Epidemiology

2

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Contents

2.1 Introduction

Syringomyelia is a polyaetiological disorder, characterized by abnormal fluid-filled cavities within the spinal cord. It causes typical neurological symptoms and signs as it expands. Many associated disorders and anomalies that can cause syringomyelia have been described (Williams 1995), including Chiari malformation type 1, trauma, intramedullary tumours and inflammation. Despite the ready availability of diagnostic methods and surgical treatments for syringomyelia in developed countries, this pathology continues to present medical and social problems. Syringomyelia accounts for about 5 % of paraplegias (Sedzimir et al. 1974; Williams 1990) and the quality of life for patients with syringomyelia is generally lower than that of the general population, being comparable with that of patients with heart failure or malignant neoplasms (Sixt et al. 2009).

2.2 Geographical and Ethnic Variation

The mean prevalence of MRI-confirmed syringomyelia ranges, in different countries, between 2 and 13 per 100,000 inhabitants (Table 2.1). There are also some small regions where the prevalence is even higher, reaching levels of 80–130 per 100,000 population (Borisova et al. 1989). The ratio of males to females varies between 1:2 and equal (Brickell et al. 2006; Sakushima et al. 2012; Sirotkin 1972).

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The recorded incidence and prevalence of syringomyelia have not been constant through time. Between 1949 and 1978, for example, in southwest Germany, recorded cases fell from 25 to less than 1 case per year, per 100,000 inhabitants (Hertel and Ricker 1978; Schergna and Armani 1985). It was suggested that the enormous change in living habits over this period might have accounted for the decrease. In contrast, an epidemiological study in New Zealand found that the incidence of syringomyelia increased between 1961 and 2001, from 0.76 to 4.70 cases per year, per 100,000 population (Brickell et al. 2006). This increasing incidence might have been due to the changing ethnic composition of the population. There are clear ethnic differences in the prevalence of syringomyelia and its associated conditions (Table 2.2), although the extent to which these variations are due to environmental influences, as opposed to genetic factors, remains unknown. Pacific people and Maori have a higher prevalence of syringomyelia than other ethnic groups, and the percentage of Maori and Pacific people in the New Zealand population increased over the study period in the Brickell et al. survey. The population of Pacific people in particular grew 11 times faster than did other ethnic groups. A second possible reason for the increase in recorded incidence in New Zealand is, of course, simply the increased detection of syringomyelia, brought about by improved access to MR imaging.

The Tartar population in the Volga-Ural region of Russia, including Bashkortostan, Tatarstan and other areas, suffers from a particularly high

Table 2.1 Prevalence of syringomyelia

Prevalence (per 100,000 inhabitants)	Geographical region	Reference source
1.94	Japan	Sakushima et al. (2012)
7	USA	Kurtzke (1996)
8.2	New Zealand	Brickell et al. (2006)
12.6	Tatarstan, Russia	Authors' data (2011)

Table 2.2 Ethnic differences in syringomyelia and related disorders

Disorders	Geographical region	Ethnic group	Prevalence (per 100,000 inhabitants)	Reference source
Syringomyelia	New Zealand	Pacific people Maori Caucasians and other	18.4 15.4 5.4	Brickell et al. (2006)
Syringomyelia associated with CM1	New Zealand	Pacific people Maori Caucasians and other	16.1 8.3 3.2	Brickell et al. (2006)
Syringomyelia	Russia, Bashkortostan	Tartars Russians Bashkirs	130 0.5–12 0.32–0.6	Borisova et al. (1989)
Syringomyelia associated with CM1	Russia, Tatarstan	Tartars Russians (mainly)	14.8 9	Authors' data (2011)
Chiari malformations with and without of syringomyelia	Russia, Tatarstan	Tartars Russians (mainly)	33.4 23.8	Authors' data (2011)
Syringomyelia associated with scoliosis	New Zealand	Maori and Pacific people	Children with scoliosis more likely than Caucasians to have syringomyelia	Ratahi et al. (2002)
Syringomyelia	USA	African-Americans and Caucasians	Syringomyelia more prevalent in African-Americans	Tipton and Haerer (1970)

Table 2.3 Geographical distribution of syringomyelia and related disorders

Disorders	Countries and regions with high prevalence (per 100,000 inhabitants)	Countries and regions with low prevalence (per 100,000 inhabitants)	Reference sources
Syringomyelia	*Germany* Southwest	*Germany* Northeast	Hertel and Ricker (1978)
	Italy Piedmont, Valle d'Aosta, Toscana and Marche		Ciaramitaro et al. (2011)
	Russia Central regions in the valleys of the rivers Volga, Kama, Vyatka, Belaya	*Russia* South regions	Borisova et al. (1989)
	Russia Bashkortostan East and Northwest (80–130) Tatarstan North (63–83) Samara region Northeast (43–62)	*Russia* Bashkortostan Southwest (0.3–0.6) Tatarstan Southeast (4.3–5.5) Samara region South (6–20)	Sirotkin (1972) Borisova et al. (1989) Borisova and Mirsaev (2007) Authors' data. (2011)
Chiari malformations with and without of syringomyelia	*Russia* Tatarstan North (100–148)	*Russia* Tatarstan Southeast (9–14)	Authors' data (2011)
Craniovertebral anomalies	*India* Uttar Pradesh, Bihar, Rajasthan, part of Gujarat		Goel (2009)
Basilar impression associated with Chiari malformation	*Brazil* Northeast		Da Silva et al. (2011)
Sagittal synostosis associated with Chiari malformation	*Finland*		Leikola et al. (2010)

