Child's Nervous System (2021) 37:3407–3415
https://doi.org/10.1007/s00381-021-05333-2

ANNUAL ISSUE PAPERS

Hydrocephalus in myelomeningocele

Sergio Cavalheiro[1,3] · Marcos Devanir Silva da Costa[1,3] · Mauricio Mendes Barbosa[2,5] · Patricia Alessandra Dastoli[1,3] · Jardel Nicácio Mendonça[1,3] · Daniela Cavalheiro[4] · Antonio Fernandes Moron[2]

Received: 17 July 2021 / Accepted: 9 August 2021 / Published online: 25 August 2021

Abstract

Purpose To investigate certain aspects of hydrocephalus in patients with myelomeningocele.

Methods We retrospectively analyzed data of 1050 patients with myelomeningocele who underwent surgical treatment between June 1991 and June 2021. These patients were divided into three groups: group 1 consisted of patients who underwent surgery after the first 6 h of life, group 2 consisted of patients who underwent surgery within the first 6 h, and group 3 consisted of patients who underwent surgery during the fetal period and before 26 6/7 weeks of gestation.

Results There were 125, 590, and 335 patients in groups 1, 2, and 3, respectively. In groups 1 and 2, 593 (83%) patients developed hydrocephalus after birth and required ventriculoperitoneal shunt placement in the maternity ward, mainly within the first 4 days of life. In contrast, in group 3, 24 (7.2%) patients required surgery to treat hydrocephalus after birth. Hydrocephalus was the primary cause of mortality in groups 1 and 2, with mortality rates of 35% and 10%, respectively. In group 3, the mortality rate was 0.8% and was not related to hydrocephalus.

Conclusion The onset of hydrocephalus is directly related to myelomeningocele closure in neurosurgery.

Keywords Hydrocephalus · Fetal neurosurgery · Myelomeningocele · Chiari type II · Folates

Introduction

Myelomeningocele (MMC) is an open dysraphism that occurs in the third week of gestation due to failure of neural tube closure in its caudal portion. Unlike other spinal dysraphisms, MMC may also present a massive number of other associated intracranial malformations that contribute to hydrocephalus onset, such as partial agenesis of the corpus callosum, thin corpus callosum, enlarged massa intermedia, tectal beaking, aqueductal stenosis, small fourth ventricle, brainstem extending into the cervical spinal canal, tonsillar herniation, heterotopias, and rhomboencephalosynapsis [1, 2].

MMC can affect any level of the spine, but the lumbar and sacral levels have been found to be the most frequently affected levels. Moreover, MMC is a dysraphism that can

✉ Marcos Devanir Silva da Costa
marcoscostaneuro@gmail.com

Sergio Cavalheiro
sergiocavalheironeuro@gmail.com

Mauricio Mendes Barbosa
mmendesbarbosa@uol.com.br

Patricia Alessandra Dastoli
paty.dastoli@uol.com.br

Jardel Nicácio Mendonça
jardelmnnicacio@gmail.com

Daniela Cavalheiro
dani.cava2000@gmail.com

Antonio Fernandes Moron
antonio_moron@uol.com.br

[1] Department Neurology and Neurosurgery, Universidade Federal de Sao Paulo, Rua Napoleão de Barros, 715, 6th Floor, Sao Paulo, SP 04024-002, Brazil

[2] Department of Fetal Medicine, Hospital E Maternidade Santa Joana, São Paulo, SP, Brazil

[3] Department of Fetal Neurosurgery, Hospital e Maternidade Santa Joana, São Paulo, SP, Brazil

[4] Faculdade de Medicina de Jundiaí, Jundiai, SP, Brazil

[5] Department of Obstetrics, Faculdade de Medicina Einstein, São Paulo, SP, Brazil

present different degrees of morbidity, including hydrocephalus, lower limb motor impairments, bladder and anal sphincter disturbances, orthopedic disorders, and sexual dysfunction. With the increased care of patients with MMC, many survive with varying degrees of sequelae, leading to psychiatric and behavioral disorders. Hydrocephalus, in particular, is an aggravating factor and accounts for up to 90% of these cases [3]. Tennant et al. demonstrated that patients who did not present with hydrocephalus had a survival rate of 86.7% in 20 years, whereas those who presented with hydrocephalus had a survival rate of 50%, possibly demonstrating that hydrocephalus was one of the main factors directly related to survival in MMC. Notably, a multicenter randomized study by Adzick et al. [4] in 2011 demonstrated a 50% reduction in hydrocephalus when MMC repair was performed intrauterine and at 26 weeks of gestation. This study marked the reemergence of fetal neurosurgery in the field of pediatric neurosurgery, with several centers worldwide following suit. However, despite early treatment in the fetal period, there are many morbidities resulting from MMC that cannot be avoided.

Therefore, the objective of this study was to analyze a cohort of 1050 patients with MMC who were treated in different periods and assess their relationship with hydrocephalus development.

Patients and methods

This retrospective study analyzed patients with MMC born between June 1991 and June 2021 at the Neurosurgery Department of Escola Paulista de Medicina and Santa Joana Hospital and Maternidade. In this period, 1122 patients were born with MMC; however, only 1050 patients in whom the surgery was performed by the senior author of this study and were subsequently included. Patients were divided into three groups based on the timing of MMC closure as follows: group 1, after 6 h of life; group 2, within the first 6 h of life; and group 3, during the fetal period. In total, 125 patients underwent surgery after 6 h of life, 590 underwent surgery within the first 6 h (ultra-early surgery), and 335 underwent surgery intrauterine at a gestational age of less than 26 6/7 weeks. Furthermore, the included patients had a minimum follow-up period of 30 days after birth.

