Scholars LITERATURE

La Prensa Medica Argentina

Research Article

DOI: https://doi.org/10.47275/0032-745X-156
Volume 105 Issue 5

Myelomeningocele Associated with Deletion of 22q11 and Normal Posterior Fossa: Prenatal Diagnosis

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Abstract

Background: Spina Bifida Myelomeningocele is the most common nonlethal neural tube defect in North America, that is associated with some anomalous development of brain structure especially chiari-malformation, musculoskeletal system, renal system, and cardiovascular system. Genetic factors are infrequent causes of NTDs such as deletion of 22q11.

Case presentation: Prenatal ultrasonography of 29 week aged fetus with normal maternal serum alpha fetoprotein found polyhydramnios and abnormal cystic mass in lower spine recommended for myelomeningocele. Fetus MRI demonstrated terminal closed myelomeningocele and tethered cord, obliteration of cisterna magna without other cerebral anomalies such as Chiari II malformation. After birth the patient had respiratory distress with the same finding. More evaluation showed multiple cardiac abnormalities and deletion of 22q11 that is a rare cause of NTDs.

Conclusion: Identification of NTDs should be considered as a warning sign for other syndrome or disorder, and prompt a thorough etiologic investigation and genetic counseling.

Keywords: Neural tube defect; Myelomeningocele; Chiarimalformation; Deletion of 22q11.

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Citation: Dadkhah A, Younesi L (2019) Myelomeningocele Associated with Deletion of 22q11 and Normal Posterior Fossa: Prenatal Diagnosis. Prensa Med Argent, Volume 105:5. 156. DOI: https://doi.org/10.47275/0032-745X-156.

Received: August 25, 2019; **Accepted:** October 02, 2019; **Published:** October 07, 2019

Introduction

Neural tube defects (NTDs) are structural defects secondary to abnormal neural tube closure that occur during early fetal development. NTDs are divided into two major groups: (a) defects involving cranial structures, such as anencephaly and encephalocele; (b) defects at the level of the spinal cord (spina bifida) [1]. Spina Bifida Myelomeningocele (SBM) is the most common nonlethal neural tube defect (NTD) in North America, affecting three to five per 10,000 births per year [2]. The defect is characterized by protrusion of the spinal cord, meninges, and nerve roots through an opening in the spine.

Genetic influences and prenatal maternal factors such as abnormal levels of folate, maternal age, maternal Illness, parity, obesity and diabetes, previous pregnancy wastage, multiple gestations and the usage of antiepileptic medication are the most important risk factors of SBM [1]. SBM is classified as either closed or open defects. Closed SBM is characterized by the nerve tissue that is covered by skin and not exposed outside the body. In contrast, open SBM involve neural tube exposure through spinal cord defects to the amniotic fluid [3]. Some anomalous development of brain structure especially posterior fossa abnormalities are associated with open SBM, such as Chiari II malformation and hydrocephalus, that are absence in closed SBM [4].

Prenatal sonography can detect most fetuses with polyhydramnios and spina bifida and identifies other concurrent abnormalities especially in the second trimester [5]. In this study we introduce a closed SBM case with polyhydramnios and some others anomaly with deletion of 22q11 as a rare association.

Case Presentation

A pregnant woman, aged 32, primigravida for MRI of fetus was referred to our imaging centre, because of abnormal cystic mass in lower spine that was found in ultrasonography of fetus at 29w. She had no history of diabetes, antiepileptic medication usage and family history of congenital disorder.

All pregnancy evaluation including CBC, U/A, U/C, TSH, GCT, biochemistry test (PAPP-A, Free β-hCG, AFP, uE3, hCG, inhibin-A) were in normal range. Maternal serum alpha fetoprotein was 17.12 IU/ml in 15 week. First and second trimester screening tests based on biochemistry and ultrasound showed that the risk of Down

syndrome, trisomy 13/18, NTD, and SLOS was less than the screening cut-off. Ultrasonography in 18 week gestation (anomaly scan), which performed in another center, showed normal fetus with appropriate growth and normal amniotic fluid.

Next ultrasonography in 29 week gestation detected polyhydramnios (Amniotic fluid index=25 cm) (Figure 1) and a 30*20 mm cystic lesion with internal septa adjacent to the posterior andlower part of spine, recommended for myelomeningocele. No obvious defect was seen in skin (Figure 2). So brain and spinal MRI was performed. MRI showed a 32*20mm cystic structure at the dorsal aspect of lower part of spine that had protruded via dorsal sacral defects in lower segment, along with connection to spinal canal. Internal septa was seen (probably nerve roots). Skin seemed to be intact and cord continued to this level (Tethered cord). Intrapelvic mass was not seen. These findings were compatible with terminal closed myelomeningocele and tethered cord (Figure 3). In the brain, cisterna magna was mildly obliterated, without Chiari II malformation. Ventricles were not dilated. Falx and interhemispheric fissure were seen in the midline. Prominent CPS was visible (Figure 4).

The patient was delivered by caesarean section at 38 week gestation. The birth weight was 2670 g (10th percentile). After birth examination revealed a fluid filled sac along the postroinferior aspect of spinal column with an ulcer on this lesion. No leakage of fluid was evident. Both fontanels were smaller than normal. Pupils were mid-size andreactive to light. He had spontaneous motion of all four extremities. He was tachypenic with respiratory rate 56 per min and O_2 saturation was 98%. Mild mottling was seen in abdominal skin. In more evaluation, brain CT scan showed mild dilation of ventricles without any evidence of posterior fossa abnormality. Multiple cardiac

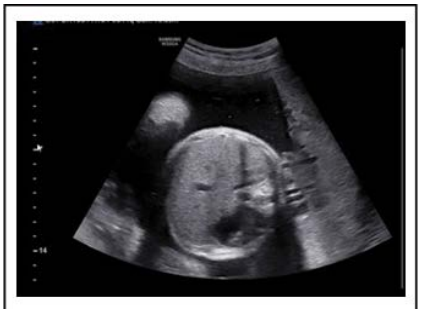

Figure 1: Ultrasonography detected polyhydramnios, Amniotic fluid index=25 cm.