prevalence of syringomyelia, at 130 per 100,000 inhabitants. In contrast, the prevalence among other ethnic groups, mainly Bashkirs and Russians, in the same geographic region, was no more than 12 per 100,000 population (Borisova et al. 1989; Borisova and Mirsaev 2007). Our own data, collected since 1998, revealed a less pronounced difference in the prevalence of syringomyelia between the Tartars and other groups, at 15 and 9 per 100,000 inhabitants, respectively. In addition, the prevalence among both Tartars and other ethnic groups varied significantly across different regions of Tatarstan, ranging between 3.7 and 93 per 100,000 adults in Tartars and between 2 and 92 per 100,000 in a population composed mainly of Russians.

Elsewhere in the world, the distribution of syringomyelia and related conditions, by country, region and even small territories, is extremely non-uniform (Table 2.3, Fig. 2.1). Such differences have been linked to environmental factors, for example, the size of a community, the distance between a patient's place of residence and a diagnostic centre, the degree of physical exertion exercised by the individual as part of his or her profession, the number of siblings in the patient' family, the order of his or her birth and the infant mortality rate in the patient's family (Borisova et al. 1989; Hertel and Ricker 1978; Sirotkin 1972). Most of the patients with syringomyelia tend to come from large families and originate from the second half of the birth order. Infant mortality is especially high among the brothers and sisters of syringomyelia patients. Patients are more likely to live in small towns and are more likely to be employed in occupations involving

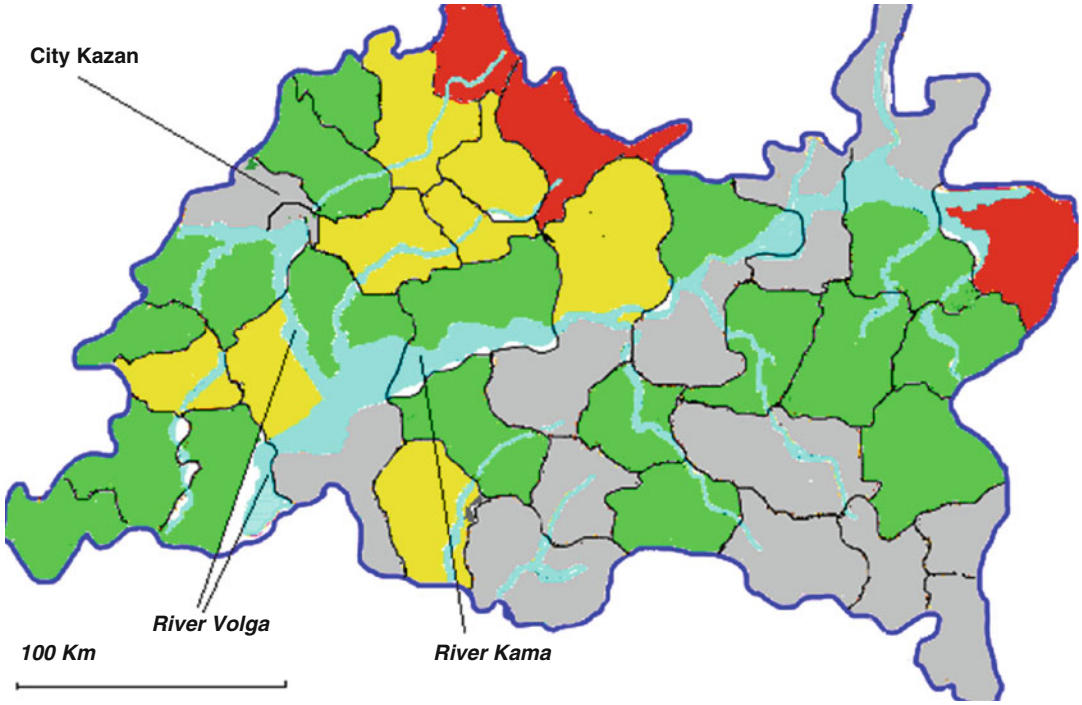

Fig. 2.1 Map of Tatarstan (Russia) with the prevalence of syringomyelia (per 100,000 adult inhabitants). *Red* = very high prevalence (>50); *yellow* = high prevalence (30–50); *green* = moderate prevalence (10–30); *blue* = low prevalence (<10). Regions with very high prevalence of syringomyelia are situated in a compact area in northern Tatarstan (Unpublished authors' data 2011)

hard physical labour. The high prevalence of syringomyelia in the north of Tatarstan may be associated not just with the predominance of the Tartar population in this region but also the employment of these people, mainly in physically demanding jobs in agriculture (author's own data). Interestingly, however, syringomyelia prevalence may also vary with the soil type (Sirotkin 1972).

