [14], Isu et al. [16], Kotil et al. [17], and Romero and Pereira [18]
[b]From meta-analysis by Durham and Fjeld-Olenec [15]

aspect of the foramen magnum, (2) opened the fourth ventricle to the subarachnoid space, and (3) "plugged the obex" [7]. His immediate postoperative results in 74 patients were as follows: 52 improved, 11 unchanged, 6 worse, and 5 dead [8]. Later Levy et al. compared craniovertebral decompression and opening of the fourth ventricle with and without obex plugging at the Cleveland Clinic [9] and found no differences in outcome. Plugging the obex could be complicated by damage to the hypoglossal and vagal nuclei and permanent neurologic deficits [10]. In the 1970s, Logue introduced a less invasive alternative to Gardner's procedure. His procedure consisted of simple bony decompression and expansion of the dura with a tissue graft and avoidance of opening of the arachnoid membrane and entrance into the subarachnoid space or fourth ventricle. They performed a clinical study comparing Gardner's procedure with their procedure of simple decompression and duraplasty and demonstrated that there was no difference in syrinx resolution between the procedures, although Gardner's operation resulted in a higher complication rate [8, 11]. Since then, some investigators have advocated a decompressive procedure that opens the arachnoid membrane, removes or shrinks the inferior portion of the cerebellar tonsils, and attempts to enlarge the CSF pathways beyond what is achievable with bony decompression and duraplasty alone [12, 13]. Syringomyelia resolves following this latter procedure in about 80 % of cases, which is similar to the results reported for simple decompression and duraplasty with preservation of the arachnoid membrane and tonsils. More recently, less invasive surgical treatments have been investigated for Chiari I malformation with and without syringomyelia, ranging from simple bony decompression to bony decompression and partial incision of the dura (Table 26.1) [14–18].

Patient Selection for Operative Treatment

Chiari I malformation is usually not associated with an underlying disease and is considered primary in most patients, although a majority of patients have underdevelopment of the posterior fossa of unknown etiology [19]. Secondary causes should be considered during evaluation of a patient with CM1 because if they are present, their treatment might make craniocervical decompression unnecessary. Such underlying conditions include craniosynostosis [20], hydrocephalus [21–25], intracerebral hypotension resulting from a spinal CSF fistula [26–30], pseudotumor cerebri, intracranial tumors, and acromegaly [31–34]. In addition, basilar invagination and instability or hypermobility at the craniocervical junction are causes for failure of craniocervical decompression craniectomy and should be excluded before performing a posterior decompression alone [35–37].

The decision to surgically decompress the craniocervical junction is based primarily on clinical, not radiologic, findings. It is imperative to avoid surgical treatment based primarily on MRI findings of Chiari I malformation in a patient with a history and neurological examination that suggests another cause for their symptoms. The proportion of the population that has MRI scan findings compatible with the diagnosis of Chiari I malformation far exceeds the proportion with symptoms of Chiari I malformation. One study found that 0.9 % of normal adults undergoing MRI studies of the brain had tonsillar herniation extending more than 5 mm below the foramen magnum [38]. Therefore, the simple presence of 5 or more millimeters of tonsillar ectopia is not adequate justification for craniocervical decompression of any type. Vigilance in patient selection for surgical treatment includes evaluating for the presence of an associated syrinx, which confirms that the Chiari I malformation is causing critical compression of the CSF pathways at the foramen magnum. In patients with Chiari I malformation without syringomyelia, the decision to operate is straightforward if subjects have cerebellar or medullary signs and symptoms, or downbeat nystagmus. Suboccipital and cough headache are also reliable symptoms of Chiari I malformation. Certain radiologic findings that support critical impaction of the tonsils at the craniocervical junction include (1) tonsils that are peg shaped, instead of rounded [2, 39], (2) narrowed CSF pathways at the foramen magnum as seen on anatomic and phase-contrast cine MRI [40, 41], and (3) tonsillar ectopia over 12 mm [42].

For subjects with CM1 and syringomyelia, or CM1 alone with neurological signs, it is essential that surgical treatment be rendered expeditiously, as delay in treatment may lead to further neurological deficit or irreversible losses in neurological function [43]. Before surgery, it is essential to counsel patients with Chiari I malformation, syringomyelia, and neurologic deficit that craniocervical decompression, if successful, will result in stabilization of the associated myelopathy and that objective improvement may occur, but is less common [12, 44]. In addition, based on the type of decompression that is being performed, it is necessary to explain the most frequent side effects of that form of treatment and the likelihood of additional surgical treatment in case the initial surgical procedure is unsuccessful. Patients with Chiari I malformation without syringomyelia should be counseled that medullary or cerebellar symptoms would be expected to improve but that complete recovery does not occur in all cases. Cough headache improves or resolves completely after surgery in most patients [39, 45, 46].

Selection of the Optimal Operative Treatment

One of the goals of operative therapy is to provide consistently successful treatment while at the same time limiting surgical complications and morbidity. Some studies define surgical success solely on a clinical basis in terms of symptomatic improvement or neurologic outcome. Imaging after surgery is either not performed or not considered pertinent if signs and symptoms are stable. Other studies evaluate surgical success not only in terms of clinical outcome but also in light of the effects of surgery on neural anatomy and physiology, seeking to confirm sufficient enlargement of the intradural volume at the foramen magnum to relieve pressure on the medulla and ectopic cerebellar tonsils, reduction in syrinx diameter, and restoration of CSF movement across the foramen magnum. In a congenital disease whose time course is usually slowly progressive, the long-term outcome of surgery may be prognosticated better if these anatomic and physiologic metrics are used to supplement findings of the patient's history and examination during the first year after surgery. Long-term follow-up of patients has been performed in many craniocervical decompression studies that include exposure of the extra-arachnoidal or intra-arachnoidal spaces. Most of these studies evaluated outcome retrospectively, but a few of them have been prospective studies [39, 41, 46]. More recent modifications of the craniocervical decompression method, including bony decompression alone or with dural scoring, have generally had shorter follow-up after surgery than older, more

invasive, methods. A prospective study in pediatric patients with Chiari I and syringomyelia has recently been designed and initiated to compare outcomes after surgery using various forms of craniocervical decompression. Without comparative studies for guidance, a neurosurgeon must decide on the type of craniocervical decompression to perform based on the (1) reported short- and long-term clinical and radiologic outcomes from the various types of decompression procedures, (2) the pathophysiology of Chiari I malformation, and (3) personal experience [47]. The ultimate goal is to select the method that provides permanent, curative therapy, while minimizing injury to neural and soft tissue structures.

Rationale for Using Craniocervical Decompression and Duraplasty for All Patients with Symptomatic CM1 or Symptomatic CM1 with Syringomyelia

Although there is increasing evidence that bony decompression alone might be adequate treatment for at least some patients with CM1, especially those without syringomyelia, these studies must be viewed cautiously, as the evaluation of treatment outcome in patients with CM1 without syringomyelia is often subjective and follow-up is usually short. Radiologic confirmation of surgical success or failure in patients without syringomyelia is not as straightforward as when syrinx size is used as a radiologic marker. Anatomic MRI rarely demonstrates expansion of the CSF pathways at the foramen magnum after bony craniocervical decompression alone. Bony decompression alone in patients with CM1 with syringomyelia results in a lower rate of syrinx resolution than does bony decompression and expansile duraplasty, which demonstrates that in many cases of CM1, bony decompression alone does not expand CSF pathways at the foramen magnum sufficiently to relieve the encroachment of the cerebellar tonsils on the CSF pathways (Table 26.1). Bony decompression alone in patients with CM1 without syringomyelia would, similarly, produce less decompression of the neural elements than would decompression and duraplasty or bony decompression and partial-thickness dural incision. For these reasons, and for those listed in the paragraphs below, we favor using a decompressive procedure that expands the CSF pathways and intradural volume to a greater extent than is provided by bony decompression alone.

One can speculate about why syringomyelia only develops in some patients with Chiari I malformation. Clinical research in patients with CM1 with syringomyelia has shown that these patients have narrowing of the CSF pathways that prevents normal CSF flow across the foramen magnum during the cardiac cycle. In this setting, expansion of the brain during cardiac systole cannot be compensated normally by the rapid flow of CSF into the spinal canal during systole. In lieu of CSF movement, the cerebellar tonsils and medulla descend every time the brain expands during cardiac systole. The resultant up-and-down motion of the cerebellar tonsils during the cardiac cycle acts as a piston on the spinal subarachnoid space, creating enlarged CSF pressure waves that drive CSF into the spinal cord to form a syrinx. After the syrinx forms, the spinal subarachnoid pressure waves propel the syrinx fluid, leading to syrinx expansion and clinical progression (Fig. 26.1) [39, 41]. This physiologic process usually takes years to create a symptomatic syrinx, perhaps explaining why syringomyelia does not usually affect patients until the age of 20–50 years. The reason that syringomyelia does not develop in other patients with CM1 may be because (1) syringomyelia has not had enough time to develop, (2) the encroachment on the CSF pathways is not severe enough to produce the above mechanism of syrinx development and progression, or (3) the encroachment on the CSF pathways is more severe than in patients with CM1-syringomyelia, preventing the piston motion of the tonsils and medulla. Because all patients with symptomatic CM1 have critical compression of the neural elements and/or the CSF pathways at the foramen magnum, the procedures to treat CM1 alone, or CM1 with syrinx, have identical endpoints in that the surgical decompression must sufficiently expand the intradural space at the foramen magnum to

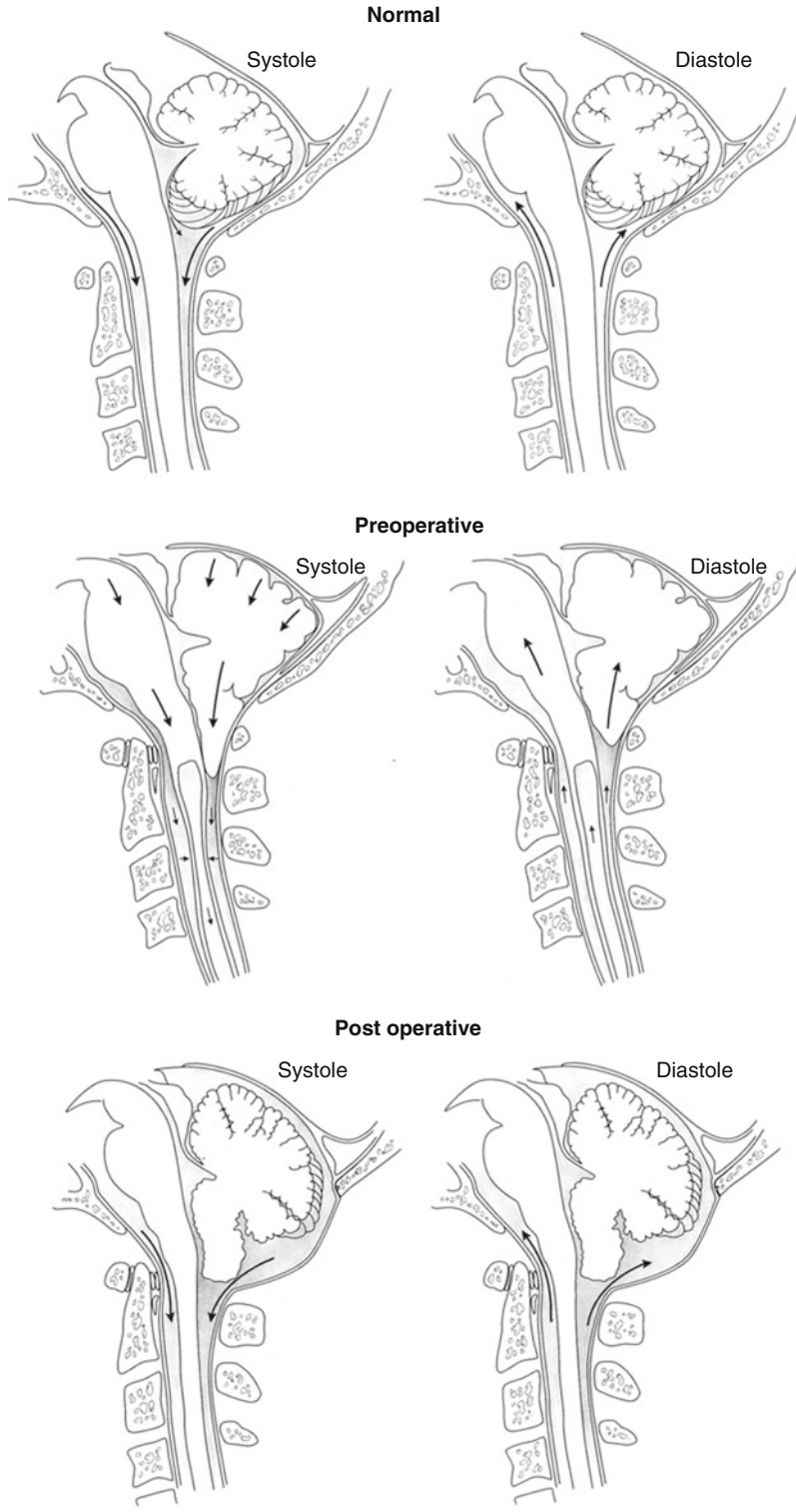

Fig. 26.1 Illustration of the (**a**) normal anatomy and flow of CSF in the subarachnoid space at the foramen magnum during the cardiac cycle, (**b**) obstructed flow of CSF in the subarachnoid space at the foramen magnum resulting in impaction of the cerebellar tonsils in the foramen magnum and in the cerebellar tonsils acting as a piston on the cervical subarachnoid space, creating cervical subarachnoid pressure waves that compress the spinal cord from without, propagating syrinx fluid movement, (**c**) relief of the obstruction of the subarachnoid space at the foramen magnum reverses the mechanism of the impaction of the cerebellar tonsils and of progression of syringomyelia. The direction of movement of CSF, brainstem, and cerebellum during systole and diastole (*arrows*) (Reproduced from Heiss et al. [39], with permission)

effectively decompress the neural elements and CSF pathways. On the other hand, patients with radiologic findings of minimal ectopia, minimal narrowing of the CSF pathways, and atypical symptoms may not be having symptoms referable to CM1, but have symptoms due to another condition. In the absence of syringomyelia, we do not recommend surgical decompression, even minimally invasive procedures, for patients who do not have symptoms that can be clearly related to the Chiari I malformation.

Rationale for Using Less Invasive Forms of Craniocervical Decompression for Patients with Symptomatic CM1 or Symptomatic CM1 with Syringomyelia

The goal of surgery in patients with Chiari I malformation is to provide sufficient subarachnoid space at the level of the foramen magnum for reversal of the impaction of the cerebellar tonsils in the foramen magnum, so that the symptoms and signs of the Chiari I malformation are reversed. Development of a strategy of surgery, then, might ask how much additional space is required at the level of the foramen magnum for successful reversal of the pathophysiology? Certain observations suggest that the additional space required is very small. For instance, Chiari I malformations in young children occasionally reverse without treatment as the skull grows faster than the brain in early childhood [48]. There are also indications that reversal of a very slight increase in thickness of the soft tissues at the level of the foramen magnum associated with acromegaly is sufficient for a Chiari I malformation to reverse after elimination of the excess growth hormone [31, 32]. Thus, the extra room required at the foramen magnum for successful surgery may be a millimeter or even a fraction of a millimeter, and it may not require much surgery to provide this.

The argument for using either bony decompression alone (without a dural incision) or bony decompression combined with a partial-thickness dural incision as the initial procedure of choice is that it reduces the risk of complications associated with opening the dura and arachnoid, it is usually successful, the patient has a more comfortable postoperative course, and it saves health care costs. For instance, in one study of pediatric patients, those undergoing PFDD (posterior fossa decompression and duraplasty) required increased health care services than patients with PFD (posterior fossa decompression alone). Patients in whom PFDD was performed were in the operating room 74 min longer than those receiving a PFD (201 ± 34 min compared with 127 ± 25 min; $p = 0.0001$), a 59 % increase [49]. Mutchnik et al. also found that morbidity was increased in the patients with PFDD; patients who underwent PFDD used low-grade narcotics, intravenous narcotics, muscle relaxants, and antiemetic medications at greater rates and longer than patients with PFD. Patients who underwent PFDD stayed in the hospital longer (4.0 vs. 2.7 days, $p = 0.0001$), and the average cost per patient undergoing PFDD was almost twofold greater than patients treated with PFD [49].

Although, in general, the surgical approaches of either bony decompression alone (without a dural incision) or bony decompression combined with a partial-thickness dural incision have been successful in 80–90 % of patients, 10–20 % of patients will require additional surgery (Table 26.1). There is substantially more information comparing the outcome of these procedures in children than there is in adults. Note that in patients with syringomyelia, the group with most objective measure of successful surgery, PFD alone had much lower likelihood of resulting in a response of the syrinx (64 % in adults, 56 % in children) compared to patients who received PFDD (100 % in adults, 87 % in children). See Table 26.1. Almost no adults who received PFDD required additional surgery compared to 9 % of the patients who were treated with PFD.

Thus, as surgical therapy has evolved in the MRI era, an era in which the outcome of surgery is easier to assess and can be assessed with higher resolution, it has become apparent that simply performing the bone decompression alone, or combining the bone decompression with superficially opening the dura (partial thickness) or removing

the outer layer of dura is successful in most patients. The arguments for using this approach as the initial procedure is that it reduces the morbidity of the procedure, it is usually successful, and these features outweigh the disadvantages of knowing that further surgery to open the dura will be required in 10–20 % of patients treated in this fashion. On the other hand, those favoring PFDD discuss the value of having the capacity to visually assess the subarachnoid space to examine for a subarachnoid abnormality (arachnoiditis, dural or arachnoid band, arachnoid cyst) after opening the dura, whether the arachnoid is left intact or not, and argue that the consistency of success and a single operation outweighs the disadvantages associated with the greater incidence of complications and additional surgery later.

Ideally, there would be a method of determining during surgery the least amount of surgery that each individual patient requires to open the subarachnoid space at the foramen magnum. That is, it would be valuable if it could be determined during surgery if removal of bone alone, removal of bone combined with a partial-thickness opening of the dura, or bone removal and opening the dura, but not the arachnoid, is sufficient in individual patients, so that the surgery could stop at the least stage that is likely to be successful. Intraoperative ultrasound has been used for this purpose to examine the distance between the inner layer of dura and the posterior edge of the cerebellar tonsils, to assess the pulsatility of the cerebellar tonsils and the spinal cord surrounding a syrinx, and to see if bony decompression or partial-thickness dural incision provided the extra space needed [16, 39, 41, 50], although its value has not been established for this purpose.

Surgical Management

As mentioned in the discussions above, a surgical procedure for CM1 should relieve the impaction of the cerebellar tonsils and the obstruction to the free pulsatile flow of CSF across the foramen magnum [39, 41]. A surgical method should be chosen that is extensive enough to target and eliminate the pathophysiologic process of the disorder. If it has equal or superior effectiveness, therapy associated with lesser risk should be selected in preference to treatment options associated with greater risk. Further, therapy with less invasion of the central nervous system (CNS) is preferable to options of equal effectiveness with more CNS invasion.

We advocate choosing between the two least-invasive procedures that effectively expand the volume of the foramen magnum beyond bony decompression alone, either selecting simple craniocervical decompression and duraplasty without opening the arachnoid membrane (Fig. 26.2) or decompression of the bone of the posterior lip of the foramen magnum and removal of the posterior arch of C1, and occasionally part of C2, with a partial-thickness dural incision. Patients are positioned in the prone position on silicone gel pads that support the chest and pelvis and that allow the abdomen to hang freely. The neck is flexed slightly. The head is held with the 3-pin Mayfield head holder (OMI Inc., Cincinnati, OH). A midline skin incision is made extending from above the inion to the level of the C2 spinous process. For duraplasty, a triangular pericranial graft is obtained from the occipital area measuring 4–5 cm in length and width. We free the skin margins from the deep fascia and open the fascia in a Y-shaped incision [51]. The Y-shaped incision is preferred to a linear fascial incision because its closure suspends the suboccipital muscles and prevents them from recessing against the dural graft. Enough bone should be removed at the foramen magnum to completely decompress the entire posterior surface of the cerebellar tonsils, usually 2 cm deep and 2.5–3.0 cm from side to side. Cervical laminectomy extends inferiorly to the tips of the cerebellar tonsils; removal of the posterior arch of C1, and occasionally at least the superior part of the lamina of C2, is required. After suboccipital craniectomy and laminectomy, but before opening the dura, ultrasound imaging is performed to assess if bony decompression is adequate to relieve impaction of the cerebellar tonsils and to search for bands and membranes within the cisterna magna and upper cervical subarachnoid space (Figs. 26.3 and 26.4)

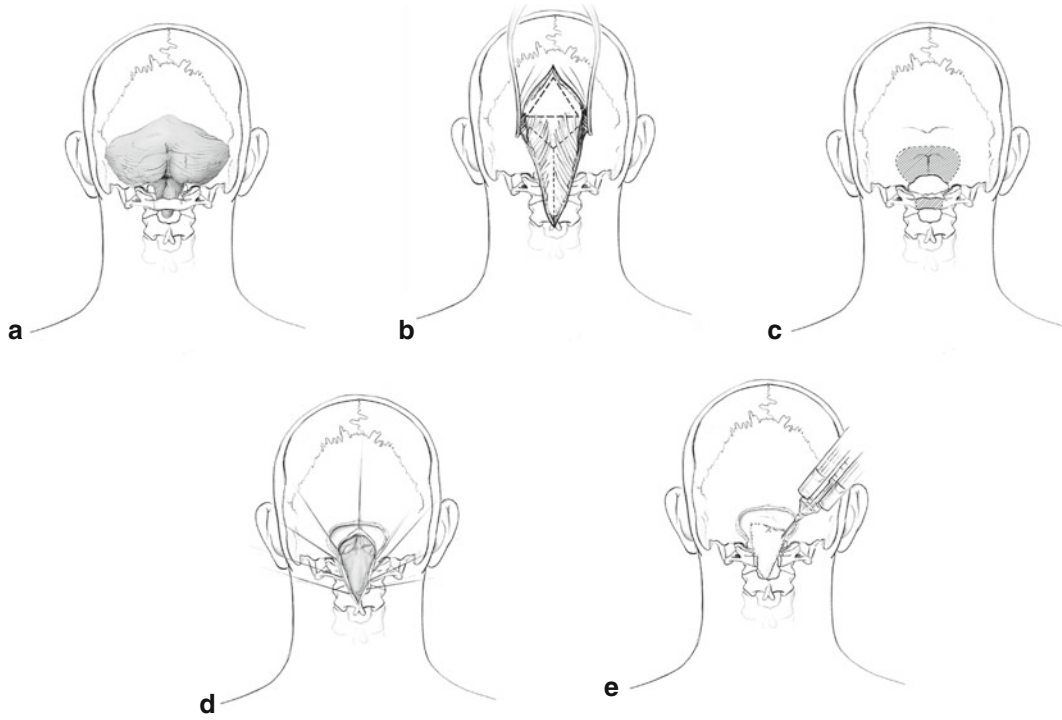

Fig. 26.2 Drawings describe decompression and duraplasty for Chiari I malformation. (**a**) The anatomic extent of the underlying cerebellum is seen through transparent posterior fossa bone and dura. (**b**) The skin, fascial, and pericranial incisions are shown. (**c**) Bone removal includes the suboccipital bone at the foramen magnum, the dorsal arch of C1, and occasionally the superior part of the lamina of C2 if the tonsils protrude to this level. (**d**) The dura has been opened while preserving the arachnoid. (**e**) A pericranial graft has been sutured to the surrounding durotomy to create an expansile duraplasty. Fibrin glue is applied to augment closure of the suture line

(Operative Video 26.1a, b). The dura is opened in the midline at the C1 level with care to avoid injury to the underlying arachnoid (Fig. 26.5). For duraplasty, the incision is carried superiorly and split just below the foramen magnum to create a Y-shaped dural opening [51]. The cisterna magna expands immediately in almost all cases. Leakage of CSF through a small hole in the cisterna magna is not uncommon and has not resulted in inferior outcomes. The dura is retracted with 4–0 multifilament nylon sutures. A pattern of the size and shape of the opening for the dural graft is created by cutting a cottonoid to the same shape and size; the cottonoid is then used to determine the size and shape of the pericranial graft. The pericranial autograft is sutured to the durotomy margins with a running 4–0 multifilament nylon suture. The graft expands the volume of the posterior fossa and provides a biological membrane that contains the CSF and prevents adhesions to the cerebellum by the suboccipital musculature. Autologous pericranium is preferred to other graft material because it seals better to the surrounding dura and is not immunogenic.

