Fetal treatment for myelomeningocele in Brazil

Silvia Lourdes Loreto Faquini [1]
https://orcid.org/0000-0003-4247-0126

Alex Sandro Rolland Souza [2]
https://orcid.org/0000-0001-7039-2052

Orlando Gomes Santos-Neto [3]
https://orcid.org/0000-0001-7216-9671

[1-3] Instituto de Medicina Integral Prof. Fernando Figueira. Rua dos Coelhos, 300. Boa Vista. Recife, PE, Brazil. CEP: 50.070-902. E-mail: alexrolland@uol.com.br

Neural tube defects (NTDs) are congenital malformations that result from the failure of the neural tube to close between the 5th and 6th week of gestation. The anatomical site where the defect occurs defines the type of defect.[1] Spina bifida (SB) is the result of neural tube failure closing in its caudal portion. It is classified as opened, in more than 90% of the cases, when the nerve structures are exposed by a defect in conjunction with the skin, and closed, which corresponds to the smallest proportion of the cases, where the nerve structures are covered by the skin.[2]

Opened spina bifida has different subtypes defined by the content within the defect. The meningocele contains only the dural sac, while the myelomeningocele also contains neural elements that are attached to the hernial sac. The term myeloschisis or rachisis is used when the neural placode is exposed without the presence of a hernial sac, and presents as a flat lesion.[3]

Every year, around 150,000 children are born with SB in the world.[4] In Brazil, the estimated prevalence is 14 cases per 10,000 births and the sum of all types of NTD reaches 24 cases per 10,000 births.[5]

Most cases of NTDs are considered to be of multifactorial origin and are influenced by a combination of geographical, ethnic, genetic and dietary factors.[6] Among the nutrients involved in the etiopathogenesis of this disease, the most established is the folate (also known as folic acid or vitamin B9). Folate is not produced by the human body and must be obtained by eating food rich in this vitamin or supplement in its synthetic form.[7] Some countries have introduced folic acid into essential food, in Brazil this fortification is carried out in wheat flour, as a way of trying to minimize the occurrence of NTD cases.[8]

This article is published in *Open Access* under the *Creative Commons Attribution license*, which allows use, distribution, and reproduction in any medium, without restrictions, as long as the original work is correctly cited.

http://dx.doi.org/10.1590/1806-9304202400000241-en

The SB diagnosis is made during prenatal care in more than 90% of cases.[9] Currently, ultrasound (USG) is considered the gold standard for this diagnosis. The sonographic characteristics of SB can be detected in the second trimester and include an abnormal skull shape with flattening of the temporal bones ("lemon sign"), abnormal appearance of the teardrop-shaped cerebral ventricles (colpocephaly), ventriculomegaly, alteration of the posterior fossa with cerebellar herniation ("banana sign") and non-visualization of the cisterna magna and alteration in the position of the feet and lower limbs (LLL) with decreased movement. In addition to these indirect signs, a direct defect in the spine can also be observed with the presence of a cystic image or sacculation and abnormal or incomplete closure of the posterior vertebral arches.[10] It is important to note that new markers for SB have been introduced in recent decades, allowing suspicion and diagnosis to be made in the first trimester, such as intracranial transluscence.[11]

Myelomeningocele is a complex congenital malformation and the most common central nervous system (CNS) anomaly compatible with life. It has a death rate of around 10%[12] and has considerable short- and long-term morbidity and mortality, including paralysis, reduced strength and movement of the lower limbs and intestinal and urinary dysfunction. At birth, they have cerebellar herniation (Arnold Chiari Syndrome type II) with obliteration of the foramen magnum, brainstem abnormalities and often hydrocephalus and the need for a ventriculo-peritoneal shunt. It is important to note that surgical revisions of the ventriculo-peritoneal shunt are common throughout life due to infection or obstruction.[13]

The classic treatment for spina bifida is performed after birth, but since the publication of the "Management of Myelomeningocele Study" (MOMS)[14] in 2011, intrauterine correction has been an option for these patients. The study showed an improvement in motor function, less herniation of the brainstem and cerebellum and a reduction in the need for surgical procedures for hydrocephalus, especially the need for peritoneal ventricle shunt, when comparing intrauterine and postnatal repair, with an improvement in quality and life expectancy for these patients.[14]

Despite the clear benefits demonstrated by the study, which led to it being discontinued before reaching the initial number of estimated patients, some limitations and maternal and fetal risks have also been described. Among the main complications was an increased risk of premature rupture of membranes (PROM) and spontaneous premature birth, with 79% occurring before 37 weeks and 36% before 35 weeks,[14] as well as maternal limitations throughout pregnancy and the need for surgical delivery for this and future pregnancies.[14]

Since the publication of the MOMS trial, the number of centers offering fetal surgery for myelomeningocele has grown significantly, especially in the United States, thus increasing regional access to the procedure, but potentially diluting the experience of individual centers.

In Brazil until 2011, fetal surgery was only performed in São Paulo, at the *Escola Paulista de Medicina of the Universidade Federal de São Paulo* (Unifesp) and later at the *Hospital e Maternidade Santa Joana* by the same team.

After the MOMS trial, other centers began offering this procedure.Initially, there were two more centers in São Paulo, the *Unidade Fetal do Hospital do Coração* (HCor) and the *Hospital Israelita Albert Einstein* (the first fetoscopic myelomeningocele repair in Brazil in 2013). Subsequently, intrauterine myelomeningocele repair could be performed in different States and medical centers in Brazil, making the procedure more available to patients. Other Brazilian centers that regularly perform intrauterine surgery include *Hospital Moinhos de Vento* - Rio Grande do Sul, *Maternidade Escola da UFRJ* - Rio de Janeiro, *Maternidade Escola Assis-Chateaubriand* (MAEC) - Ceará and *Hospital Vila da Serra* - Minas Gerais.