After birth, the patients underwent head circumference measurements using Doppler ultrasound of the fontanel and/or magnetic resonance imaging (MRI) of the skull. When the ventricular indices were greater than 50% and associated with increased head circumference and resistance index in the anterior cerebral arteries and mean on Doppler, ventriculoperitoneal (VP) shunt was indicated. More specifically, for patients weighing less than 2 kg, an Accuo-Flo type valve without a reservoir, with an opening pressure varying from 2 to 5 cm of H2O, was used, whereas for patients weighing more than 2 kg, a CODMAN® HAKIM® precision system (after 2010, CODMAN® HAKIM® micro programmable shunt system), with a fixed medium-to-low opening pressure, was used. VP shunt in both cases was performed according to the protocol proposed by Choux et al. [5]. Following MMC management, these patients were followed up quarterly in the first year, which was accompanied by fontanelle ultrasound using Doppler study. At 1 year, MRI of the skull and whole spine was performed to evaluate brain alterations related to MMC and accurately establish its level. After the first year, these patients were followed up every 6 months by a multidisciplinary team including pediatricians, neurosurgeons, urologists, orthopedists, and physical therapists. During these periods, various management strategies were employed for each situation, as detailed below. If there was any intercurrence of hydrocephalus, brain MRI was performed. However, if the third ventricle floor presented a satisfactory anatomy, endoscopic third ventriculostomy (ETV) was preferably performed, and the valve was removed accordingly. In patients older than 6 months of age who developed hydrocephalus with a favorable third ventricle floor, we preferably performed ETV. In Group 3 patients who began to present a cephalic perimeter increase, cranial MRI was performed. If the aqueduct was patent, the Chiari malformation would have disappeared, with the third ventricle floor presenting a flat or convex curvature. Clinical treatment was preferred for this situation, and 83 mg of acetazolamide was introduced every 8 h until cephalic perimeter normalization. If there was persistence in the progressive increase of the cephalic perimeter, VP shunt was indicated, and if the third ventricle floor presented a concave curvature (Fig. 1), i.e., when the floor was bulging toward the dorsum sellae and interpeduncular cistern, EVT was indicated. Patients with VP shunt presenting with dysfunction and favorable anatomy underwent endoscopy. If the anatomy was complex in these patients, shunt revision was performed. In contrast, in patients with certain abdominal complications, ETV was preferably performed. In all three groups, we analyzed the clivus-supraocciput angle (CSA) to infer the size of the posterior fossa (Fig. 2). Furthermore, shunt infection was considered when an infectious event occurred within the first 6 months after implantation. Descriptive statistics of the data were performed using the Prism 8 software for Mac OS, version 8.0.1 (GraphPad Software, San Diego, CA, USA).

Results

Among the 1050 patients with MMC included in the study, 617 (58.7%) developed hydrocephalus. Among them, 522 (73%) patients in groups 1 and 2 were diagnosed with hydrocephalus antenatally, with ventricular

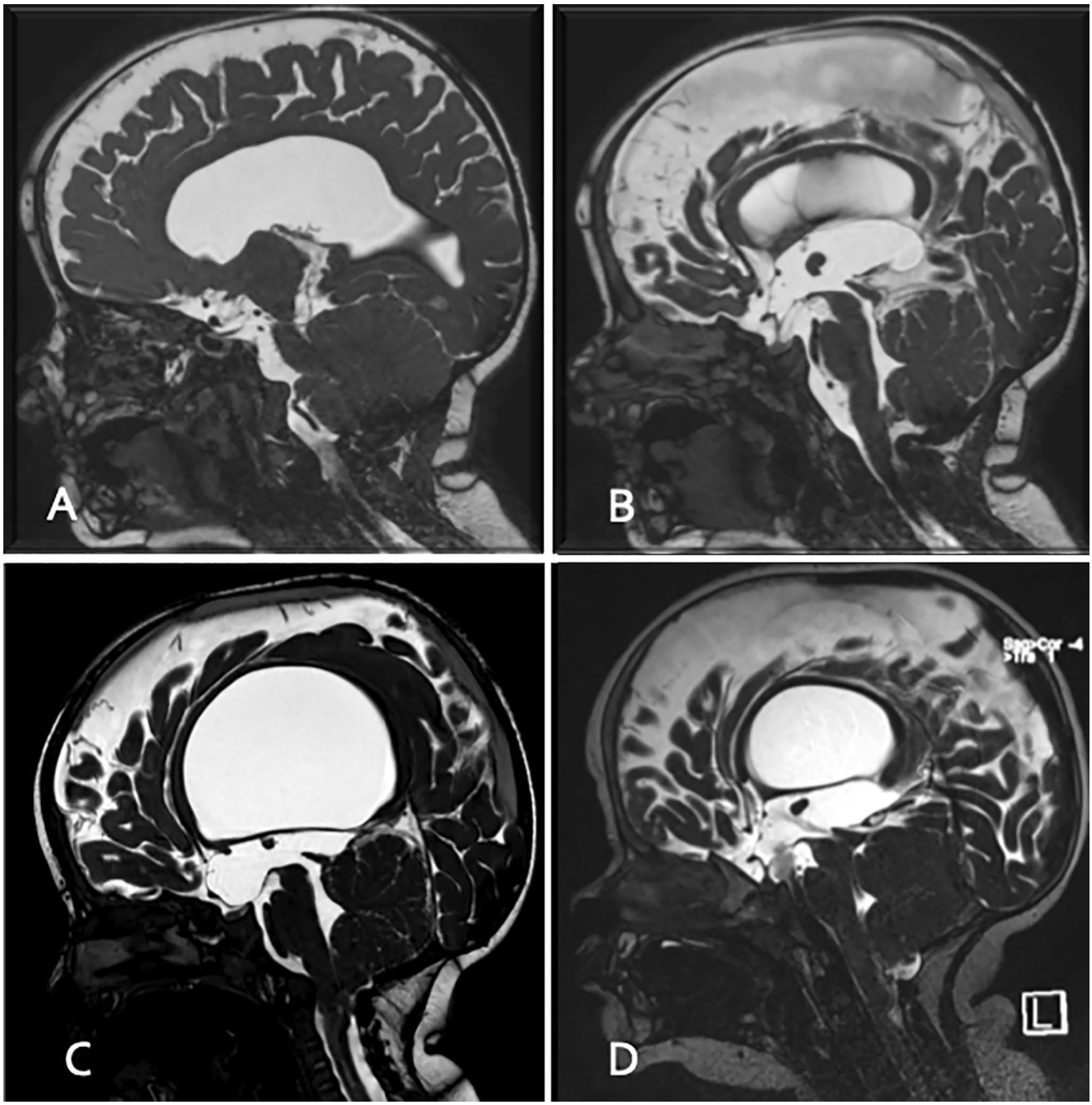

Fig. 1 **A**, **B** MRI of a skull of a patient from group 3 showing subarachnoid CFS accumulation, cerebral patent aqueduct, and a convex the third ventricular floor. **C** Findings of ventriculomegaly showing a patent aqueduct, cerebellar tonsillar impaction, and a convex third ventricular floor. **D** Flow study on the floor of the third ventricle after endoscopic third ventriculostomy