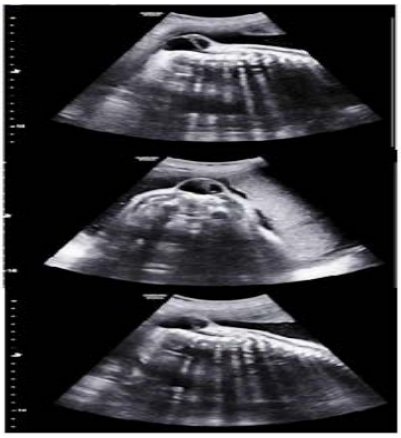

Figure 2: Ultrasonography showed cystic lesion with internal septa adjacent to the posterior and lower part of spine, recommended for myelomeningocele.

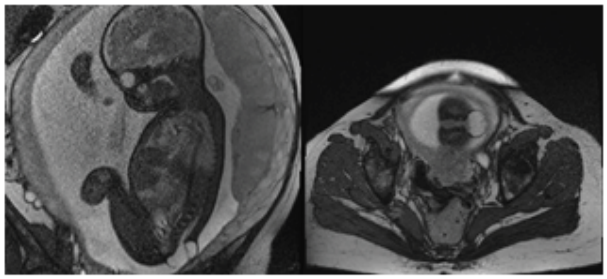

Figure 3: MRI demonstrated cystic structure at the dorsal aspect of lower part of spine that had protruded via dorsal sacral defects in lower segment, along with connection to spinal canal. Internal septa was seen (probably nerve roots). Skin seemed to be intact.

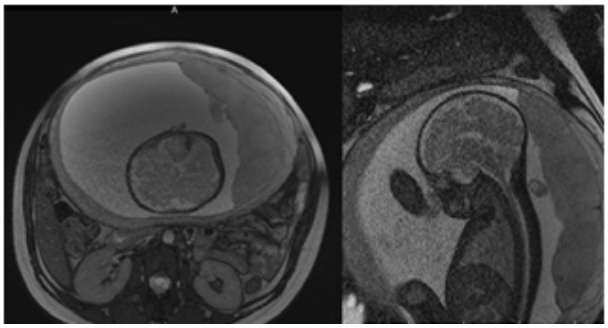

Figure 4: MRI showed cisterna magna was mildly obliterated, without Chiari II malformation. Falx and interhemispheric fissure were seen in the midline.

abnormalities were seen in CT angiography of heart and pulmonary arteries including large ASD, large VSD, PDA (5 mm), right atrium enlargement, right ventricle enlargement, interrupted aortic arch, descending aorta originated from PDA, subclavian artery originated from descending aorta, dilated main pulmonary artery with confluent branches. So patient with these cardiac anomalies was not operable. Finally, four day new-born died because persistent bradycardia and unsuccessful CPR process. In future genetic evaluation deletion of 22q11 founds in dead new-born.

Discussion Spina Bifida Myelomeningocele (SBM), the most common neural tube defect, is classified as either closed or open defects. Some anomalous development of brain structure are associated with open SBM, including Chiari II malformation, hydrocephalus, agenesis or hypoplasia of corpus callosum, thickening or thinning and gyrification of cortex [6].

In the case of open NTDs, Chiari type II anomaly develops when intracranial brain structures herniate toward the spinal canal as cerebrospinal fluid escapes through the NTD area. Such malformations present as characteristic intra-cranial signs on ultrasound, such as ventriculomegaly, small biparietal diameter, scalloping of the frontal bone (“lemon” sign), obliteration of the cisterna magna, and compressed cerebellum (“banana” sign) [7].

Closed defect in closed SBM prevents the free leakage of cerebrospinal fluid into the amniotic cavity, thus reduces the probability of intracranial sign manifestation and will not show an elevation of AFP and amniotic fluid [5,7]. So that is the differentiation between open and closed spina bifida is best shown by the sonographic demonstration of abnormal or normal cranial anatomy and amniotic fluid [8]. Whoever we had a closed SBM case with polyhydramnios and some cranial anomaly including obliterated cisterna magna and mild dilation of ventricles after birth. It is noteworthy that a few studies

showed pathological changes in the brain occurred in the presence of both open and closed spinal lesions [9].

Associated anomalies are frequent in infants with NTDs such as malformations in the face (oral clefts), musculoskeletal system, renal system, and cardiovascular system [10]. Similar to our case, cardiac anomalies especially conotruncal defects are associated with spina bifida disorder because both of them are neural crest abnormalities and also they have common genetic factors such as: 118 SNPs of folaterelated genes and risks of spina bifida and conotruncal heart defects and Deletion of 22q11as a rare genetic cause [11,12].

Deletion of 22q11 is an infrequent cause of NTDs and some case report studies have shown that spina bifida is recognized as a feature of the variable phenotype associated with this microdeletion. So it is recommended to perform cytogenetic and molecular studies to detect 22q11 deletion in all children with both NTDs and congenital heart defects, either has cleft palate or not [11-14].

Conclusion

All myelomeningocele in prenatal sonography are not associated with posterior fossa abnormality especially closed types. However identification of NTDs should be considered as a warning signs for other syndromes or disorders, and prompt a thorough etiologic investigation and genetic counselling.

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