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Peritrigonal And Temporo-Occipital Heterotopia With Apple Core Corpus Callosal Agenesis And Hippocampal Malrotation

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Abstract

Malformations of cortical development is one of the leading causes of developmental delay in children. They can be due to abnormal neural proliferation, migration and cortical organization. We herein report a case of one and a half years old child who presented with developmental delay with imaging features of peritrigonal and temporo-occipital nodular heterotopia along with dysgenesis of corpus callosum and hippocampal malrotation. Periventricular nodular heterotropia is known to be associated with corpus callosal dysgenesis. Corpus callosal dysgenesis is closely linked to hippocampal development. Although findings of cerebral malformations are revealed by seizures, they can also be found in cases of developmental delay.

Keywords: Corpus callosum dysgenesis, Developmental delay, Hippocampal malrotation, Malformation of cortical development, Periventricular nodular heterotropia

Introduction

Malformations of cortical development (MCDs) are a wide category of disorders that are a common cause of neurodevelopmental delay and epilepsy which are brought about by the defects in the intricate process of cortical genesis of brain [1].

Delay in development is defined as delayed attainment of milestones in one or more domains but in an expected sequence when compared to a normally developing child [2]. Malformations of cortical development can bring about developmental delay in children. The severity of developmental delay can vary depending on the specific type of malformation of neuronal development and extent of brain damage. All stages of cortical development, including neurogenesis, neuronal migration and postmigrational development can be affected by abnormalities that result in a wide range of malformations of cortical development (MCD). MRI of brain plays a key role in identifying this. Early diagnosis is crucial for managing developmental delay by special education, physical therapy, speech therapy and to counsel the parents.

Case Report

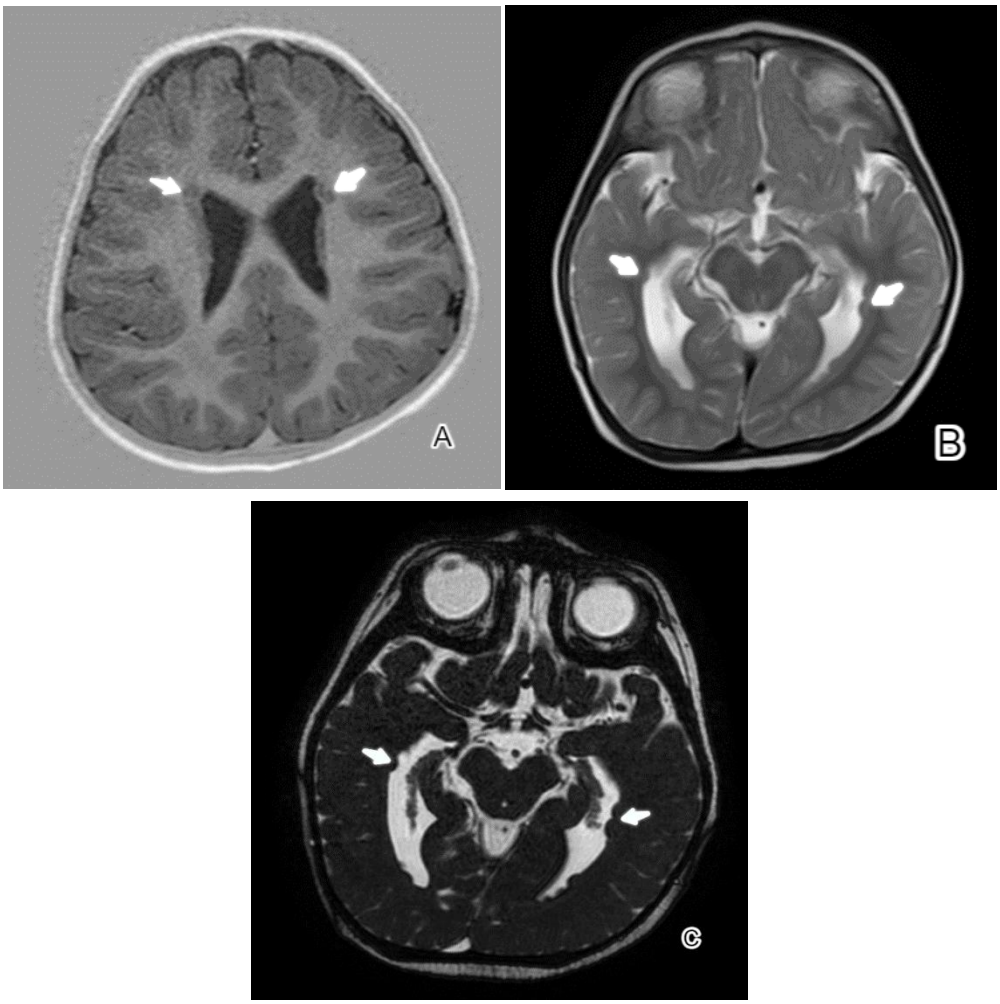
One and a half years old male child was referred for neuroimaging in view of global developmental delay. The child was born to a 2nd degree consanguineous marriage. Birth history was unremarkable with no NICU (neonatal intensive care unit) admission during postnatal period. There was no history of seizures, fever or trauma.

