

Prenatal Diagnosis and Pregnancy Management of MMC

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Abstract

Open spina bifida (myelomeningocele) is a specific kind of neural tube defect (NTD) resulting from a trouble of closure of the caudal region of the neural tube early in embryogenesis. The diagnosis and management of open spina bifida has changed significantly over the past century. Significant advances in the prevention, diagnosis and treatment of open spina bifida have been made over the last years. The most significant strategy for the prevention of open spina bifida has been with folic acid supplementation. Although progress in the field of myelomeningocele diagnosis and treatment has revolutionised the medical treatment of open spina bifida, the postnatal treatment of myelomeningocele evolved significantly and is now complicated by issues surrounding prenatal diagnosis, including availability, economic feasibility, and selection for invasive fetal surgery and management of pregnancy.

Keywords: Myelomeningocele/ Spina bifida / folic acid supplementation / ultrasound scan /surgery.**Copyright © 2022 The Author(s):** This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Congenital anomalies (CA) are a real public health problem due to their prevalence of approximately 14% of live births worldwide [1, 2] and it's the leading cause of infant mortality in the world (more than 25%). Major or severe CA concerns 3% of all births and 20% of all the CA. Among these major anomalies, 25% are cardiac, 20% of limb anomalies and 15% of the central nervous system [3]. Spina bifida is the most common CA of the central nervous system. Its most common form is myelomeningocele (MMC).

Open spina bifida (myelomeningocele) is a devastating congenital defect of the central nervous system, a specific type of neural tube defect resulting from a failure of closure of the caudal region of the neural tube early in embryogenesis. MMC is characterized by protrusion of the meninges and spinal cord through open vertebral arches leading to lifelong paralysis.

In utero as well as after birth MMC is not a lethal disease but a severe progressive disease with damage to the central and peripheral nervous systems responsible of severe handicaps.

In addition, MMC patients are often limited by various degrees of mental retardation, bowel and bladder dysfunction, and orthopedic disabilities. While the etiology of MMC remains poorly understood, primary failure of either neural tube or mesenchymal closure at the caudal neuropore in the embryonic period results in exposure of the developing spinal cord to the uterine environment [4].

Without protective tissue coverage, secondary destruction of the exposed neural tissue by trauma or amniotic fluid may occur throughout gestation.

The diagnosis and management of open spina bifida has evolved dramatically over the past century. Over the past years, improvements in prenatal diagnosis and advancements have been made in fetal therapy, with the publication of a randomized-controlled trial demonstrating benefit of fetal surgical repair of myelomeningocele [5]. Although progress in the field of myelomeningocele diagnosis and treatment has revolutionized the medical treatment of open spina bifida.

Until 15 years ago, treatment of MMC consisted of surgical closure of the spinal canal at birth and lifelong supportive care. Since that time the clinical

experience with midgestational human repair has been shown to improve neurologic function and reduce morbidity from hydrocephalus.

Prenatal diagnosis

Advances in prenatal diagnosis now permit diagnosis of spina bifida as early as the first trimester, and extensive research into the etiology of neural tube defects has elucidated both genetic and micronutrient causes.

The use of maternal serum alpha-fetoprotein levels as a primary modality for screening for open/closed spinal dysraphism should be practiced especially in a pregnant patient with a pre-pregnancy body mass index (BMI) greater than or equal to 35 or greater, or in the presence of geographical access or clinical access factors that affect the implementation of timely and good quality ultrasound screening at 18-22 weeks' gestation.

In the context of maternal serum aneuploidy screening, maternal serum alpha-fetoprotein levels can be used as a secondary screening tool in the second trimester [8].

Maternal serum alpha-fetal protein is a sensitive screening tool for NTDs, with a screening sensitivity of about 80–85% when the screen positive cut-off is set at 2.5 multiples of the median [6–7]. With improving detection rates of NTD by ultrasound, the role of routine MSAFP screening has been challenged, and is useful for early diagnosis.

The Ultrasound Screening has consistently been identified as a sensitive tool for the detection of NTDs, and is considered the gold standard for the prenatal diagnosis of NTDs. Recent studies have reported detection rates by ultrasound, ranging from 96–100%. With advances in ultrasound technology, however, the need for amniocentesis for this purpose has become obsolete [9, 10].

