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Case Report

Lissencephaly with agenesis of corpus callosum: A rare anomaly

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ARTICLE INFO

Article history:

Received 17 November 2015

Accepted 18 March 2016

Available online 8 May 2016

Keywords:

Lissencephaly

Corpus callosal agenesis

MRI

Introduction

Lissencephaly means smooth cerebrum with lack of normal convolutions of brain. It is a rare disorder caused by defect in migration of neurons, which occurs between 12 and 24 weeks of gestation period.¹ The prevalence of type I lissencephaly in Netherlands was found to be 11.7 per million births.² It may be associated with other developmental anomalies in brain, such as cerebellar hypoplasia and pachygyria, but its association with agenesis of corpus callosum is very rare. We present a case of lissencephaly with corpus callosal agenesis.

Case report

A 2-month-old male infant patient presented with history of generalized tonic-clonic seizures, difficulty in swallowing, and

regurgitation of milk while feeding. On clinical examination, length of the infant was 57 cm, weight was 4.2 kg, and head circumference was 39 cm; there was facial dysmorphism and hypotonia of muscles. Systemic examination revealed normal air entry into chest, normal heart sounds with no murmur. The liver was just palpable below the costal margin, and there was no splenomegaly. Ultrasound abdomen was normal. The patient was subjected to MRI examination to look for cause of facial dysmorphism and hypotonia. Axial T1W and T2W MR images revealed bilateral diffuse smoothening of brain surface with absence of gyration and sulcation, and shallow and wide Sylvian fissures giving a “figure of 8” appearance to the brain (Fig. 1). Sag T1WI showed complete absence of corpus callosum with high riding third ventricle (Fig. 2). Axial T2WI showed lateral ventricles oriented parallel to each other giving a racing car appearance. Coronal T2W imaging revealed ‘moose head’ or ‘Viking helmet’ appearance of frontal horns of lateral ventricles (Fig. 3a, b).

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<http://dx.doi.org/10.1016/j.mjafi.2016.03.013>

0377-1237/© 2016 Published by Elsevier B.V. on behalf of Director General, Armed Forces Medical Services.

Fig. 1 – MRI Axial T1W image showing bilateral diffuse smoothing of brain surface with shallow and wide Sylvian fissures giving a “figure of 8” appearance to the brain.

Fig. 2 – Sag T1WI showing complete absence of corpus callosum (arrow).

Discussion

The term lissencephaly was first coined by Owen in 1868 to describe the smooth surface of brain seen in this condition.³ It occurs because of migrational arrest of neurons during brain development between 12 and 24 weeks.

Children with lissencephaly present with seizures and developmental delay, hypotonia, microcephaly, and facial dysmorphism.⁴ Our case did not have microcephaly, as often these children have head circumference within normal limits at birth, but they develop microcephaly by one year of age, as

the head growth is slow. In our case, the facial dysmorphic features were evident as asymmetry of palpebral fissure, short nose, flat mid face, deformed lower lip, and small chin (Fig. 4). The facial asymmetry also pointed to possible congenital facial nerve palsy. Degree of brain malformation determines the prognosis for children with lissencephaly. Survival after the age of 10 years in more severe cases is rare, and these children do not show milestone development beyond a 3- to 5-month-old level. Aspiration into respiratory tract with its complications or severe seizures lead to death in most of these cases.

Lissencephaly has been classified as classic (type I) or cobblestone (type II).⁵ Classic or type I lissencephaly is associated with mutations in 4 genes, namely LIS1, DCX, RELN, and ARX, as these genes are known to have a role in normal cell migration. The LIS1 gene mutation can be

Fig. 3 – (a) Axial T2W showing lateral ventricles oriented parallel to each other giving a racing car appearance. (b) Coronal T2W image shows Moose head or Viking helmet appearance of frontal horns of lateral ventricles.

Fig. 4 – Image of the child showing facial dysmorphic features of asymmetry of palpebral fissure, short nose, flat mid face, deformed lower lip, and small chin.

subdivided into type 1 isolated lissencephaly or associated with Miller–Dieker syndrome where agyria is associated with facial dysmorphism and microcephaly. The *doublecortin* (DCX) gene is X-linked and more commonly seen in females, with abnormal gyration in the frontal lobe. The *relin* (RELN) gene is rare and patients have a small cerebellum, hypoplastic brain stem, and mild reduction of the cortical gyri. The ARX gene is characterized by agyria with agenesis of the corpus callosum, and ambiguous genitalia.⁶ Our case was probably due to defect in ARX gene as the agyria was associated with agenesis of corpus callosum. However, it did not have ambiguous genitalia. The penis was normal in length with stretched penile length of 3.2 cm and a normal scrotal sac with fully descended testis (Fig. 5).

Type II lissencephaly or cobblestone lissencephaly has characteristic nodular brain surface, ocular anomalies, and congenital muscular disorder. It includes Walker–Warburg syndrome, Fukuyama congenital muscular dystrophy, and muscle-eye-brain disease.⁷

MRI is the imaging modality of choice for diagnosis of this condition and plays an important role in assessing the severity and any other associated anomalies of the brain. It shows classical findings of lissencephaly with smooth cortical surface and shallow and wide Sylvian fissure due to lack of or incomplete operculization, giving a figure of 8 or hourglass appearance to the brain as was seen in our case. MRI can also detect agenesis of corpus callosum easily due to its inherent ability in tissue characterization. Though this condition can also be diagnosed in utero on antenatal ultrasound or MRI after 24 weeks,⁸ most of the patients present after birth early in life, which was also seen in this case. In our case, the patient had

Fig. 5 – Image of the child depicting external genitalia with normal sized penis and scrotal sac.

undergone an anomaly scan at 20 weeks, which was reported as normal. Third trimester ultrasound was not done in our patient.

Lissencephaly is a rare disorder, which may be associated with other anomalies in the brain; however, its association with agenesis of corpus callosum is even rarer and occurs due to defect in ARX gene. The cases of ARX gene defect are associated with ambiguous genitalia. However, though the gene analysis was not done, this case is unique in that there was no association of these anomalies with ambiguous external genitalia.

Conflicts of interest

The authors have none to declare.

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