Fetal Schizencephaly Associated with Complex Cardiac and Limb Defects

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Abstract

We report a case of prenatally diagnosed schizencephaly in association with cardiac and limb defects. The diagnosis was made by antenatal ultrasound and fetal echocardiography at 28 weeks of gestation and corroborated by fetal MRI. There was unilateral open lip schizencephaly along with limb defects and cardiac anomalies such as common arterial trunk and large ventricular septal defect. The newborn delivered at term expired immediately after birth. Schizencephaly is rarely diagnosed in prenatal life with most cases recognized after birth. As prognosis is related to the extent of the lesion and associated malformations, prenatal diagnosis of schizencephaly should prompt a thorough evaluation for the same.

Introduction

Schizencephaly is a rare congenital anomaly characterized by deep clefts in the brain surrounded by heterotopic gray matter and may extend from ependyma of the ventricles to the pia mater. It is rarely diagnosed prenatally with most cases recognized only after birth. We report a case of schizencephaly with associated cardiac and limb anomalies in a fetus and propose a model for the hypothesized theory of vascular insult in the pathogenesis.

Case report

A 23-year-old second gravida at 28 weeks of gestation with one previous normal child, was referred in view of multiple anomalies in the fetus. Other than Rh incompatibility and previous Caesarean section, there was no relevant antenatal or family history. Routine antenatal investigations including the blood sugars and thyroid function tests were normal. Antenatal ultrasound revealed a unilateral deep clefting of the Sylvian fissure in the left cerebral hemisphere extending up to the lateral ventricle. Fetal MRI showed the extent of the cleft and confirmed the open type, large, unilateral schizencephaly (Figure 1 A & B). On fetal echocardiography, there was a large ventricular septal defect and a common arterial trunk (Figure 1C). Amniocentesis followed by fetal karyotyping and fluorescence in situ hybridization (FISH) for 22q deletion were done, which were reported to be normal. Poor fetal outcome was explained to the parents in view of multiple major anomalies. A male baby, weighing 2.8 kg was delivered at term, who expired soon after birth. An external examination of the baby revealed ectrodactyly and no other obvious malformation. Fetal autopsy for internal examination could not be done as parents declined the same. We propose that the schizencephaly in this fetus could have been the result of an early vascular insult secondary to major cardiac defects.

Discussion

Schizencephaly is defined as a fluid-filled cavity in the fetal brain, which may communicate with the lateral ventricle and subarachnoid space. The incidence is estimated to be 1.54 in 100,000 live births (Howe et al., 2012). Schizencephaly is thought to be secondary to multiple factors leading to a final common manifestation of abnormal neuronal migration. It could be the result of a congenital malformation of cortical development or follow a destructive process with various factors implicated in pathogenesis such as toxins, maternal warfarin, cytomegalovirus infection, genetic factors and vascular injury and can occur in association with various syndromes (Montenegro et al., 2002).