Several investigators have recently examined ultrasound findings of open NTDs in the first-trimester: Small biparietal diameter has been associated with open spina bifida from 11–13 weeks [11], 50% of cases of open spina bifida have a BPD below the fifth centile [33]. Subsequently, this group showed that the combination of first trimester BPD below the fifth centile with maternal serum markers MSAFP, and free HCG, improves the detection rate for open spina bifida to 70% [12]. First-trimester examination of the posterior fossa has also been further refined with the use of three-dimensional ultrasound. Cisterna magna width and measurements of the brainstem compared with brainstem-occipital bone distance have been identified as potential first-trimester screening signs for open spina bifida [13].

Abnormal development of the neural tube leads to the development of a Chiari II malformation resulting from herniation of the cerebellar vermis, fourth ventricle, and medulla oblongata through the foramen magnum into the upper cervical canal. The classic cerebellar and cranial findings seen on ultrasound associated with the Chiari II malformation were described by Nicolaides *et al.* [14] in 1986 as the banana sign and lemon sign. The sonographic cerebellar signs associated with open spina bifida have been found to be the most reliable diagnostic signs. Despite nearly 100% of neonates born with an open myelomeningocele having evidence of hydrocephalus at the time of birth, but only 70% will develop hydrocephalus during fetal life [14, 15].

Ultrasound imaging of the spinal lesion in cases of spina bifida can be quite obvious when there is an open lesion with the formation of a cystic myelomeningocele (Fig1.). The location of bony dysraphism is more difficult in cases of a closed neural tube defect, or small myelomeningoceles, particularly lesions isolated to the sacral spine.

The use of three-dimensional ultrasound may be more accurate for the localisation of lesion level compared with two-dimensional ultrasound, but a discrepancy exists with the clinical significance of the improved accuracy, which is generally in the region of one spinal level compared with postnatal findings [16, 17].

The fetal MRI has become an important adjunct tool for perinatologists and paediatric neurosurgeons to aid in counselling and surgical planning for fetuses diagnosed with spina bifida on ultrasound by its ability to characterise accurately the level of myelomeningocele within one to two vertebral levels in 89% of cases using MRI. Compared with ultrasound, MRI seems to be equally accurate for the prediction of the highest affected vertebral [25, 26].



Fig-1: Open spina bifida / myelomeningocele - Gynecology-obstetrics and endoscopy Department, Maternity Souissi/ University hostpital center IBN SINA

Management of Pregnancy in the Presence of MMC

Following the detection of an isolated open/closed spinal dysraphism, families should be offered a choice of obstetrical management options following the results of diagnostic and genetic screening tests. The offer of these options should include information about prenatal repair of myelomeningocele and its prognosis, postnatal surgical repair of myelomeningocele and its prognosis, and termination of pregnancy (not allowed in Islamic countries) and conducting an autopsy [8].

Caesarean section is the most common mode of delivery in the fetus with myelomeningocele, regardless of presentation (cephalic or Breech); however, cesarean delivery is obligatory in cases of breech presentation. The performance of a vaginal delivery with intrapartum fetal heart rate monitoring may be considered in certain cases of MMC in cephalic presentation, in the absence of macrocephaly (depending on the gestational age) and in the presence of a small MMC sac.

Management of the delivery of a fetus with multiple and complex anomalies (including neural tube defect) should be determined on the basis of an individualized foundation by the multidisciplinary team of care providers at the center where the delivery is to take place, based on the differential diagnosis, identified congenital anomalies, results of prenatal screening results, prenatal care requirements, anticipated neonatal morbidity or mortality, results of family consultation and family requests.

Many Investigations are improving prenatal therapy for open spina bifida repair. Currently, minimally invasive surgical techniques using fetoscopy have proven to be inferior to open fetal surgery; however, with advancing technology, some of the technical fetoscopic approach may improve over time [18].

The more promising treatment and exciting area of innovation has been with a non-traditional approach using engineered tissues held in a flexible patch, sponge or hydro-gel matrix to create a watertight protective seal over the defect using a single fetoscopic port or a percutaneous approach with an amniocentesis needle [19, 20].