2.3 Causes of Syringomyelia

A study analysing autopsy results over a 38-year period identified 175 patients with tubular cavitations of the spinal cord. Just over a half of these cases were male and the mean age was just over 40 but with a range from 1 day to 87 years old. Non-neoplastic syringomyelia was found in 60 %, neoplastic cysts in 10 % and syringomyelia ex vacuo (i.e. atrophic syringes occurring with myelomalacia) in 30 % (Milhorat 2000). The reported frequency of the main causes of syringomyelia does, however, vary between clinical and MRI studies (Table 2.4).

The cause of syringomyelia varies between different age groups, with Chiari malformation type 2 being the most common cause in younger patients, whereas in adolescents and adults, Chiari malformation type 1 predominates. In older age groups the cause of the syringomyelia may not always be apparent, and cases are more likely to be given the label of idiopathic (Sakushima et al. 2012).

2.3.1 Chiari Malformations

Most cases of syringomyelia are associated with Chiari malformation type 1, which in turn comprises the commonest abnormality encountered at the craniovertebral junction. It is characterized by underdevelopment of the posterior cranial

Table 2.4 Syringomyelia by cause

Underlying cause	Proportion of all causes of syringomyelia (%)	Geographical region	Reference source
Chiari malformation type 1	26	Germany	Roser et al. (2010)
	32	UK	Williams (1995)
	48	Japan	Sakushima et al. (2012)
	48	Italy	Ciaramitaro et al. (2011)
	50	New Zealand	Brickell et al. (2006)
	77	USA	Speer et al. (2003)
Chiari malformation type 2	4.6	Italy	Ciaramitaro et al. (2011)
	8	Japan	Sakushima et al. (2012)
	2–14	USA	Speer et al. (2003)
Trauma	4	USA	Speer et al. (2003)
	8	Japan	Sakushima et al. (2012)
	10	New Zealand	Brickell et al. (2006)
	19	Germany	Roser et al. (2010)
	24	UK	Williams (1995)
Tumours	0.4	USA	Speer et al. (2003)
	3	UK	Williams (1995)
	5.2	Japan	Sakushima et al. (2012)
	12	Germany	Roser et al. (2010)
	32	Croatia	Orsolic et al. (1998)
Inflammations of the spinal cord and meninges	2	Germany	Roser et al. (2010)
	4	USA	Speer et al. (2003)
	4.4	New Zealand	Brickell et al. (2006)
	5	Japan	Sakushima et al. (2012)
Idiopathic	13–25	Japan	Sakushima et al. (2012)
	16	New Zealand	Brickell et al. (2006)
	28	Germany	Roser et al. (2010)

fossa with overcrowding of an otherwise normally developed hindbrain (Milhorat et al. 1999; Nishikawa et al. 1997). A ubiquitous feature is compression of the retrocerebellar CSF spaces, and about nine out of ten cases have a tonsillar herniation that is at least 5 mm below the level of foramen magnum. Very commonly there are also radiographic signs of cranial base dysplasia, of varying degree (Milhorat et al. 1999). Chiari malformation type 1 has a reported male to female ratio of between 1:0.7 and 1:3.7 (Da Silva et al. 2011; Meadows et al. 2000; Milhorat et al. 1999; Takeuchi et al. 2007). The reported rate of Chiari malformation type 1 as an incidental finding on MRI of the brain ranges from 0.04 to 0.9 % (Meadows et al. 2000; Morris et al. 2009; Vernooij et al. 2007). The reported incidence is higher from studies using high-resolution MRI sequences. One study reported cerebellar tonsillar herniation in as many as 14.4 % of patients presenting with neck pain and/or upper limb symptoms (Takeuchi et al. 2007).

The reported occurrence of syringomyelia in association with Chiari malformation type 1 ranges from 65 to 80 % (Speer et al. 2003). Chiari type 1-related syringomyelia has also been reported as an incidental finding on MRI (Meadows et al. 2000; Nishizawa et al. 2001).

Chiari malformation type 2 is found only in patients with myelomeningocele. It is the leading cause of death in affected individuals under the age of 2, and up to 15 % of patients with early clinical manifestation of Chiari malformation type 2 die by the age of 3 years and nearly a third of survivors have some form of permanent neurological disability (Stevenson 2004). Outcomes in older children, presenting with myelopathy and/or pain, are much better, ranging from 79 to

Table 2.5 Pathologies leading to Chiari type 1 hindbrain hernias

Cranial constriction
Spinal cord tethering
Cranial settling
Intracranial hypertension
Intraspinal hypotension

Table 2.6 Causes of hindbrain hernias

Chiari malformation type 1	57 %
Chiari malformation type 2	1.5 %
Basilar impression/invagination	18–64 %
Hydrocephalus	3–23 %
Tethered cord syndrome	7 %
Craniosynostosis	0.7–17 %

100 % improvement in symptoms following surgery. The prevalence of Chiari malformation type 2 in the general population is 1 in 3,600.

