Case Report

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Schizencephaly: A Neuronal Progression Disorder

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Abstract

Schizencephaly is a congenital cleft in cerebral mantle extending from pial surface to the lateral ventricle. It is lined by heterotopic grey matter. It is rare, with a prevalence of 1.48/1,00,000 births. In this case study, adult female brain specimen showed unilateral open lipped cleft - schizencephaly, in the left hemispheric perisylvian region communicating with the left lateral ventricular cavity. Cleft was lined by heterotopic grey matter. Schizencephaly is considered as the neuronal progression or migration disorder. It is also thought to be a brain segmentation disorder. This disruptive birth defect may have ischaemic - vascular injury at its root or it could be a presence of infection like Cytomegalo virus. Mutations in Homeobox gene EMX2 have been also implicated in this congenital anomaly. Our study indirectly confirms that unilateral cases of Schizencephaly may lead long life remaining undiagnosed till death.

Keywords: Unilateral Cerebral Cleft; Perisylvian; Open Lipped Cleft; Heterotopia.

Introduction

Schizencephaly is a rare congenital disorder in which there is a cleft in cerebral mantle from pial surface to lateral ventricles. Such clefts are lined by heterotopic grey matter. It is of two types – closed lip and open lip, depending upon relation of the cleft with the lateral ventricle.

Any abnormality in the process of cortical neuronal migration results in various congenital anomalies like agyria, polymicrogyria, schizencephaly, lissencephaly. [1]

Case Report

We came across this brain from adult female cadaver, around 45 years old, while working on museum specimens.

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The specimen showed presence of type II - unilateral left side open lip schizencephaly.

Cleft involved frontal and parietal lobes (precentral and postcentral gyurs), above posterior ramus of lateral sulcus (Perisylvian), in the territory of middle cerebral artery.

The surface opening was large, circular with average diameter of 55.28 mm. [Figure 1- line A]

The communication with the lateral ventricle was smaller, circular with average diameter of 14.76 mm. [Figure 1 – line B and Figure 2]

The cleft was 27.5 mm deep occupying full thickness of hemisphere from surface to ventricle.

The cleft was medium size being slightly more than 1/3rd of the length (frontal to occipital pole) of the left hemisphere (150 mm).

The cleft was lined by heterotopic cortical grey matter extending up to ventricle.

There was complete absence of septum pellucidum. Normalcy of optic nerve could not be commented upon. Corpus callosum was present. Flattening of pyramid of medulla oblongata was observed on the left side.

Samples from lip and subependymal region of the cleft were stained with 'Luxol fast blue and Cresyl violet' stain. Heterotopic cortical grey matter was found in subependymal region.

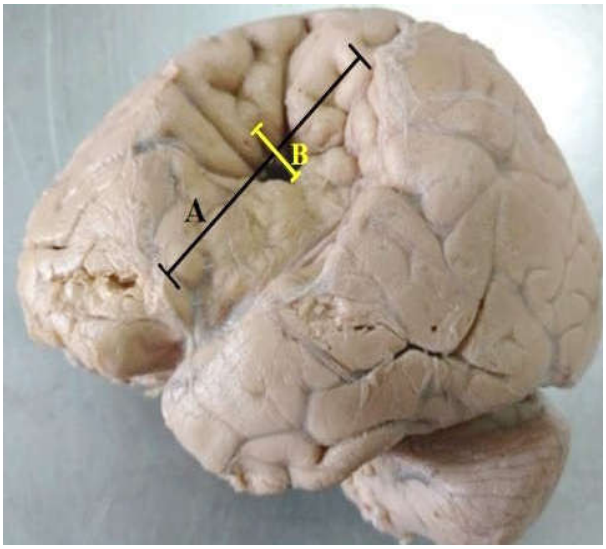

Fig. 1: External view of the left open lip cleft, Line A–surface opening, Line B–ventricular opening

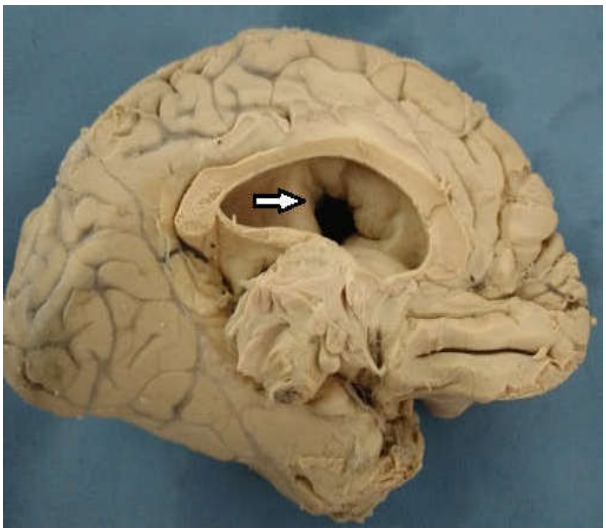

Fig. 2: Ventricular view of the left open lip cleft, White arrow–pointing to the ventricular opening

Discussion

Schizencephaly is a rare congenital brain anomaly, with a prevalence of 1.48/1,00,000 births [2].

