

Cortical Clefts and Cortical Bumps: A Continuous Spectrum

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ABSTRACT

Cortical ‘clefts’ (schizencephaly) and cortical ‘bumps’ (polymicrogyria) are malformations arising due to defects in postmigrational development of neurons. They are frequently encountered together, with schizencephalic clefts being lined by polymicrogyria. We present the case of an eight-year-old boy who presented with seizures. Imaging revealed closed lip schizencephaly, polymicrogyria and a deep ‘incomplete’ cleft lined by polymicrogyria not communicating with the lateral ventricle. We speculate that hypoperfusion or ischaemic cortical injury during neuronal development may lead to a spectrum of malformations ranging from polymicrogyria to incomplete cortical clefts to schizencephaly.

Keywords: Brain, Development, Malformation, Polymicrogyria, Schizencephaly

CASE REPORT

An eight-year-old boy presented with history of seizures, generalised tonic clonic in nature, lasting for three minutes, with post-ictal loss of consciousness. There was no history of fever, headache or vomiting. He had a birth history of asphyxia with a consequent low APGAR score and required ventilatory support for one week. His past history and family history was otherwise unremarkable. General physical examination was normal. Higher mental functions for his age and cranial nerve examination were normal. Spino motor system sensory and cerebellar examination were within normal limits. There were no meningeal signs.

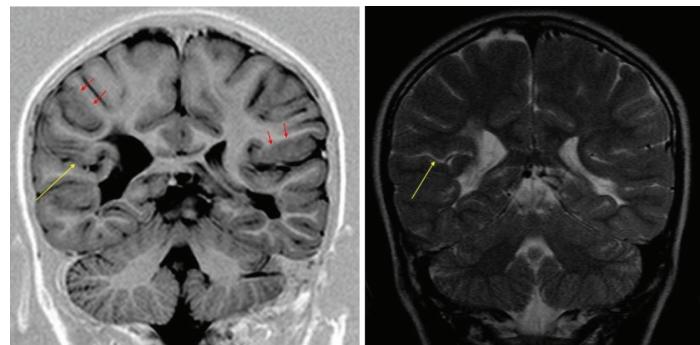
Blood glucose, serum electrolytes including calcium and magnesium were normal. An inter-ictal EEG was performed which was normal. MRI revealed a right sided CSF intensity cleft with apposed margins lined by grey matter which was communicating with the right lateral ventricle, suggestive of closed lip schizencephaly [Table/Fig-1,2]. A left sided cleft was noted which did not communicate with the lateral ventricle [Table/Fig-3]. The cleft was lined by polymicrogyria. Regions of polymicrogyria in bilateral temporoparietal cortex and an incidentally detected cavum septum pellucidum were also noted [Table/Fig-4].

The patient was started on sodium valproate 200mg BD and showed good response. He is currently on daily antiepileptics for the last one year and has not had breakthrough seizures. He is doing well at school.

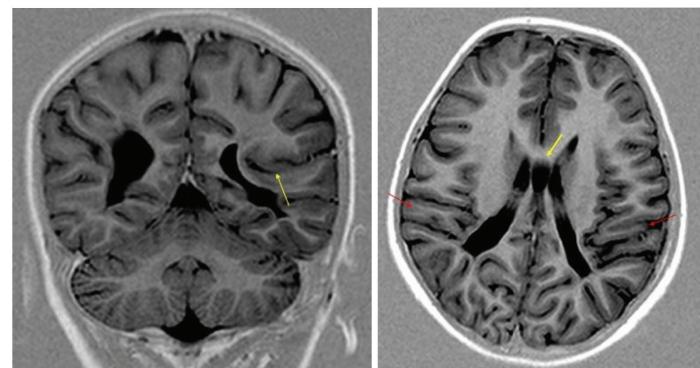
DISCUSSION

Schizencephaly and polymicrogyria are developmental disorders which were classified as disorders of late neuronal migration and organization [1]. Advances in molecular biology, genetics and imaging have led to reclassification of the same under malformations secondary to post migrational development [2]. Since polymicrogyria lines schizencephalic clefts [3], it is reasonable to assume that a common aetiologic factor may predispose to these conditions. Varying severities of ischaemic insult, toxic and infectious causes have been proposed as the aetiological factors by Barkovich and Kjos [4].