Almost all patients respond to decompressive surgery [39, 44]. In rare patients, opening the dura will not result in expansion of the cisterna magna with CSF, signaling that bands or membranes are binding the arachnoid to the cerebellum and spinal cord. This contingency requires opening of the arachnoid of the cisterna magna, cutting the bands or membranes, and tacking the arachnoid to the durotomy margin. In the unusual patient in whom the syrinx fails to resolve after decompressive surgery, it is because the pathophysiologic mechanism has not been eliminated [52]; in these cases a second operation usually resolves syringomyelia by correcting conditions that prevented the subarachnoid space

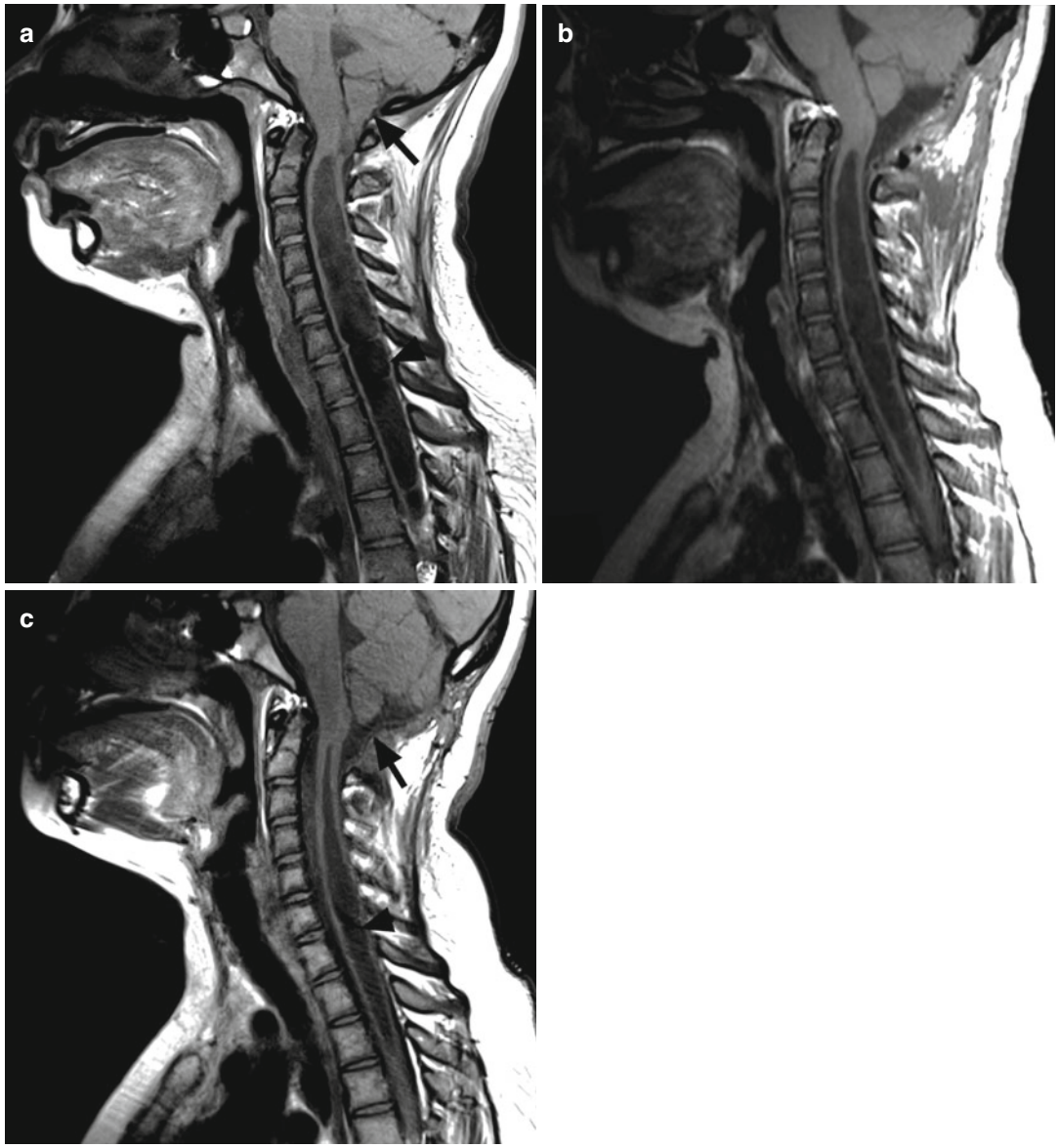

Fig. 26.3 T1-weighted MRI of the cervical spine in the midsagittal plane in a young woman with a 7-month history of cough headache and more recent onset of nystagmus, bilateral upper extremity dissociated sensory loss, and ataxia. Before craniocervical decompression and duraplasty (**a**), a Chiari I malformation (*arrow*) and large-diameter syrinx (*arrow head*) are seen. The syrinx diameter decreases progressively at 1 week (**b**) and 3 months (**c**) after surgery (*arrow head*); CSF is clearly seen posterior and inferior to the cerebellar tonsils (*arrow*), whose shape has begun to change from a pointed (**a**, *arrow*) to a rounded shape (**c**, *arrow*) as a result of no longer being impacted into the foramen magnum with each pulse. Headache, nystagmus, and ataxia resolved and upper extremity sensation improved after surgery

posterior to the cerebellar tonsils from expanding, such as inadequate bone removal or an extradural pseudocyst [52–56]. In the rare patient with severe primary or secondary arachnoiditis, syringomyelia cannot be treated successfully using an approach that opens CSF pathways at the foramen magnum. Syrinx shunts are an option, but carry risks of neurologic deficits developing from their placement

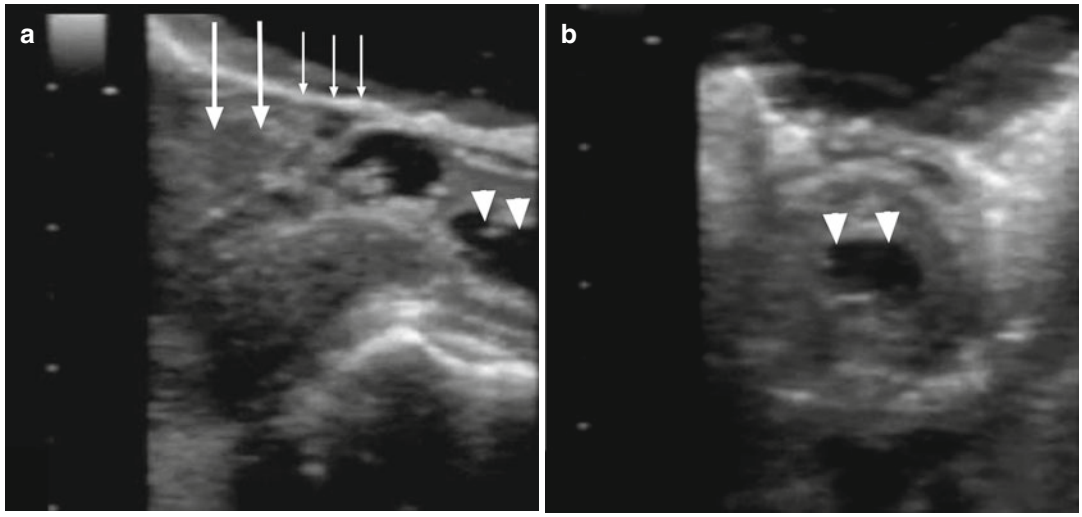

Fig. 26.4 (See also Operative Video 26.1a, b) Sagittal (**a**) and axial (**b**) intraoperative ultrasonographic images of the craniocervical junction were obtained on the patient described in Fig. 26.3 after bony decompression of the foramen magnum and laminectomy of C1. The dorsal dura (*thin arrows*) is superficial to the cerebellar tonsils (*thick arrows*), which have a pointed shape because of their pulsatile impaction into the foramen magnum. The syrinx is shown by *arrowheads* in (**a**) and (**b**)

(20 %) or delayed cord tethering, occlusion and malfunction over time, and foreign body-related infection [13, 57–60]. Because of these risks, in patients with Chiari I and syringomyelia, syrinx shunts should only be used in cases of syringomyelia that cannot be treated using an approach which opens CSF pathways at the foramen magnum.

In recent years, it has become apparent that simply performing the bone decompression and superficially opening the dura (partial thickness) or removing the outer layer of dura results in resolution of the syrinx in most patients, with 10–35 % failing to respond. The argument of using this approach as the initial procedure is that it reduces the risk of a pseudomeningocele associated with opening the dura and arachnoid, it is usually successful, and these features outweigh the disadvantages of knowing that further surgery to open the dura will be required more often in patients treated in this fashion (Table 26.1) [61].

Complication Avoidance

The most frequent cause of surgical failure is inadequate removal of bone at the foramen magnum, which results in persistent compression of the cerebellar tonsils and CSF pathways [52, 62, 63]. Another frequent reason for failure is the development of a persistent leak of CSF through the dural graft that results in the formation of a pseudomeningocele dorsal to the dural graft; the pseudomeningocele presses the dural graft anteriorly and creates adhesions between the graft and the underlying cerebellum that obliterates the dorsal CSF pathway [64]. Maintaining the arachnoid membrane during craniocervical decompression prevents CSF leakage and provides an additional biological barrier to scar formation between the graft or duraplasty suture line and the underlying neural elements. Cerebrospinal leakage through the skin should not occur if the dural closure and the fascial closure are secure, except for cases in which hydrocephalus or pseudotumor cerebri is present. Hydrocephalus and pseudotumor cerebri should be assessed for before surgery because syringomyelia may improve after ventricular shunting in patients with associated hydrocephalus and decompressive surgery at the foramen magnum is rarely successful and uncomplicated in patients with a Chiari I malformation caused by high intracranial pressure [65, 66]. Leakage of

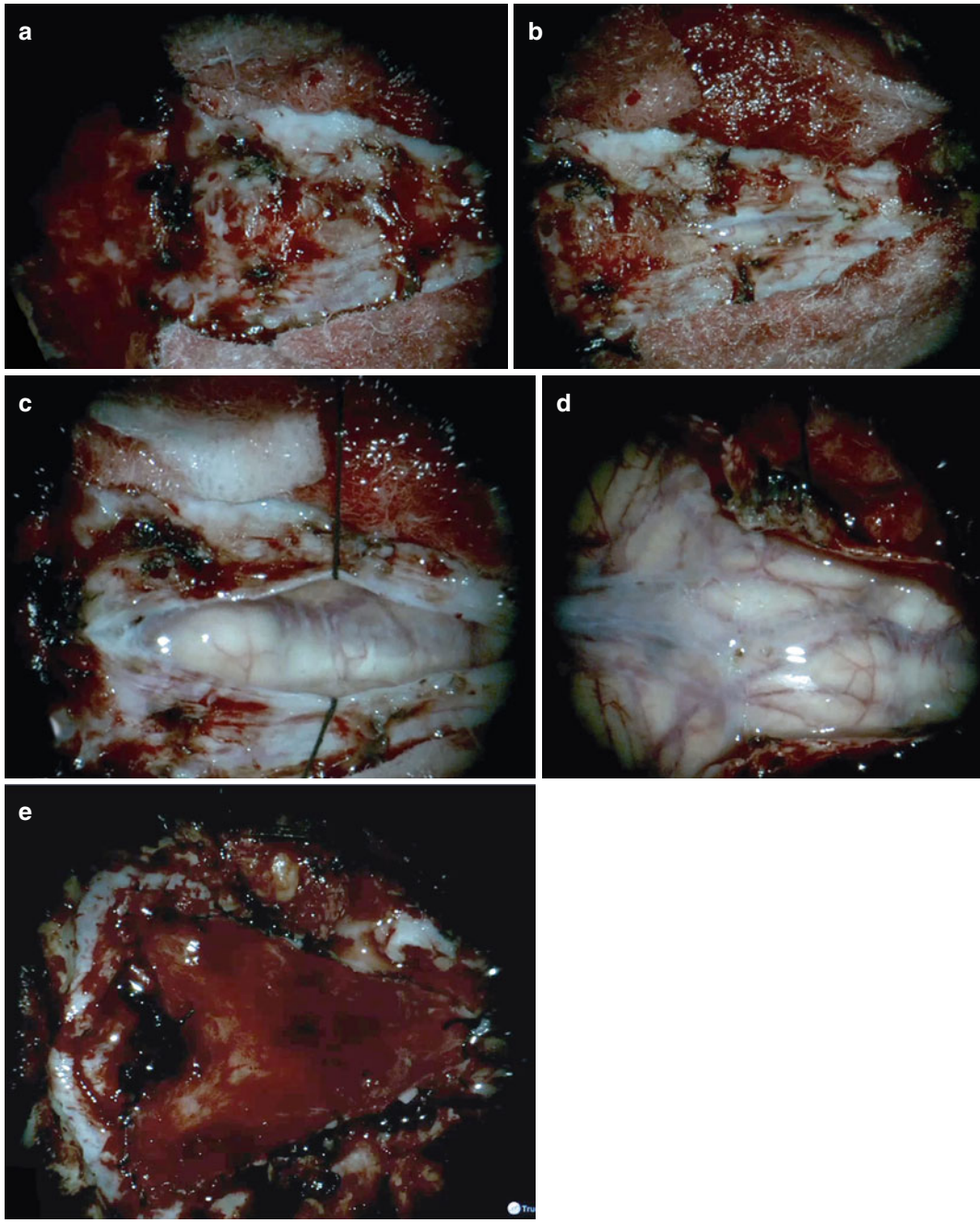

Fig. 26.5 (See also Operative Video 26.2) Operative photographs were taken sequentially after suboccipital craniectomy and C1 laminectomy was performed on the patient described in Fig. 26.3 with Chiari I malformation and syringomyelia. In each photograph, *left* is cephalad and *right* is caudal. (**a**) The dura in the upper cervical spinal canal is almost translucent in this case. (**b**) The spinal dura is opened in the midline while preserving the underlying arachnoid membrane. (**c**) The dural opening is elongated exposing the caudal aspect of the left cerebellar tonsil. (**d**) The inferior part of the cerebellar hemispheres, the cisterna magna, and the upper spinal canal are exposed; the arachnoid remains intact. (**e**) A triangular piece of autologous pericranium has been sutured to the surrounding dura to create an expansile duraplasty

CSF through the skin incision is treated initially with skin sutures. If CSF leakage persists, a CT scan should be obtained to evaluate for hydrocephalus and extradural hematoma. External drainage of CSF and/or reoperation to replace or repair the dural graft may be required. Excessive drainage of lumbar CSF may increase tonsillar ectopia [67]. Treatment should be prompt because development of meningitis or graft infection may lead to surgical failure from secondary arachnoiditis at the surgical site.

Postoperative Care

The patient is observed overnight after surgery in the intensive care unit for changes in neurological status and is given a level of narcotic analgesia that allows participation in hourly neurological examinations. Rarely, hydrocephalus may develop and is signaled by persistent lethargy. An urgent head CT scan should be performed in such patients and treatment of hydrocephalus rendered. After leaving the ICU, most patients report symptoms of pain and local muscle spasm for 1–2 weeks after surgery, which are relieved with a regimen of narcotic analgesic, muscle relaxant, and NSAID. All patients receive DVT prophylaxis including (1) sequential compression stockings (SCS) beginning before induction of anesthesia and continuing throughout hospitalization when the patient is in bed and (2) low-dose subcutaneous heparin.

The results of surgical therapy of syringomyelia can be evaluated noninvasively using MRI. Clinical stabilization or improvement after treatment follows reduction in syrinx diameter [68]. MRI scans of the cervical spine and posterior fossa should be performed at 3–12 months after surgery to evaluate if CSF pathways have been restored at the foramen magnum and if the syrinx is becoming progressively smaller (Fig. 26.3). Elimination of the active pathophysiological process causing the syringomyelia is demonstrated by collapse of a syrinx and reduction in the spinal cord edema as seen on MRI [10, 44, 69, 70].

Patients may desire additional treatment because of symptoms of myelopathy that persist after surgery. Neuropathic pain often continues after surgery, despite surgery being successful surgery and collapse of the syrinx. Various medications from the antidepressant (amitriptyline) and antiepileptic groups (gabapentin) may be tried to control this symptom, but the need for chronic treatment may require consultation with a pain control specialist. Craniocervical decompression and duraplasty should be revised only if the syrinx maintains its size or enlarges after surgery and neurological deficits progress. Symptomatic hydrocephalus, if present, should be treated.

Procedures for Chiari I malformation that effectively open the CSF pathways to provide normal pulsatile flow across the subarachnoid space at the foramen magnum provide effective and lasting treatment of syringomyelia with low morbidity (Figs. 26.1 and 26.2). After successful craniocervical decompression surgery for Chiari I and syringomyelia, the cerebellar tonsils lose their conical shape, the CSF pathways expand at the foramen magnum, and the syrinx decreases to less than 50 % of its presurgical diameter, although it may take several months for the collapse of the syrinx to occur [44].

Summary

Chiari I malformation is not a primary neural malformation but rather a secondary malformation that results from deformation of the neural elements in response to reduced volume of the inferior part of the posterior fossa [19, 71, 72] and impaction of the cerebellar tonsils into the foramen magnum with every heartbeat [39, 41]. Because of this, a surgical procedure that expands the volume of the foramen magnum relieves compression on the neural elements and CSF pathways and opens the obstruction to the free pulsatile flow of CSF during the cardiac cycle. Medullary and cerebellar symptoms usually improve after decompression of CM1. Syringomyelia and cough headache reliably resolve following restoration of normal CSF flow at the foramen magnum.

This chapter contains updated and adapted material from previous chapters on the same subject by the authors [73].

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Treatment of the Pediatric Chiari I Malformation

27

W. Jerry Oakes

Abstract

Decompression of the craniocervical junction for the Chiari I malformation is a safe and effective procedure for appropriately selected patients. Postoperatively, associated syringes are likely to resolve and, if small, do not usually progress, and Valsalva-related occipital headaches are predictively relieved immediately after surgery and do not recur. Serious surgical complications are rare. Although pathology is not usually identified, we believe that evaluation of the intradural contents is important in order to verify for intradural pathology (e.g., arachnoid webs) and to avoid continued symptoms and the necessity for reoperation. Avoiding subarachnoid blood and other subarachnoid irritants enhances recovery, and free cerebrospinal fluid egress from the fourth ventricular outlets is critical. Preoperative evaluation of potentially associated hydrocephalus and craniocervical instability is important.

Surgical intervention for a pediatric CIM is a simple and usually uncomplicated procedure. The more difficult portion of the care is deciding which patients will benefit and how likely that benefit is to occur. The procedure has generated significant controversy as to the extent of the surgery and the exact details that make up each step in the decompression. In general, the purpose of the procedure is to relieve compression at the craniocervical junction and re-establish free CSF egress from the midline fourth ventricular outlet. Other aspects of the surgery have been judged to be sufficiently important that we have devoted separate chapters to them (treatment of hydrocephalus and a discussion of dural opening). We plan simply to outline what is done at our institution and attempt to justify why we take the steps we do. Although we will mention alternative techniques, short of a randomized trial, the opinions expressed are solely ours based on our experience [5]. Because other chapters deal with the presentation and evaluation, little will be mentioned concerning those subjects. We would comment that the presence of a syrinx seems to be a reasonable justification for surgical intervention even with the understanding that some patients with a syrinx will have spontaneous

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resolution [1]. The decision to recommend surgery rests on the remote likelihood that resolution will occur contrasted with the risk of developing a fixed deficit resistant to delayed surgical intervention. The type of headache that responds to intervention is also worthy of mention. The three headache characteristics that predictably yield a satisfactory outcome are [1] occipital or high cervical pain [2], reproducibly brought on with some type of Valsalva maneuver, and [3] relatively short duration (few seconds/minutes). With these three characteristics present, the likelihood of relieving the pain is quite high (>95 % in our experience). As soon as the headache description deviates from these characteristics, the rate of surgical success falls precipitously, and reoperation because of a lack of headache relief is illogical and unjustified. We have not seen it necessary to reoperate on patients because of a return of the characteristic Chiari-type headache.

Once a decision for surgical intervention is made and the risks accepted by the family, the patient is brought to the operating room and positioned prone with the neck flexed (Fig. 27.1). Pin fixation is used and the head of the bed is elevated 30° to decrease venous pressure. Even small infants may have the judicious application of pin fixation with minimal pressure to ensure maintenance of a flexed position. The area of the foramen magnum is exposed through a midline incision from a point just below the external occipital protuberance to the spinous process of C-2. I have rarely found it necessary to expose or remove any of C-2 even in the presence of significant caudal displacement of the cerebellar tonsils. In avoiding C-2 removal, we have not seen the development of postoperative kyphosis, which is a serious and difficult to treat postoperative complication. The relative avascular midline of the cervical musculature is easily divided and retracted to expose the area of the foramen magnum and dorsal arch of C-1 (Fig. 27.2). One should keep in mind that this is a midline operation and that there is no need for significant lateral exposure. Especially in the presence of major bony anomalies of the craniocervical junction, the course of the vertebral artery laterally around C-1 is less predictable [6]. The extent of the bony opening need not be wider than the width of the spinal cord. One can easily judge this because the dura begins to become vertical in its orientation. In patients below 2 years of age, this is usually 22–25 mm. Bone at the foramen magnum may be removed with a high-speed drill or craniotome and rongeurs. The width of the foramen magnum opening again is to the point where the dura begins to course vertically. The height rarely needs to be greater than 20–25 mm. By avoiding excessive bony removal, the serious complication of cerebellar slump may be avoided. In select patients, with significant side-to-side compression at the foramen magnum, a portion of the medial condyle may be removed to provide additional room laterally at the point of maximum compression. This situation is seen most commonly in patients with achondroplasia or other similar syndromes. The surgeon should remind himself that the pathology in this condition is in the area of the foramen magnum and not more cephalad in the posterior fossa. The various techniques of replacing bone or other physical restraints exactly where the intradural contents had been compressed seem counterintuitive and unnecessary. The dorsal arch of C-1 is removed with rongeurs. The lateral and anterior ligaments connecting C-1 to the remainder of the spine can easily be overpowered by a surgeon with significant leverage and a mechanical advantage. This is especially true in young infants. Bony removal should be done with crisp side-to-side bites and never place an instrument under the posterior arch of C-1 where the intradural contents are crowded.

At this point, the surgeon has a choice to close or proceed on to a dural opening. I would agree that the majority of patients with symptomatic CIM will improve by simple bony decompression. However, a significant percentage of patients (6–10 %) [7] will have intradural pathology not allowing free egress of CSF out of the fourth ventricular outlets. This is the group that will need an intradural exploration for the opening of these channels, and bony decompression alone will not suffice. The trade-off is the likelihood of creating a large inflammatory response from blood spilled into the subarachnoid space versus the likelihood

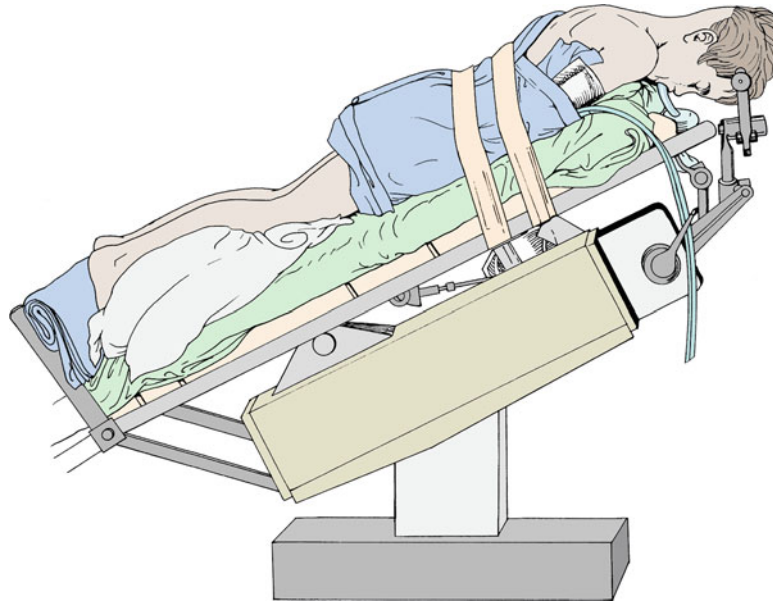

Fig. 27.1 Positioning for posterior fossa decompression for patients with Chiari malformation

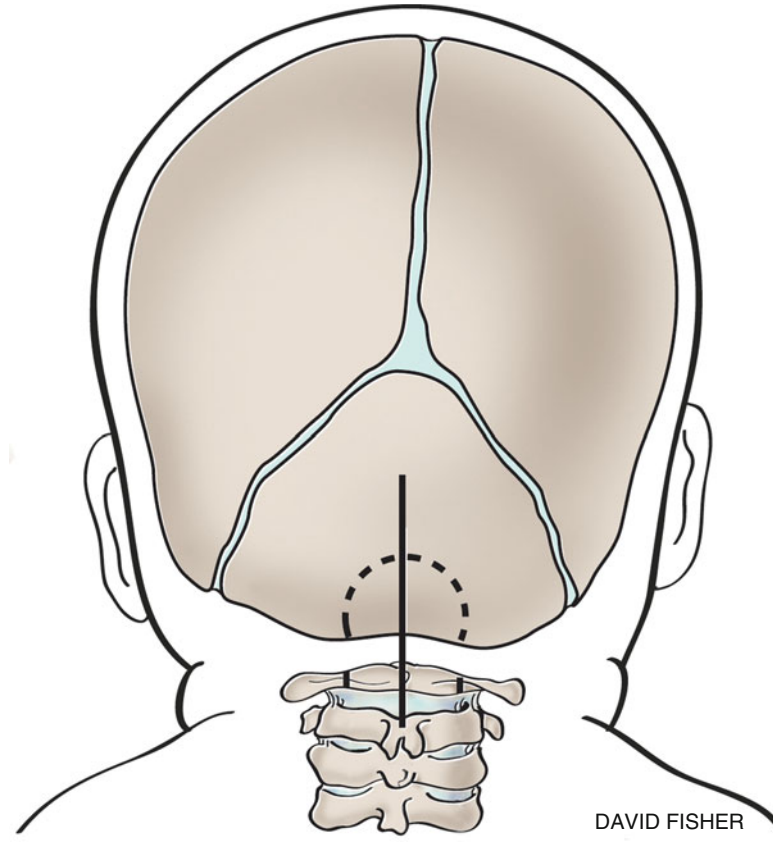

Fig. 27.2 Schematic drawing of the posterior craniocervical junction noting skin incision and areas of bony removal

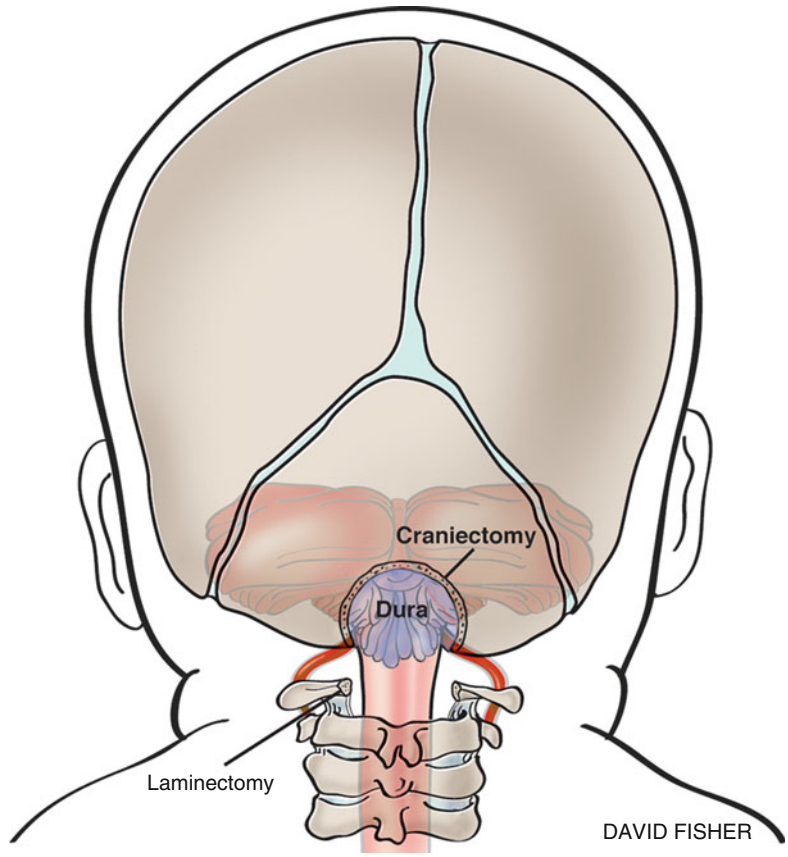

Fig. 27.3 Schematic drawing illustrating regional anatomy and intradural contents

of finding a fourth ventricular veil or some other obstructions to CSF egress [7]. I would argue that most skilled neurosurgeons can open and graft the dura of the posterior fossa with a very low morbidity and mortality, well less than 6–10 %, and therefore, dural opening should proceed.