Chiari malformation type 2 is associated with syringomyelia in 35 % of cases (Speer et al. 2003), and it accounts for up to 8 % of the total cases of syringomyelia, with a higher percentage in paediatric practice.

Borderline tonsillar herniation, 2–4 mm below the foramen magnum, has an estimated prevalence of 2.6 per 100,000 population, from all MRI scans of the brain (Takeuchi et al. 2007). Syringomyelia was found in just over half of these patients (Milhorat et al. 1999).

The definition of Chiari malformation type 1 is evolving from that of a simple anatomical description to the concept of it representing the clinical expression of a number of different pathologies. Five broad mechanisms causing cerebellar tonsillar have been described (Table 2.5) (Milhorat et al. 2010; De Souza et al. 2011). These include those which affect the development of the craniocervical structures. For example, the development of Chiari malformation type 1 was seen in 29 % of patients suffering from rickets and in 73 % of all cases of Crouzon's disease. A tight filum terminale has an associated Chiari malformation type 1 in 10 % of cases. Twenty-four percent of pseudotumour cerebri patients had inferiorly displaced cerebellar tonsils. In addition, venous sinus occlusion can be the cause of reversible hindbrain herniation (Novegno et al. 2008). The frequency of these different causes of cerebellar herniation is very variable (Table 2.6) and also has ethno-geographical differences (Da Silva et al. 2011; Milhorat et al. 1999, 2009, 2010; Novegno et al. 2008; Strahle et al. 2011a). Our own observation of 900 adult patients with Chiari malformations, over a 10-year period, found basilar impression in 17 % and non-syndromic craniosynostosis in 7.4 %. The incidence of hydrocephalus, when defined as an Evans' index greater than 0.30, was present in as many as 54 % of patients. In contrast, the prevalence of basilar impression associated with Chiari malformation in the northeast of Brazil was more than 60 % (Da Silva et al. 2011). It may well be that differences in the frequency of cranial constriction, cranial settling and mild deformations of cranial shape can explain ethno-geographical differences in syringomyelia prevalence.

2.3.2 Post-traumatic Syringomyelia

The causes of spinal cord injury vary from country to country, depending on social and economic factors. Post-traumatic syringomyelia was previously thought to be an infrequent but serious sequel to such injuries, and clinical and CT studies suggested that it occurred with an incidence of between 1 and 5 % (Barnett et al. 1971; Biyani and El Masry 1994; El Masry and Biyani 1996). Since the introduction of MRI, the reported radiological incidence has increased up to 22 % (Burt 2004; Squier and Lehr 1994), which is consistent with the frequency of 17–20 % identified in post-mortem studies (Squier and Lehr 1994; Wozniewicz et al. 1983). Cystic necrosis of the spinal cord, confined to the level of injury, is generally considered to be a myelomalacic cavity and not syringomyelia, but asymptomatic cavitations, extending above and below the levels of injury, are often detected radiologically in victims of spinal cord injury, and these outnumber cases of symptomatic post-traumatic syringomyelia. Which asymptomatic cavities are likely to become symptomatic and over what length of

time is, however, unknown. Progression may depend upon the original mechanism of injury or a variety of conditions inherent to the individual or both (Byun et al. 2010; Ohtonari et al. 2009).

Males are more likely to be victims of spinal cord injury than are females, in a ratio of about 6:1 (Burt 2004; El Masry and Biyani 1996). The interval between injury and diagnosis ranges from 2 months to 34 years (Biyani and El Masry 1994; El Masry and Biyani 1996). Full neurological recovery following the original spinal cord injury does not eliminate the possibility of post-traumatic syringomyelia developing later.

2.3.3 Syringomyelia in Patients with Non-traumatic Arachnoiditis

Syringomyelia is a rare sequel (less than 1 %) of infectious and non-infectious central nervous system inflammatory disease (Williams 1995). There are two main mechanisms by which inflammation may lead to the formation of syringomyelia: arachnoiditis and myelitis. Infection may also be a factor precipitating the onset of symptoms in Chiari-associated syringomyelia, in up to 7 % of patients (Milhorat et al. 1999).

Primary spinal syringomyelia is commonly secondary to post-inflammatory scarring, which leads to obstruction to the normal spinal CSF flow. Arachnoiditis might also cause syrinx formation by causing obliteration of the spinal microvasculature, leading to local cord ischaemia. Patterns of arachnoiditis seen range from focal meningeal cicatrix formation to diffuse adhesive spinal arachnoiditis (Caplan et al. 1990).

Foramen magnum arachnoiditis, in the absence of Chiari malformations, is a rare cause of syringomyelia (Klekamp et al. 2002). The mean interval between the presumed causative event (meningitis or trauma) and the development of syringomyelia-related symptoms can be up to 10 years. Compared with patients with Chiari malformation type 1, individuals with syringomyelia due to foramen magnum arachnoiditis have a much poorer long-term outcome. A stable clinical course was demonstrated in only 14 % of patients in whom surgery was not performed. Following surgery, 57 % of patients will have recurrence of symptoms within 5 years of the procedure.