CONCLUSION

Several risk factors have been studied in association with spina bifida; the strongest established risk factor for an NTD is a family history. Several studies have estimated that women with a history of a child with an NTD carry a 3–8% risk of and NTD, including spina bifida.

Also Folic acid and genes related to folate metabolism have been identified to play a strong role in

neural tube development. Folic acid deficiency has been associated with a two- to eight-fold increased risk of NTDs [21]. Several gene variants involved in the folate metabolism pathway have been identified in association with abnormal neural tube closure in human beings [22]. Of recent discovery has been the complicated interaction between maternal and embryonic genes and the role of regulators of neural tube closure that are not involved in folate metabolism [21-23].

Many studies showed a significant benefit of 4 mg of folic-acid supplementation in the preconceptional period to prevent NTD recurrence [24].

The increase in the number of births of children with SB should make the medical community aware of the importance of a global and multidisciplinary care of this pathology, which requires experienced centers from the neonatal period to adulthood to allow the best possible life for these people. The increase in the number of diagnosed cases should allow to alert the public authorities to the need for national prevention campaigns and the need to raise awareness among doctors, especially general practitioners and obstetrician-gynecologists who are in the front line of prevention.

REFERENCES

1. Rosano, A., Botto, L. D., Botting, B., & Mastroiacovo, P. (2000). Infant mortality and congenital anomalies from 1950 to 1994: an international perspective. *Journal of Epidemiology & Community Health*, 54(9), 660-666.
2. EUROCAT, W. (2004). A review of environmental risk factors for congenital anomalies.
3. EUROCAT WG. (2002). Surveillance of Congenital Anomalies in Europe, 1980–1999. University of Ulster, Northern Ireland: E.S.o.C.A. EUROCAT, Editor. EUROCAT, European surveillance of congenital anomalies: Newtownabbey; 2002.
4. Hutchins, G. M., McGowan, K. D., & Blakemore, K. J. (1992). Spinal dysraphia: Not a neural tube defect. *Am J Hum Genet*, 51(suppl 1), A319.
5. Adzick, N. S., Thom, E. A., Spong, C. Y., Brock III, J. W., Burrows, P. K., Johnson, M. P., ... & Farmer, D. L. (2011). A randomized trial of prenatal versus postnatal repair of myelomeningocele. *New England Journal of Medicine*, 364(11), 993-1004.
6. Wald, N. J., Cuckle, H., Brock, J. H., Peto, R., Polani, P. E., & Woodford, F. P. (1977). Maternal serum-alpha-fetoprotein measurement in antenatal screening for anencephaly and spina bifida in early pregnancy. Report of UK collaborative study on alpha-fetoprotein in relation to neural-tube defects. *Lancet (London, England)*, 1(8026), 1323-1332.
7. Cheschier, N. (2003). ACOG practice bulletin. Neural tube defects. Number 44, July