To open the dura at the craniocervical junction, start caudally at the exposed dura. At the level of C-1, the leaves of the dura are generally fused and bleeding is more easily controlled. As you work cephalad, especially in young infants, a marginal or occipital sinus may be encountered. Unfortunately, this is exactly at the point of maximum compression and near the opening of the fourth ventricle. This venous sinus can be dealt with by staying extra-arachnoidal during the initial opening to help avoid subarachnoid blood spillage and working slowly and methodically keeping the leaves of the dura approximated. This can be accomplished with bipolar coagulation and Weck clips or simply by suturing the edge of the dura on each side as it is opened. The dura is opened the vertical length of the bony exposure (Fig. 27.3). If the point of maximum compression still appears constricted, a horizontal T incision at the point of maximum compression can expand the dural opening more. This may even be done bilaterally. The arachnoid is opened as a separate layer and clipped to the dura in an attempt to avoid the uncommon complication of acute hydrocephalus from a CSF subdural effusion occurring postoperatively [2]. The tonsils are separated and, if present, the outlet veil is lysed. For initial procedures without life-threatening symptoms or without a huge syrinx, I generally do not advise burning or shrinking of one or both tonsils. Care is taken to manipulate the pial surface of the tonsil minimally, especially the medial surface where adhesions can re-establish fourth ventricular outlet occlusion. If a decision is made to decrease the volume of cerebellar tonsil over the ventricular outlet, the pia should be coagulated

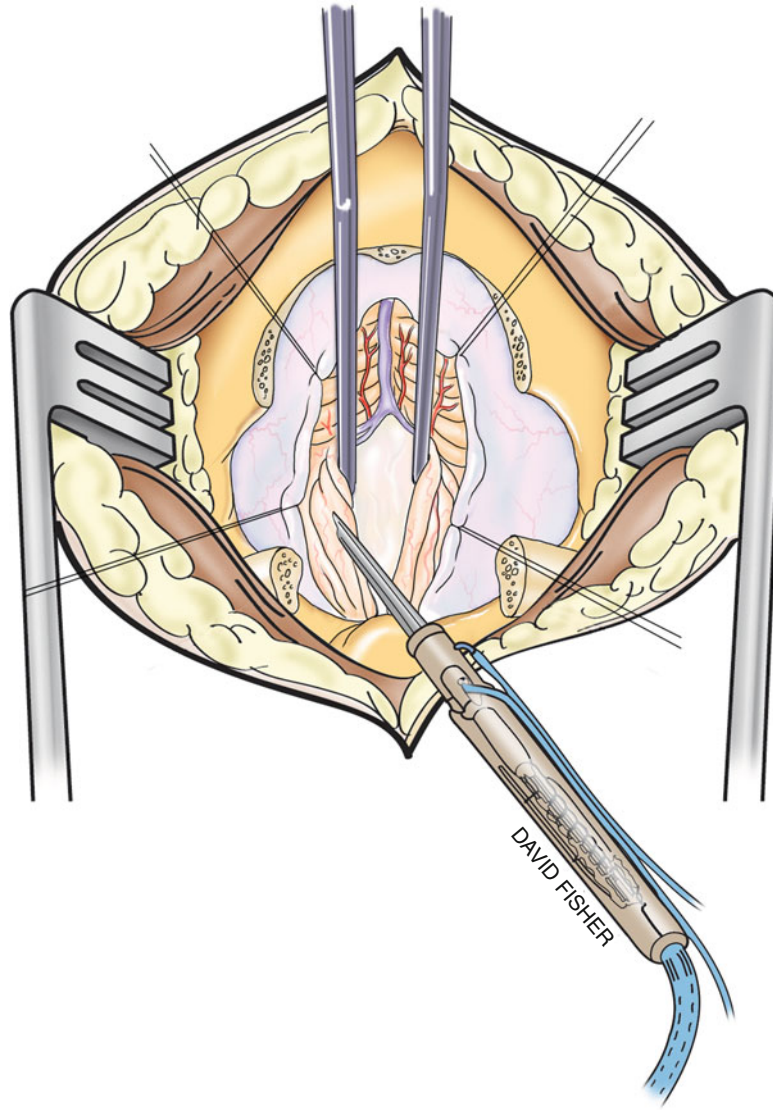

Fig. 27.4 Schematic drawing illustrating subpial resection of the cerebellar tonsil

on the *dorsal* tonsilar surface and the removal done from within the pia (Fig. 27.4). This minimizes scarring across the outlet postoperatively.

There are numerous graft materials one can choose from for the dural closure. Not closing the dura and allowing blood and other irritative fluids to react within the subarachnoid space defeats the goal of establishing free and easy egress of CSF out of the fourth ventricle. Of all of the graft materials, the one that has the highest likelihood of being sterile and not causing some type of reaction is the patient's own tissue. A convenient place to harvest a piece of appropriate graft material is the periosteum over the posterior skull. I generally do this through a separate incision. A usual graft size is 4×1 ½cm, and it is sewn in place with an attempted watertight closure. The remainder of the closure is routine.

The patient is nursed in an intensive care unit overnight and is generally available for discharge home in 2–3 days. Steroids are not given and postoperative chemical meningitis almost never occurs with a good dural closure. Blood transfusion is almost never needed, and pain management is adequate with alternating ibuprofen and acetaminophen with something being given every

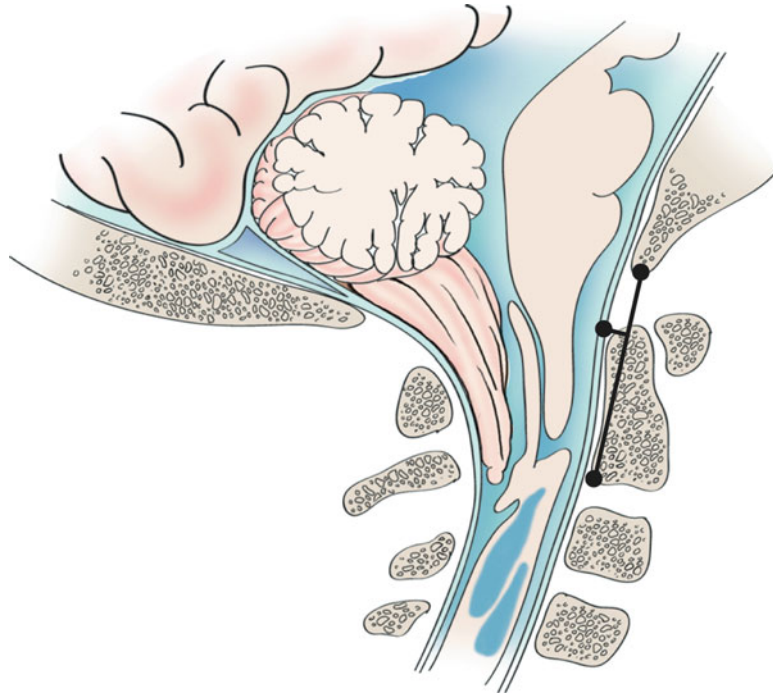

Fig. 27.5 "Rule of 9 mm." Patients may be in danger of postoperative decline when the perpendicular distance (to anterior dura mater) from a line connecting the basion to the posterior aspect of the base of C-2 vertebra exceeds 9 mm. This reflects the degree of retroflexion of the odontoid process

3–4 hours [4]. With experience, the procedure can routinely be done in less than 90 min.

Postoperative complications will be covered in a separate chapter, but acute hydrocephalus may be seen in as many as 3 % of patients. This problem appears to be lessened by clipping the arachnoid to the dura [5]. Acute medullary compromise may occur when there is significant anterior or ventral compression [3]. In those patients that violate a line drawn from the basion to the posterior inferior aspect of the C-2 vertebral body by more than 9–10 mm, acute ventral compression is possible (Fig. 27.5). Preparing the family and patient for this possibility is important. In our experience, this does not occur without significant medullary symptoms preoperatively. Postoperative pseudomeningoceles are generally handled conservatively, and with time, most will resolve spontaneously. Large syringes associated with longstanding neurological dysfunction may resolve more slowly if not incompletely.

In summary, CIM decompression is a safe and effective procedure for appropriately selected patients. Syringes are likely to resolve or if small, not progress, and occipital headache associated with Valsalva maneuvers is predictively relieved immediately and does not recur. Serious complications are rare.

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Treatment of the Chiari II Malformation

28

W. Jerry Oakes

Abstract

Our understanding of the clinical entities known as the Chiari malformations has tremendously increased over the past 40 years. We have moved from a position of grouping the CIM and syringomyelia patient in the degenerative category to a fundamental understanding of the pathophysiology. This has led to surgical intervention that has generally favorable outcomes. Our understanding that patients with the Chiari II malformation must have adequate CSF diversion is of paramount importance. Additional patients with complex issues of ventral compression and micromovement at the craniocervical junction challenge even the experienced neurosurgeon. However, the understanding of few diseases has progressed so far in such a short time.

In discussing the therapeutic intervention for the Chiari II malformation, it would be important to emphasize from the beginning our clear understanding that these lesions rarely become symptomatic beyond infancy and when medullary symptoms or a syrinx do occur, the primary culprit is the lack of adequate shunt function. In this day of trying to avoid shunt placement in this population, the development of sleep apnea, aspiration pneumonia, or other medullary symptoms in the absence of a shunt should first be addressed by placing a valve-regulated ventriculoperitoneal shunt. If a shunt exists, then its function should be surgically verified. Many of us have learned this lesson at the expense of prior patients. In the setting of a small ventricle on the side of the ventricular catheter and an "unchanged" enlargement on the opposite side (Fig. 28.1) or in the setting of a "totally unchanged ventricular system" and the development of new or progressive medullary or craniocervical junction symptoms, one should suspect the shunt. Manipulating the posterior fossa contents without this first and essential step has been the ruin of many a patient. To paraphrase a common neurosurgical saying, "It's the shunt until proven otherwise." This proof demands surgical inspection with good flow from the ventricular catheter and no adherence within the brain. If the catheter fails on either count or if the data are confusing, it should be replaced without going on to Chiari II decompression.

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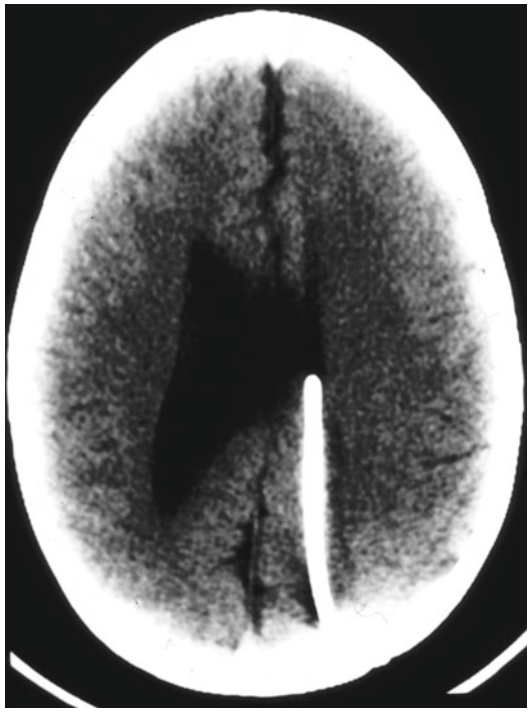


Fig. 28.1 Patient with CIIM presenting with lower cranial nerve dysfunction and this CT image demonstrating minimal contralateral dilatation of the ventricular system. The official reading for this image was "unchanged"

Both symptoms of Chiari II malformations and evaluation preoperatively have been covered in other chapters. Only the highlights will be mentioned here. If you are convinced the symptoms relate to the craniocervical junction and the shunt has been explored, then the decision to consider Chiari II decompression is reasonable. Many of the symptom complexes are life threatening, and the risk of surgical intervention is easily justified. There is no medical treatment for this condition, and confusion with other explanations for a myelomeningocele infant with a loud inspiratory stridor is generally the inexperience of a poorly informed clinician. Preoperative evaluation of respiration both while awake and during sleep is prudent. Excess snoring is a frequent symptom of medullary compromise, and evaluation will add objective data to assess and allow comparison postoperatively. Swallow studies to determine if aspiration is present and the extent of aspiration are less objective but still useful data. Radiologic evaluation of the craniocervical junction is mandatory. It is helpful if the MRI is done both with and without contrast. The purpose of the contrasted study is to evaluate the position of the choroid plexus as it marks the outlet of the fourth ventricle. The choroid plexus tissue begins embryologically as an extraventricular structure and with normal development rotates into the roof of the ventricle. This migration is arrested in the myelomeningocele patient, and the choroid plexus marks the foramen of Magendie. It is a useful intraoperative marker for the surgeon to avoid dissection through delicate marginally functioning tissue of the lower medulla, trying to find access into the fourth ventricle. Intraoperative ultrasound may also be helpful, but because of the tissue distortion, these may be quite difficult to interpret. Preoperative studies are also critical to determine the position of the torcular. With the small posterior fossa characteristically seen in myelomeningocele patients, the torcular may be caudally displaced and lie at or just above the foramen magnum (Fig. 28.2a). Opening into this venous channel can be avoided simply by knowing its position and extent. Not knowing its position or recognizing its potential for being low lying is not easily excused. Additionally, flexion-extension evaluation of the cervical spine has occasionally revealed bony instability that had not previously been detected. Not knowing about this finding can result in a serious neurological deficit during positioning.

Chiari II decompression, particularly in the infant, can be as difficult a technical challenge as is faced in pediatric neurosurgery. Contamination of the subarachnoid space with blood must be avoided to prevent further obliteration of the fourth ventricular outlet; the dural opening itself can be associated with significant loss of blood in a fragile infant. Finding a safe surgical corridor into the floor of the fourth ventricle can be the most challenging of all, but not to pursue this step makes surgical intervention unlikely to be helpful. As with CIM patients, free and unimpeded egress of CSF from the fourth ventricular outlet is the goal of operation.

The procedure is planned to expose the lower brain stem to the outlet of the fourth ventricle

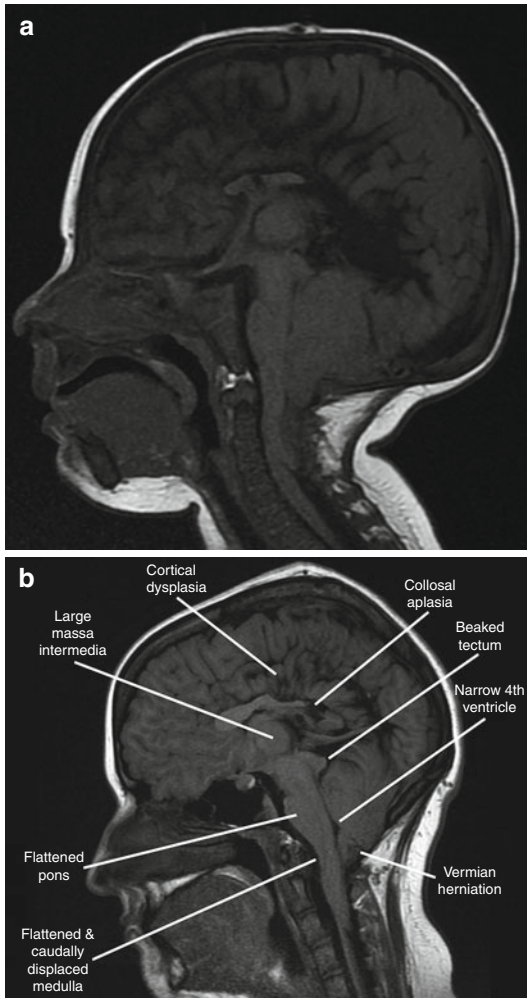


Fig. 28.2 (**a**) Typical MRI of CIIM. Note the near-vertical straight sinus and torcular near the foramen magnum. (**b**) Sagittal MRI noting typical features of the CIIM

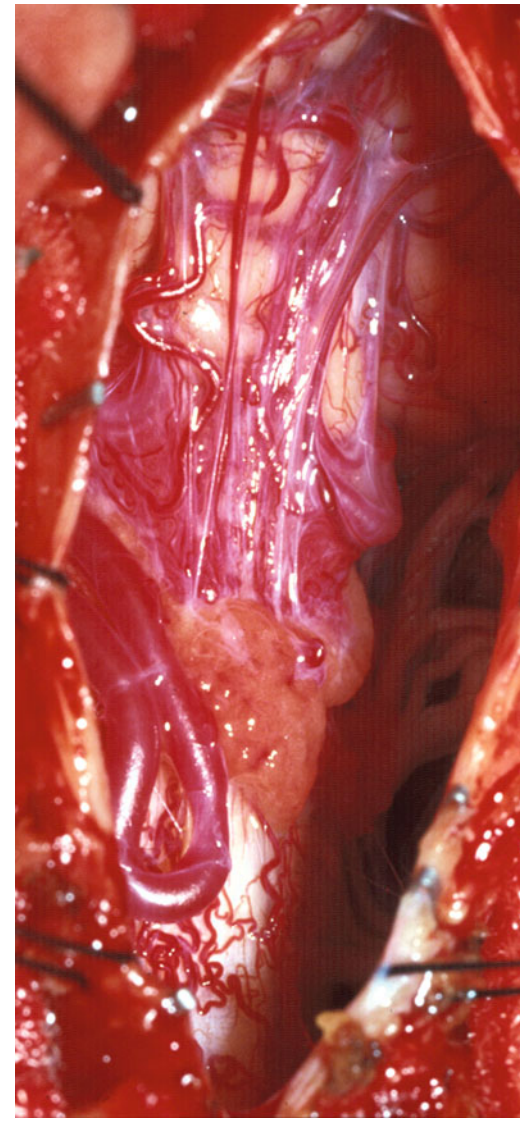


Fig. 28.3 Intradural CIIM illustrating the ectopically positioned choroid plexus and a caudal loop of the posterior inferior cerebellar artery

(Fig. 28.2b). Again, this is frequently marked by the maintenance of the embryological position of the choroid plexus (Fig. 28.3). It is not necessary to expose the medullary kink, and excess bony removal in the presence of a large cervical syrinx can be associated with the development of a significant kyphotic deformity postoperatively. The bony opening should be limited to the necessary dorsal bony elements only (Fig. 28.4). Bone removal to expand the foramen magnum is rarely necessary and if the torcular is caudally displaced, this can be life threatening.

The patient is positioned prone with the neck flexed and the head of the bed elevated. Despite the thin nature of the infant skull, pin fixation can be used with minimal pressure to maintain constant position. Soft tissue exposure of the appropriate dorsal bony elements is accomplished in the usual manner as well as a standard laminectomy. This is a midline procedure and far lateral exposure is unnecessary. Replacement of the bony elements has not proven necessary or easily accomplished in my hands. After bony decompression, if the dura protrudes dorsally and is

tense, the intracranial pressure and shunt function should again be assessed. We believe this to occur only in the presence of uncontrolled intracranial hypertension. Again, it is the shunt or lack of CSF diversion causing the problem, and if this intraoperative finding occurs, reevaluation of shunt function is necessary immediately. A band of tissue representing the periosteum of the dorsal arch of C-1 may be present and appear constrictive. It should be sectioned and burned back with bipolar coagulation. With the dura exposed, it is opened, usually from caudal to cranial. Above C-1 the dura may contain a large venous sinus. Bipolar coagulation of the outer leaf simply enlarges the opening in the sinus and therefore worsens the bleeding. The solution is to have control of both leaves of the dura and keep them approximated. This may be accomplished with suture or clips. I prefer to maintain sutures opposing both leaves, and if a significant sinus is encountered, simply sew the edges together as you open the dura. This necessitates that the original opening of the dura be in an area where bleeding is minimal to allow clear visualization of both leaves. Under the arch of C-1 usually accomplishes this purpose. Once the dura is open, the arachnoid is opened as a separate layer and clipped with small titanium clips to the opened dura. The characteristic globular orange-yellow appearance of the choroid plexus is then sought (Figs. 28.4 and 28.5). The dorsal surface of the neural elements may be seen to be covered with a fine excessive network of vessels. This is thought to be due to the chronic ischemia of the caudally displaced neural tissue. Working through and on each side of the choroid plexus will eventually allow visualization of the avascular floor of the fourth ventricle. The opening is enlarged until, at rest, it is maintained (Fig. 28.6). This is the goal of surgery, and not to complete this step is likely not to benefit the patient.

Manipulation of the pial surface and blood contamination of the subarachnoid space should be minimized. What can make the procedure difficult is when the opening into the fourth ventricle is not obvious or is blocked by a dominant vessel. Here the decision may be aided by intraoperative ultrasound although, these may be difficult to interpret. Not opening into the fourth ventricle carries much less chance of helping the patient.

With the floor visualized, a small pericranial graft is harvested and sewn into place as a dural substitute. Many other tissues and substances have been used for grafting; none is more likely to be sterile or to minimize a foreign body reaction than the patient's own tissue.

The patient is maintained intubated until spontaneous respiration is assured and airway protection is judged to be adequate.

The essential points of the procedure are first and foremost to ensure adequate CSF diversion prior to the procedure. Outside the neonatal age range, this first step will eliminate the need for consideration of further surgery. Once the procedure is deemed justified, maintain dural control with stay sutures, minimize blood contamination of the subarachnoid space, and open into the fourth ventricle.