The *Instituto de Medicina Integral Prof. Fernando Figueira* (IMIP) is a reference hospital for fetal malformations and neurosurgery in the State and Northeast region of Brazil.Since 2013, fetal medicine and neurosurgery service at IMIP have been performing and offering patients from the *Sistema Único de Saúde* (SUS) (Public Health System) intrauterine myelomeningocele repair, making it the fourth center in Brazil to perform this procedure. The surgery performed at our service is "open", using the mini-hysterotomy technique[15] and adapted for our institution.[16] It is worth noting that the surgical complications at IMIP were similar in frequency to those reported in the literature,[14] such as PROM, which was approximately 48%.[16]

The group of IMIP has performed more than 80 procedures over the years, and the team is made up of specialists in fetal medicine, neurosurgery and anesthesia. As well as specialist physicians, we have the support of resident physicians, undergraduate students, nursing professionals, surgical block and the intensive care unit (ICU). This multidisciplinary team is extremely important for the support and monitoring of each patient.

Despite the progress made in recent years in terms of the availability of specialized fetal medicine centers in Brazil, intrauterine surgery still lacks centers in all regions of the country. Currently, patients still have to travel around Brazil in an attempt to find specialized centers, and there is little publicity about the possibility of this repair while still in the womb, which ends up with the loss of opportunity to perform it, since it must be carried out in the 2nd gestational trimester.

Authors' contribution

All the authors contributed equally for the design of the article and declared no conflicts of interest.

References

1. Greene ND, Copp AJ. Neural tube defects. Annu Ver Neurosci. 2014; 37: 221-42.
2. Masisni L, De Luca C, Noia G, Caruso A, Lanzone A, Rendeli C, et al. Prenatal Diagnosis, natural history, postnatal treatment and outcome of 222 cases of spina bífida: experience of tertiary center. Ultrasound Obstet Gynecol. 2019; 53 (3): 302-8.
3. Yilmaz A, Müslüman AM, Dalgic N, Cavuşoğlu H, Ayhan Kanat A, Colak I, et al. Shunt insertion in newborns with myeloschisis/ myelomeningoceles and hydrocephalus. J Clin Neurosci. 2010; 17 (12): 1493-6.
4. Gotha L, Pruthi V, Abbasi N, Kulkarni AV, Church P, Drake JM, et al. Fetal spina bífida: What we tell the parentes. Prenat Diagn. 2020; 40 (12): 1499-1507.
5. Lopes-Camelo JS, Cartilla EE, Oriolli IM. Folic acid flour fortification: Impact on the frequencies of 52 congenital anomaly types in three South American countries. Am. J. Med Genet. 2010; 152 (10): 2444-58.
6. Copp AJ, Adzick NS, Chitty LS, Fletcher JM, Holmbeck GN, Shaw GM. Spina bifida. Nat Rev Dis Primers. 2015; 1: 15007.
7. Daly LE, Kirke PN, Molloy A, Weir DG, Scott JM. Folate levels and neural tube defects. JAMA. 1995; 274 (21): 1698-1702.
8. Canfield MA, Collins JS, Botto LD, Willians LJ, Mai CT, Kirby RS, et al. Changes in the birth prevalence of selected birth defests after grain fortification with folic acid in the United States: findings from a multistate population-based study. Birth Defects Res A Clin Mol Teratol. 2005; 73 (10): 679-89.
9. Bodin CR, Rasmussen MM, Tabor A, Westbom L, Tiblad E, Ekelund CK, et al. Ultrasound in prenatal diagnostics and its impact on the epidemiology of spina bifida in a national cohort from Denmark with a comparison to Sweden. Biomed Res Int. 2018; 2018: 9203985.
10. Sepulveda W, Corral E, Ayala C, Be C, Gutierrez J, Vasquez P. Chromosomal abnormalities in fetuses with open neural tube defects: prenatal identification withbultrasound. Ultrasound Obstet Gynecol. 2004; 23 (4): 352-6.
11. Meller C, Aiello H, Otano L. Sonographic detection of open spina bifida in the first trimester: review of the literature. Childs Nerv Syst. 2017; 33 (07): 1101-6.
12. Manning SM, Jennings R, Madsen JR. Pathophysiology, prevention and potencial treatment of neural tube defects. Ment Retard Dev Disabil Res Rev. 2000; 6: 6-14.
13. Caldarelli M, Di Rocco C, La Marca F. Shunt complications in the first postoperative year in child with meningomyelocele. Childs Nerv Syst. 1996; 12: 748-54.
14. Adzick NS, Thom EA, Spong CY, *et al*. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med. 2011; 364 (11): 993-1004.
15. Botelho RD, Imada V, Costa KJR, Watanabe LC, Rossi Jr. R, Salles AAF, et al. Fetal Myelomeningocele Repair through a Mini-Hysterotomy. Fetal Diagn Ther. 2017; 42 (1): 28-34.
16. Callou RT, Faquini SL, Santos-Neto OG, Faquini I, Furtado G, Furtado MF, et al. Maternal and perinatal outcomes after prenatal or postnatal surgical repair of myelomeningocele. Cuad Educ Desarrollo. 2024; 16 (5): 1-24.

Received on September 5, 2024
Final version presented on September 6, 2024
Approved on September 9, 2024

Invited by Editor in Chief: Lygia Vanderlei