Schizencephaly consists of a cleft extending from the pial surface to the ventricle which is lined by grey matter. It was first described by Wadsworth and Yakolev in 1946 [5,6]. Polymicrogyria consists of irregular gyri, regions of apparent thickened cortex and a stippled grey-white matter interface [7].



[Table/Fig-1]: Coronal T1 inversion recovery image showing a right sided cleft extending from the pial surface to the lateral ventricle with apposed margins (yellow arrow) suggestive of closed lip schizencephaly. Also, seen are regions of polymicrogyria (red arrows). [Table/Fig-2]: Coronal T2 weighted image showing the right sided CSF intensity cleft with apposed margins (yellow arrow).



[Table/Fig-3]: Coronal T1 inversion recovery image showing a left sided deep cleft lined by polymicrogyria which is NOT communicating with the lateral ventricle (yellow arrow). [Table/Fig-4]: Axial T1 inversion recovery image showing cavum septum pellucidum (yellow arrow) and regions of polymicrogyria in bilateral temporo-parietal lobes (red arrows).

These malformations present with a wide spectrum of clinical manifestations, ranging from asymptomatic to epilepsy and developmental delay. This case illustrates features of both schizencephaly and polymicrogyria, and also an intermediate ‘incomplete cleft’ not fully satisfying the criteria for schizencephaly. We aimed to highlight that these malformations are part of a spectrum that arise due to varying severities of hypoxic insult.

Schizencephaly may be of the open or closed type. These are based on whether the cleft margins are separate or apposed [5,6]. It can be unilateral or bilateral, symmetric or asymmetric [4].

Association with optic nerve hypoplasia, pachygyria, polymicrogyria, heterotopia, and arachnoid cysts have been described [8].

Polymicrogyria is a malformation of cortical development consisting of excessive small gyri with narrow sulci and an irregular, 'bumpy' appearance of the cortical surface and grey-white matter junction [8]. It may be focal, multifocal or diffuse, unilateral or bilateral [9]. It most commonly occurs in the perisylvian regions [10], although involvement of most cortical regions have been described [9].

These malformations are now classified under malformations of post migrational development [2]. MRI is useful for diagnosing disorders of cortical development. Schizencephaly can be diagnosed upon identifying a CSF filled cleft lined by gray matter that extends from the pial surface to the ventricle [8]. Polymicrogyria is diagnosed by the presence of increased cortical thickness, an abnormal gyral pattern, and irregularity of the cortical-white matter junction [7].

Normal development of the nervous system begins with primary neurulation (at 3-4 weeks), followed by development of the prosencephalon (2-3 months), neuronal proliferation (3-4 months), neuronal migration (3-5 months), neuronal organization (5 months to after birth) and myelination (after birth) [3]. Neuronal migration begins in the eighth week of gestation with the neurons migrating radially outward from the germinal matrix in the walls of the lateral ventricles to form the cerebral cortex [11]. Interruption of the normal processes of development due to lack of normal gene expression, by either an abnormal gene or interference of normal gene function due to external causes such as infection or ischaemia can lead to schizencephaly and polymicrogyria [12].

Schizencepalic clefts are lined by polymicrogyria [3]. The theory supporting this association is that schizencephaly and polymicrogyria arise due to hypoperfusion or ischaemic cortical injury with mild ischaemic insult causing polymicrogyria without cortical infolding and more severe insults resulting in clefts lined by polymicrogyria [4,13]. Barkovich has postulated that cortical infolding of various depths lined by dysplastic cortex could indicate that schizencephaly and polymicrogyria share a common pathogenesis [4]. This theory explains our patients imaging findings with varying degrees of ischaemic insult occurring during development leading to schizencephaly, an incomplete cortical

cleft and polymicrogyria. A similar imaging finding has been described by Leventer et al., as a 'novel' form of polymicrogyria. It consisted of a cleft lined by polymicrogyria directed towards the lateral ventricle but not communicating with it. The authors in the study postulated that such a cleft may be an incomplete form of schizencephaly and that a spectrum of clefting may exist ranging from schizencephaly to deep clefts lined by polymicrogyria but not communicating with the ventricles [9].

CONCLUSION

We thus highlight that schizencephaly and polymicrogyria are part of a continuum of disorders of cortical development at the post migrational level.

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