General physical examination was under normal limits. On assessment of milestones, the child could sit with support but could not sit without support,

corresponding to developmental age of 6 months. Pincer grasp was attained in fine motor milestone examination corresponding to developmental age of 9 months. The child was able to say a monosyllable in language assessment corresponding to developmental age of 9 months. Under social milestone assessment, the child could smile corresponding to developmental age of 4 months. Overall, there was a developmental delay <70%.

MRI imaging of brain showed multiple subependymal grey matter nodules lining the wall of bilateral frontal and occipital horns of lateral ventricles which was suggestive of periventricular nodular heterotropia (Fig. 1). It was in peritrigonal and temporo-occipital distribution. There was hypoplasia of splenium of corpus callosum causing apple core corpus callosal agenesis (Fig. 2A). There was incomplete hippocampal inversion (Fig. 2B) on left side which was suggested by pyramidal shaped hippocampus, longer craniocaudal diameter of hippocampus and more vertical orientation of dominant inferior temporal sulcus (DITS). Prominent occipital and temporal horns of lateral ventricles were observed.

Figure 1: 1.5T MRI of the brain: (A) axial T1-weighted inversion recovery (IR); (B) axial T2-weighted; (C) axial balanced fast field echo.



Findings: Periventricular nodular lesions ranging 1-5 in number which are lining the walls of frontal horn, body (A) and occipital horns (B, C) of bilateral lateral ventricles following gray matter signal intensity.

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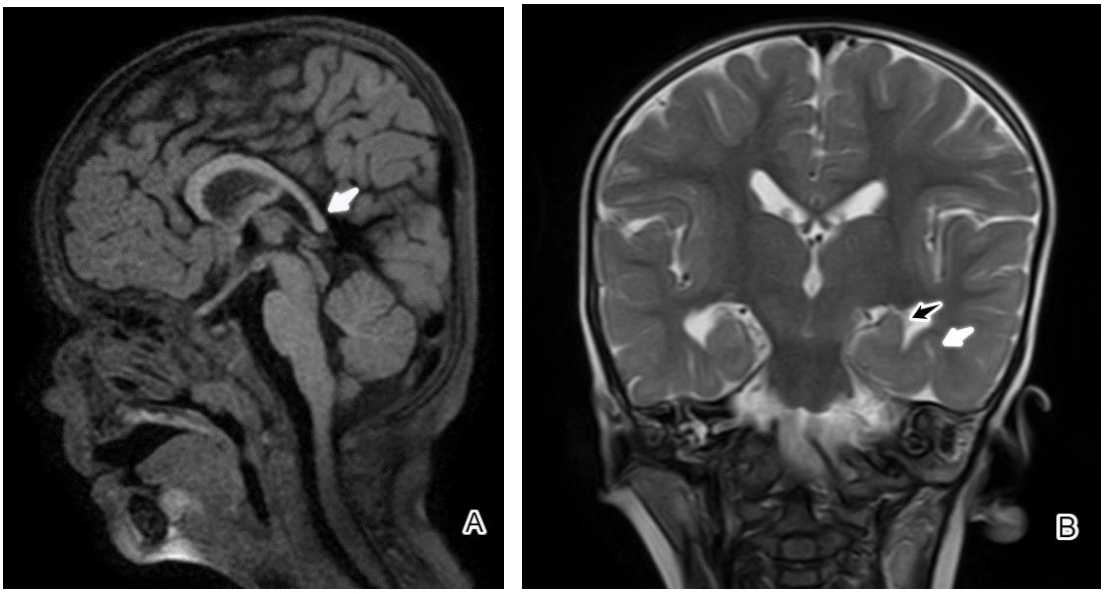
Figure 2: 1.5T MRI of the brain: (A) sagittal T1-weighted; (B) coronal T2-weighted.