Non-infectious inflammatory diseases of the nervous system are also sometimes associated with syringomyelia (Ravaglia et al. 2007; Zabbarova et al. 2010) and transient syringomyelia is occasionally encountered and associated with various types of non-infectious myelitis. Syringomyelia also occurs in 4.5 % of patients with multiple sclerosis (Weier et al. 2008) and in 16 % of patients with neuromyelitis optica (Devic's disease) (Kira et al. 1996). Reversible hydromyelia has been reported in patients with transverse myelitis (Wehner et al. 2005).

Syringomyelia arising as a complication of tuberculous meningitis is rare, in the context of the overall incidence and prevalence of this disease (Kaynar et al. 2000). Published literature consists, for the most part, of single case studies or small series, reporting patients who developed syringomyelia as a late complication of tuberculous meningitis. Examples of gross pathology include intradural extramedullary tuberculomas (Gul et al. 2010; Muthukumar and Sureshkumar 2007), tuberculous meningitis with a cranial nerve palsy (Katchanov et al. 2007) and spinal tuberculous arachnoiditis (Paliwal et al. 2011).

Spinal intramedullary haematoma is an uncommon lesion, and spontaneous, non-traumatic, intramedullary haemorrhage, without any obvious underlying pathology, is distinctly rare. Predisposing conditions that have been reported include pregnancy and childbirth, spinal angioma, spinal artery aneurysm, haemophilia and syringomyelia (Leech et al. 1991). The latter condition was originally described by Gowers in 1904 and consequently has been termed Gowers' syringal haemorrhage (Sedzimir et al. 1974). A slowly developing haematomyelia, within an existing syringomyelia cavity, may originate from a torn intraspinal vein, which is deprived of its normal neural and glial support (Ayuzawa et al. 1995). Trauma is not a predisposing cause of such haemorrhages.

2.3.4 Idiopathic Syringomyelia

Idiopathic tubular cavitations of the spinal cord account for between 13 and 28 % of all reported cases of syringomyelia (Brickell et al. 2006; Roser et al. 2010; Sakushima et al. 2012). A study of adult patients presenting to a neurosurgical department, with an MRI diagnosis of syringomyelia, found that 28 % had a central canal with no underlying associated pathology (Roser et al. 2010). A distinguishing feature of these lesions was that there was no accompanying clinical or radiological progression. A study of 794 MRI investigations of the spinal cord, for a variety of indications, found 1.5 % of patients had a filiform intramedullary cavity (Petit-Lacour et al. 2000). These patients did not have any other anatomical factors predisposing to syringomyelia and they, too, were clinically asymptomatic.

Various terms have been used to refer to idiopathic syringomyelia including hydromyelia, idiopathic localized hydromyelia and syringohydromyelia (Roy et al. 2011). Primary or idiopathic hydromyelia is typified by a slitlike expansion of the central canal, without any pathology of CSF dynamics, congenital or acquired (Holly and Batzdorf 2002; Novegno et al. 2008; Roser et al. 2010). Idiopathic, slitlike or "filiform" cavities usually represent a benign condition, and in 50 % of these patients, medical assessment may reveal alternative conditions as being responsible for the presenting symptoms (Holly and Batzdorf 2002).

An explanation for many apparently idiopathic syringomyelia cavities may be simple persistence of the embryonic central canal of the cord (Holly and Batzdorf 2002). This structure is still present at birth but becomes progressively obliterated during childhood and adolescence. Clinical and experimental studies have shown that expansion of the central canal is an early, non-specific and potentially reversible manifestation of disturbed intraspinal fluid circulation, caused by both internal and external factors (Josephson et al. 2001; Milhorat et al. 1993; Petit-Lacour et al. 2000; Weier et al. 2008).

Some cases of syringomyelia that appear to be idiopathic may actually be associated with morphometric abnormalities of the skull, in particular a small posterior fossa, with resultant compression of the subarachnoid cerebrospinal fluid (CSF) pathways (Bogdanov et al. 2004; Chern et al. 2011). This so-called Chiari 0 malformation represents a very small cohort of patients within the spectrum of all individuals with Chiari malformation, and the diagnosis of Chiari 0 malformation can only be made after other aetiologies of syringomyelia have been eliminated conclusively.

2.4 Natural History and Presentation by Age

Clinical manifestations of type 1 Chiari malformation vary according to the age at which they first appear (Klekamp and Samii 2002; Luciano 2011; Vannemreddy et al. 2010). Symptoms are often caused by compression of the brainstem, and in patients under 2 years of age, this often manifests with stridor, crying, apnoea, cyanosis, increased muscle tone and life-threatening respiratory problems. In older children the greatest problem is the development of scoliosis secondary to syringomyelia and an ataxic gait. In both adolescents and adults, chronic brainstem compression may be manifested by occipital headache, nystagmus and hyperaesthesia in the trigeminal nerve territory. In children, onset of clinical features may be associated with the rapidly growing cerebellum, and later resolution of symptoms can be related to increasing skull volume and gradual ascent of the child's cerebellar tonsils (Klekamp and Samii 2002; Novegno et al. 2008).