It presents as a cleft in the cerebral mantle extending from the pial surface to the lateral ventricles. The cleft is lined by heterotopic grey matter [3].

It is of 2 types –

Type I is closed lipped with edges of cleft appearing to be fused at pial-ependymal seam.

Type II is open lipped with widely separated cleft communicating with the lateral ventricle and lined by heterotopic grey matter.

In 70% of the cases it involves frontal and parietal lobes around central sulcus [4].

Causative developmental mechanism of schizencephaly is poorly understood and heterogenous.

Normally the cerebral cortex develops from the roof and lateral walls of the telencephalon. Neural development is said to be a longitudinal assemblage along a spatial grid at a specific time.[3]

The whole process of the human cortical development can be divided into five stages like, neuronal precursor proliferation at the ventricular zone, neuroblast departure from the ventricular zone, neuroblast migration, migration arrest, and neuronal organization.[5]

The cell migration starts in eighth week and continues for two months, mostly getting over in sixteenth week. After this, there is cell migration in smaller waves stretching up to 25 weeks [6].

To establish boundaries of various areas of forebrain, OTX 1, EMX1 and 2 are expressed in overlapping pattern in the future forebrain region of neural plate [7].

One of the causes of cleft formation can be failure of regional specification of clones of cells in germinal matrix of future cerebral cortex. It could also be vascular disruptive birth defect occurring early in gestation at critical time of neuronal development, but before end of neuronal migration [3].

Cortical mantle development flaws of cell migration in the first trimester or an encephaloclastic process due to ischaemic injury in middle cerebral artery distribution, in the third trimester (31 to 35 weeks) have also been suggested as a cause for cleft formation [8].

Causative agents could be teratogens like warfarin, alcohol or cocaine [3].

Cleft formation has also been associated with infections from Cytomegalo virus and Herpes virus.

Familial cases of schizencephaly suggest genetic factor. Commonly implicated factor is a germline mutation in homeobox gene EMX2 [8]. This gene is required in patterning of forebrain and cortical arealization.

As per Wayne et al [9] classification of cortical malformations, based on the primarily disturbed developmental process, schizencephaly comes in fourth group, as destructive lesion. They say it could be resulting from vascular disruptive lesion happening before 25 weeks of gestation. It can happen due to attempted abortion, amniocentesis, vehicular

accident. Mostly the territory of middle cerebral artery is involved.

Trudy Pang et al [5] consider schizencephaly as part of large spectrum of disorders under heading of Malformations of Cortical Development (MCD). They say that, but for the advent of MRI, many of these cases were previously directly seen at the autopsy. They categorize schizencephaly as a disorder due to abnormal neuronal organization. Neuronal organization is the last stage in the process of cortical development and involves synaptogenesis, neuronal maturation, synapse pruning and apoptosis. In this spectrum schizencephaly is considered to be an extreme form of polymicrogyria.

Utku Senol et al [10] has reported a rare case of dizygotic twins. One of the twins showed bilateral closed lip schizencephaly while the other had focal cortical dysplasia. There was involvement of the same parietal lobe in both the cases. They have discussed, that not only the focal cortical dysplasias (FCDs) are most commonly associated with schizencephaly, but also they seem to be resulting from the same pathologic process. Either FCD or schizencephaly develops depending on whether the anomalous process involves only superficial layer of brain or full thickness of hemispheric cortex. Both their 'study twins' also had absent septum pellucidum, which they have reported to be associated with scizencephaly in 80 to 90% of the cases.

M Avellanet et al [6] also agree that schizencephaly is associated with absent septum pellucidum in 80% cases, out of which 40% also have optic dysplasia.

But Bhatnagar S. et al [2] say that schizencephaly is associated with septo-optic dysplasia (SOD) in 25% cases. They also claim maternal age as important factor in schizencephaly with young mothers being at higher risk.

Depending on clinical manifestations, age at detection may range anywhere between 8 months to 30 years. 17% cases of schizencephaly have mild deficits or no problem [1].

Persons with unilateral clefts may lead a long good quality life. The case studied by M Avellanet et al [6] was unusual, with bilateral schizencephaly having a seizure free life in her 40s. The bilateral clefts otherwise usually present severe impairment. They present a range of neurological disabilities in accordance with their cortical involvement.

Post mortem detection of cleft in our 40 year old female brain, indirectly confirms the possibility of long life in unilateral cases of schizencephaly.

Conclusion

Even though schizencephaly is rare, its unilateral cases may go undiagnosed till adulthood, with possible detection only after death.

Conflict of Interest

NIL

Source(s) of Support

NIL

Presentation at a Meeting

NIL

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