atria larger than 16 mm. In contrast, 25% patients in group 3 had ventricular atria, with measurements ranging from 11 to 16 mm. In particular, two patients in group 3 had atria larger than 16 mm and were treated in utero with a ventricular amniotic shunt. They also required VP shunt placement after birth. Furthermore, these patients were followed up for a period ranging from 30 days to 30 years, with a mean follow-up period of 15.6 years. In groups 1, 2, and 3, the mean follow-up period was 22, 15, and 3.4 years, respectively.

In groups 1 and 2, 593 (83%) patients developed hydrocephalus after birth and required VP shunt placement in the maternity ward, mainly within the first 4 days of life. In contrast, in group 3, 24 (7.2%) patients required surgery to treat hydrocephalus after birth, but these patients underwent surgery after more than 6 months of life on an average.

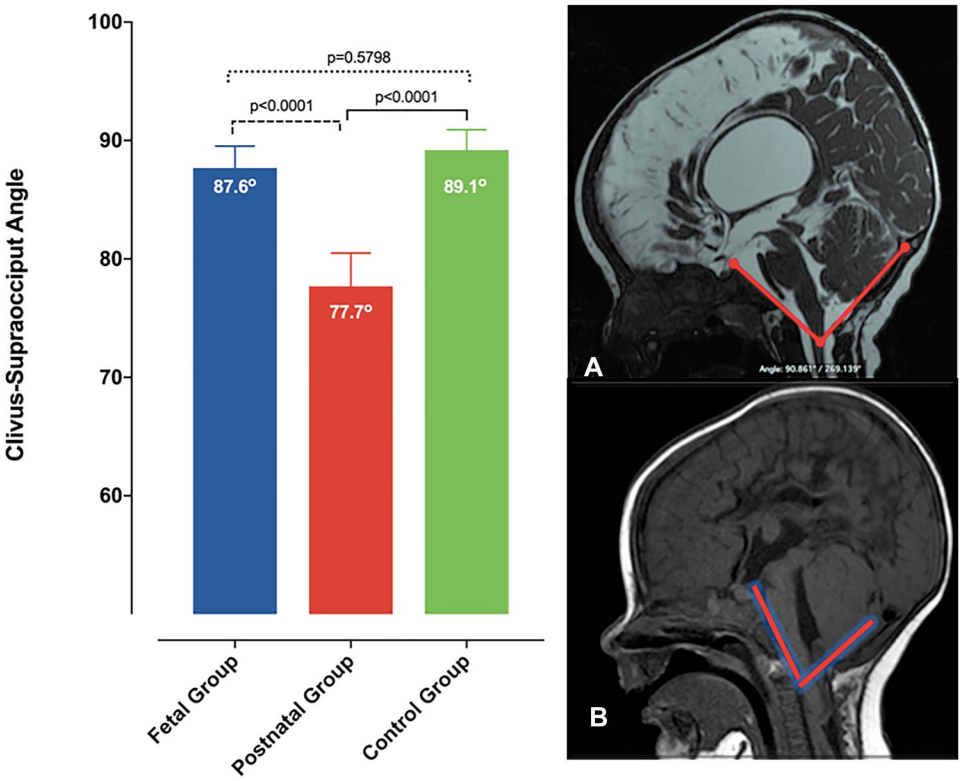

Fig. 2 The chart shows a comparison between the means with 95% confidence intervals of the clivus-supraocciput angles (CSA) in the fetal, postnatal, and control groups, comprising 65 children under 12 months of age who underwent brain MRI that revealed normal anatomy, which was as confirmed by a radiologist. **A** The CSA in a patient who underwent intrauterine surgery. **B** The CSA in a patient who underwent surgery after birth. Adapted from da Costa et al. [15], with permission from the publisher

Specifically, 15 (62.5%) patients underwent ETV, and six (40%) patients required VP shunt. In group 1, 7% patients had VP shunt infection within the first 6 months after shunt implantation, which was higher than the 1% incidence in group 2 and 0% incidence in group 3.

The overall mortality of patients in group 1 was 35% for those with hydrocephalus and 1.5% for those without hydrocephalus. In group 2, the mortality rate was 10.5%, of which 7% was directly related to the valve. In group 3, the mortality rate was 0.8%, and deaths were related to prematurity.

Additionally, in groups 1 and 2, we noticed a clear relationship between the MMC level and hydrocephalus onset, in which all cases with high MMC levels developed hydrocephalus. However, this relationship was not observed in group 3. Specifically, in groups 1 and 2, the MMC level was similar, with 17% cases considered high, which was distributed as follows: 1.1% (eight patients) at T12–L1, 15.9% (114 patients) at L2–L3, 58% (415 patients) at L4–L5, and 24.9% (178 patients) at L5–S1. In group 3, only 5.9% cases were considered high as follows: 0.6% (two patients) at T12–L1, 5.3% (18 patients) at L2–L3, 69.2% (232 patients) at L4–L5, and 24.7% (83 patients) at L5–S1.