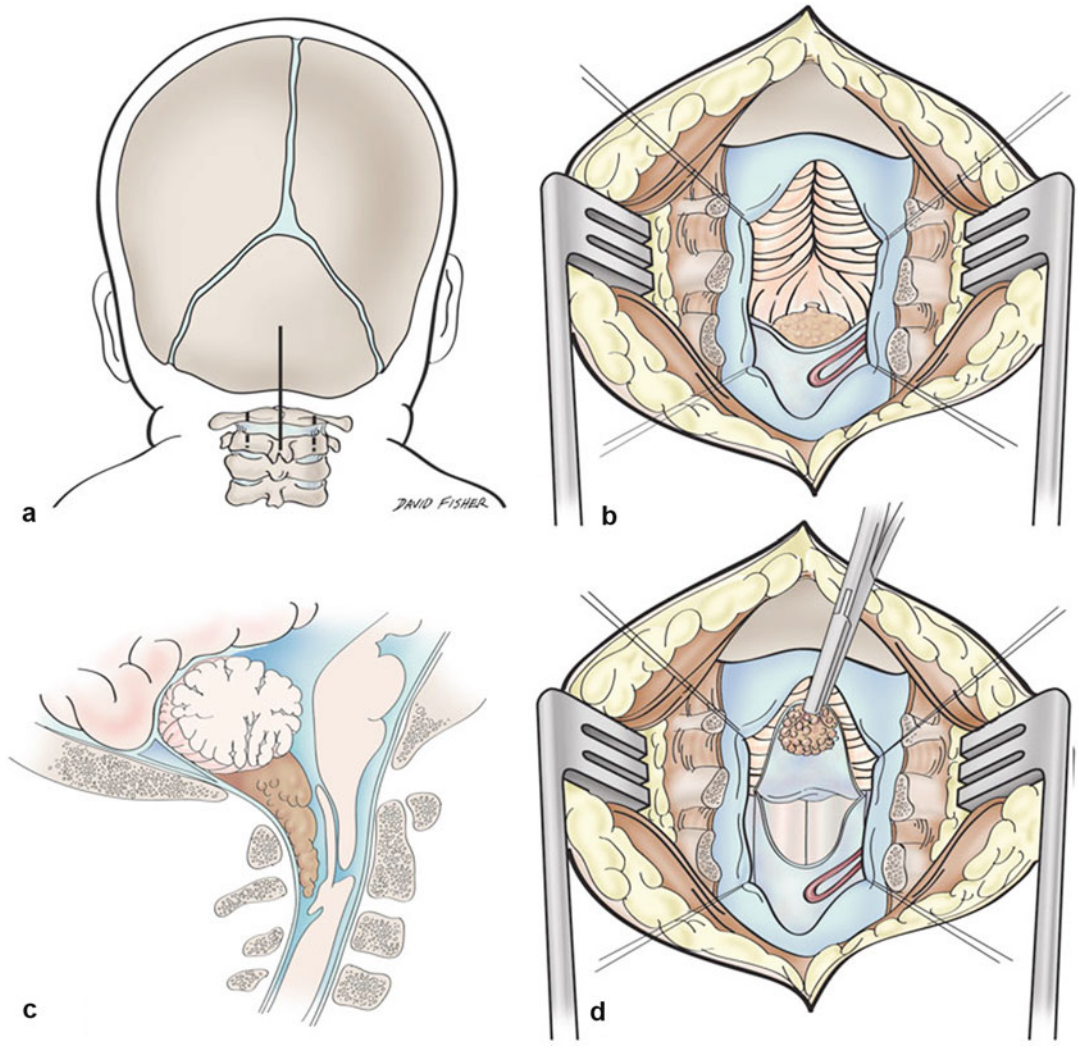


Fig. 28.4 Schematic representation of operative intervention for the CIIM. (**a**) Skin incision over bony elements. (**b**) Following soft tissue and bone removal, the dura is opened. (**c**) Sagittal image noting the vermian herniation. (**d**) The extraventricular choroid is identified and lifted (forceps) to secure entrance into the fourth ventricle

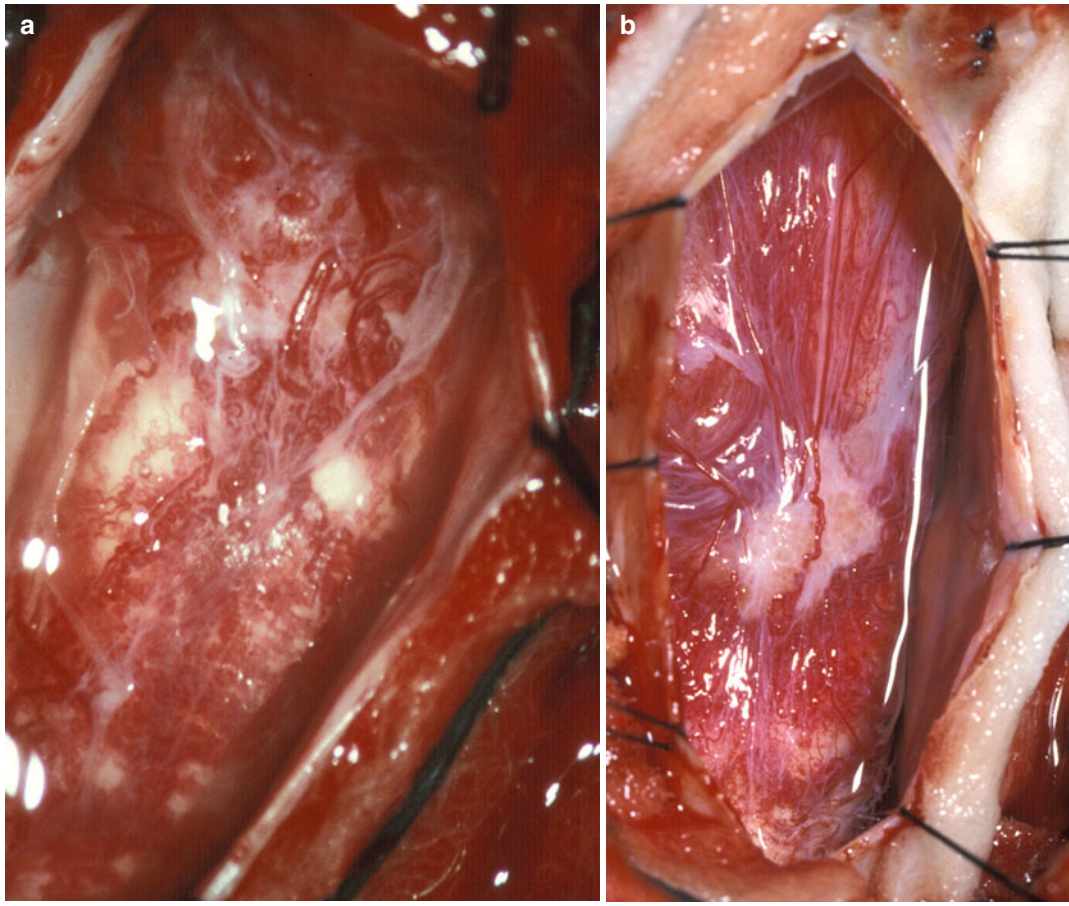


Fig. 28.5 (**a**) Intraoperative view of CIIM. The position of the choroid plexus and entry into the fourth ventricle is problematic. The hypervascularity of this region is impressive. (**b**) Intraoperative view of CIIM. The hypervascularity of the region with elongation of the dorsal vessels is striking. The site of entrance into the fourth ventricle is not obvious. (**c**) With dissection laterally of (**b**), access to the fourth ventricle is eventually obtained. (**d**) Similar patient to patient seen in (**b**, **c**), but in this patient, a cleft is present in the floor of the fourth ventricle. (**e**) Another intraoperative view of the CIIM. Here, the demarcation between the spinal cord and cerebellar tissue is more apparent. (**f**) With dissection of (**e**), the more dorsal tissue is shown to be the medullary kink and NOT a corridor into the fourth ventricle

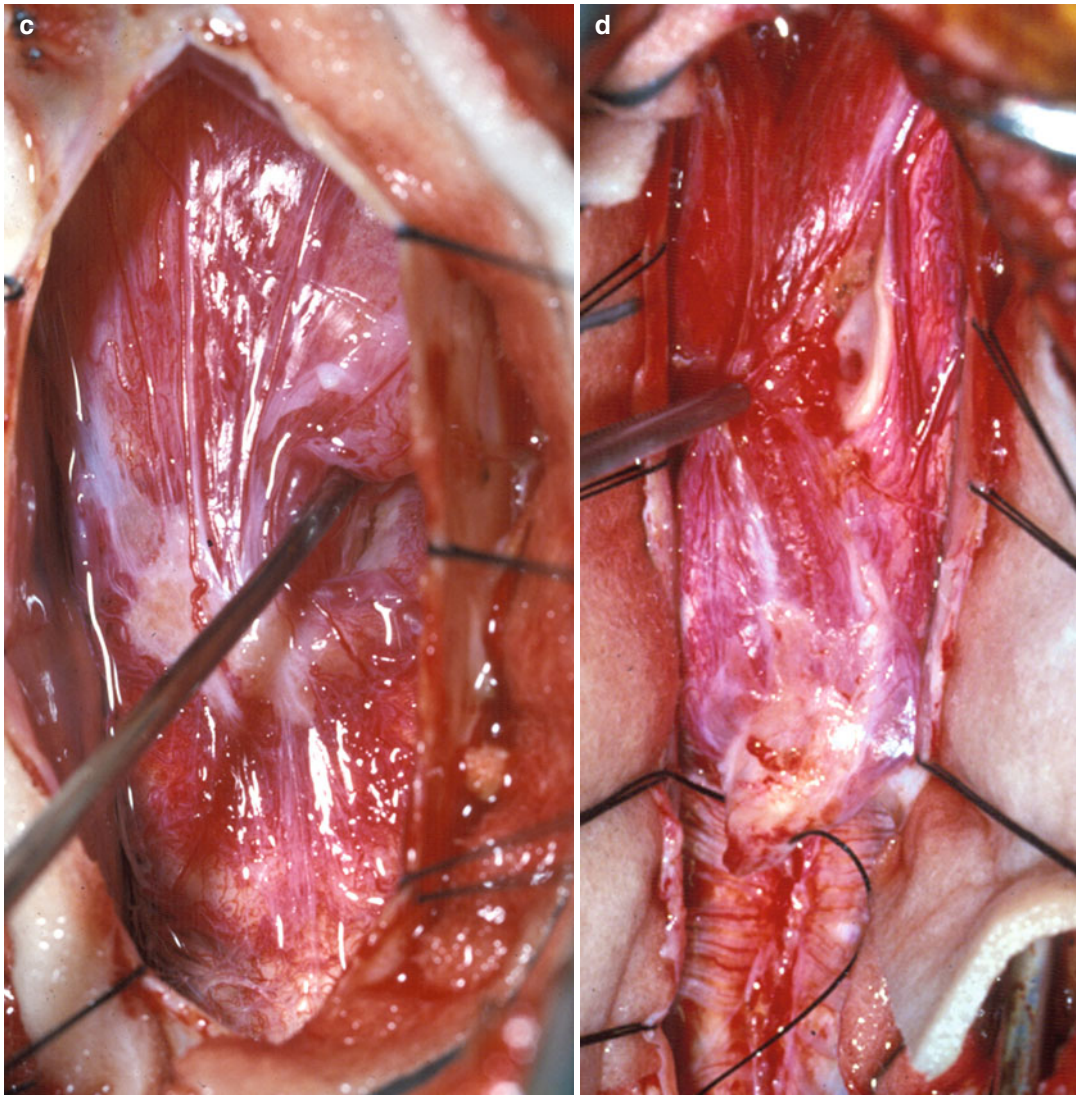
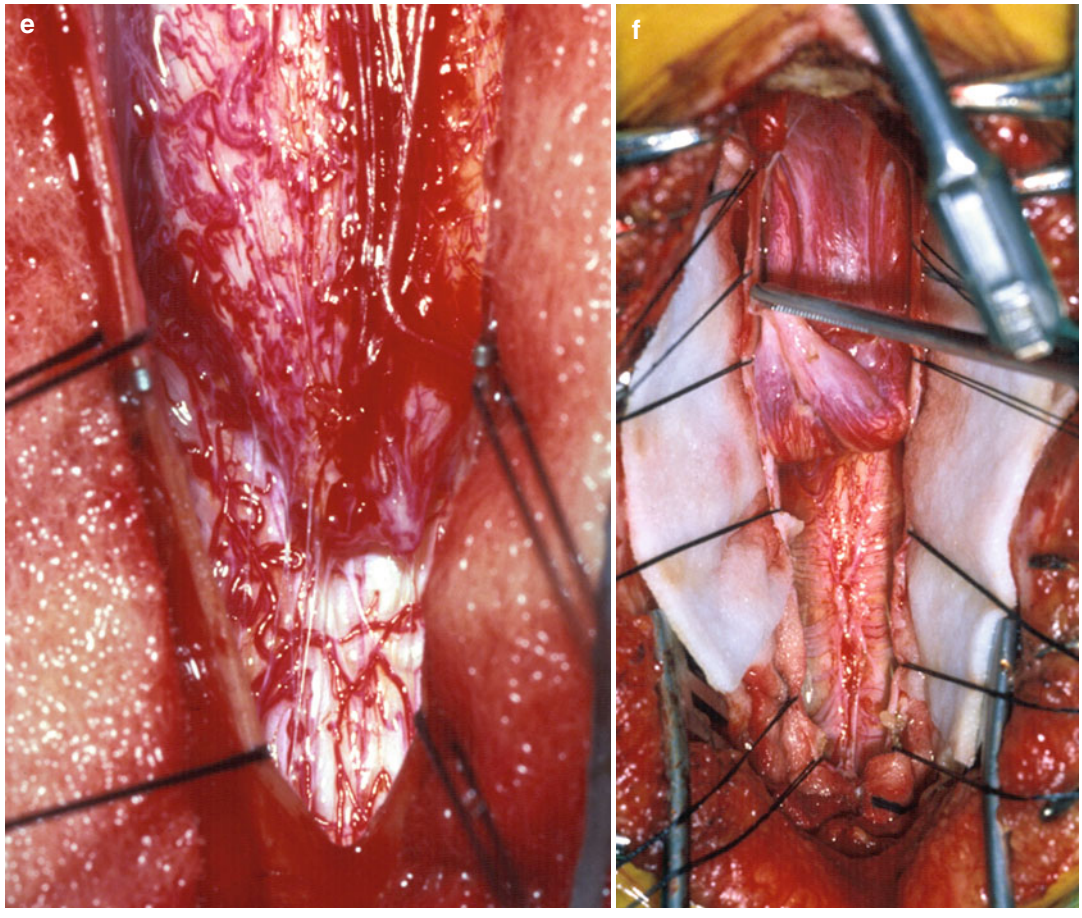


Fig. 28.5 (continued)



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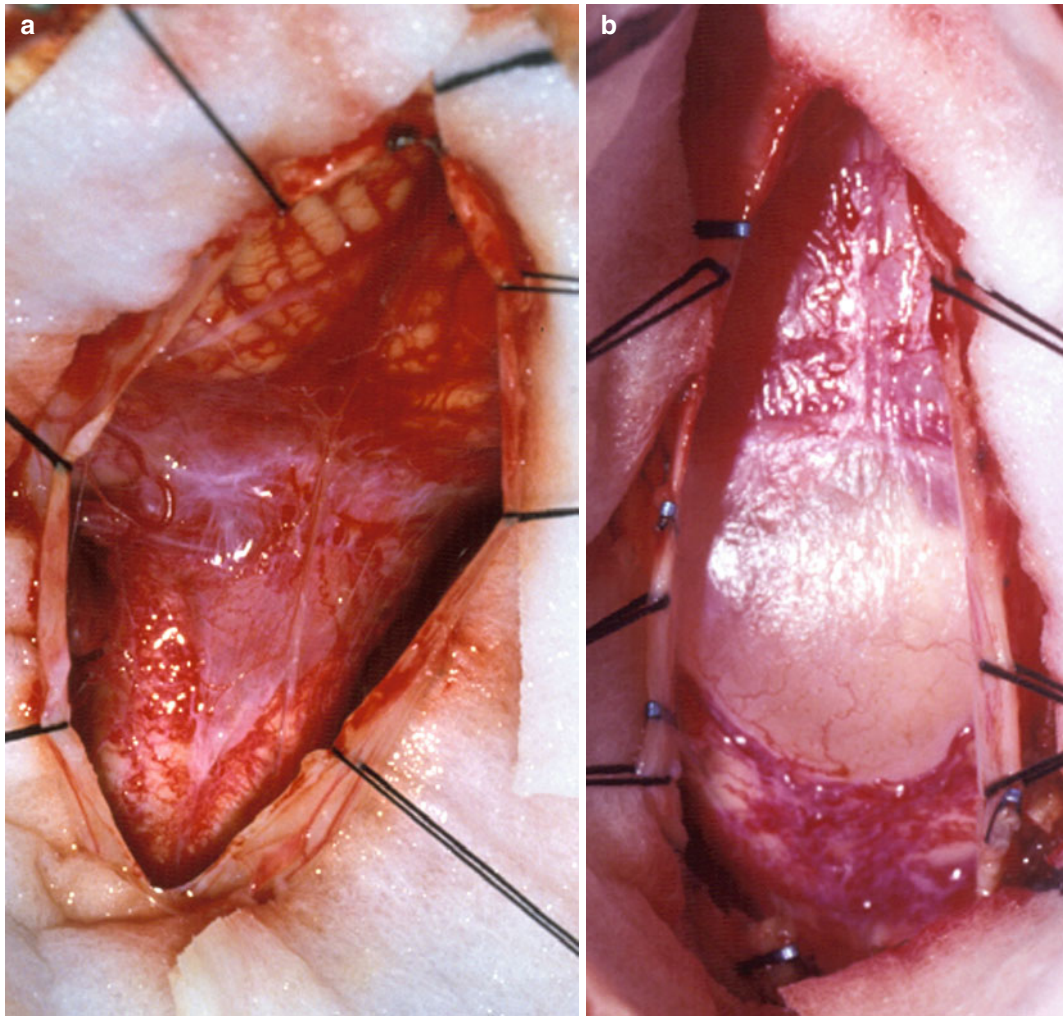

Fig. 28.6 (**a**) A veil over the fourth ventricle is seen as a thin membrane and is easily opened to reestablish outflow. (**b**) Craniocervical exposure with dura retracted laterally. A membrane over the fourth ventricular outlet is seen as a thin almost transparent sheet. (**c**) Following opening the membrane seen in (b), the relatively avascular floor of the fourth ventricle is obvious

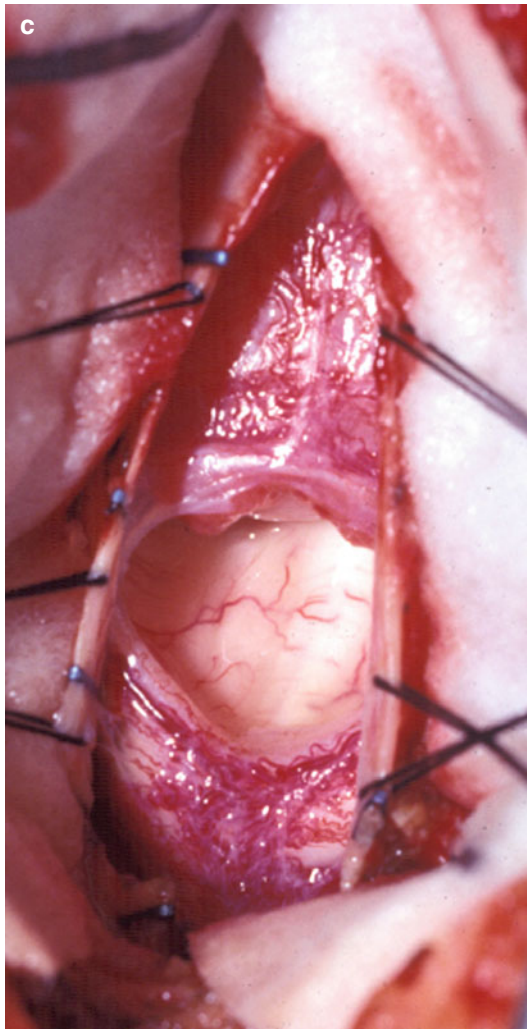

Fig. 28.6 (continued)

Complications of Chiari Surgery

29

Tyler S. Auschwitz and Frederick A. Boop

Abstract

Suboccipital decompression for Chiari has been performed for years with a wide range of reported complications. These complications can be divided into those related to misdiagnosis, complications associated with improper surgical technique, and common complications of properly performed surgery. This chapter reviews the extant literature of reported complications of Chiari surgery.

Although suboccipital decompression is thought to be a relatively simple and safe procedure with a low complication rate, reported surgical complications occur in 20 % of patients. The chapter will familiarize the reader with errors in diagnosis, errors in surgical judgement, and in the avoidance and management of complications associated with Chiari surgery. It is hoped that by reading this chapter, the readers may avoid the mistakes of those who have gone before them.

Suboccipital decompression for the treatment of Chiari-related symptoms has been one of the most satisfying surgeries the neurosurgeon can perform due to the fact that most patients derive appreciable and durable benefit from the operation. Having said that, if one looks at the complication rate from suboccipital decompression, it is not as low risk as many of us would like families to believe. Published series report a complication rate ranging from 3 to 40 % for this procedure [1]. This chapter will review the current literature on these complications in hopes of helping the reader reduce the likelihood of errors. We will detail the complications in an individual format starting with the most common complications and ending with those occurring only rarely. The chapter will not discuss the management of basic wound infections, wound breakdown, and those complications with which all neurosurgeons should be familiar. The authors divide the complications into those related to misdiagnosis and those related to surgical technique.

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Complications of Misdiagnosis

When first seeing a patient referred to the neurosurgery clinic with an MRI diagnosis of Chiari malformation, it is important for the neurosurgeon to differentiate the clinical diagnosis from the radiologic picture. The vast majority of patients referred to the neurosurgery clinic with the diagnosis of Chiari I will have mild tonsillar ectopia on a scan unrelated to the clinical condition. The family or the patient has been on the Internet reading about their diagnosis and comes to clinic certain that many of the symptoms they have read about belong to them as well. Most of the time, the reassurance that this finding has been present since birth and assuring the family that the patient's examination is normal are all that is necessary. Likewise, the small persistent dilatation of the thoracic central canal is often something that can be followed either clinically or radiologically and should not be considered an indication for surgery. One learns quickly that incising the neck muscles in a patient who has muscle tension headaches or fibromyalgia will lead to poor results and a patient who is dissatisfied. Thus, it is of paramount importance that the patient's clinical symptoms suggest a Chiari syndrome (e.g., tussive headaches).

It is not uncommon for the neurosurgeon to see a patient who has radiologic evidence of tonsillar ectopia but whose presenting symptoms are those of raised intracranial pressure (ICP). These patients fall into two subsets. First are patients who present with progressive generalized headaches, visual symptoms, nausea, and perhaps vomiting and who have on imaging either small- or normal-sized ventricles. They may or may not have papilledema, but their symptoms are those of increased intracranial pressure rather than the classic tussive headaches or Chiari symptoms. These patients may have tonsillar ectopia secondary to raised intracranial pressure from pseudotumor cerebri, occult sinus thrombosis, or other causes. In the teenage male, this is often a child who has been started on minocycline for acne, causing a drug-induced pseudotumor. The clinician must recognize that their presenting symptoms are not those of a Chiari patient but instead are those of a patient with raised intracranial pressure. If the clinical suspicion is raised but cannot be confirmed by eye exam, then intracranial pressure monitoring may be necessary. To perform a posterior fossa decompression on such a patient without first addressing the cause of the increased intracranial pressure may lead to further tonsillar descent, brain stem herniation, or neurological deterioration. In papers published looking at patients who present with radiologic evidence of Chiari and have a decompression but continue to be symptomatic, 41 % who failed decompression had pseudotumor. This was diagnosed by cine MRI establishing flow and then confirmed by high-flow lumbar puncture with resolution of symptoms [2]. One study, examining the prevalence of Chiari I malformation in patients with pseudotumor cerebri, showed that out of 68 patients with pseudotumor, 7 had MRI evidence of Chiari I; of note, all patients with cerebellar descent in their study were overweight females [3].

The second group of patients is those who again have clinical symptoms of raised intracranial pressure but who have on imaging tonsillar ectopia associated with increased ventricular size. Until proven otherwise, these patients have hydrocephalus causing their cerebellar tonsils to be pushed through the foramen magnum by chronically raised ICP.

Hydrocephalus associated with Chiari malformation has been debated for a long time with regard to pathogenesis. Some authors suggest that hydrocephalus may be associated with 7–10 % of patients with Chiari I malformation [4]. In such cases it has been theorized that supratentorial hypertension causes downward pressure on the cerebellum creating a radiologic "Chiari picture" [5]. Though rare, performing a suboccipital craniectomy and duraplasty on such patients may lead to both tonsillar and brain stem descent and has been associated with acute neurological decompensation. Thus, if one feels compelled to perform a suboccipital decompression in patients with ventriculomegaly, consideration should be given to first controlling the intracranial pressure through placement of a ventriculostomy.

Similarly, clinicians will also be asked to treat Chiari II patients shunted early in life and who present with suboccipital headaches, brain stem symptoms, or a progressive syrinx absent of any change in ventricular size. These patients are likely to have a subtle shunt malfunction. Shunt malfunction should be the primary diagnosis in any spina bifida child who presents with neck pain, new onset of bulbar symptoms, or a new cervicothoracic syrinx [6]. In such cases, shunt exploration is warranted before considering suboccipital decompression.

Another surgical complication that can be avoided with careful preoperative inspection is the patient presenting with a Chiari malformation associated with ventral compressive pathology. Patients with basilar invagination, os odontoideum, a rheumatoid pannus at C1, or atlantoaxial assimilation are at risk to decompensate with dorsal decompression alone. In such patients, careful consideration should be given to addressing their ventral pathology first. Patients with symptomatic anterior compression causing brain stem dysfunction, myelopathy, lower cranial nerve palsies, or quadriparesis often experience no relief with a posterior decompression even with radiologic evidence of Chiari malformation. It is important that these pathologies be recognized preoperatively. In some instances, these patients may improve with traction to reduce the ventral pathology. If not, one must consider ventral decompression before undertaking a suboccipital decompression. These patients will virtually all require occipitocervical stabilization and fusion for long-term stability.