Findings: Hypoplasia of splenium indicating apple core corpus callosum (A). Pyramidal shaped left hippocampus (white arrow) and verticalization of deep inferior temporal sulcus (black arrow) in (B) indicating hippocampal malrotation.

Discussion

Malformations of cortical development (MCDs) are a wide category of disorders that are a common cause of neurodevelopmental delay and epilepsy which are brought on by the defects in the intricate process of cortical genesis of brain [1]. Malformations of cortical development (MCD) are development abnormalities of microscopic and macroscopic structure of the cerebral cortex that arise due to interruption in all stages of cortical development during fetal development which is determined by genetic or environmental factors [3]. According to Barkovich classification, MCDs are classified into three groups- (1) malformations due to abnormal neural proliferation, (2) malformations due to abnormal neuronal migration, and (3) malformations due to abnormal cortical organization [4]. They collectively account for 3% of intellectual disability [5]. Malformations of cortical development can bring about developmental delay in children.

Gray matter heterotropia: Gray matter heterotropia occurs due to impaired migration of neurons from approximately 6^{th} to 16^{th} weeks of gestation. Heterotropia can take form of nodules or in laminar form. Various types of heterotropia are periventricular heterotropia (PNH), subcortical gray matter and subcortical band heterotropia (SBH). Periventricular heterotropia is the most common type of gray matter heterotropia [5]. The most frequent cause of bilateral symmetric PNH is heterozygous loss of function mutations in Xq28 located Filamin A(FLNA) gene [6]. These mutations which primarily affect females result in a variety of phenotypes causing cortical malformations. Large cytoplasmic actin binding and cross-linking protein encoded by FLNA serves a variety of purposes, including promoting cell migration, blood coagulation and maintaining the integrity of blood vessel walls.

Diffuse periventricular nodular heterotropia (PNH) is associated with callosal anomalies [4,5]. Numerous structural and functional MRI studies have shown that PNH involves specific cortical regions, particularly, corpus callosum [6].

Corpus callosal dysgenesis: Corpus callosum is the largest commissure connecting both the cerebral hemispheres. Dysgenesis of corpus callosum can be either partial or complete. Dysgenesis of corpus callosum is due to insult occurring between 8 to 20 weeks of gestation [7]. Prefrontal fibres either project to or from the genu and the body contains fibres associated to motor cortical areas, while temporal commissural fibres cross the splenium. Splenium is the posterior most part of corpus callosum. Hypoplasia of posterior corpus callosum gives rise to

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apple core corpus callosal agenesis. According to more recent research, including those that used MR tractography, the anterior body develops first and then continues in a bidirectional manner, with the anterior portions (genu) developing earlier than the posterior portions [8]. About half of patients with dysgenesis of corpus callosum exhibit mental disability [9].

Hippocampal malrotation: Hippocampus is a bilaminar gray matter structure that is located medially in the temporal lobe protruding into temporal horn of the lateral ventricle [10]. Incomplete hippocampal inversion occurs due to incomplete infolding of medial temporal structures during embryonic brain development. It resembles fetal orientation of hippocampus that is present at 14-20 weeks of gestation. Diagnosis of hippocampal malrotation (HIMAL) can be made by imaging features like rounded or pyramidal appearance of hippocampus, verticalization of the dominant inferior temporal sulcus, curved lateral aspect of hippocampus and enlarged lateral aspect of hippocampus [11]. It is usually left sided with other morphological abnormalities of brain [12].