Of patients diagnosed with Chiari malformation type 1 on MRI, the reported number that is asymptomatic varies between a third and a half (Benglis et al. 2011; Elster and Chen 1992; Meadows et al. 2000; Novegno et al. 2008; Wu et al. 1999). The frequency of asymptomatic syringomyelia has been reported as being 23 % (Sakushima et al. 2012).

Most patients with syringomyelia and Chiari malformation type 1 first become symptomatic during adult life (Table 2.7). Adults diagnosed with Chiari malformation type 1 are more likely to have an associated syringomyelia than are children: 14–58 % of children and 59–76 % of adults (Aitken et al. 2009). The mean age at onset

Table 2.7 Incidence of tonsillar herniation in different age groups

Age group	Takeuchi et al. (2007) (%)	Authors' data (2011)		
		Chiari type 1, without syringomyelia (%)	Chiari type 1, with syringomyelia (%)	Chiari type 1, all cases (%)
<29	5	27	10	19
30–39	20	17	21.7	19
40–49	12	29	38	33
50–59	17	19	20	20
60–69	17	8	10	9
>70	12	–	0.3	0.1

of symptoms in patients with Chiari malformation type 1 is between 11 and 25 years (Aitken et al. 2009; Milhorat et al. 1999). The mean age at onset of symptoms of syringomyelia is between 28 and 40 years (Brickell et al. 2006; Sakushima et al. 2012).

Syringobulbia was found in between 1 and 6 % in patients with syringomyelia (Sakushima et al. 2012; Tubbs et al. 2009).

Syringomyelia is a disorder that can have a varying prognosis (Table 2.8). The course of symptoms after initial diagnosis is not uniform, with deterioration in 20–51 %, 10–80 % remaining unchanged and 11 % improving (Table 2.8). Spontaneous reduction of tonsillar herniation is uncommon, but may occur, in 11–18 % of cases (Novegno et al. 2008). Spontaneous resolution of syringomyelia in adult patients with cerebellar ectopia is rare, although cases have been reported (Perrini 2012). Probable mechanisms include spontaneous drainage between the syrinx and the subarachnoid space or restoration of abnormal CSF dynamics at the craniovertebral junction (Bogdanov et al. 2000, 2006; Kyoshima and Bogdanov 2003; Perrini 2012).

A study of patients with Chiari malformation type 1, who initially elected for nonsurgical management, found no significant change in the mean volume of cerebellar herniation over a 4-year period. There was, however, worsening CSF flow at the foramen magnum in 16 %, but there was also an improvement in flow in 31 %. Development of a spinal cord syrinx was seen in only 5 % and spontaneous resolution of an existing syrinx in 2 % (Strahle et al. 2011b). Ten percent of patients went on to undergo surgical treatment. Other series have reported that, overall, surgical management is required for 29–44 % patients with Chiari malformation type 1 (Benglis et al. 2011; Milhorat et al. 1999). Surgical management is performed in 69 % of patients with syringomyelia in Japan (Sakushima et al. 2012). In the paediatric population syringomyelia often (94 %) remains stable in children managed nonsurgically (Singhal et al. 2011).

Table 2.8 Clinical course of syringomyelia

Clinical course	%	Reference source
Acute presentation	11	Bogdanov and Mendelevich (2002)
Deterioration	20–51	Bogdanov and Mendelevich (2002)
Slow/moderate progressive	>47	Borisova and Mirsaev (2007)
Rapid progressive	15–20	Nakamura et al. (2009)
Stop after progression	5–6	Sakushima et al. (2012)
Unchanged at 10 years or more	10–80	Bogdanov and Mendelevich (2002), Boman and Livanainen (1967), Borisova and Mirsaev (2007), Nakamura et al. (2009), Sakushima et al. (2012)
Improved	11	Sakushima et al. (2012)
Collapse of cavity	10	Bogdanov and Mendelevich (2002)
Spontaneous remission	3.2	Sakushima et al. (2012)
Dead (or the status was unknown) during 40 years of observation	5.8–20	Boman and Livanainen (1967), Brickell et al. 2006

A retrospective analysis of 103 adult patients with un-operated hindbrain-related syringomyelia looked at the prognostic significance of syrinx size and morphology. Patients with the widest cavities, as measured by their anteroposterior diameter, presented with a short duration of symptoms and a rapidly progressive clinical course. Those with smaller diameter cavities had

symptoms of longer duration and a slower rate of progression (Bogdanov and Mendelevich 2002).