Regarding Chiari malformations, in group 1, 11 (8.8%) patients presented with Chiari symptoms with apnea, difficulty in swallowing, and stridor, among which 4 (3.2%) required posterior fossa decompression. The other cases were controlled with VP shunt placement/revision (Fig. 3). In group 2, the incidence was similar to that in group 1, wherein 47 (7.9%) patients developed symptomatic Chiari, among which 18 (3%) required posterior fossa decompression. In contrast, no symptomatic Chiari cases were noted in Group 3.

Regarding the CSA, no variation was found between groups 1 and 2, with a mean angle of 78.3°. In contrast, the CSA in group 3 was significantly higher, with a mean of 87.6° ($p < 0.0001$), which was similar to that of the average population (89.1°). Moreover, in group 3, 30% patients presented with an increased cephalic perimeter due to bilateral frontal collections and communicating ventriculomegaly, prompting acetazolamide treatment. The curve of the head circumference in groups 1, 2, and 3 is shown in Fig. 4.

In the long-term evaluation, 10% patients did not need VP shunt revision, 50% needed one revision, 30% needed two revisions, 15% needed three revisions, and five% needed more than three revisions. The most common mechanical complication was ventricular catheter blockage, followed by over-drainage, while the most common biological complication was abdominal pseudocyst formation. In 85 patients, it was possible to reverse valve use for ETV, with a success rate of 73.4%.

Among all patients, 18.5% of their mothers reported regular folic acid use for a period of more than 2 months before pregnancy. The age of the mothers of these patients ranged from 16 to 45 years, with a mean of 31.6 years of age. Regarding sex, 588 (56%) of the included patients were women.

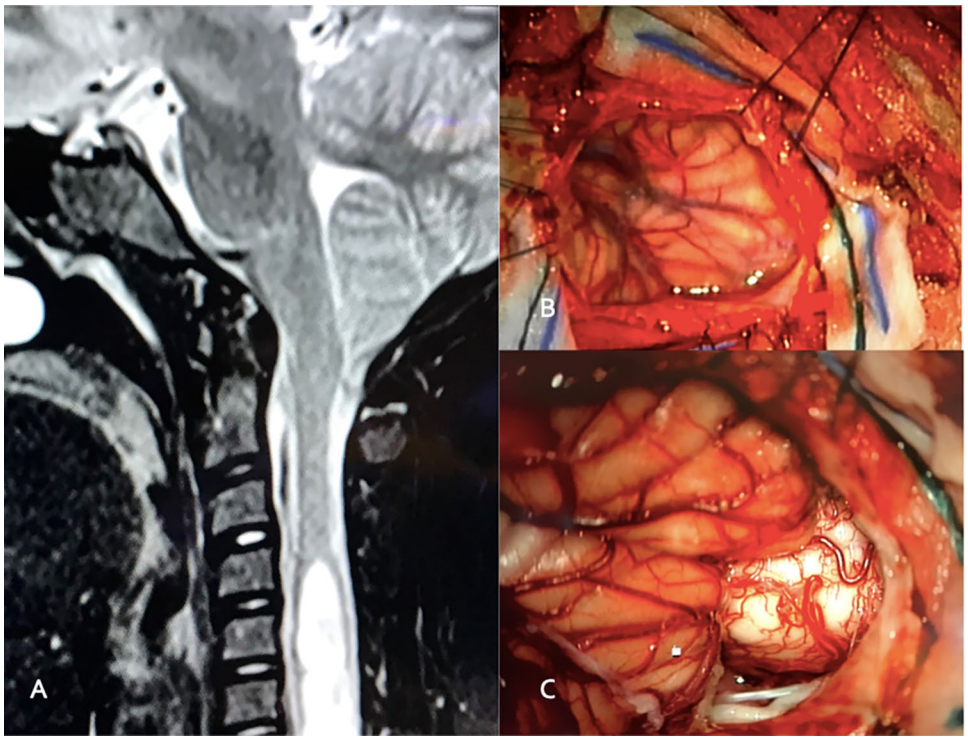

Fig. 3 **A** Brain MRI of a group 1 patient showing symptomatic Chiari and syringomyelia. **B** Intraoperative view of the cerebellar tonsillar herniation in the foramen magnum. **C** Intraoperative view after posterior fossa decompression

Discussion

For many years, MMC has been neglected by the medical community. As a result, many patients die due to neurosurgical and related urological complications, leading to renal failure. In many countries, pregnancy termination is legalized, and feticide is performed regularly in these cases [6–9]. In 1983, Mc Lone proposed a multidisciplinary treatment approach, promoting an improvement in the survival of these patients. [10]

Hydrocephalus is the most severe complication associated with MMC, with an incidence varying from 60 to 90% in cases, which is related to the level of MMC [11–13]. This finding was verified in groups 1 and 2 of our study; however, this relationship was not verified in group 3. More specifically, the level of the lesion was not related to hydrocephalus development, but the number of high MMCs in group 3 was lower than that in groups 1 and 2.

The timing of MMC correction was directly related to mortality in these patients. Patients born without diagnosis and who underwent surgery much later presented a mortality rate of 36.5%, with complications of hydrocephalus and shunt infection being the most significant causes of death. In group 2, mortality was much lower, with a rate of approximately 10.5% in long-term follow-up. In group 3, the mortality rate was 0.8% and was related to prematurity rather than hydrocephalus. Given these findings, it is clear that a planned delivery, with neurosurgeon assistance at the time of delivery and with the protection of MMC and surgery within the first 6 h of life, leads to a better result since it reduces infection rates. However, if this surgery is performed in uterus and before 26 6/7 weeks of gestation, the results would be even better.

At the end of gestation, in groups 1 and 2, 73% patients presented with hydrocephalus on fetal ultrasound, increasing to 83% after MMC correction. It was then up to the neurosurgeon to decide the timing and type of delivery considering the deleterious effects of hydrocephalus counterbalanced with those of prematurity. In these cases, cranial circumference measurement is essential for sonographic evaluation prior to delivery. For example, many patients with ventricular atrial dilatation had partial agenesis of the corpus callosum, which is not truly a hypertensive hydrocephalus but rather a colpocephaly.