The final preoperative pathology we will discuss that can be associated with hindbrain herniation is assimilation of the atlas. Atlas assimilation is caused by failed segmentation of the fourth occipital sclerotome and the first spinal sclerotome, usually occurring in conjunction with other abnormalities, specifically Klippel-Feil. This pathology leads to basilar invagination secondarily. In one large series of 5,300 patients evaluated for cranio-vertebral junction abnormalities, 550 patients had atlas assimilation. Of these, hindbrain herniation occurred in 38 % due to diminished posterior fossa volume [7]. This pathology can be compounded with segmentation failures of second and third cervical vertebrae [8]. If this occurs along with atlas assimilation, it leads to atlantoaxial instability due to abnormal load on this motion segment [9]. This motion segment then leads to a pannus or basilar invagination, which may be reducible with traction up to about 14 or 15 years of age. In older patients, the lesion becomes an irreducible basilar invagination [10]. Hence, an operation just focusing on posterior decompression without addressing the potential for instability can lead to unfortunate results.

The next section addresses the common complications associated with suboccipital decompression, the most common of which is pseudomeningocele. Pseudomeningocele is defined as an abnormal collection of cerebrospinal fluid (CSF) that communicates with the CSF space around the brain or spinal cord (Fig. 29.1). It is the most common complication of Chiari surgery with some papers reporting an incidence as high as 30 %. These complications have been attributed to different types of dural patch grafts, both allograft

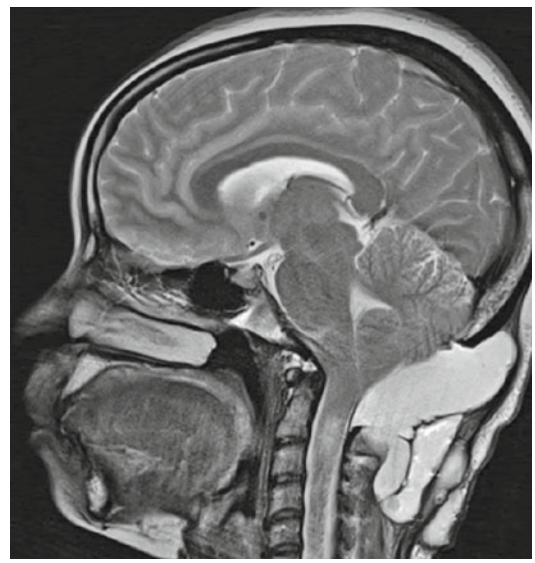

Fig. 29.1 T2-weighted sagittal MRI showing a postoperative pseudomeningocele

vs. autograft. Absent the patient with raised intracranial pressure, pseudomeningocele most commonly occurs when a patient vomits, cries, strains, or lifts a heavy object in the postoperative period, thus tearing a suture loose in their dural repair. It is not uncommon, at re-exploration, to find a single small hole in the closure, which is responsible for the whole pseudomeningocele [1]. In discussing pseudomeningocele, it is important to recognize that at some centers with large series and good results, the advocated surgical technique is to perform a bony decompression, leave the dura open, and to close the paracervical muscles and skin with the intent of creating a pseudomeningocele [12]. Thus, the presence of a small asymptomatic pseudomeningocele should be little cause for concern. Concern arises when a small defect in a dural closure allows CSF to progressively accumulate in the epidural space or to leak through the wound. A progressively expanding mass, which threatens the skin, or causes the patient pain, will require additional treatment. Having said that, whenever a large pseudomeningocele occurs in the early postoperative period, it should raise the suspicion of a CSF absorption problem such as pseudotumor cerebri or occult hydrocephalus. In patients with a preexisting ventriculoperitoneal shunt, a pseudomeningocele should suggest the need to rule out a shunt malfunction.

As mentioned, the most common finding at re-exploration is that of a small dural defect where a dural suture has pulled loose either from head movement or from Valsalva such as crying or vomiting in the acute postoperative period. Although meticulous closure of the dura and muscular layers is essential, requesting that anesthesia extubate the patient a bit deeply and then bag them with a facemask to prevent bucking on the endotracheal tube may reduce the incidence of this complication. In the early postoperative period, scheduled antiemetics can also reduce the risk of retching and disruption of the dural suture line.

As mentioned previously, the presence of a small asymptomatic pseudomeningocele should not be cause for alarm. Parents benefit from knowing this prior to surgery so that they are not surprised by it in the event that they see it postoperatively. Once a pseudomeningocele is deemed concerning, there are several treatment options to be considered.

Re-exploration of the wound for an early acute pseudomeningocele allows the surgeon the most immediate repair of a dural defect. In younger children, this may be the most expeditious means of curing the problem and getting the child home. Since the surgical risks are small, these authors prefer wound re-exploration as the most direct way of dealing with a symptomatic pseudomeningocele in the early postoperative course. Another method of dealing with a pseudomeningocele is by the placement of a lumbar drain. To do so, one must be confident that a good decompression was accomplished at surgery and that CSF flow is restored. Only then is it safe to place a lumbar drain. This allows diversion of CSF flow, which, in return, will hopefully allow the dural closure time to heal. Once the lumbar drain is placed, it is typically left in place from 3 to 7 days. By doing so, the surgeon hopes to avoid another operation. Lumbar drains may not be tolerated well in young infants and children and may be technically difficult to place in patients with concomitant tethered spinal cords or other lumbar pathologies. This treatment requires prolonged hospitalization but is an option for patients with comorbidities which may make return to surgery less appealing.

Some surgeons may elect to percutaneously tap a fluid collection at the bedside. This may differentiate a CSF collection from a wound infection or seroma but is not a treatment for pseudomeningocele. Since this treatment does nothing for the dural defect, it may promote further CSF flow into the epidural space, which may then leak through the needle tract placing the patient at risk for meningitis. Given this, therapeutic tapping of pseudomeningoceles is mentioned only to be condemned. Similarly, there have been case reports of using a blood patch in the epidural space. This is performed by draining the pseudomeningocele and

injecting blood mixed with fibrin glue in multiple settings [11].

Meningitis

The second most common complication encountered in Chiari surgery is meningitis. A study by Dubey et al. of 500 patients undergoing posterior fossa surgery reported this complication rate at 9 % [12]. Having said this, the incidence of bacterial meningitis following Chiari decompression is normally quite low. The most common cause of meningeal inflammation is aseptic meningitis or inflammatory meningitis due either to the spillage of blood products into the subarachnoid space or related to an idiosyncratic reaction to a dural allograft. Surgical technique can help decrease this complication. If lysis of arachnoidal adhesions is not planned during the operation, carefully opening the dura and leaving the arachnoid intact decreases the chance of blood spillage into the subarachnoid space. Another surgical technique is placing a temporary Gelfoam patty at the inferior aspect of the opening stopping any blood products from contaminating the spinal subarachnoid space.

Aseptic meningitis is usually diagnosed subacutely, within 3 weeks of surgery. The diagnosis is made by lumbar puncture with the expected findings of mononuclear pleocytosis, elevated protein, and a negative gram stain and culture. This complication may either be treated with corticosteroids or by serial lumbar punctures until the symptoms improve.

Bacterial meningitis, though less common, is a more serious complication. Although Staphylococcus species are most common, one must rely upon cultures to direct appropriate therapy. In some instances, early return to surgery for removal of an infected dural patch graft may be prudent.

Cerebellar Slump, Sag, or Ptosis

Cerebellar ptosis is a rare iatrogenic complication caused by an excessively large suboccipital craniectomy. Over time, CSF pulsations and gravity may pull the cerebellum through the defect created during the craniectomy causing cerebellar herniation. The once decompressed posterior fossa now has a new interface between the brain stem and cerebellar tonsils. As adhesions form between the cerebellum and dura, the CSF outflow, which was once reestablished after surgery, may gradually become obstructed leading to recurrence of a syrinx or preoperative symptoms [13]. Avoidance of an overaggressive craniectomy can help lead to reduction of this complication. A craniectomy of 3×5 cm is generally adequate for most straightforward Chiari I patients.

Although the timing of this complication has been seen within the same calendar year as surgery, it may present much later. Cerebellar sag most commonly manifests as the insidious return of Chiari symptoms, the most common being headache. Although different in nature than the classic tussive headaches, these have been described as intractable with radiation to jaw and orbit. Because of the acquired CSF outflow obstruction, patients may develop syringomyelia. Once symptomatic ptosis has occurred, surgical correction is generally required. If a patient returns with symptoms related to syringomyelia, one treatment option is a syrinx shunt. A more physiological correction is a suboccipital cranioplasty with dural exploration, allowing visualization and decompression of the cerebellum and dura [14] (see Fig. 29.2).

Cranio-cervical Instability/Kyphosis

Another complication, though usually not of clinical significance, is radiologic evidence of cranio-cervical instability following occipito-cervical decompression. In a recently published retrospective review of this complication, the authors reported that five of nine patients (56 %) showed evidence of radiologic instability of their cervical spines following surgery for Chiari II malformations. Of the five patients, none developed clinical instability requiring fusion [15]. It should be pointed out, absent congenitally abnormal anatomy, that this complication is generally only seen following laminectomy of C2 and

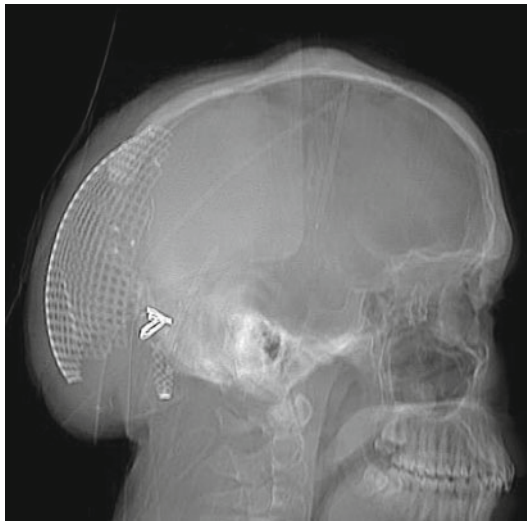

Fig. 29.2 This lateral skull x-ray was taken in a patient who presented after a large occipital decompression at another institution. His presentation was unilateral vocal cord paralysis secondary to syringobulbia secondary to cerebellar sag. Although his vocal cord paralysis was permanent, his syrinx improved with occipital cranioplasty using titanium mesh

below. It is very uncommon to see instability with just removal of the posterior arch of C1. Thus, in Chiari I children, even though the cerebellar tonsils may extend down to the level of C2, effort should be made to preserve the spinous process and lamina of C2, even if a partial laminectomy of the superior half of C2 is necessary to disimpact the tonsils. Disrupting the facet joints intraoperatively may also lead to a higher probability of instability. Once post-laminectomy deformity develops, it will usually progress until surgical stabilization and fusion corrects the problem.

Recurrent Syringomyelia

Though not always thought of as a complication, the persistence or recurrence of a syrinx following decompression has been reported in 10–40 % of cases [16]. This complication is typically seen months to years following surgery, but underscores the need for long-term follow-up of this patient population. One of the arguments favoring intradural exploration for Chiari patients is to confirm that CSF flow has been reestablished and that no arachnoidal webs overlie the fourth ventricular outlet. A delayed postoperative MRI of the cervical spine in patients with syringomyelia will serve as both proof that the syrinx has deflated and to offer a comparison study should future symptoms develop. In most cases, if the syrinx has regressed and symptoms have improved, it is uncommon for the syrinx to return. If the syrinx has not changed in size but the clinical symptoms have improved, it is at this time that assessment of the syrinx and CSF velocity and flow using cine phase-contrast MR imaging may be of benefit. If, by this imaging test, good CSF flow is observed, then one may follow the patient clinically and radiologically. If the patient's symptoms recur, suboccipital re-exploration should be entertained. The authors have one patient in whom recurrence of syringomyelia 10 years postoperatively was associated with quadriparesis. Review of the original operative report noted a paucity of CSF from the foramen of Magendie during the original surgery, and, at re-exploration, a missed congenital web of arachnoid over the obex was identified. Once resected, the syrinx collapsed and the patient's weakness improved (Fig. 29.3 a, b)

In conclusion, in the current era the radiologic finding of Chiari I malformation has become very common. Most of these patients and their primary care physicians will not be satisfied until they have had formal neurosurgical evaluation. The majority of these patients are either asymptomatic or have clinical symptoms unrelated to the radiologic picture and will require no intervention. Although neurosurgeons consider suboccipital decompression to be a benign procedure, a careful review of the literature or of one's own series will demonstrate that serious complications can and do occur. It is of paramount importance that the operating surgeon is sure the patient's clinical picture is appropriate before undertaking surgery. Once the operation has been performed, meticulous attention to detail and to postoperative recovery will allow for a healthy patient who is pleased with their surgeon and the results of their surgery.

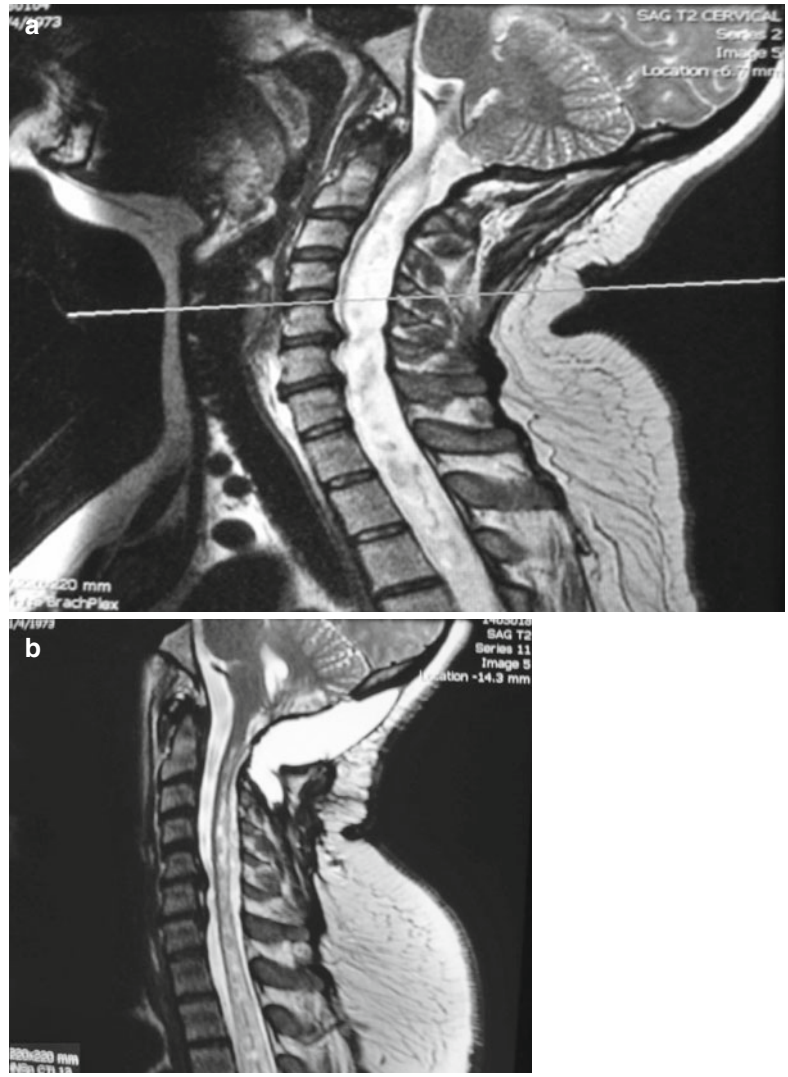

Fig. 29.3 (**a**) This adult female presented with quadriparesis related to a large recurrent syrinx, as noted on her T2-weighted MRI. Note her small posterior fossa. Her syrinx had failed prior suboccipital decompression and had been shunted twice before, each time with recurrence. At re-exploration she was found to have a congenital veil of arachnoid over her obex, which had been missed at the initial operation a decade before. (**b**) Postoperative T2-weighted sagittal MRI in this same patient shows resolution of her syrinx and enlargement of her posterior fossa following reoperation. Her quadriparesis was significantly improved

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Outcomes for the Surgical Management of Chiari I and Chiari II Malformations

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Abstract

An up-to-date, evidence-based review of the neurosurgical literature reveals that clinical outcomes following the operative management of Chiari I and II malformations have improved dramatically since these congenital disorders were first recognized as surgical diseases. A detailed assessment of major measurable postoperative parameters, including improvement in clinical signs and symptoms, resolution of syringomyelia, and progression of scoliosis, proves these procedures to be safe and effective when performed in a timely manner by an experienced neurosurgeon. Patients with CM-I routinely report a significant reduction in headache, neck pain, apnea, and syrinx-related symptoms and encounter low rates of complication or reoperation after posterior fossa decompression using a bone-only or intradural approach. Neonates and infants with CM-II have higher rates of symptomatic improvement and reversal of impairment when an operative intervention is made at the first sign of brainstem dysfunction. The current trend of less invasive bone-only surgical approaches, if shown in larger prospective trials to be superior to traditional decompressions with dural opening, will only add to the modern-day neurosurgeon's ability to achieve excellent clinical outcomes with minimal risk in the treatment of patients with Chiari I and II malformations.

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The details regarding classification, embryology, epidemiology, pathology, presentation, evaluation, and management of these entities will be discussed elsewhere in this text. The objective of this chapter is to provide a literature-based description of the clinical outcomes observed and reported following the surgical treatment of Chiari I and II malformations (CM-I and CM-II). The major measurable parameters include the improvement of clinical signs and symptoms, resolution of syringomyelia, and progression of scoliosis. Endpoints such as duration of surgery, findings on

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intraoperative ultrasonography, and length of hospital stay, each of which has been evaluated in more recent investigations, will be discussed as well. Complications and rates of reoperation will be noted but have been addressed in another chapter. The differences in results documented in patients with CM-I or CM-II that have undergone either bony decompression alone or in conjunction with duraplasty will also be outlined. In light of the fact that Chiari I and II malformations are congenital disorders truly distinct from one another, they will be addressed separately here.

Chiari I Malformation (CM-I)

First described in 1891 by Hans Chiari, Chiari malformation type I (CM-I) refers to a caudal descent of the cerebellar tonsils through the foramen magnum – sometimes as low as the mid-cervical spine – that results in a variety of clinical signs and symptoms [1]. Multiple theories exist regarding the proposed pathogenesis of CM-I, the most routinely cited being that of an anomalous differential craniospinal pressure gradient across the foramen magnum; the lack of pressure equilibration between the intracranial and spinal subarachnoid spaces in this location permits the development of a caudal vector of force that results in worsening downward displacement of posterior fossa tissues [2–10].

The diagnosis of CM-I, typically made by magnetic resonance imaging (MRI) criteria, is being delivered with increasing frequency in both children and adults as the threshold for obtaining radiologic studies in the setting of minor clinical complaints has continued to decline. Unlike CM-I patients of a half-century ago that presented with severe ataxia, quadriplegia, and signs of elevated intracranial pressure, patients today are frequently diagnosed earlier with minor deficits, permitting more elective surgical management [11–13]. An excellent retrospective review of the 20-year institutional experience with pediatric CM-I at a major children's hospital conducted by Tubbs et al. revealed the two most common presentations to be headache/neck pain (40 % of patients) and scoliosis (18 %); they also found that only 20 % of patients referred with radiological CM-I actually had symptoms likely to be improved by surgical intervention [14]. Numerous authors have similarly determined headache (exertional, Valsalva-induced) and pain to be the dominant presenting complaints in adults [15–19]. In the large pediatric study population evaluated by Tubbs and colleagues, less than 10 % of patients presented with cranial neuropathies and fewer than 5 % had central sleep apnea. Other common findings included irritability, opisthotonus, upper extremity pain, paresthesias and weakness, ataxia, and lower extremity hyperreflexia. Among associated diagnoses, shunted hydrocephalus, retroversion of the dens, and scoliosis were observed most often [14].

Syringomyelia (SM), a condition caused by the abnormal accumulation of fluid within the spinal cord, is seen in up to 20 % of asymptomatic patients with CM-I and 75 % of those with symptoms [5, 20–26]. Although difficult to separate from the clinical findings in CM-I itself, these patients typically complain of suboccipital headaches and neck pain that may occur in conjunction with uni- or bilateral numbness, weakness or atrophy, and spasticity depending on the size and location of the syrinx. It is well-recognized from the Boman and Iivanainen study from the 1960s describing the natural history of untreated cervical SM that the condition will gradually progress and ultimately lead to both early disability and death if a timely intervention is not made [27].

Although no causal relationship has been definitively proven, the association between CM-I, SM, and scoliosis is well established and has been extensively studied [28–30]. It is believed by many that impairment of the lower motor neurons in the setting of syringomyelia results in aberrant innervation of the trunk musculature and creates an imbalance that directly contributes to the development of scoliotic deformity [31–33]. Several reviews have determined that not only is scoliosis often the earliest presenting sign of SM in children and teens but that it may be present to varying degrees in up to 85 % of young patients with SM [34, 35]. The likelihood of an individual case of idiopathic scoliosis (coronal spinal curve with Cobb angle > 11°) being associated with CM-I

and SM is increased in the setting of left-sided thoracic or otherwise atypical curves, hyperkyphosis, loss of thoracic apical segment lordosis, rapidly progressive curves, male gender, pain, and neurological deficits; the evaluation of scoliotic patients with such findings must therefore include spinal MRI [28, 30, 32, 36–46].

Operative Management of CM-I

With the exception of medical pain management, surgery is the only proven treatment available for CM-I. Although traditional approaches have included operations to address the syringomyelia itself via syrinx fenestration and shunting, the mainstay of therapy involves procedures directed at the presumed mechanism of syrinx development. Since some of the first descriptions in the literature of successful surgical management of CM by McConnell and D'Errico in 1938, studies by Fischer, Galarza et al., Krieger et al., and Navarro et al. have demonstrated the safety and efficacy of multiple techniques for decompression of the posterior fossa [47–52]. More recently, as the debate regarding the advantages and disadvantages of performing a "bone-only" extradural decompression via removal of the suboccipital bone with or without cervical laminectomy and lysis of fibrous epidural bands (PFD) versus the more invasive intradural maneuvers (PFDD) has grown stronger, Durham et al. and Hankinson et al. published meta-analyses of the current literature comparing the results of both approaches [53, 54]. Mutchnick and colleagues added to this growing body of class IIb and III data in 2010 with a single-institution retrospective review comparing 121 CM-I patients that underwent either PFD or PFDD [55]. As has been mentioned previously, however, there is no level I or IIa evidence comparing posterior fossa decompression without dural opening (PFD) to posterior fossa decompression with duraplasty (PFDD).

Clinical Outcome

In their meta-analysis composed of five retrospective cohort studies and two prospective cohort studies in which both surgical techniques were directly compared, Durham and Fjeld-Olenec found that 65 % of patients undergoing PFD experienced clinical improvement as compared to 79 % of the PFDD patients [53]. Hankinson and colleagues also reviewed the relatively limited database of studies retrospectively assessing the efficacy of PFD and PFDD separately. Some of these included the use of intraoperative ultrasonography to determine whether or not to perform intradural maneuvers, while others used electrophysiological evidence or preoperative factors to support the selection of PFD versus PFDD [52, 56–61]. Two retrospective studies from Italy reviewed by Hankinson et al. in which patients underwent PFD-only demonstrated complete symptom resolution in 81.3 % of patients [24] and a significant improvement in clinical condition at nearly 5 years of follow-up in 93.3 % of patients [62].

A wealth of class III evidence exists in the form of retrospective, single-institution studies analyzing the outcomes in patients with CM-I managed primarily with PFDD. Reports from the 1980s and 1990s by Paul, Nagib, and Nohria, respectively, showed that the majority of patients treated with PFDD experienced either improvement or stabilization of symptoms related to CM-I following surgery [25, 63, 64]. Outcomes were better when the onset of symptoms occurred less than 2 years prior to operative intervention [17]. Numerous small studies have shown a range of clinical improvement from 92 to 100 % with fairly low complication rates [51, 56, 57, 65–70]. In their extensive analysis of 500 pediatric patients treated for CM-I, Tubbs et al. demonstrated relief of preoperative symptoms or signs in 83 % of patients; headache (particularly Valsalva-induced and occipital in location), sleep apnea, and syringomyelia were affected more reliably than were preoperative motor or sensory abnormalities [14].

Syrinx Resolution

In the Durham and Fjeld-Olenec meta-analysis reviewing studies in which PFD and PFDD patients were directly compared, radiological

syrinx improvement rates were 56 % in the PFD patients and 87 % in those undergoing PFDD, although this finding did not reach statistical significance [53]. In the study by Genitori et al., eight of ten patients that presented with syringomyelia achieved complete syrinx resolution following PFD alone; Caldarelli and colleagues showed that 50 % had a decrease in syrinx size following bony decompression and 16.7 % experienced postoperative syrinx growth and persistent or worsening symptoms [24, 62].

Among studies looking at PFDD alone, investigators have reported rates of syringomyelia reduction ranging between 55 and 100 %, though no universal criteria defining improvement in syrinx exist [51, 56–58, 65, 67, 69–71]. Tubbs et al. found that of 285 patients with syringomyelia who underwent decompression with duraplasty, only 4 patients were found to have syrinx progression at follow-up 6 months to 1 year postoperatively; 80 % of patients had resolution of syringomyelia symptoms following the first operation and 95 % of patients achieved relief following a second operation [14]. Zhang and colleagues reviewed 200 cases and demonstrated collapse or diminished size of syrinx in 60 % of CM-I patients following PFDD [72]. Although case reports exist in the literature, the likelihood of delayed syrinx resolution is low, and reoperation is recommended for persistent symptomatic syringomyelia at the 3–6-month postoperative time point [73].