Little is known about effect of syringomyelia on life expectancy or what is the most common cause of death of patients with Chiari-associated syringomyelia. Death rates in patients with syringomyelia ranged from 6 to 20 % in studies involving 30 and 40 years of observation (Boman and Livanainen 1967; Borisova et al. 1989; Brickell et al. 2006) and do not exceed the overall rate in the population. Chiari malformation type 1 can very occasionally be associated with respiratory and cardiovascular compromise, which can potentially lead to sudden death (De Souza et al. 2011). The overall risk of such catastrophes must be small and unless a patient reports himself or herself as having suffered blackouts, brought on by Valsalva-like manoeuvres, then surgery still remains an option, rather than an essential treatment. There have been cases reported of people dying in motor vehicle collisions and who have been found, at subsequent post-mortem examination, to harbour a previously asymptomatic Chiari malformation. Forced hyperextension of the neck, to a degree not normally expected to cause serious injury, leads, presumably, to lethal medullary contusion, caused by the herniated cerebellar tonsils. Reported cases are rare and are mostly children, so this sort of tragedy may be related to the increased mobility and poorer musculature of the neck (James 1995; Mäkelä 2006; Rickert et al. 2001; Wolf et al. 1998). It would be wrong, therefore, to advocate surgery for Chiari malformations, solely on the basis that the patient is at marginally increased risk of injury during a road traffic accident.

2.5 Inheritance of Chiari and Syringomyelia

It has been reported that 3–12 % of patients with Chiari malformation type 1 have a family history of Chiari malformation (Milhorat et al. 1999; Schanker et al. 2011). The incidence of a positive family history in our Chiari population was 4.7 %, and the mean prevalence of familial cases was 2 per 100,000 adult inhabitants but ranging from less than 1 to over 100 per 100,000 adult inhabitants, with the highest prevalence found in 2 neighbouring villages in the northern region of Tatarstan. The highest prevalence of familial cases of syringomyelia and Chiari malformation was in the regions with the highest prevalence of all cases of this pathology (Figs. 2.1, 2.2 and 2.3). Genetic studies would help clarify the nature of the prevalence of sporadic and hereditary forms of disease.

Evidence of a genetic contribution to Chiari type 1 malformation and syringomyelia comes from at least three sources: familial aggregation, twin studies and known genetic syndromes associated with Chiari and syringomyelia (Speer et al. 2003). One study identified 31 pedigrees, in which two or more individuals were affected with Chiari malformation type 1 and syringomyelia (Speer et al. 2000). In this study, when MRI of asymptomatic first-degree relatives of affected patients was obtained, 21 % were diagnosed as having Chiari malformation type 1 and syringomyelia. There were no cases of isolated familial syringomyelia without an underlying Chiari malformation, suggesting that familial syringomyelia is more accurately classified as familial Chiari type 1-associated syringomyelia (see Chap. 5).

Chiari malformation with syringomyelia occurs in association with a variety of syndromes of established inheritance patterns (Table 2.9) (Speer et al. 2003). These syndromic cases are likely to account for less than 1 % of the total Chiari population. It has been suggested that the underlying gene or genes involved in Chiari malformation type 1 and syringomyelia will have pleiotropic[1] effects, influencing bone morphology at the skull base, posterior fossa volume and the extent of cerebellar tonsillar herniation (Speer et al. 2000). Such pleiotropic manifestations may or may not be clinically relevant, but one possible condition within such a pleiotropic spectrum may be the Chiari 0 malformation, which is found in individuals with volumetrically small posterior fossa, some of whom have been shown to respond to decompressive surgery.

The genetics of Chiari malformation are discussed in more detail in Chap. 5 of this book.

[1] When a single gene influences more than one phenotypic characteristic.