However, in 2011, with the publication of the results of the MOMS study by Adzick et al. [4], the scenario of this disease has changed tremendously. Several centers for fetal medicine have been created, even in countries with interrupted pregnancies that have begun to devote themselves to fetal life treatment.

In reality, the most significant benefit of performing MMC correction in the fetal period is hydrocephalus rate reduction. In particular, the MOMS study showed a 50% reduction in hydrocephalus cases. However, in our series, the reduction rate was 7.2%. These differences in the reduction rate may be explained by understanding the pathophysiology of hydrocephalus in MMCs [14, 15].

In fact, studies on encephalic fetal alterations and their transformations after birth in patients undergoing fetal

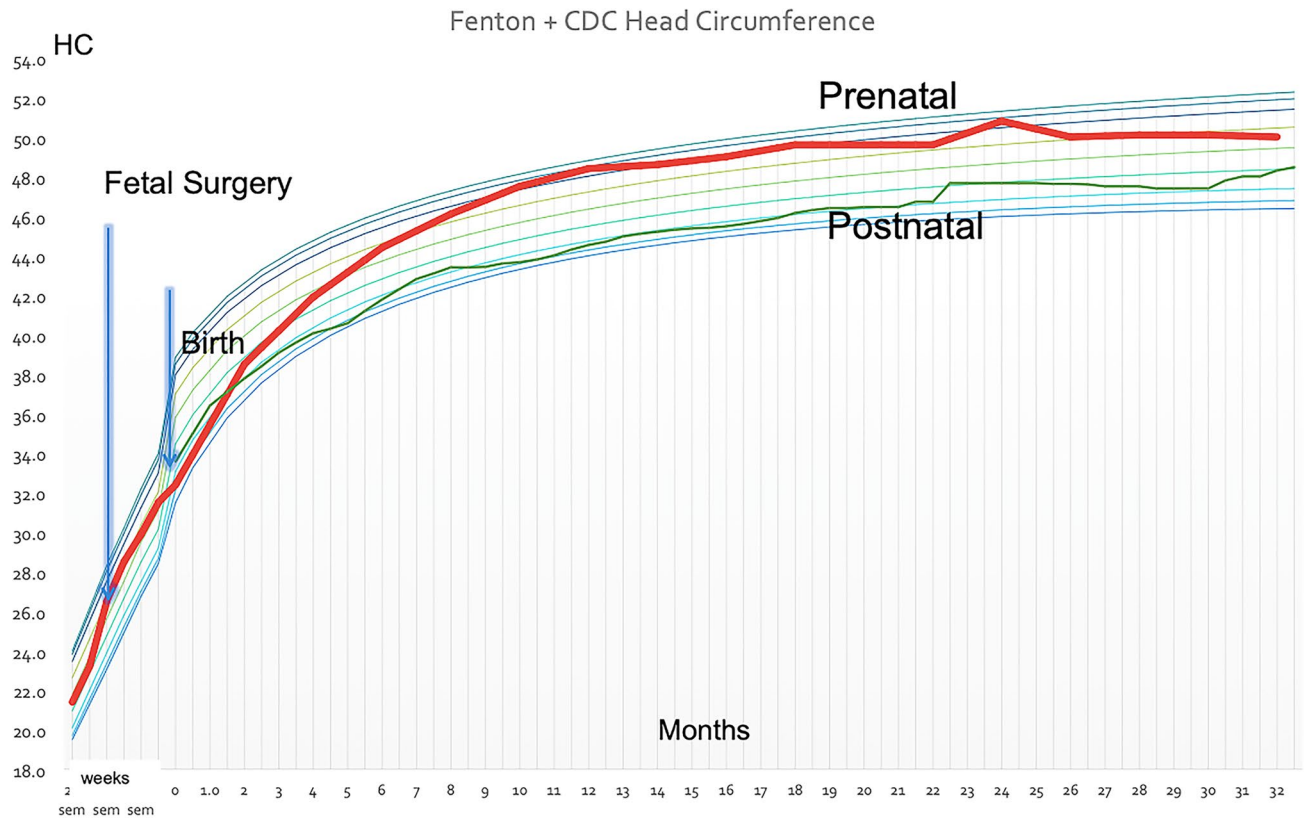

Fig. 4 Cranial circumference curve in patients who underwent surgery in utero (group 3) (red) and after birth (groups 1 and 2) (green)

surgery have allowed us to understand the physiopathology of this disease, which is mainly related to hydrocephalus.

One finding is that there is primary neurulation failure in MMC, probably due to a lack of carbohydrate expression on the neuronal surfaces in the developing neural tube. Although embryological events involving MMC onset begin around the third to fourth week of gestation, the effects of this embryological failure generate a cascade of consequences that may affect other segments of the central nervous system, causing, for example, Chiari syndrome type II and hydrocephalus. In 1989, McLone, D., and Knepper, P., published a unified theory to explain the pathophysiology of Chiari syndrome type II, proposing the unification of four mechanisms [16]. The first was neurulation failure, which was defined as an a priori condition for Chiari syndrome II formation. Due to continuous cerebrospinal fluid (CSF) leakage from neural tube closure failure, there would also be a failure in neurocele distention, consequently resulting in a failure in the apposition of forces on the neural tube medial walls during human brain development. This would lead to a failure in ventricular system distension, and in turn, the ventricular system would develop with anomalies but without exerting mechanical force on the bone-forming mesenchyme of the posterior fossa. This so-called dry brain is characterized by the lemon sign on ultrasonography, which is the wedging of the frontal bones caused by intracranial hypotension (Fig. 5), presenting in 90% fetal MMC cases.

From there, the rhombencephalon would continue to develop and increase in volume, but the compass with the posterior fossa bone formation would have been lost, causing a disproportion between the content and space in the posterior fossa. This phenomenon results in tonsillar herniation, inferior displacement of the bulb, low implantation of the tentorium, and apposition of the thalami with significant inter-thalamic adherence [16]. Within this context, hydrocephalus may also be a consequence of the extracellular matrix and cellular activity changes in the CSF circulation and absorption pathways, which are influenced by time-dependent inductive factors related to CSF flow obstruction through the fourth ventricle and foramen magnum [16]. The other mechanisms capable of explaining hydrocephalus in cases of Chiari type II with small posterior fossa include cerebellar displacement into the spinal canal, cerebral aqueduct compression and subsequent aqueduct stenosis, and occlusion of the foramen of Luscka and Magendie.