Scoliosis Improvement

There is a paucity of literature regarding the management of scoliotic CM-I patients with PFD alone. Genitori et al. documented radiologic improvement in two of three patients, and Caldarelli's paper reported mild improvement in two of two patients [24, 62]. Attenello et al. detailed a single patient who had progression of scoliosis requiring reoperation with duraplasty following an initial PFD [74]. The likelihood of improvement in CM-I patients with syringomyelia and scoliosis is better defined for the PFDD approach. A detailed search of the literature reveals at least 15 published clinical studies retrospectively evaluating scoliosis outcomes in patients treated primarily with PFDD. Though confounded by a lack of uniformity in surgical criteria and approaches across these series, rates of scoliosis improvement and progression range between 0–73 and 18–72 %, respectively [75–86]. An association has been made between better outcomes and both a younger age at intervention and a smaller presenting Cobb angle [75, 76, 82–84]. Isu and colleagues demonstrated that two-thirds of patients with CM-I-related syringomyelia and scoliosis might have both a postoperative reduction in the Cobb angle as well as lower rate of scoliosis progression when preoperative Cobb angles were less than 40° [32]. Nagib found that 6 of 10 patients with Cobb angles less than 30° improved and 4 patients with preoperative angles greater than 30° stabilized after PFDD [63]. Tubbs et al. observed that 18 % of patients in their large series had scoliosis, 82 % of whom had syringomyelia; 40 patients (8 % of all subjects) ultimately required spinal fusion for deformity correction. The authors observed that a preoperative Cobb angle of more than 40° was associated with higher rates of scoliosis progression even in the setting of decreased syrinx size following surgery [14]. Attenello et al. found that in addition to a larger preoperative Cobb angle, scoliosis located at the thoracolumbar junction and a lack of radiographic improvement in syrinx size following surgery were predictive of scoliosis progression [74]. Most recently, Krieger and colleagues published a 10-year retrospective review of 79 pediatric patients found to have CM-I and syringomyelia greater than 6 mm in diameter during an evaluation for scoliosis [86]. Each patient underwent PFDD, and none of the 49 patients with curves less than 20° had progression of their curves postoperatively; 70 % of the patients with curves between 25 and 80° required either bracing or spinal instrumentation and fusion for scoliosis after the Chiari decompression. In total, 87 % of the 79 patients had a significant size reduction of the syrinx following PFDD, but this, along with the magnitude of the preoperative curvature (in patients with Cobb angle > 20°), did not predict the need for subsequent deformity correction. Krieger and colleagues concluded appropriately

that timely intervention was the key to improving neurological signs and symptoms and to preventing the need for later spinal fusion surgery [86].

Reoperation Requirement and Complications

In the Durham and Fjeld-Olenec meta-analysis, patients who underwent duraplasty were less likely to require reoperation for persistent or recurrent symptoms (2.1 % vs. 12.6 %) but were more likely to sustain cerebrospinal fluid (CSF)-related complications (18.5 % vs. 1.8 %) [53]. McGirt et al. published a 3 % incidence of CSF leak in a 2009 retrospective review of 393 adult patients undergoing PFDD [87]. Mutchnick et al. found that 12.5 % of PFD patients needed a subsequent PFDD for symptomatic recurrence, though none suffered a complication; only 2 (3.1 %) patients receiving an upfront PFDD in their series underwent a repeated PFDD for lack of symptom improvement, and 3 patients suffered minor complications [55]. Tubbs and colleagues reported a complication rate of 2.4 % in 500 patients; these included posterior fossa extra-axial fluid collections causing acute hydrocephalus (managed with external ventricular drainage), severe brain stem compression within 48 h of surgery requiring transoral odontoidectomy and occipitocervical fusion, two aborted operations due to excessive occipital sinus bleeding, one case each of chemical and bacterial meningitis, and one patient with CSF leak secondary to untreated hydrocephalus that resolved with shunt placement [14]. Fifteen of 500 patients required reoperation (3.2 %). It is estimated that the annual expected mortality rate following CM-I decompression is between 2.5 and 4.5 % [88].

Operative Time and Length of Stay

In the retrospective review of their own institutional experience published in 2011, Tubbs et al. reported the mean operative duration to be 95 min for PFDD [14]. The average hospital stay for their patients (all but 1 of whom underwent PFDD) was 2–7 days with a mean of 3 days; the length of time away before returning to school ranged between 7 and 16 days, with a mean of 12 days. Mutchnick and colleagues found that those patients in their series undergoing PFDD spent a longer time in the operating room (201 ± 34 min vs. 127 ± 25 min) and in the hospital (4.0 vs. 2.7 days) than the patients who underwent PFD [55]. The 2005–2008 national normative data showed mean lengths of stay between 4.5 and 6 days [88].

Chiari II Malformation (CM-II)

Chiari malformation type II (CM-II) is a disorder of hindbrain development observed in the setting of myelomeningocele that was initially described by Hans Chiari in 1891 and is now known to include a variety of supra- and infratentorial anomalies [89]. In addition to caudal displacement of the cerebellar vermis, brain stem, and fourth ventricle, CM-II may include cerebellar inversion, a small posterior fossa, low-lying torcular Herophili, enlargement of the massa intermedia, shallow to absent cerebellar folia, a medullary "kink," and heterotopias [90–94]. The hypothesis currently favored by most neurosurgeons that best explains the myriad of findings in CM-II is the unified theory championed by McLone and Knepper; the combination of cranial constriction and settling, spinal cord tethering or traction, intracranial hypertension and intraspinal hypotension present in this malformation leads to the aforementioned spectrum of anatomical abnormalities [95].

Clinical signs of CM-II include apnea and respiratory stridor, neurogenic dysphagia, aspiration, hypotonia or spasticity, and para- or quadriparesis. Symptoms of the disease, which occur in one-third of patients with CM-II, range from very subtle to life threatening; symptomatic CM-II is the leading cause of death in children less than 2 years old with myelomeningocele, and surgical decompression is required in up to one-third of symptomatic patients with CM-II [96–100]. Although the malformation is present to variable degrees in every child born with a myelomeningocele and the diagnosis is straightforward, some patients become symptomatic only

later in adolescence with deficits or pain related to the more chronic effects of syringomyelia or scoliosis; these older children will manifest classic effects of cervical myelopathy with upper extremity weakness, spasticity, loss of dexterity, ataxia, and occipital headaches and are treated operatively in a more elective fashion [83, 101].

Operative Management of CM-II

The evaluation of symptomatic CM-II in a young child begins with a determination of the presence or absence of hydrocephalus, as many of these children require shunting at birth or shortly thereafter; in those patients with a shunt, the possibility of a malfunction must be addressed first. Because of the potentially fatal nature of the symptoms with which these young children present, whether secondary to cranial nerve traction, lower brain stem compression, or congenitally malformed cranial nerve nuclei, the workup and, if necessary, surgical decompression must be completed in an urgent manner [102–108].

Once hydrocephalus and/or shunt malfunction has been eliminated as the etiology of the CM-II patient's symptoms, the options for surgical intervention include suboccipital craniectomy, cervical laminectomy, and durotomy with or without dural augmentation [109–111]. As in CM-I operative management, controversy exists regarding the decision to perform a bony decompression only versus the more invasive durotomy and even fourth ventricular fenestration; each technique has been shown in separate investigations to be safe and effective for the treatment of CM-II, but the data remains class IIb or III [112–114]. The advantages of staying outside the intradural space include reduced risk of bleeding and decreased exposure to general anesthesia, while avoidance of a suboccipital craniectomy eliminates the chance of violating the low-lying torcular in these patients [115, 116].

Clinical Outcome

Overall, the prognosis for patients with symptomatic CM-II remains guarded, as up to 15 % of these patients die by 3 years old and an additional one-third suffer a permanent neurological disability [98]. Prior to the recognition of hindbrain compression as the cause of apnea, bradycardia, and cranial neuropathies and the establishment of an effective and aggressive surgical treatment, mortality rates for patients presenting with brain stem dysfunction that underwent "less urgent" surgical decompression ranged between 50 and 70 %; more recent studies in which surgery was undertaken early in an attempt to reverse the signs of brain stem compression reported postoperative mortality rates between 15 and 23 % [105, 108, 117, 118]. Conversely, outcomes in children and adolescents presenting with symptoms related to myelopathy or syringomyelia may mirror those of CM-I patients, with mortality rates near 0 % and clinical improvement in 79–100 % after surgery [105, 119].

As stated earlier, controversy exists regarding the optimal approach for craniovertebral decompression in these patients, in particular whether to include a suboccipital craniectomy and the utility of durotomy with dural augmentation. Tubbs and Oakes found in a 2004 evidence-based review of the literature regarding CM-II evaluation and management that all data were class III in nature and no reliable conclusions or recommendations could be made at that time [111].

With regard to the more invasive techniques, Pollack et al. published in 1992 on the use of a suboccipital craniectomy, cervical laminectomy, dural decompression, and, in patients with syringomyelia, a fourth ventricular shunt, in 25 CM-II patients with symptoms of increasing brain stem compression and deterioration [105]. The authors found that this approach resulted in near-complete or total reversal of clinical symptoms in 17 patients, while 3 others had mild-moderate residual deficits and 5 experienced no change. They established an association between worse preoperative neurological status, particularly bilateral vocal cord paralysis, and poorer outcomes, with an emphasis on the importance of expeditious treatment. Pollack and colleagues subsequently published a prospective report in 1996 in which children underwent the aforementioned decompression in a protocolized manner at the earliest

signs of CM-II-related brain stem dysfunction [104]. Ten of 13 patients returned to normal or near-normal brain stem function shortly after surgery, and only one required a temporary gastrostomy with no tracheostomies in the group. The remaining three patients presented with bilateral vocal cord paralysis and severe central apnea prior to operative intervention and achieved no meaningful recovery of function following surgery.

In 1992, Vandertop et al. retrospectively reviewed the management of 17 CM-II neonates over a decade with cervical laminectomy and duraplasty alone, finding that 88 % of patients achieved complete recovery with a mean follow-up of 65 months; one patient expired from respiratory arrest 8 months after surgery and the other died from a remote shunt infection 7 years later [108]. The authors argued that the relatively spacious size of the foramen magnum in CM-II patients eliminated the need for routine suboccipital craniectomy as part of the decompression.

With regard to the least-invasive end of the surgical spectrum, a 1996 investigation by Yundt and colleagues found that two children presenting with CM-II and stridor experienced clinical improvement following osseous decompression alone [116]. A later retrospective review by James et al. of 22 patients with CM including 18 children with CM-II that underwent a bony decompression only reported no surgical morbidities or mortality and partial or total symptomatic improvement in 86 % [115].

Most recently, Akbari, Limbrick, and colleagues conducted a retrospective analysis of 33 patients that underwent bony decompression with or without dural augmentation for the treatment of symptomatic CM-II and compared outcomes in patients managed with each approach [120]. Twenty-six patients had an osseous decompression alone, including 21 with cervical laminectomy and 5 others with both laminectomy and suboccipital craniectomy; seven patients underwent cervical laminectomy with or without suboccipital craniectomy and upfront duraplasty. At a median follow-up of 5 years, nearly 70 % of patients had symptomatic improvement, 62 % of those undergoing bone-only decompression compared to 57 % of the patients with dural augmentation (though this did not reach statistical significance). Signs including apnea, opisthotonus, stridor, and dysphagia were most responsive to surgical intervention, and the intraoperative blood loss, time under general anesthesia, and length of hospital stay were less in the bony decompression group, though statistical significance was not achieved. Rates of repeat surgery for lack of improvement or symptomatic recurrence were higher but not statistically significant in the bone-only cohort (19.2 % vs. 14.3 %); outcomes were not different between the patients that underwent cervical laminectomy alone compared to those that also had a suboccipital craniectomy. Overall, 6 of 33 patients required tracheostomies after surgery, and one patient died secondary to fungal sepsis unrelated to the Chiari decompression. The authors concluded that the less invasive approach of cervical laminectomy and sectioning of the dural band alone avoided the inherent risks of performing a suboccipital craniectomy and durotomy, including injury to the torcular herophili, CSF leak, pseudomeningocele, and meningitis, and should be considered a first-line option in the operative management of children with CM-II. Emphasis must also be placed on the critical need to evaluate each CM-II patient for active hydrocephalus or shunt malfunction, whether through radiographic imaging, shunt tap, or exploration, prior to undertaking a decompressive surgery. Undoubtedly, the need exists for a larger retrospective series or randomized controlled trial comparing the aforementioned approaches in order to make an outcomes-based decision regarding the optimal technique for CM-II treatment.

Fetal Myelomeningocele Repair and Improvement in Hindbrain Herniation

Finally, no discussion of CM-II outcomes would be complete without mention of the recently published prospective, randomized controlled trial of prenatal versus postnatal repair of myelomeningocele [121]. Though the primary findings of this

study included reduced need for shunting and improved motor outcomes at 30 months, the multi-institutional investigation also revealed that the proportion of infants without evidence of hindbrain herniation was higher (36 %) in the prenatal surgery cohort than in the postnatal surgery group (4 %) at 12 months of age. Similarly, the rate of moderate or severe herniation was lower (25 %), as were brain stem kinking, abnormal fourth ventricle location, and syringomyelia, in the prenatal surgery group than in the postnatal surgery patients (67 %). These data suggest that interruption of CSF flow through the myelomeningocele neural placode in utero, if performed early enough, may halt or even reverse abnormal hindbrain development. Although more work remains to be done, the impact of these findings on the future neurosurgical management of CM-II may be enormous.

Summary

An up-to-date, evidence-based review of the neurosurgical literature reveals that clinical outcomes following the operative management of Chiari I and II malformations have improved dramatically since these congenital disorders were first recognized as surgical diseases a century ago. A detailed assessment of major measurable postoperative parameters including the improvement of clinical signs and symptoms, resolution of syringomyelia, and progression of scoliosis proves these decompressive procedures to be safe and effective when performed in a timely manner by an experienced neurosurgeon. Patients with CM-I now routinely report a significant reduction in headache, neck pain, apnea, and syrinx-related symptoms and encounter low rates of complication or reoperation whether a bone-only or intradural posterior fossa decompression is performed. Neonates and infants with CM-II, though facing more significant deficits and frequently presenting in an emergent fashion, have higher rates of symptomatic improvement and reversal of impairment when an operative intervention is made at the first sign of brain stem dysfunction. The current trend of less invasive and faster bone-only surgical approaches, if shown in larger prospective trials to be truly superior to traditional intradural decompressions, will only add to the modern-day neurosurgeon's ability to achieve excellent clinical outcomes with minimal risk in the treatment of patients with Chiari I and II malformations.

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A Multidisciplinary Clinic for the Management of Chiari I Malformations

31

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Abstract

This chapter describes the experiences of a multidisciplinary clinic specializing in the diagnosis and management of Chiari 1 malformations (C1M). Data were collected regarding reasons for referral and outcomes and indicate that approximately half of referred patients were appropriately diagnosed radiographically with CIM. Moreover, of patients who actually had consistent imaging, only about one-third reported symptoms attributable to C1M. These findings illustrate pertinent issues relating to health-care resources and delivery of multidisciplinary care.

Introduction

A distinction of the Chiari malformation is that it is often a radiologic diagnosis, with no definitive clinical correlates [1, 2]. While certain objective findings, such as ataxia or cranial nerve deficits, may be localizable and consistent with a Chiari 1 malformation (C1M), these features in no way distinguish it from other posterior fossa pathologies [3]. Therefore, the diagnostician is often confronted with the task of reconciling symptoms with radiologic findings. There is ample literature

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describing both typical and atypical symptomatic C1M to aid the clinician in this respect. However, the increasing availability of computerized axial tomography (CT) and magnetic resonance imaging (MRI), coupled with the reported incidence of C1M, virtually ensures that referrals to specialty clinics will include patients whose signs and symptoms have no relationship to the radiologic diagnosis.

Given that management of a symptomatic C1M typically involves surgery, most patients are referred to a neurosurgeon for consultation. These referrals may come from neurologists, pediatricians, internists, family practitioners, or any health-care provider who has obtained a diagnostic MRI and been provided with a report that indicated the presence of a C1M. Anecdotally, at our institution, the frequency of symptomatic C1M is well under half of referred patients. This illustrates the problem of how to provide efficient and appropriate care for these individuals in a manner that not only addresses the question of whether or not a C1M is symptomatic but also deals with contemporaneous symptoms. Such a situation has been clearly operant at our institution with a neurosurgical interest in the surgical management of C1M in childhood [4]. Because of the need to address symptoms that are likely distinct from the C1M, a member of the pediatric neurology faculty (LSD) was enlisted to begin development of a multidisciplinary approach to C1M referrals. In addition, this clinic served as a resource for data collection to examine the characteristics of referrals, the nature of attendant complaints, and the outcomes. This chapter will serve as a summary of the first 16 month's experience of the clinic.

Methods

The Children's Hospital of Alabama (TCHA) is a freestanding tertiary care facility that serves not only the state of Alabama but is a resource for the adjoining states of Georgia, Florida, Mississippi, and Tennessee. Subspecialty pediatric care for children in the region is provided in large measure by physicians at TCHA, and this is particularly true for neurosurgical services.

Since 1992, TCHA has offered a neurosurgical clinic specifically focusing on the diagnosis and management of C1M, under the direction of a single neurosurgeon with significant interest in the C1M (JO). Children are typically referred to this clinic after a radiologic diagnosis of C1M is made. Beginning in January, 2010, children referred to this clinic were seen and their care incorporated into a multidisciplinary care model, involving a neurosurgeon (JO, CR) and a neurologist (LD, TM). Inclusion and evaluation was undertaken only if imaging was available to confirm or exclude a C1M.

In each child, a comprehensive history and physical examination was performed, along with review of radiologic studies. The primary goals of this initial evaluation were to determine (1) if radiologic evidence supported the diagnosis of C1M and (2) if the chief complaint or presenting symptoms could be attributed to a C1M. In situations where these goals were met, the care and management plan remained neurosurgical, typically involving a recommendation for surveillance or, more rarely, the offer of a surgical intervention. However, in patients for whom these criteria were not met, a neurological consultation was obtained, in order to identify other possible etiologies for the presenting complaints. In these latter cases, appropriate recommendations for care and management were made.

Results

From January 2010 to May 2011, 12 clinics were held, and 74 unique patients evaluated. Patient demographics are illustrated in Table 31.1. In the group of 74 children, 44 % were male and 56 % female. Eighty-three percent were identified as Caucasian, with 17 % of African-American ethnicity. The average age was 9.6 years, with a range of 9 months to 17 years. In terms of age distribution, 17 % (12) were from 0 to 4 years old, 25 % (18) were 5–8 years old, 29 % (21) were aged 9–12 years, and 29 % (21) were between 13 and 17 years of age.

All patients had undergone MRI of the head, and review of these studies revealed that in 36

Table 31.1 Patient demographics

Gender	Male	32
	Female	40
Ethnicity	Caucasian	60
	African-American	12
Age	Average	9.6 years
	Range	9 months–17 years
Age distribution	0–4 years	12
	5–8 years	18
	9–12 years	21
	13–17 years	21

Table 31.2 Indications for obtaining MRI

	No radiographic Chiari	Radiographic Chiari
Headache	24	16
Endocrinologic evaluation	1	2
Head trauma/concussion	3	2
Musculoskeletal pain	3	2
Other	5 (visual changes, deafness, anxiety (2), gait disturbance)	14 (tremor, tics, developmental delay, nystagmus, epilepsy (2), apnea, syncope, multiple congenital anomalies, macrocephaly, gait disturbance, hypotonia, dysmorphism, family history of C1M)

(50 %) of the children, radiologic findings were inconsistent with a C1M, with an absence of tonsillar herniation greater than 5 mm. Of the other 36 cases with the presence of a C1M, 22 (61 %) were felt to be of mild to moderate severity, as defined as tonsillar herniation measuring between 6 and 10 mm. The remaining 14 (39 %) C1M were classified as significant, on the basis of herniation greater than 10 mm. Five of 16 patients with significant C1M were also noted to have an accompanying cervical syrinx.

Presenting complaints in the entire population were wide ranging, but headaches predominated, with 40 (56 %) being the chief reason for undergoing an MRI. Headache was the primary complaint in 24 of 36 (67 %) of the patients who did not meet criteria for a radiologic C1M, while the same was true in 16 of 36 (44 %) of individuals who met criteria. Other reasons for obtaining an MRI in these patients included endocrinologic evaluations, assessment of head trauma and concussion, and investigation of musculoskeletal pain of the head and neck, among other complaints. Table 31.2 details the range of reported indications for imaging.

Upon review of MRI findings, clinical history, and the neurologic examination, a determination was made for each child by the neurosurgeon and neurologist of the plan of care. For the 36 patients whose MRI findings did not meet criteria of a C1M, the neurologist assumed the majority of medical management. Of this group, the most of the 24 children presenting with headache fell into the categories of tension headache or migraine. Appropriate recommendations were made, and follow-up was required in only two patients. Similar strategies were employed for all other patients.

Of the 36 patients whose imaging studies were consistent with C1M, correlation of the imaging studies, clinical history, and examination was done to determine if symptoms were related to the C1M. Twenty-four patients' symptoms were not felt to be secondary to the C1M. This group reported a variety of complaints, summarized in Table 31.3. The most common complaint was that of headache, in some cases diagnosed as tension headache or migraine. Few of these children exhibited characteristic complaints such as headache associated with a Valsalva maneuver, cough, or exercise, and none manifested abnormal findings referable to C1M. None of the children with headaches (10/24) reported a severity that suggested a significant impact on everyday activities. The next most common instance of detecting a radiologic C1M was as an incidental finding as part of a genetic or endocrinologic evaluation (4/24). In terms of ongoing management, 9 of these children were referred back to their primary physician for continued observation or to the

Table 31.3 Complaints elicited in 24 patients with radiographic C1M, but not felt to be symptomatic

Complaint	Number
Headache	10
Endocrinologic/genetic	4
Musculoskeletal	2
Concussion/injury	2[a]
Movement disorder	2
Behavioral disturbance	2
Syncope	1
Nystagmus	1

[a]Includes one child with an asymptomatic C1M + syrinx who underwent surgical decompression

neurologist for medical management. Fourteen patients were directed to continue follow-up with the neurosurgeon, with surveillance imaging. The criteria for this course of action related in some instances to the radiologic morphology of the C1M and in others to historical features that might evolve into symptoms more readily attributable to a C1M. The one remaining child in this group had undergone an MRI after being struck by lightning and was clinically asymptomatic, but radiologic findings included a large C1M and a cervical syrinx and were of such a magnitude that surgery was offered to the family for decompression of the C1M [5].

The final group of 12 children included those whose radiologic findings were consistent with C1M and whose clinical history or examination was consistent with a symptomatic process. In all but one case, neurologic examination was unremarkable. Five children were noted to have reproducible headaches with cough or Valsalva, and an additional two indicated occipital or nuchal pain as primary symptoms. Two children had previously undergone C1M decompression and were seen as second opinions. They were considered symptomatic as one had experienced significant postoperative complications, and the other manifested C1M as a component of a complex skeletal deformity involving the base of the brain and cervical spine. Another child was reported to have frequent falls but was a toddler and required further follow-up to obtain a better clinical assessment. One child reported events of apnea in the context of a C1M, previously diagnosed as epilepsy. The final child was the only one to have an abnormal examination, felt to be consistent with a sensory ataxia. In this case, a syrinx was also present. In addition, these latter two symptomatic cases were the only two of this group to undergo surgical decompression during the period of time encompassed by this analysis.

Discussion

In this report, we summarize our experience with a multidisciplinary model for the management of referrals to a tertiary care facility with interest in the evaluation and management of C1M. The findings are of interest on a number of levels. Of 72 consecutive patients seen in the clinic, only half of the patients were felt to have radiologic evidence of C1M. It has been the practice in this clinic to evaluate all children referred with a diagnosis of C1M, but it is clear that radiologic diagnoses were made that are inconsistent with guidelines regarding the entity [1]. A limitation of this study is that data were not collected regarding official radiologic interpretations, and therefore, no conclusions can be drawn with respect to the possibility that radiographs were either misinterpreted or that guidelines were applied conservatively. However, physicians referring to the clinic did so as a consequence of these radiologic interpretations, suggesting a lack of familiarity with diagnostic criteria for C1M, as well as the clinical features.

Although there is ample literature indicating the frequency of incidental findings on MRI [6, 7], subsequent evaluation and assessment typically falls to subspecialists who must determine if any relationship exists between radiologic abnormalities and clinical phenotypes. In this series, the situation in half of the cases was one of a diagnosis being applied without radiologic abnormality, thus highlighting a need for either better communication between radiologists and referring physicians or greater education regarding the significance of radiologic findings. A somewhat broader issue is highlighted by our experience, relating to the fact that in our cohort, over 50 % of the referred patients had undergone

an MRI for an indication of headache. In the context of management of headache in childhood, it has been demonstrated in a variety of studies that the clinical utility of imaging is low, despite the fact that incidental findings (including C1M) may approach 20 % [8, 9]. Thus, it could be argued that overuse of neuroimaging, in combination with misinterpretation of findings, led to the high incidence of inappropriate referrals to our clinic. These findings carry significance in relation to practice patterns and allocation of resources and point toward an important issue for further study.

Another result of our analysis is the fact that upon evaluation of children with a consistent radiologic finding, two-thirds of these individuals were not felt to have symptoms consistent with a symptomatic C1M. Fourteen of these children were recommended to have ongoing follow-up with repeat imaging, to assess for the possibility of progression, while nine were referred back to their primary physician, or their symptoms were to be managed by the neurologist. The one remaining child was felt to have a strong likelihood of becoming symptomatic, and surgery was offered, despite having at the time no complaints referable to the C1M and syrinx. Only two other children underwent surgical decompression for a symptomatic C1M during the course of this study. While consistent with other large studies of C1M [2, 10], these findings further underscore a need for better understanding of the clinical features of C1M by referring physicians. Alternatively, the results suggest that a clinic dedicated to C1M evaluation and management should at the very least have access to resources appropriate to care for other diagnoses.