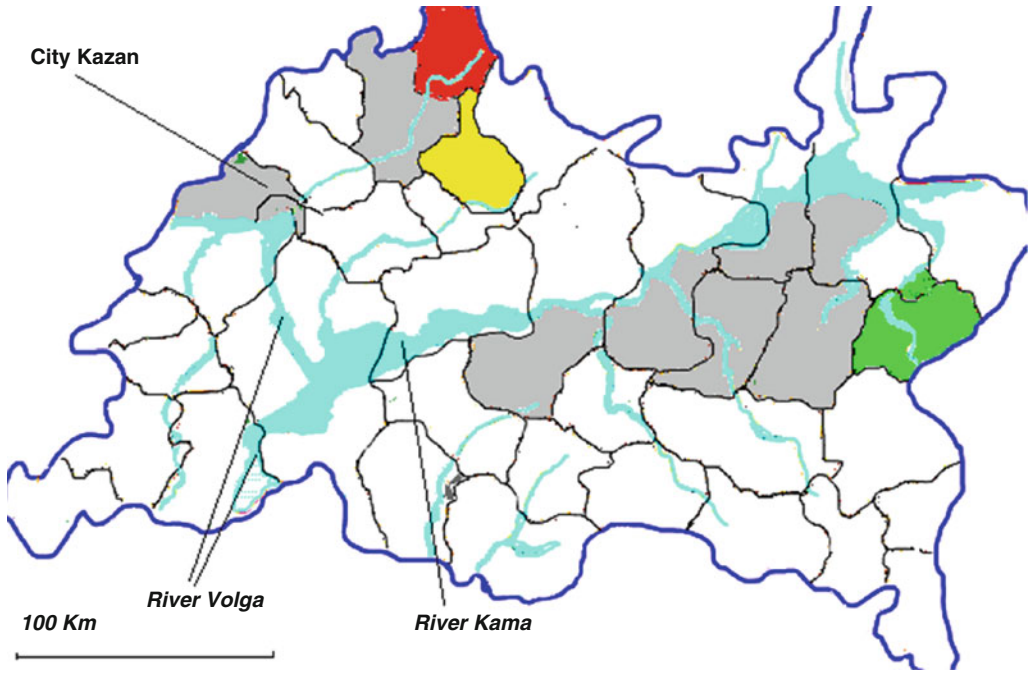

Fig. 2.2 Map of Tatarstan (Russia) with the prevalence of familial cases of Chiari malformation/syringomyelia (per 100,000 adult inhabitants). *Red* = very high prevalence (117.4); *yellow* = high prevalence (34.8); *green* = moderate prevalence (17.6); *grey* = low prevalence (<10). *White* reveals regions without familial cases of Chiari malformation/syringomyelia (Authors' data 2011)

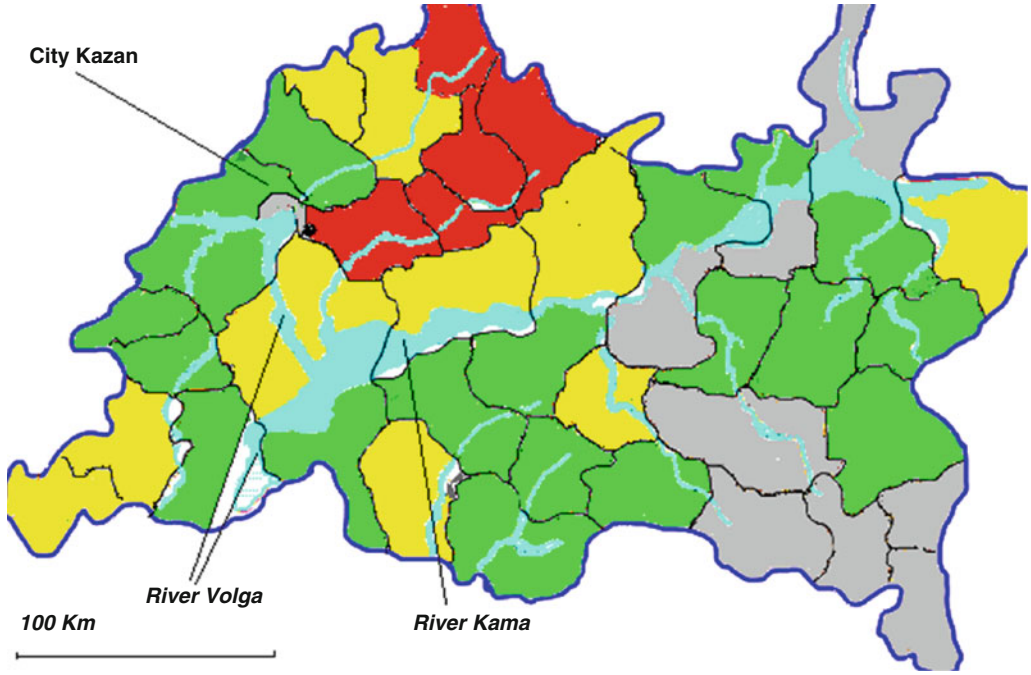

Fig. 2.3 Map of Tatarstan (Russia) with the prevalence of Chiari malformations with or without syringomyelia (per 100,000 adult inhabitants). *Red* = very high prevalence (>100); *yellow* = high prevalence (60–100); *green* = moderate prevalence (20–60); *grey* = low prevalence (<20) (Authors' data 2011)

Table 2.9 Inherited syndromes associated with Chiari and syringomyelia

Achondroplasia
Cleidocranial dysplasia
Crouzon's syndrome
Cystic fibrosis
Familial osteosclerosis
Growth hormone deficiency
Paget's disease of bone
Klippel-Feil sequence/syndrome
Hypophosphataemic rickets

Conclusions

The prevalence of syringomyelia varies widely in different geographic regions and between ethnic groups. These variations can probably be explained by ethno-geographical differences of cranial construction and cranial settling, including mild deformations of cranial shape. Most cases of syringomyelia are associated with Chiari malformation type 1. Among patients with Chiari malformation type 1, with or without syringomyelia, up to 50 % are asymptomatic. Some patients not undergoing surgical treatment may have a favourable disease course with minimal progression of clinical signs and, in a minority, spontaneous reduction of their hindbrain hernia or even resolution of their syringomyelia cavity.

There are clearly limitations as to how far we can draw meaningful conclusions from the data presented in this chapter, and there is a need for international collaboration in gathering more data, if we are to understand better the epidemiology of Chiari malformations and syringomyelia.

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