In our study, in group 3 patients, the CSA normalized, demonstrating an increase in the posterior fossa, with the reversal of Chiari and possibly obstructive hydrocephalus.

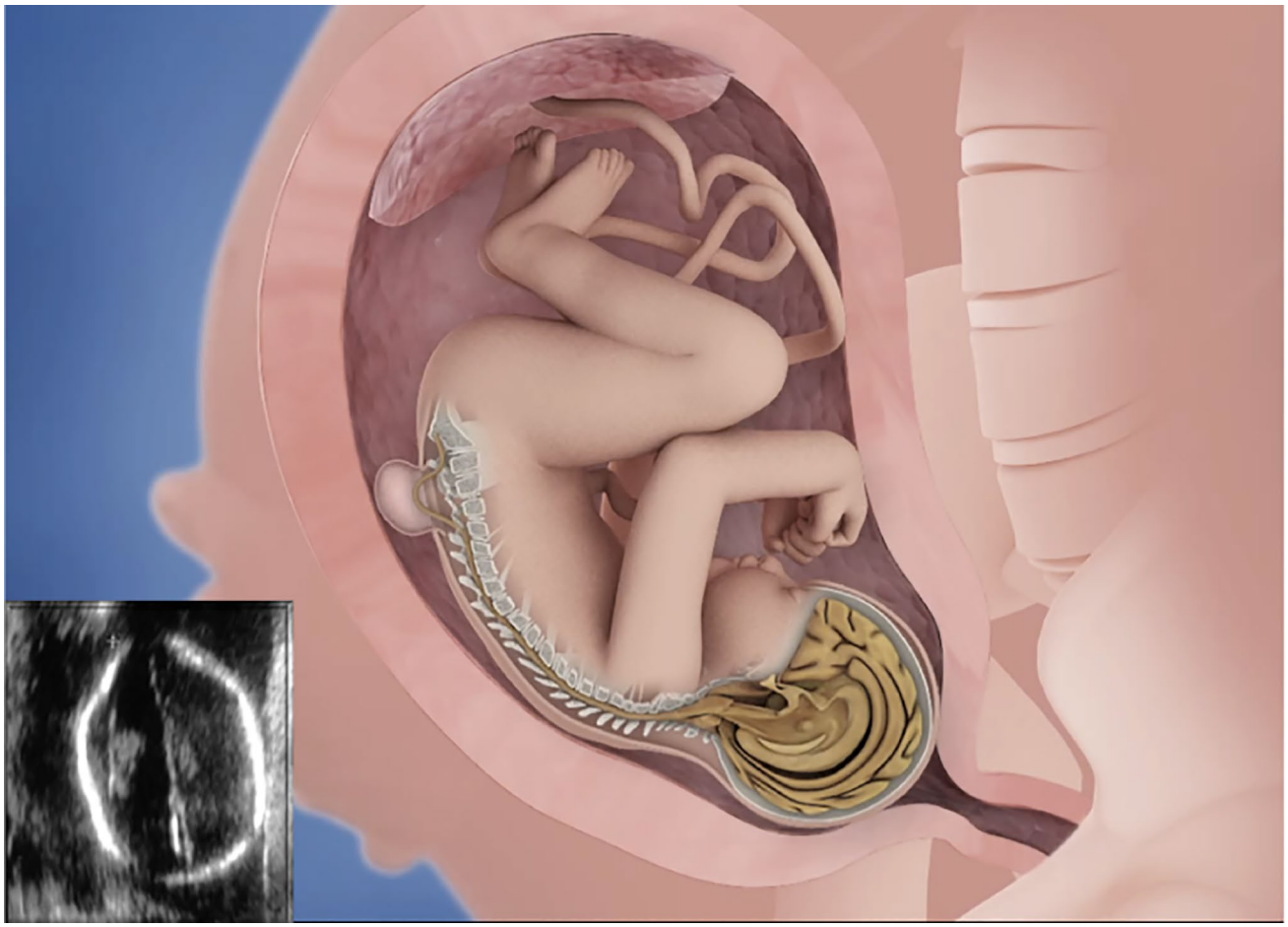

Fig. 5 Chiari malformation type II with cerebellar tonsillar herniation into the spinal canal and ultrasonography demonstrating the lemon sign, with the thrust of the frontal bones (dry brain)

We also found no significant differences between the CSA of group 3 patients and that of the average population [15]. However, when we compared this to the CSA of patients who underwent surgery after birth, the CSA was significantly lower, showing no expansion of the posterior fossa volume and explaining the decreased need for posterior fossa decompression in the so-called symptomatic Chiari [15]. In groups 1 and 2, we had to perform posterior fossa decompression in 8.8% and 7.9% patients, respectively; however, posterior fossa decompression was not needed in any patients in group 3. This finding was consistent with that reported by Adzick et al., who demonstrated a reduction of posterior fossa decompression from 5 to 1% in intrauterine surgery.

Thus, we believe that this increase in posterior fossa amplitude should occur after MMC closure during gestation. This phenomenon allows CSF retention within the cerebrospinal space, stimulating posterior fossa enlargement and adequate CSF circulation, which should occur in cases without neural tube closure defects [17, 18].

The timing of MMC closure is critical for posterior fossa expansion, and the occipital bone also plays a role in this process. However, although MMC was operated intrauterine, patients did not benefit from this phenomenon after 27 weeks of gestation [19].