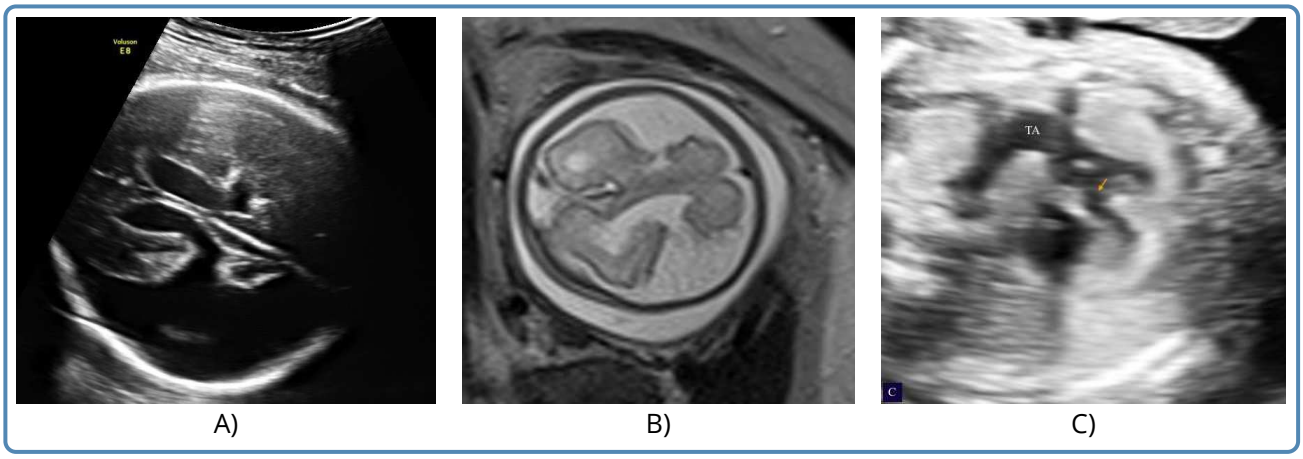

Figure 1 A) Fetal sonogram showing unilateral deep clefting of the Sylvian fissure in the left cerebral hemisphere extending up to the lateral ventricle. B) Fetal MRI showing the open type, large, unilateral schizencephaly. C) Fetal echocardiogram showing a common arterial trunk and ventricular septal defect (indicated with the yellow arrow).

Familial cases have been reported, suggesting a possible genetic origin and heterozygous mutations of the *EMX2* gene have been associated with schizencephaly (Granata et al., 1997). The only significant and probably etiological factor in our case was the presence of complex cardiac defects which could have resulted in an early vascular injury.

The clefts of fetal schizencephaly may extend through the hemispheres from the ventricles to the pial surface. It can be unilateral or bilateral and of the closed-lip or open-lip variety. Closed-lip schizencephaly is characterized by gray matter–lined lips that are in contact with each other (type 1) and open-lip schizencephaly has separated lips and a cleft filled with cerebrospinal fluid (CSF), extending to the underlying ventricle (type 2) (Yakovlev & Wadsworth, 1946). Schizencephaly is a rare diagnosis in prenatal medicine and most cases have been diagnosed after 28 weeks of gestation or after birth (Howe et al., 2005). Two-dimensional ultrasonography is the main prenatal diagnostic tool; however, the clefts are often not easily identified on ultrasound and it may be necessary to use other imaging modalities such as magnetic resonance imaging (MRI). MRI can also aid in differentiating schizencephaly from other possible diagnosis and in delineating associated brain anomalies. Various CSF containing lesions of the brain can be confused as schizencephaly which include developmental lesions like arachnoid cyst, mono ventricle in holoprosencephaly, agenesis of corpus callosum with an interhemispheric cyst and destructive lesions such as porencephalic cyst, ventriculomegaly and hydranencephaly (Oh et al; 2005). The prenatal ultrasonogram and fetal MRI in this case revealed a deep cleft in the region of Sylvian fissure extending all the way from the surface of brain up to the left lateral ventricle. Thus, a diagnosis of unilateral (left) schizencephaly of open-lip type 2 variety was made.

The clinical phenotypes associated with schizencephaly vary widely, depending on the size of the defect, unilateral versus bilateral defect, and open versus closed-lip defect. Affected individuals most often present with varying degrees of developmental delay, motor impairment and seizures. Open-lip clefts usually result in the most significant impairment, while unilateral clefts have a less severe clinical phenotype. If there is a small, unilateral closed-lip cleft without involvement of the motor cortex, the patient is usually normal except for seizures (Guerrini & Carrozzo, 2001; Liang et al., 2002). Schizencephaly can be associated with other anomalies including facial malformations, ventriculomegaly, polymicrogyria, pachygyria, heterotopias and lissencephaly, absence of the cavum septum pellucidum, agenesis of the corpus callosum and septo-optic dysplasia (Yakovlev & Wadsworth, 1946). Prenatal diagnosis of schizencephaly should therefore prompt a thorough search for other anomalies and counseling should be based on the extent of lesion, gestational age at diagnosis and associated anomalies. In our case, there was a large, unilateral open cleft in the brain along with complex major cardiac defects. Hence, parents were counselled about the expected poor outcome which was later evident with the early death of the

baby.

Conclusion

Prenatal diagnosis of schizencephaly is possible by ultrasound and fetal MRI can aid in further characterization of the extent and type of cleft. As no postnatal therapeutic options exist at present, accurate delineation of the extent of lesion and a thorough search for associated malformations should be done to help in counseling the parents about the prognosis, outcome and further management.

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