In our clinic, we chose to incorporate neurologic expertise to assist in management of children referred for C1M. With regard to the provision of care, this was successful, as all children were able to access services appropriate to their chief complaints. The model of a multidisciplinary approach to childhood diseases has been successfully implemented for a variety of conditions, including sickle-cell disease [11], genetic disorders [12], and diabetes [13, 14], among others, with significant benefits in terms of clinical outcomes. In addition, it has also been shown that multidisciplinary clinics can have a favorable effect on overall health-care costs [13, 15] while also serving as foundations for innovation and research. On the other hand, as opposed to other medically complex conditions, our experience could be construed as illustrating an overabundance of access, given that 50 % of the patients referred to a clinic ostensibly directed at neurosurgical management of C1M had no evidence of the disorder. Therefore, another strategy under consideration would be to develop a screening process, with evaluation of neuroimaging prior to appointing a referral. This could have the effect of more appropriate utilization of subspecialty resources but will demand a higher level of education among primary care providers.

Conclusion

In summary, we have reported our experience with a multidisciplinary approach to the management of C1M in children. Although successful from the standpoint of patient access and care, our findings indicate somewhat problematic issues with respect to utilization and interpretation of radiologic findings in children. We anticipate that our results and conclusions will serve to inform other similar efforts.

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Chiari Malformations: A Patient's Guide

32

Nadine Bradley and E. Haley Vance

Abstract

The Chiari malformations are becoming more frequently diagnosed due to technological advancements. Many patients will be diagnosed with this type of brain herniation but will be asymptomatic. Others, however, will have medical problems related to the brain tissue that is displaced into the upper neck. These latter patients may undergo surgery to treat their Chiari malformation. In experienced hands, this procedure has a low complication rate and often effectively treats the Chiari malformation symptoms/signs.

Introduction

The purpose of this chapter is to provide patients and family members with general medical information concerning the diagnosis and treatment of a Chiari malformation. It is not intended as medical advice. Specific questions or concerns about this diagnosis should be directed toward the treating physician.

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Anatomy of the Brain and Spine

To understand you or your family member's diagnosis of a Chiari malformation, it is important to first understand the basic anatomy of the brain and spine. The brain is made up of three main portions: the cerebrum, cerebellum, and brain stem (Fig. 32.1). The cerebrum is the largest portion of the brain and is responsible for many higher functions such as hearing, vision, speech, emotion, movement, and sensation. The cerebellum is the second largest portion and is located at the back of the brain. The cerebellum controls things such as balance, coordination, and movement. The brain stem is the portion of the brain that connects to the spinal cord and controls many functions critical for life, such as breathing, swallowing, and heart rate. The spine is made of small vertebrae (bones), which are strong but flexible. The spinal cord is located inside the spinal canal that is surrounded by the spine.

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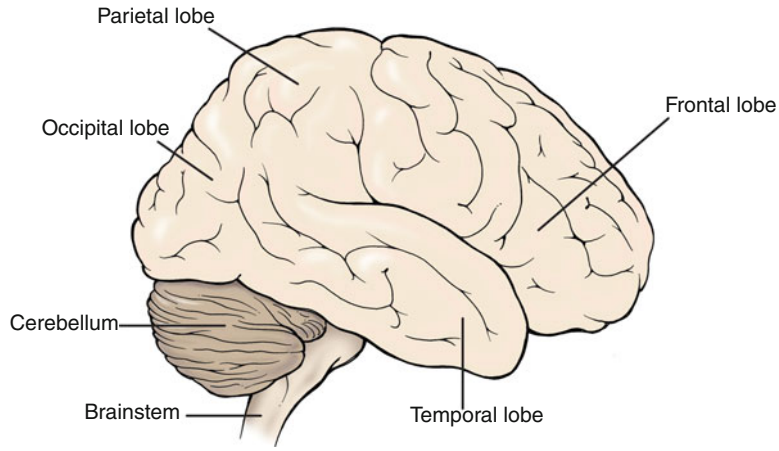

Fig. 32.1 Schematic drawing of the major parts of the brain

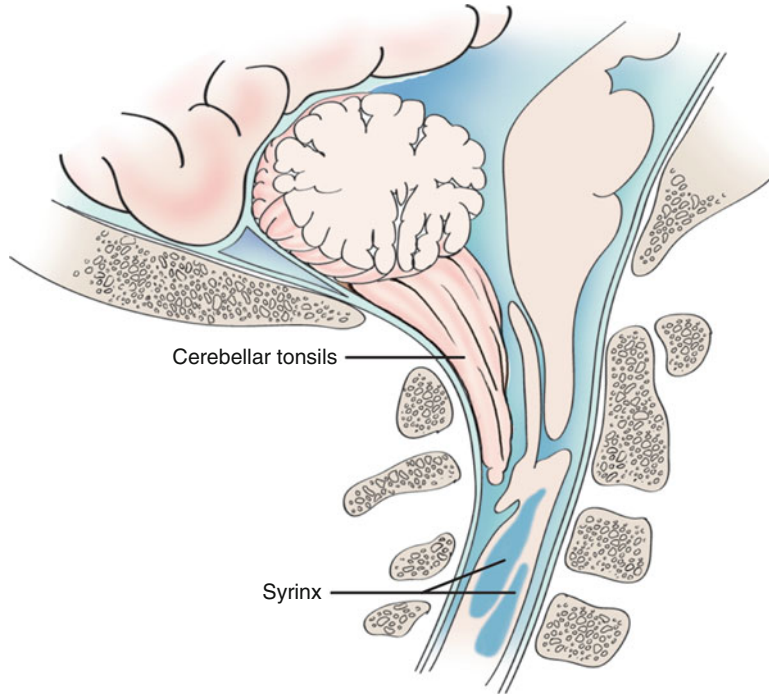

Fig. 32.2 Schematic drawing of the Chiari I malformation with a syrinx

What Is a Chiari Malformation?

A Chiari malformation (Fig. 32.2) occurs when a portion of the cerebellum is found outside of the skull and downward into the spinal canal. When the cerebellar tonsils (bottom portion of the cerebellum, i.e., Chiari I malformation) are located in the spinal canal, this disrupts the flow of cerebrospinal fluid (CSF) and may cause it to build up in the spinal cord. This buildup of fluid within the spinal cord is called a syrinx (Fig. 32.2).

To be considered a Chiari I malformation, the cerebellar tonsils must extend downward into the spinal canal at least 5 mm. Typically, individuals are thought to be born with this malformation; however, some patients may be found to have cerebellar tonsils that are pathologically descended into the spinal canal due to too much pressure in the head or due to brain tumors. More

than one family member may be diagnosed with a Chiari malformation.

Chiari malformations can be classified into several types including:

- Chiari 0 – The presence of a syrinx without evidence of frank tonsillar herniation (movement of the cerebellar tonsils into the spinal canal). These cases are only diagnosed once surgery results in an improved syrinx.
- Chiari I – At least 5 mm of tonsillar herniation into the cervical spine, with or without a syrinx. This is the most common form of these malformations.
- Chiari II – Seen only in patients with spina bifida (born with the membranes and/or parts of the spinal cord in a sac on the back). The cerebellum and brain stem herniate into the spinal canal and there may or may not be a syrinx.
- Chiari III – Very rare and the most severe form of cerebellum and brain stem movement into a sac on the back of the head.

Signs and Symptoms

Symptoms of the Chiari malformations vary depending on age and the type of malformation. The most common symptom in these patients is headaches. The headaches are located at the base of the skull/neck area. They are brought on by certain activities such as coughing, sneezing, straining, or exercise and do not last a long time. Headaches have a quick onset and quick relief when the patient stops the activity. Other symptoms may include severe snoring, hoarse voice, difficulty swallowing, choking, abnormal eye movements, weakness, numbness, or tingling in the arms/legs. The list of potential symptoms can be long.

Sometimes a Chiari malformation is diagnosed when a patient is found to have an abnormal curvature of the spine called scoliosis. When present, the scoliosis is due to an underlying syrinx, which is caused by the Chiari malformation. When the Chiari is operated and the syrinx improves, the scoliosis often improves if not severe to begin with.

Diagnosis

A Chiari malformation is best diagnosed with an MRI of the brain and neck. To be considered a Chiari I malformation, the cerebellar tonsils must extend downward into the spinal canal at least 5 mm. A CT scan alone cannot reliably diagnose a Chiari malformation. Occasionally, a Chiari malformation is found when a patient is being evaluated for another condition. Once a Chiari malformation is identified, the individual will be evaluated by a neurosurgeon. The neurosurgeon may request additional tests to be performed to further assist with the diagnosis and treatment. These may include plain x-rays of the neck, MRI of the spine, and swallowing and sleep studies. The MRI of the complete spine will allow the neurosurgeon to evaluate for the presence of a syrinx. The sleep and swallowing studies help evaluate brain stem function.

Treatment Options

Not every individual with a Chiari malformation will require surgery. In fact, most children seen because of an x-ray diagnosis of a Chiari malformation do not have symptoms caused by the malformation. If the individual is not experiencing any symptoms related to the Chiari malformation, the neurosurgeon may recommend routine follow-up to monitor for any future changes. If the individual's symptoms are not related to the Chiari malformation, they may be referred to a neurologist for medical management of their symptoms.

If the neurosurgeon determines that the symptoms are worsening or becoming life altering, surgery may be recommended. If a patient has a large syrinx with a Chiari malformation, then surgery is usually offered.

Surgery

The surgical procedure (called a posterior fossa decompression) carries risks and should not be taken lightly. The goal of this procedure is to

make more room at the base of the skull for the herniated cerebellum and allow the spinal fluid to flow in a normal fashion.

The surgical team consists of a neurosurgeon, an anesthesiologist, and the operating room staff. Once the patient is in the operating room, the anesthesiologist will administer medication to put them to sleep. At this time, the neurosurgeon will assist in positioning the individual face down on the operating table holding the head in a surgical frame. The surgical area, extending from the base of the skull to the upper neck, is prepped with a cleaning solution and the hair will be clipped or shaved. The neurosurgeon will start by making an incision in the skin and pulling back the muscles and other soft tissues to expose the skull and upper neck. A portion of the skull is removed at this time (Fig. 32.3). Depending on the severity of the Chiari malformation, it may be necessary to remove a portion of the upper cervical spine. The neurosurgeon may or may not open the covering of the brain (called the dura mater). If the decision is made to open the dura, then a patch will be sewn over the opening to provide more room. This procedure may take several hours.

Postoperative Period

After surgery, the patient is observed in the intensive care unit overnight. They will be monitored closely for any complications. If no problems occur overnight, the individual will be transferred to a room, usually on the surgical floor. Neck pain/stiffness is the main complaint after this type of surgery. Nausea and vomiting may also occur but, in general, last for the first 2 days. The estimated hospital stay is 2–4 days.

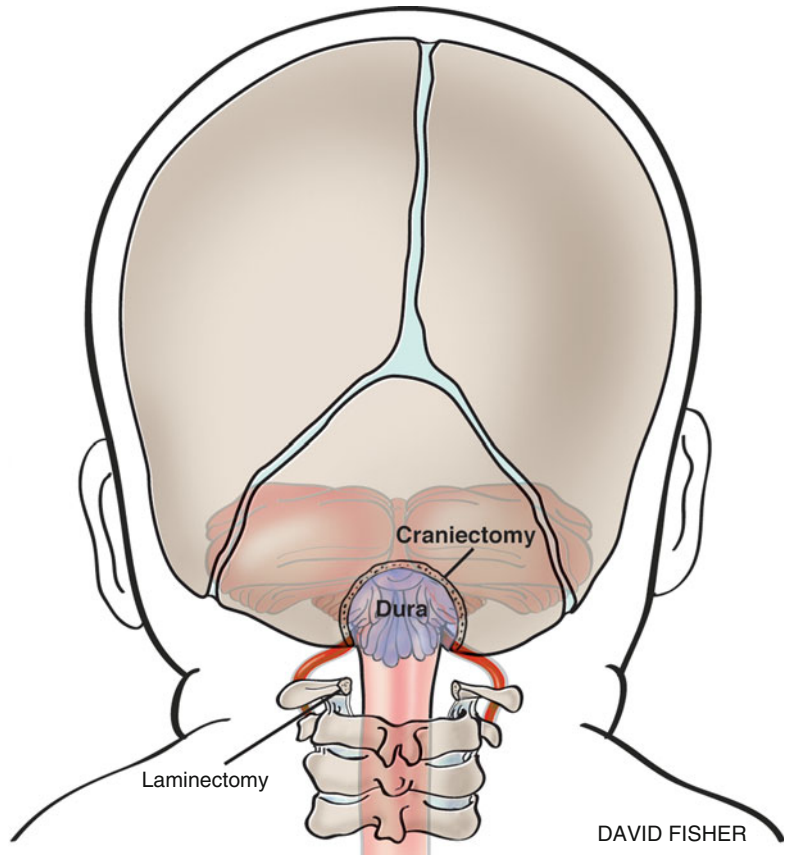

Fig. 32.3 General illustration of the parts of the skull and upper spine that are removed during a posterior fossa decompression

Complications

The risk of complications with this surgical procedure is quite low.

The complications that may occur include:

- Bleeding
- Infection – This can either be on the outside of the incision (superficial) or deep in the incision. If the infection is superficial, the neurosurgeon may choose to treat the infection with antibiotics that are taken by mouth. If an infection appears to be more severe, then the patient may need to return to the operating room for the incision to be washed out and reclosed. The patient may require IV antibiotics for 10–14 days.
- Cerebrospinal fluid (CSF) leak – This usually occurs only if the surgeon opens the dura (coverings) during the surgical procedure. This increases the risk of an infection called meningitis. Once a leak occurs, the neurosurgeon may place additional sutures (stitches) in the deeper layer of the wound. If the spinal fluid continues to leak, additional surgery may be performed to repair the leak.
- Fluid collection under the incision – Fluid can accumulate under the skin without leaking through the incision. This is called a pseudomeningocele. The treatment for this depends on the size and duration of the fluid collection. If the fluid increases in size over several days, the individual may need additional surgery.

Post Hospitalization

Wound Care

The surgeon will typically place a dressing over the incision site. The dressing will be removed by your surgeon. After this, the incision site should be washed daily with plain soap and fresh tap water. The incision should be gently washed and not scrubbed with the fingernails. Do not apply lotions or creams to the site unless instructed to by your surgeon. Do not submerge the incision under water for the first week after surgery.

Activity

After surgery, patients will be tired and have some discomfort near the operative site. Most pain can be treated with over-the-counter pain medicines. The postoperative discomfort will gradually get better over days to weeks. The patient may resume normal activities when they feel they have returned to their baseline. This time varies from patient to patient but is usually in a few weeks. Patients should try to avoid trauma to the area of operation. For pediatric patients, it is recommended that they do not participate in P.E. or sports for 3 months.

Reasons to Call Your Surgeon

Fever – 101.5 F or higher that is persistent or not relieved by medication
Any drainage from the incision site – red like blood, white like puss, or clear like spinal fluid
Headaches that increase in frequency or severity and are not relieved with over-the-counter medications
Continued nausea or vomiting
Altered sensations in the arms or legs
Worsening pain
Fluid collection at the incision site

Follow-Up

You will see your neurosurgeon after surgery for a wound check in 1–3 weeks. This visit may consist of removing sutures/staples, evaluation of symptom relief, discussion of returning to school or work, and planning of future testing and appointments. An MRI is not necessary for this appointment. If a preoperative syrinx was present, an MRI will be scheduled 3–6 months after the procedure to allow time for improvements.

Further Reading

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Duraplasty Versus Non-dural Opening for the Treatment of Pediatric Chiari Malformation, Type I

33

Olufemi Ajani and Todd C. Hankinson

Abstract

Chiari Malformation, Type I (CMI) is characterized by the herniation of the cerebellar tonsils through the foramen magnum and into the upper cervical spinal canal. Children with CMI may present symptomatically or this entity may be found incidentally. When intervention is required, surgery, generally through posterior fossa decompression, represents first-line treatment for children with CMI. In the pediatric population, there is variability with regard to whether or not the dura is opened as a component of this procedure and if additional intradural maneuvers are performed. This chapter discusses the current literature relevant to this aspect of surgical treatment for children with CMI.

Introduction

Chiari Malformation, Type I (CMI) is characterized by the herniation of the cerebellar tonsils through the foramen magnum and into the upper cervical spinal canal. Children with CMI may present symptomatically or this entity may be found incidentally. When intervention is required, surgery, generally through posterior fossa decompression, represents first-line treatment for children with CMI. In the pediatric population, there is variability with regard to whether or not the dura is opened as a component of this procedure and if additional intradural maneuvers are performed. This chapter discusses the current literature relevant to this aspect of surgical treatment for children with CMI.

Of note, if hydrocephalus is present, appropriate CSF diversion should be undertaken prior to any other surgical intervention. This may be accomplished through the insertion of a ventricular shunt or performance of an endoscopic third ventriculostomy [1, 2]. Additionally, this chapter does not discuss the role of intradural maneuvers (i.e., tonsillar reduction/resection) that may be performed along with dural opening procedures. Surgical management for patients with the more recently described Chiari 0 (syringohydromyelia in the absence of cerebellar tonsillar herniation) and Chiari 1.5 (tonsillar herniation with associated brain stem herniation) are based on the principles that will be discussed here in the context of CMI.

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General Concepts in Surgical Intervention for CMI

First-line surgical therapy for patients with CMI in the absence of hydrocephalus is posterior fossa decompression (PFD) via midline suboccipital craniectomy and (generally) removal of the posterior arch of the atlas. This procedure may be completed with or without subsequent dural opening. PFD attempts to reestablish bidirectional CSF flow across the craniocervical junction. This is accomplished through the expansion of the posterior fossa subarachnoid space, which provides decompression of the cerebellar tonsils and brain stem. PFD may also eliminate the craniospinal CSF pressure differential that is postulated to contribute to syrinx formation [3]. For the remainder of this discussion, the term "posterior fossa decompression," when used alone, will refer to bony suboccipital decompression with dural scoring or splitting but without the opening of both layers of the dura mater or the underlying arachnoid mater. Most commonly, PFD is undertaken with duraplasty (PFDD) with or without cerebellar tonsil coagulation or resection. Other intradural interventions, such as fourth ventricular stenting and syrinx shunting, have been largely abandoned or are reserved for second- or third-line therapies [4–7].

Decision-Making Regarding Surgical Technique

Once the decision to operate has been made, the surgeon must determine the most appropriate extent of decompression. The goals of surgery in the CMI population include improvement/resolution of symptoms, stabilization/improvement of scoliosis (when present), and diminution of radiographic syringomyelia (when present). With regard to the postoperative assessment of syringomyelia, there is some debate regarding the extent and timing of diminution that is necessary to demonstrate effective treatment [8, 9].

Studies Directly Comparing Surgical Techniques

Despite significant literature describing the treatment of CMI, no randomized trials comparing PFD against PFDD have been completed. The current literature includes retrospective single institutional series, one meta-analysis, and three surveys [5, 7, 10, 11] (Table 33.1).

Durham and Fjeld-Olenec [10] published a meta-analysis of studies that directly compare cohorts of pediatric patients who underwent PFD with cohorts that were treated with PFDD. A total of 7 studies met their inclusion criteria [12–18]. The authors concluded that patients who undergo duraplasty are less likely to require reoperation (2.1 % vs. 12.6 %) for persistent or recurrent symptoms but are more likely to experience CSF-related complications (18.5 % vs. 1.8 %). There was no statistical difference in clinical outcomes between the two groups, specifically with regard to symptom improvement and syringomyelia. Rates of clinical improvement were 65 % in the PFD patients and 79 % in the PFDD patients. Rates of radiological syrinx improvement were influenced by small numbers in some studies, but were 56 % in the PFD patients and 87 % in those undergoing PFDD. The authors appropriately acknowledged that their conclusions were limited by the patient selection methods of the studies they examined. Among the 7 papers, 5 used intraoperative ultrasound to help determine whether or not to perform a dural opening [13–15, 17, 18]. The inherent subjectivity of this technique limits the extent to which the resultant findings may be generalized. Additionally, no study included randomization or blinding.

Haroun and colleagues [5] assessed expert opinion as an indicator of current practice. In 2000, they reported that 25 % of survey respondents would perform PFD for children with symptomatic CMI, while 32 % recommended PFDD, and 55 % recommended further intradural manipulations (some respondents chose >1 intervention). Schijman and Steinbok [7] surveyed the membership of the International Society of Pediatric Neurosurgery. Their results indicated

Table 33.1 Rates of symptom/syrinx improvement and reoperation in studies including both techniques

Author (year)	Pts	Dural opening	Clinical improvement (%)	Syrinx improvement (%)	Scoliosis stable/ improvement (%)
Mutchnick (2010) [11]	56	N	49 (87.5)[a]	NR	NR
	64	Y	62 (96.9)[a]	NR	NR
Galarza (2007) [16]	20	N	4 (33.3, $n=12$)	2 (40, $n=5$)	NR
	21	Y	11 (73.3, $n=15$)	0 (0, $n=2$)	NR
	19	Y[b]	8 (88.9, $n=9$)	7 (100, $n=7$)	NR
Yeh (2006) [13]	40	N	36 (90.0)	4 (66.7)	1 (100)
	85	Y	83 (97.6)	17 (85)	9 (100)
Limonadi (2004) [17]	12	N	1.67[c]	NR	NR
	12	Y	1.53[c]	7 (70, $n=10$)	NR
Navarro (2004) [18]	56[d]	N	40[d] (72.2)	NR	NR
	24[d]	Y	16[d] (68.4)	NR	NR
	29[d]	Y[b]	17[d] (60.8)	NR	NR
Ventureyra (2003) [14]	6	N	4 (66.7)	0 (0, $n=2$)	NR
	10	Y	10 (100)	5 (100, $n=5$)	NR
Munshi (2000) [12]	11	N	8 (72.7)	3 (50.0, $n=6$)	NR
	21[e]	Y	18 (85.7)	7 (63.6, $n=11$)	NR

NR not reported
[a]Extrapolated from reoperation rates
[b]With intradural maneuvers
[c]Aggregate scoring system with range from −1 to 2, with 2 = all preoperative symptoms resolved (p = NS)
[d]Extrapolated from percentages
[e]Dural opening as initial procedure

that 76 % of pediatric neurosurgeons always open the dura mater when treating CMI. More recently, Rocque and colleagues [19] published the results of a 2006 survey of the attendees of the American Society of Pediatric Neurosurgery annual meeting. The respondents were presented four cases of a child with CMI, each with a "large" syrinx. Details regarding symptom severity, patient age, and syrinx location varied between the scenarios. With regard to the cases presented, 63–80 % of respondents indicated that they would perform duraplasty with or without further intradural maneuvers, while 8–14 % indicated that they would perform bony decompression alone or with intraoperative ultrasonography to determine if duraplasty was necessary. The results of this survey have been used in the design of a prospective clinical trial that intends to use radiographic evidence of syrinx reduction as the primary outcome measure.

Mutchnick and colleagues [11] published a retrospective review of their institutional experience performing PFD for children without syringomyelia and PFDD for those with a syrinx. There were a total of 121 patients. The authors found that 12.5 % of PFD patients required reoperation for symptom recurrence while 3.1 % of PFDD patients required reoperation. Conversely, the authors report significantly shorter operative time and length of hospital stay with PFD. They also report lower requirements regarding analgesic use and lower cost associated with PFD. As such, they conclude that there is a role for PFD although at this time it is difficult to know which patients are likely to have a suboptimal clinical outcome.

Studies of PFD Without Dural Opening

Intraoperative electrophysiological assessments have provided evidence of functional decompression during PFD. Groups from the Children's Hospital of New York/Columbia University and Ohio State

University reported that improved conduction of nerve impulses through the brain stem occurs after bony decompression rather than after dural opening [20–22]. Additionally, several groups report the utility of intraoperative ultrasound findings to aid their decision-making with regard to dural opening in children with CMI [13, 18, 23–25]. Yeh and colleagues [13] assessed preoperative characteristics that were associated with successful surgical treatment. The authors reported that age less than 1 year was associated with a high rate of success following PFD. Spinal symptoms (motor, sensory, or scoliosis) and a greater magnitude of tonsillar descent were more likely to require PFDD.

Clinical Outcome

A pair of single-center series from Italy reports excellent results in children who underwent PFD alone [8, 26]. Caldarelli and colleagues [8] reviewed their experience with PFD in 30 children. After a mean follow-up period of 4.7 years, 28 patients (93.3 %) demonstrated a "significant improvement in their clinical condition." Genitori and colleagues [26] reported the results of their experience using PFD in 26 patients. Among 16 (61.5 %) patients without syringomyelia, 13 (81.3 %) had complete symptom resolution and the remaining 3 (18.8 %) had partial resolution. Among 10 patients with syringomyelia, symptoms improved or resolved in all cases with the exception of one of three cases of scoliosis (33.3 %) and one of five cases of sensory loss (20 %). Rates of complete symptom resolution, however, ranged from 25 % (sensory loss) to 100 % (vertigo). Two patients (7.7 %) required reoperation. The authors acknowledged that it is difficult to draw definitive conclusions from their study due to the small numbers in each group.