Notably, the occipital bone has a complex embryology and is formed by eight ossification nuclei [20]. Particularly, intracranial hypotension in MMC could cause earlier occipital bone ossification, preventing its expansion when the correction is made later or even immediately after birth. As mentioned earlier, the other mechanisms capable of explaining hydrocephalus in cases of Chiari type II with small posterior fossa include cerebellar displacement into the spinal canal, cerebral aqueduct compression, and subsequent aqueduct stenosis. Fortunately, postoperative growth of the posterior fossa can reverse obstructive hydrocephalus. However, severe aqueductal ependymal compression may lead to permanent aqueductal stenosis and hydrocephalus.

In patients who underwent intrauterine surgery, we analyzed their cranial circumferences, verifying the tendency to be smaller than the average cranial circumference prior to fetal surgery (Fig. 4). After intrauterine MMC correction, the head circumference was progressively increased, and by 6 months, it was measured to be on average (above two standard deviations), which could possibly be the opportune moment for VP shunt. However, when analyzing their skull MRIs, we found that the vast majority presented reversal of Chiari type II, cerebral aqueduct patency, ventriculomegaly without transependymal edema, a convex or flat third ventricular floor, and subarachnoid CSF accumulation. This transformation from obstructive to communicating hydrocephalus was most likely due to an imbalance between CSF production and absorption. Given this presentation, we introduced acetazolamide every 8 h to stabilize the cephalic perimeter. We maintained this medication for 6 months or until subarachnoid CSF reabsorption and head circumference normalization occurred favorably in the patient. Some patients presented with acidosis at acetazolamide initiation, prompting dosage reduction for a few days before returning to the ideal dose. With these measures, it was possible to avoid placing shunts in a large number of patients. In group 3, only 7.2% patients required VP shunt. Specifically, two patients who already presented with hydrocephalus were operated on intrauterine with ventricular amniotic shunt placement using the Pudens type valve (Accuo-Flo-Codman Ro); however, after birth, these patients required VP shunt. Perhaps these cases should not have been operated intrauterine since the main objective of fetal surgery is to avoid hydrocephalus. Thus, cases with ventricles larger than 16 mm should not be operated on since the possibility of becoming valve less is very slight. This conservative strategy and shunt placement delay reduced the rates of needing shunts from 50 to only 7.2%. Given this shunt placement postponement, and if the floor of the third ventricle was favorable, we opted to perform ETV. Among the 15 cases that underwent ETV, six required VP shunt placement. In previous studies, ETV failure in children with MMC and under 1 year of age varied from 50 to 100% (mean: 75%) [21, 22], although some researchers have found lower success rates of ETV in this group of patients [23]. It is important to note that no primary ETV was performed in groups 1 and 2; usually, this group of patients requires hydrocephalus treatment in the first week after birth, when the success rate of ETV is low [24], in contrast to when group 3 patients require surgery. Group 3 patients usually undergo surgery after 6 months of life, and it seems reasonable to attempt primary ETV [23].

Shunt placement in a patient with MMC does not mean that the patient will be permanently dependent on the shunt. In cases of shunt dysfunction, it is possible to perform ETV and reverse this situation. However, the association of multiple brain malformations with these patients may hinder the performance of this procedure. Particularly, among the 85 patients included our series, 73.4% were shunt-free. ETV is very complex, and certain details must be detailed as follows: (1) inter-thalamic adhesions hinder navigation in the third ventricle in these patients; (2) the Lilliequist membrane is usually far from the tuber cinereum, making it necessary to open both membranes; and (3) the floor of the third ventricle is usually thicker than average, but in these cases, a stent can be left in the tuber cinereum if necessary.

Furthermore, patients shunted at birth will more frequently present with ventricular catheter obstruction and slit-ventricle in the long-term follow-up. With the use of programmable shunt systems, we reduced the number of slit-ventricle cases. However, in many patients, shunt dysfunction symptoms can develop without ventricular system enlargement, delaying a prompt review and causing intellectual deterioration in these patients.

Although many advocate use folic acid during pregnancy for neural tube defect prevention, 18.5% mothers with fetuses presenting with MMC took supplemental folate for more than 3 months and were unable to prevent the disease, as observed in our series. This can be explained in part because folic acid competes with contraceptives, consequently preventing folate absorption. Furthermore, environmental pollution with these hormones could be a factor responsible for the increased incidence of MMC, even in women using folic acid as a prophylactic. Thus, the introduction of folate and methyl-folate in contraceptives could reverse this situation, given that more than half of the pregnancies are reported to be unplanned [24–26].

Regarding the differences in mortality rates between the groups, there was a possible confounding factor. Families who obtain early diagnosis and either undergo fetal surgery or planned early postnatal surgery are likely to have better prenatal care, in general, than those who are diagnosed only postnatally. This might also represent a difference in the socioeconomic status of the families, which can also impact childhood outcomes and, consequently, mortality rates. When analyzing the mortality rates with those reported in other series, the mortality in group 1 was 35% during a mean follow-up of 15.6 years, which is less than that reported by Tennant et al. [3], who reported a mortality rate of 46.7% in patients during a 15-year follow-up and 50% during a 20-year follow-up, demonstrating that one of the most important factors related to mortality in cases of MMC is the presence of hydrocephalus [3].

In this study, we still have little follow-up time for patients operated in utero, with only 10 years remaining. However, reducing shunt placement in these patients will allow a better quality of life and better survival rate. MMC as a disease is the neurosurgeon's responsibility, and it is up the doctor to monitor these patients throughout their intrauterine life.

In conclusion, the most significant cause of morbidity and mortality in patients with MMC is related to hydrocephalus development and the timing of its correction. An earlier

MMC correction surgery was attributed to better outcomes, and the development of fetal neurosurgery was directly related to improving the quality of life of these patients.

Funding Not applicable.

Data availability Not applicable.

Code availability Not applicable.

Declarations

Ethics approval The study was approved by the Research Ethics Committee of Universidade Federal de São Paulo, São Paulo, Brazil, under opinion number 2461706 (CAAE 79580517.6.0000.5505) on January 08, 2018. The requirement for informed consent was waived owing to the retrospective nature of the study.

Conflict of interest No conflicts to disclose.