- 2003.(Replaces committee opinion number 252, March 2001). *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, 83(1), 123-133.
8. Wilson, R. D., Audibert, F., Brock, J. A., Campagnolo, C., Carroll, J., Cartier, L., ... & Popa, V. (2014). Anomalies fœtales affectant le tube neural: Dépistage/diagnostic prénatal et prise en charge de la grossesse. *Journal of Obstetrics and Gynaecology Canada*, 36(10), 940-942.
 9. Nadel, A. S., Green, J. K., Holmes, L. B., Frigoletto Jr, F. D., & Benacerraf, B. R. (1990). Absence of need for amniocentesis in patients with elevated levels of maternal serum alpha-fetoprotein and normal ultrasonographic examinations. *New England Journal of Medicine*, 323(9), 557-561.
 10. Nadel, A. S., Green, J. K., Holmes, L. B., Frigoletto Jr, F. D., & Benacerraf, B. R. (1990). Absence of need for amniocentesis in patients with elevated levels of maternal serum alpha-fetoprotein and normal ultrasonographic examinations. *New England Journal of Medicine*, 323(9), 557-561.
 11. Karl, K., Benoit, B., Entezami, M., Heling, K. S., & Chaoui, R. (2012). Small biparietal diameter in fetuses with spina bifida on 11–13-week and mid-gestation ultrasound. *Ultrasound in obstetrics & gynecology*, 40(2), 140-144.
 12. Bernard, J. P., Cuckle, H. S., Bernard, M. A., Brochet, C., Salomon, L. J., & Ville, Y. (2013). Combined screening for open spina bifida at 11-13 weeks using fetal biparietal diameter and maternal serum markers. *American Journal of Obstetrics and Gynecology*, 209(3), 223-e1.
 13. Scheier, M., Lachmann, R., Pětroš, M., & Nicolaides, K. H. (2011). Three-dimensional sonography of the posterior fossa in fetuses with open spina bifida at 11–13 weeks' gestation. *Ultrasound in obstetrics & gynecology*, 38(6), 625-629.
 14. Nicolaides, K. H., Gabbe, S. G., Campbell, S., & Guidetti, R. (1986). Ultrasound screening for spina bifida: cranial and cerebellar signs. *The Lancet*, 328(8498), 72-74.
 15. Pilu, G., Romero, R., Reece, E. A., Goldstein, I., Hobbins, J. C., & Bovicelli, L. (1988). Subnormal cerebellum in fetuses with spina bifida. *American journal of obstetrics and gynecology*, 158(5), 1052-1056.
 16. Lee, W., Chaiworapongsa, T., Romero, R., Williams, R., McNie, B., Johnson, A., ... & Comstock, C. H. (2002). A diagnostic approach for the evaluation of spina bifida by three-dimensional ultrasonography. *Journal of ultrasound in medicine*, 21(6), 619-626.
 17. Zugazaga Cortazar, A., Martín Martínez, C., Duran Feliubadalo, C., Bella Cueto, M. R., & Serra, L. (2013). Magnetic resonance imaging in the prenatal diagnosis of neural tube defects. *Insights into imaging*, 4(2), 225-237.
 18. Bruner, J. P., Tulipan, N. B., Richards, W. O., Walsh, W. F., Boehm, F. H., & Vrabcak, E. K. (2000). In utero repair of myelomeningocele: a comparison of endoscopy and hysterotomy. *Fetal diagnosis and therapy*, 15(2), 83-88.
 19. Kohl, T., Tchatcheva, K., Merz, W., Wartenberg, H. C., Heep, A., Müller, A., ... & Gembruch, U. (2009). Percutaneous fetoscopic patch closure of human spina bifida aperta: advances in fetal surgical techniques may obviate the need for early postnatal neurosurgical intervention. *Surgical endoscopy*, 23(4), 890-895.
 20. Watanabe, M., Li, H., Roybal, J., Santore, M., Radu, A., Jo, J. I., ... & Flake, A. (2011). A tissue engineering approach for prenatal closure of myelomeningocele: comparison of gelatin sponge and microsphere scaffolds and bioactive protein coatings. *Tissue Engineering Part A*, 17(7-8), 1099-1110.
 21. Mitchell, L. E., Adzick, N. S., Melchionne, J., Pasquariello, P. S., Sutton, L. N., & Whitehead, A. S. (2004). Spina bifida. *The Lancet*, 364(9448), 1885-1895.
 22. Finnell, R. H., Gould, A., & Spiegelstein, O. (2003). Pathobiology and genetics of neural tube defects. *Epilepsia*, 44, 14-23.
 23. Leung, K. Y., De Castro, S. C., Savery, D., Copp, A. J., & Greene, N. D. (2013). Nucleotide precursors prevent folic acid-resistant neural tube defects in the mouse. *Brain*, 136(9), 2836-2841.
 24. Laurence, K. M., James, N., Miller, M. H., Tennant, G. B., & Campbell, H. (1981). Double-blind randomised controlled trial of folate treatment before conception to prevent recurrence of neural-tube defects. *Br Med J (Clin Res Ed)*, 282(6275), 1509-1511.
 25. Chao, T. T., Dashe, J. S., Adams, R. C., Keefover-Hicks, A., McIntire, D. D., & Twickler, D. M. (2011). Fetal spine findings on MRI and associated outcomes in children with open neural tube defects. *American Journal of Roentgenology*, 197(5), W956-W961.
 26. Aaronson, O. S., Hernanz-Schulman, M., Bruner, J. P., Reed, G. W., & Tulipan, N. B. (2003). Myelomeningocele: prenatal evaluation—comparison between transabdominal US and MR imaging. *Radiology*, 227(3), 839-843.