Syrinx Resolution

At this time, there are no clear guidelines regarding the extent or timing of syrinx resolution that should be expected following surgical treatment for CMI (Fig. 33.1). Wetjen et al. [9] have stated that the absence of syrinx distention is more important than complete collapse. Caldarelli and colleagues [8] state that, in the context of clinical improvement, radiological change (either in syrinx size or posterior fossa subarachnoid volume) may not be mandatory for a successful result. In their series, syringomyelia was present preoperatively in 12 of 30 patients (40 %). Postoperatively, half of these patients (6) had a decrease in the size of the syrinx. Two patients (6.7 %) demonstrated recurrent symptoms and postoperative syrinx growth (one de novo and another who had a syrinx preoperatively) and required reoperation. In only the PFD groups of the studies included in their meta-analysis, Durham and Fjeld-Olenec [10] reported an aggregate 56.3 % (9 of 16 patients) rate of syrinx reduction. This did not differ statistically from the 87.0 % (40 of 46 patients) rate calculated for the PFDD group. As previously mentioned, in the series of Genitori and colleagues [26], 10 of 26 (38.5 %) patients presented with syringomyelia. Following PFD, the syrinx disappeared in 8 (80 %). The remaining 2 children (7.7 %) had an initial clinical improvement but underwent duraplasty for persistent syringomyelia.

Scoliosis Improvement

The two previously mentioned Italian studies describe outcomes with regard to scoliosis following PFD without duraplasty in a very small number of patients. Genitori and colleagues [26] reported improvement in 2 of 3 patients, and Caldarelli and colleagues [8] reported mild improvement in 2 of 2 patients. In their series of 21 patients with CMI, syringomyelia, and scoliosis, Attenello and colleagues [27] described a single patient who underwent PFD. This patient had scoliosis progression and underwent reoperation with duraplasty.

Studies of PFD with Dural Opening

Clinical Outcome

In a series of 500 pediatric patients with CMI who underwent surgical treatment with PFDD, Tubbs and colleagues reported a 3 % rate of reoperation for continued symptoms or persistent "large syringomyelia," a 2.4 % complication rate, and an 83 % rate of relief of preoperative signs or symptoms. Of note, the authors reported no cases of aseptic meningitis [28]. Clinical improvement rates of 92–100 % and complication rates of 0–21.1 % have been reported in other series

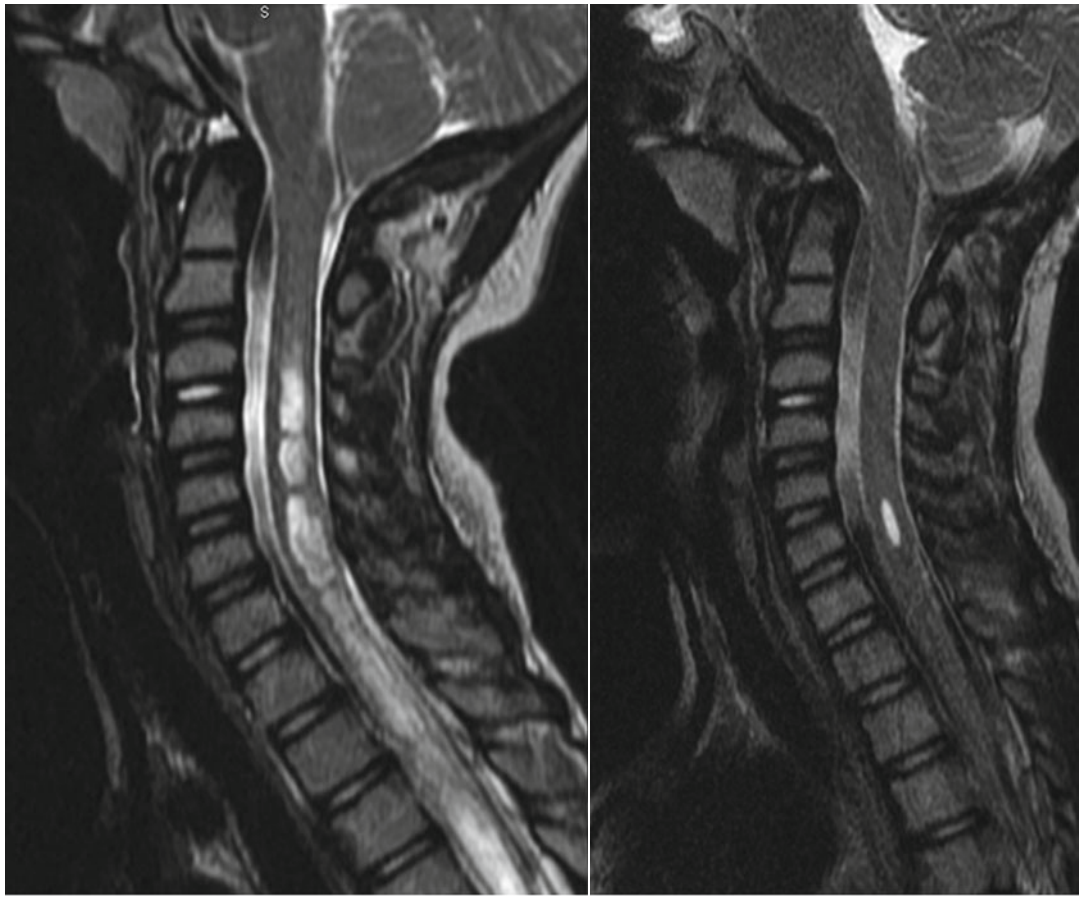

Fig. 33.1 Pre- and postoperative sagittal T2-weighted MRI demonstrating significant improvement of holocord syringomyelia in a child with CMI who was treated with PFD without duraplasty. The postoperative image was acquired 13 months after surgery (Courtesy of N. Feldstein)

[20, 21, 29–37]. Attenello and colleagues [35] examined outcomes and complication rates comparing different materials for duraplasty (autograft vs. synthetic allograft). The authors reported mild to moderate symptom recurrence at 16 months follow-up in 14/67 (20.9 %) patients, with 4 of these (6.0 %) requiring revision decompression. Seventeen percent of patients ($n=10$) demonstrated a radiographic pseudomeningocele with only 1 of these becoming symptomatic. A total of 5 patients (7 %) suffered CSF-related complications: 2 (3 %) with CSF leak and 2 (3 %) with aseptic meningitis. Parker and colleagues [37] reported a doubling of their CSF-related complication rate (to as high as 56 % in one subgroup) when specific combinations of dural graft and tissue sealant were employed.

Syrinx Resolution

Radiographic syrinx improvement following PFDD in pediatric series is reported to range from 55 to 100 % [20, 21, 24, 28, 30, 32–36]. As previously mentioned, Durham and Fjeld-Olenc [10] found an overall rate of 87 % syrinx reduction in the PFDD arms of studies that compared PFD with PFDD. The reliability of data regarding syrinx outcomes may result both from the lack of a standard definition of syrinx improvement and also from the small sample size of many studies. Additionally, the clinical relevance of specific changes in syrinx characteristics is not well understood (Fig. 33.2).

Following initial PFDD in 500 patients, Tubbs and colleagues [28] reported that 13 of 285 (4.6 %) required reoperation for "persistent syrin-

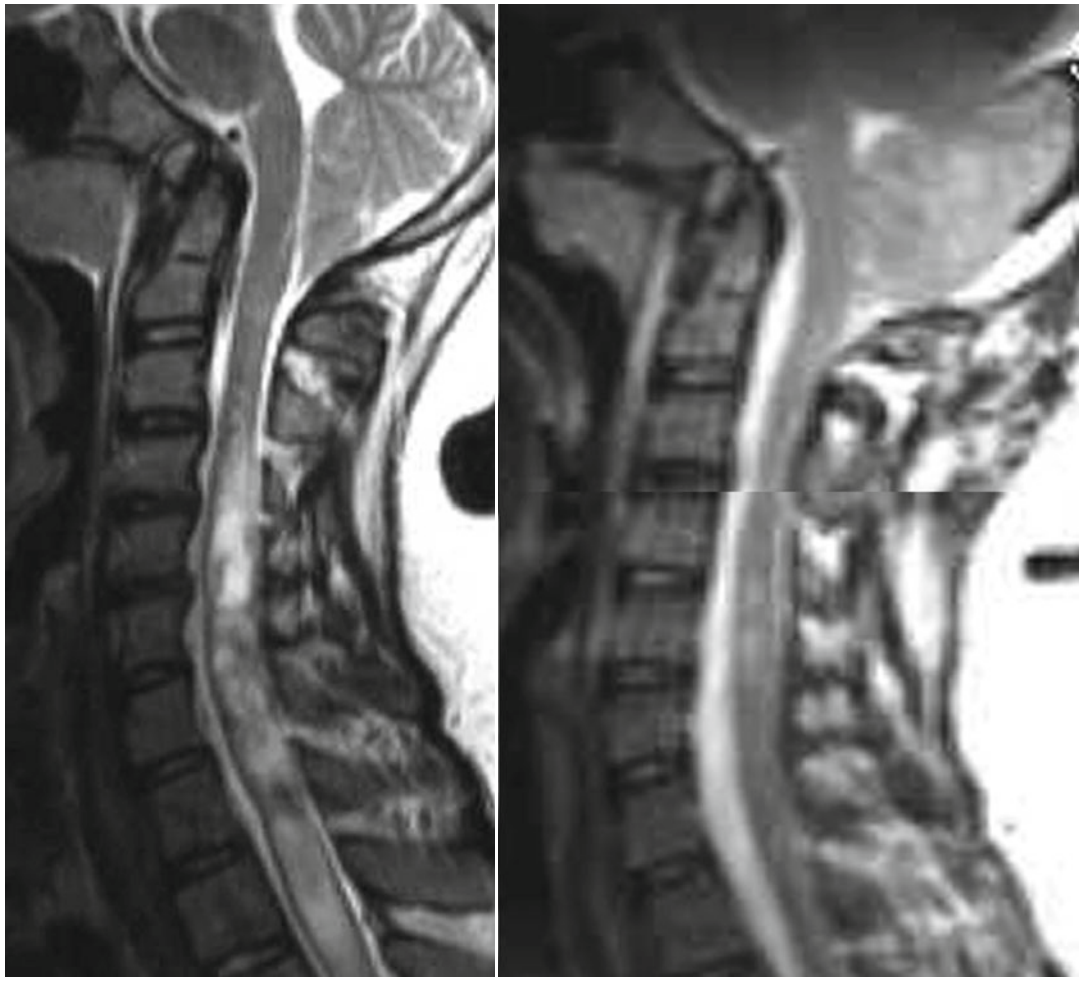

Fig. 33.2 Pre- and postoperative sagittal T2-weighted MRI demonstrating significant improvement of holocord syringomyelia in a child with CMI who was treated with PFD with duraplasty. The postoperative image was acquired 3 months after surgery (Courtesy of M. Handler)

gomyelia". Eleven of these (84.6 %) resolved with reoperative decompression including unilateral tonsillar coagulation (Fig. 33.1). Attenello and colleagues [24] retrospectively examined the syrinx response rate following hindbrain decompression in 49 consecutive children with CMI, 46 of whom underwent PFDD and 3 PFD alone. They reported a 55 % overall syrinx improvement rate at 14 months, with 56.5 % (26/46) of those in the PFDD group improving. Of 5 (10.2 %) patients who underwent repeat decompression, 1 (2.0 %) was due to syrinx expansion at 5 months after PFDD. Thirty-nine of 49 (79.6 %) patients had preoperative symptoms attributable to syringomyelia. Twenty-one (54 %) of these experienced symptom resolution. Complications included aseptic meningitis and wound breakdown in 2 patients (4 %) each and pseudomeningocele in 1 (2 %). None of these complications required reoperation. In the PFD group, 2 of the 3 did not have syrinx improvement. One required reoperation with duraplasty and another underwent spinal fusion for scoliosis.

As previously stated, there is currently no standard definition for the rate or magnitude of syrinx regression that reflects satisfactory treatment. A subjectively significant decrease in the syrinx size on the first postoperative imaging examination is reassuring to the surgeon; however, syrinx obliteration is likely unnecessary [8, 9]. Additionally, delayed syrinx dissipation has been reported [38].

Scoliosis Progression

In the vast majority of cases, scoliosis in the context of CMI is associated with syringomyelia [39]. Details regarding the neurological impairments that connect these two entities are yet to be elucidated. It is believed, however, that scoliosis may result from imbalanced innervation of axial musculature due to syrinx-generated lower motor neuron injury [40–42]. Consistent with this theory, multiple authors have reported scoliosis improvement following PFDD in children with CMI, although Brockmeyer and colleagues found that a decrease in syrinx size did not necessarily correlate with scoliosis improvement [43]. Reported rates of scoliosis improvement and progression vary widely. Rates of improvement are reported at 0–73 % and rates of progression are 18–72 % [6, 43–51]. In some series, younger children (less than 8–10 years) have been less likely to suffer from scoliosis progression [6, 43, 45, 50, 51]. Female gender and a smaller presenting Cobb angle have also been associated with improved outcomes. In 20 pediatric patients with CMI-associated scoliosis treated by PFDD, Attenello and colleagues [27] reported that 8 (40 %) demonstrated a postoperative improvement of their scoliosis and 9 (45 %) progressed. The authors reported that an increased magnitude of scoliosis curve at presentation was predictive of scoliosis progression, as were thoracolumbar junction scoliosis and a lack of postoperative radiological syrinx response.

Summary

The Case for PFD

Electrophysiologic data support the assertion that effective PFD occurs with bony decompression and dural scoring, not necessarily requiring dural opening [20–22]. Although rates of reoperation for persistent or recurrent symptoms are higher with PFD, the technique is attractive because it minimizes potential surgical complications. Theoretical complications that are avoided with PFD include pseudomeningocele, chemical meningitis, bacterial meningitis, arterial injury, venous sinus bleeding, stroke, and hydrocephalus. Several studies have demonstrated that CSF-related complication rates are lower with PFD than PFDD [11–13, 17, 18]. Additionally, non-dural opening PFD is likely to require less operative time [11, 17], results in less postoperative pain, and may be of lesser financial burden to the healthcare system [11]. The case for PFD is additionally strengthened by the inability of studies that directly compare PFD to PFDD to demonstrate a statistically significant difference in clinical outcomes. Furthermore, while many studies have demonstrated a trend toward a greater pace and magnitude of syrinx collapse following PFDD, the relevant details of this outcome measure are yet to be determined, making syrinx resolution a suboptimal method for the assessment of efficacy regarding hindbrain decompression for CMI. Lastly, the use of PFD does not in any way preclude patients from undergoing further decompression should this become necessary (Table 33.2).

The Case for PFDD

Although direct comparisons have not demonstrated a statistically significant difference in clinical outcomes, many consider PFDD to be the treatment that offers the greatest likelihood of improving the presenting signs and symptoms in any given child. Most reports that discuss the clinical efficacy of PFDD demonstrate rates of improvement superior to those of PFD [12–15]. Durham and Fjeld-Olenec [10] demonstrated a significantly lower rate of reoperation following PFDD than PFD (2.1 % vs. 12.6 %), as did Mutchnick and colleagues [11]. Although the meta-analysis also demonstrated a higher com-

Table 33.2 Relative advantages of PFD and PFDD

PFD	PFDD
Lower CSF-related complication rate	Lower reoperation rate
Shorter operative time	Better radiological outcomes
Optional shorter incision	Allows inspection of arachnoid veils/scarring
± Adequate syrinx decompression	± Better clinical outcomes
Shorter hospital stay	
Less postoperative pain	
± Lower cost	

plication rate with PFDD, it must be acknowledged that multiple groups have reported very low complication rates with PFDD [28, 31, 32]. Additionally, up to 12 % of patients with CMI and syringomyelia may harbor a radiographically occult arachnoid veil, which cannot be treated without dural opening [28, 52]. Lastly, there are circumstances, such as rapidly progressive neurological decline or scoliosis, where there is very little debate that PFDD is necessary.

Conclusions

At this time, pediatric neurosurgeons lack high-quality (Class I or II) evidence to guide decision-making with regard to the most appropriate surgical technique for the management of CMI. Most authors concur that, in the absence of hydrocephalus, hindbrain decompression represents the best first-line treatment for CMI. However, there is still debate regarding the role of dural opening. Current data leave the surgeon and family to choose between a procedure that is more likely to require reoperation (PFD) and one that is more likely to result in perioperative CSF-related complications (PFDD). The frequency of these suboptimal outcomes (12.6 and 18.5 %, respectively, in Durham and Fjeld-Olenec's meta-analysis [10]) does little to clarify which approach is most appropriate for a given patient. Furthermore, wide ranges of clinical efficacy and complications have been reported, and additional complicating factors (such as length of hospital stay, perioperative pain, and hospital cost) cloud decision-making. Lastly, the spectrum of presentation in children with CMI extends from asymptomatic to potentially life-threatening symptomatology. It is therefore not surprising that no single surgical approach is universally recommended. Efforts to standardize outcome reporting [53] and perform clinical trials for this patient population [19] will hopefully inform future decision-making. Nevertheless, the treating neurosurgeon must always consider the individual characteristics of her/his patient and practice when choosing an operative strategy.

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Conclusions

34

R. Shane Tubbs and W. Jerry Oakes

Abstract

Our understanding of the clinical entities known as the Chiari malformations has tremendously increased over the past 40 years. We have moved from a position of grouping the CIM and syringomyelia patient in the degenerative category to a fundamental understanding of the pathophysiology. This has led to surgical intervention that has generally favorable outcomes. Our understanding that patients with the Chiari II malformation must have adequate CSF diversion is of paramount importance. Additional patients with complex issues of ventral compression and micromovement at the craniocervical junction challenge even the experienced neurosurgeon. However, the understanding of few diseases has progressed so far in such a short time.

The reader of this text has experienced the breadth of knowledge concerning the Chiari malformations. Every aspect of the conditions we could justify has been included. We are that sure other areas will come to us following the publication, but for now, this is the limit of our knowledge. As stated in the introduction, we included a section on syringomyelia not caused by CSF equilibrium issues at the craniocervical junction. This was done because the entities are so tightly linked clinically.

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Much of the background information concerning the embryology and anatomy is discussed in great detail because it is on this material that our fundamental understanding of the disease process is built. Even a cursory glance at the embryology chapters will impress the reader as to how much we actually understand about the early development of this region. No other reference we are aware of has a section of its equal.

Dr. Heiss has provided us with insight into the epidemiology of the human occurrence of these conditions. This area is just beginning to be investigated. The genetics that have been expertly presented goes to emphasize how early we are in our understanding of these problems.

Our two pathology chapters recount the wealth of information concerning the CIIM but how little pathology plays into our understanding of

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the CIM. By investigating the association of CIM with other disease entities, we might gain insight that would help with the genetics analysis as well as the pathophysiology of the conditions. Numerous disease processes may cause a hindbrain hernia as a final common pathway.

One of the most intriguing chapters was contributed by Dr. Marino, our veterinary colleague. Through clinical insight, the discovery of the relatively common occurrence of CIM and syringomyelia in certain dog breeds is of genuine interest. We would wonder if it will be possible to evaluate many of the technical issues associated with the human surgical decompression by randomizing treatment options in the veterinary arena. Few surgical areas are as ripe for exploration as this one.

Dr. Barkovich and colleague review the explosion of information that has occurred in the radiological diagnosis of these conditions. They rightly emphasize that the movement of the cerebellar tonsils through the foramen magnum is not a true congenital anomaly but simply a reaction to other forces. If there is a pressure differential between the intracranial and intraspinal compartments in utero prior to the full development of the cerebellar tonsils, the vermis and brain stem move caudally. If this same pressure differential occurs later in development, once the tonsils have formed, then they are displaced. The cause for this displacement may be elevated intracranial pressure (hydrocephalus, brain tumor, etc.) or inadequate skull growth (growth hormone deficiency, some forms of craniosynostosis, etc.). Alternatively, the cause of the tissue displacement may be abnormally low intraspinal pressure either in utero (myelomeningocele) or following delivery from some type of spinal CSF leak or diversion (e.g., lumboperitoneal shunt).

These issues and relationships are further explored by Dr. Iskandar and colleague in their discussion of the pathophysiology and CSF flow characteristics of CIM patients. Much more will come from this area in the future. At this point in time, CSF flow studies are interesting but of little concrete assistance in making clinical decisions.

The reader is treated to a brief glimpse into the wealth of experience of a true master of the craniocervical junction region in Dr. Menezes' discussion of the bony anomalies found in this region. It is truly difficult to condense the experience of thousands of patients into this succinct chapter, but we believe it was accomplished.

As mentioned previously, the chapter on syringomyelia unassociated with hindbrain hernias was specifically added to help the reader analyze patients who present with similar complaints and findings as those seen with syringes due to a CIM. We specifically asked Dr. Klekamp to address the subarachnoid webs causing syringes, which are quite difficult to detect radiologically and are only now appreciated as another cause of an "idiopathic" syrinx. His second chapter is devoted to reoperation of adults with continued clinical symptoms. The honest discussion of a difficult group of patients is well worth the reading and we can all profit from his experience.

Scoliosis and the CIM have a separate chapter because of the importance of this clinical problem. In addition to more conventional information, Dr. Brockmeyer and colleague mention scoliosis seen in CIM patients without the presence of a syrinx. This subgroup of patients is worth additional attention in the future.

Of all the chapters, the discussion of the natural history of both the CIM and CIIM is one of the most important to include in any text devoted to a single clinical entity. How can a physician advise a patient on a course of action or inaction without first knowing what will happen without intervention? What becomes obvious from reading this section is that with the advent of readily available MRI imaging, large numbers of patients are presenting to the neurosurgeon frightened and concerned about their future. Both this chapter and the discussion of our experience in a multidisciplinary Chiari clinic have gone a long way to reassure asymptomatic patients that surgery is not inevitable and that many individuals remain asymptomatic throughout their length of follow-up.

We then summarize two new entities that do not conveniently fit within Chiari's original classification. It is important to point out that the Chiari "0" malformation as described was seen exclusively in the presence of a large syrinx, which resolved following posterior fossa decompression. The hybrid condition known and the Chiari 1.5 has

aspects of the CIM with caudal movement of the cerebellar tonsils without a neural tube defect and caudal movement of the brain stem typical of the CIIM. These patients have more significant challenges in regard to their treatment and outcome.

The clinical presentation of both the pediatric and adult patients with CIM is summarized and commented on by two experienced clinicians. Their insight into the clinical presentation of this group of patients will be helpful to the reader with limited experience or even a senior consultant.

Additional presentations that are unconventional are divided into two sections: those with objective findings and those without. It appears clear that the weight of evidence dismisses any association between the patient with fibromyalgia and any form of hindbrain hernia. The chapter devoted to "unconventional" presentations is a most intriguing group of patients. Many are unique in their presentation, which makes pattern recognition by their primary care physician difficult. Many times, the only hint of the problem is localization of the symptoms to the medullary region of the brain stem. Again, the ready availability of MRI has generated many a surprised referring physician and neurosurgeon with a patient and study of singularly unique findings and symptom complex. This aspect of CIM patients is most interesting and a strong stimulus to look for other unusual situations. The balance between explaining an unusual patient's symptoms localized to the medulla and trying to cure every headache patient with an operation is the difficulty.

One of the more difficult areas to discuss is the association of hydrocephalus and pseudotumor to hindbrain hernias. We do not believe the last work has been written in this area, but the authors summarize the state of our current knowledge.

Dr. Blount discusses the clinical presentation of children with the CIIM. He emphasizes the need to suspect raised ICP as a common determinant in most patients. Surgical inspection of the shunt is mandatory before any consideration of posterior fossa surgery. The surgical emergency of the situation in infancy is worth reemphasis.

Treatment of the adult CIM patient is summarized by Drs. Heiss and Oldfield based on their extensive experience at the National Institutes of Health. The reader would be well advised to take many of their surgical tips to heart in approaching their own patients.

The two chapters dealing with the surgical techniques employed in pediatric Chiari decompression do not explore what options are available but rather walk the reader through a single approach and attempts to warn the neurosurgeon of potential pitfalls and how to avoid them. The myriad of surgical options will continue to be explored as long as more than one neurosurgeon is doing these procedures.

Of the various techniques that are available, the controversy over opening or not opening the dura is most poignant. Dr. Hankinson and colleague summarize the known information well and outline the advantages and disadvantages of each technique in an evenhanded manner.

No text on a surgical subject would be complete without a section on complications and outcomes. Both of these areas are covered in detail by experts with significant experience.

We include a brief lay comment written by two experienced nurses on what to expect as a patient being operated upon for a CIM or CIIM. We attempt to pitch this section at the average patient/parent level and use language that would be understood by the vast majority of the public. We hope this section could be shared with potential surgical patients and their families.

All in all, one could not but be impressed with the progress we have made in our understanding of these clinical entities in the past 40 years. We have moved from a position of grouping the CIM and syringomyelia patient in the degenerative category to a fundamental understanding of the pathophysiology. This has led to surgical intervention that has generally favorable outcomes. There are many exceptions to this statement with generalized headaches that do not resolve to patients whose CSF egress from the fourth ventricle is made worse because of iatrogenic contamination of the subarachnoid space with blood and surgical trauma to the pial surface of the medial cerebellar tonsil. Additional patients with complex issues of ventral compression and micromovement at the craniocervical junction challenge even the experienced neurosurgeon. However, few diseases have progressed so far in such a short time.

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