References

1. Van Allen MI, Kalousek DK, Chernoff GF et al (1993) Evidence for multi-site closure of the neural tube in humans. Am J Med Genet 47:723–743. https://doi.org/10.1002/ajmg.1320470528
2. Tortori-Donati P, Rossi A, Cama A (2000) Spinal dysraphism: a review of neuroradiological features with embryological correlations and proposal for a new classification. Neuroradiology 42:471–491. https://doi.org/10.1007/s002340000325
3. Tennant PW, Pearce MS, Bythell M, Rankin J (2010) 20-year survival of children born with congenital anomalies: a population-based study. Lancet 375:649–656. https://doi.org/10.1016/S0140-6736(09)61922-X
4. Adzick NS, Thom EA, Spong CY et al (2011) A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med 364:993–1004. https://doi.org/10.1056/NEJMoa1014379
5. Choux M, Genitori L, Lang D, Lena G (1992) Shunt implantation: reducing the incidence of shunt infection. J Neurosurg 77:875–880. https://doi.org/10.3171/jns.1992.77.6.0875
6. Cooperman EM (1977) Meningomyelocele: to treat or not to treat. Can Med Assoc J 116:1339–1340
7. Robertson JA, Fost N (1976) Passive euthanasia of defective newborn infants: legal considerations. J Pediatr Surg 88:883–889
8. Verhagen A, Sol J, Brouwer O, SAuer P (2005) Deliberate termination of life in newborns in the Netherlands; review of all 22 reported cases between 1997 and 2004. Ned Tijdschr Geneeskd 149:183–188
9. Johnson CY, Honein MA, Dana Flanders W et al (2012) Pregnancy termination following prenatal diagnosis of anencephaly or spina bifida: a systematic review of the literature. Birth Defects Res. Part A - Clin Mol Teratol 94:857–863
10. McLone DG (1983) Results of treatment of children born with a myelomeningocele. Clin Neurosurg 30:407–412. https://doi.org/10.1093/neurosurgery/30.cn_suppl_1.407
11. Steinbok P, Irvine B, Cochrane DD, Irwin BJ (1992) Long-term outcome and complications of children born with meningomyelocele. Childs Nerv Syst 8:92–96. https://doi.org/10.1007/BF00298448
12. Cochrane D, Wilson D, Steinbok P et al (1996) Prenatal spinal evaluation and functional outcome of patients born with myelomeningocele: information for improved prenatal counselling and outcome prediction. Fetal Diagn Ther 11:159–168. https://doi.org/10.1159/000264297
13. Messing-Jünger M, Röhrig A (2013) Primary and secondary management of the Chiari II malformation in children with myelomeningocele. Childs Nerv Syst 29:1553–1562. https://doi.org/10.1007/S00381-013-2134-4
14. Cavalheiro S, da Costa M, Moron A, Leonard J (2017) Comparison of prenatal and postnatal management of patients with myelomeningocele. Neurosurg Clin N Am 28:439–448. https://doi.org/10.1016/J.NEC.2017.02.005
15. da Costa MDS, Nicacio JM, Dastoli PA et al (2020) Alterations in skull base anatomy in intrauterine and postnatal repaired myelomeningoceles. Child's Nerv Syst 11:2757–2763. https://doi.org/10.1007/s00381-020-04587-6
16. McLone DG, Knepper PA (1989) The cause of Chiari II malformation: a unified theory. Pediatr Neurosci 15:1–12. https://doi.org/10.1159/000120432
17. d'Addario V, Pinto V, Del Bianco A et al (2001) The clivus-supraocciput angle: a useful measurement to evaluate the shape and size of the fetal posterior fossa and to diagnose Chiari II malformation. Ultrasound Obstet Gynecol 18:146–149. https://doi.org/10.1046/J.1469-0705.2001.00409.X
18. Woitek R, Dvorak A, Weber M et al (2014) MR-based morphometry of the posterior fossa in fetuses with neural tube defects of the spine. PLoS ONE 9:e112585. https://doi.org/10.1371/JOURNAL.PONE.0112585
19. Tulipan N, Sutton LN, Bruner JP, Cohen BM, Johnson M, Adzick NS (2003) The effect of intrauterine myelomeningocele repair on the incidence of shunt-dependent hydrocephalus. Pediatr Neurosurg 38:27–33. https://doi.org/10.1159/000067560
20. Matsumura G, England MA, Uchiumi T, Kodama G (1994) The fusion of ossification centres in the cartilaginous and membranous parts of the occipital squama in human fetuses. J Anat 185:295
21. Fritsch MJ, Kienke S, Mehdorn HM (2004) Endoscopic aqueductoplasty: stent or not to stent? Childs Nerv Syst 20:137–142. https://doi.org/10.1007/S00381-003-0860-8
22. Mori H, Nishiyama K, Yoshimura J, Tanaka R (2007) Current status of neuroendoscopic surgery in Japan and discussion on the training system. Childs Nerv Syst 23:673–676. https://doi.org/10.1007/S00381-007-0329-2
23. Elbabaa SK, Gildehaus AM, Pierson MJ, Albers JA, Vlastos EJ (2017) First 60 fetal in-utero myelomeningocele repairs at Saint Louis Fetal Care Institute in the post-MOMS trial era: hydrocephalus treatment outcomes (endoscopic third ventriculostomy versus ventriculo-peritoneal shunt). Childs Nerv Syst 33:1157–1168. https://doi.org/10.1007/S00381-017-3428-8
24. Kulkarni AV, Drake JM, Mallucci C et al (2009) Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus. J Pediatr 155:254–259. https://doi.org/10.1016/J.JPEDS.2009.02.048
25. Silva CP, Otero M, Esteves V (2012) Processes for the elimination of estrogenic steroid hormones from water: a review. In: Environmental Pollution. Environ Pollut pp 38–58
26. Shere M, Bapat P, Nickel C et al (2015) The effectiveness of folate-fortified oral contraceptives in maintaining optimal folate levels to protect against neural tube defects: a systematic review. J Obstet Gynaecol Canada 37:527–533. https://doi.org/10.1016/S1701-2163(15)30229-2