The development of the splenium is preceded by the formation of the hippocampal commissure. Both the corpus callosum and hippocampus develop in parallel and their development is closely related. It appears that callosal agenesis interferes with the regular process of hippocampus formation and growth, leading to underdevelopment, which could explain some learning and memory problems in those who have callosal agenesis in later life [13].

Conclusion

Overall, the difference in FLNA mutation suggests that FLNA plays a specific function in maintaining corpus callosal integrity in this disorder and this may indicate the different pathogenic processes in FLNA-mutated and nonmutated PNH patients. According to earlier studies, PNH frequently exhibits abnormal corpus callosum morphology, with the splenium experiencing the most volume loss [1]. This is in accordance with findings in our case.

When hippocampal malrotation (HIMAL) is observed, it is crucial to evaluate for other cerebral developmental malformations as in our case. Corpus callosal dysgenesis is accompanied by malformations in hippocampus.

Although findings of cortical malformations are revealed by seizures, they can also be found in cases of developmental delay.

References

1. Pardoe HR, Mandelstam SA, Hiess RK, Kuzniecky RI, Jackson GD, Alzheimer's Disease Neuroimaging Initiative, Epilepsy Phenome/Genome Project Investigators. Quantitative assessment of corpus callosum morphology in periventricular nodular heterotopia. Epilepsy research. 2015 Jan 1;109:40-7.
2. Brown KA, Parikh S, Patel DR. Understanding basic concepts of developmental diagnosis in children. TranslPediatr. 2020 Feb;9(Suppl 1):S9-S22. doi: 10.21037/tp.2019.11.04. PMID: 32206580; PMCID: PMC7082247.
3. Leventer RJ, Guerrini R, Dobyns WB. Malformations of cortical development and epilepsy. Dialogues in clinical neuroscience. 2022 Apr 1.
4. González G, Vedolin L, Barry B, Poduri A, Walsh C, Barkovich AJ. Location of periventricular nodular heterotopia is related to the malformation phenotype on MRI. American Journal of Neuroradiology. 2013 Apr 1;34(4):877-83.
5. Oegema R, Barkovich AJ, Mancini GM, Guerrini R, Dobyns WB. Subcortical heterotopic gray matter brain malformations: Classification study of 107 individuals. Neurology. 2019 Oct 1;93(14):e1360-73.
6. Liu W, An D, Niu R, Gong Q, Zhou D. Integrity of the corpus callosum in patients with periventricular nodular heterotopia related epilepsy by FLNA mutation. NeuroImage: Clinical. 2018 Jan 1;17:109-14.
7. Tang PH, Bartha AI, Norton ME, Barkovich AJ, Sherr EH, Glenn OA. Agenesis of the corpus callosum: an MR imaging analysis of associated abnormalities in the fetus. American Journal of Neuroradiology. 2009 Feb 1;30(2):257-63.

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8. Huang H, Zhang J, Wakana S, Zhang W, Ren T, Richards LJ, Yarowsky P, Donohue P, Graham E, van Zijl PC, Mori S. White and gray matter development in human fetal, newborn and pediatric brains. Neuroimage. 2006 Oct 15;33(1):27-38.
9. Kułak P, Gościk E. Abnormalities of the corpus callosum: Magnetic resonance imaging analysis in children. Progress in Health Sciences. 2012 Dec 1;2(2).
10. Dekeyzer S, De Kock I, Nikoubashman O, Vanden Bossche S, Van Eetvelde R, De Groote J, Acou M, Wiesmann M, Deblaere K, Achten E. "Unforgettable"–a pictorial essay on anatomy and pathology of the hippocampus. Insights into imaging. 2017 Apr;8(2):199-212.
11. Tsai MH, Vaughan DN, Perchyonok Y, Fitt GJ, Scheffer IE, Berkovic SF, Jackson GD. Hippocampal malrotation is an anatomic variant and has no clinical significance in MRI-negative temporal lobe epilepsy. Epilepsia. 2016 Oct;57(10):1719-28.
12. Cury C, Toro R, Cohen F, Fischer C, Mhaya A, Samper-González J, Hasboun D, Mangin JF, Banaschewski T, Bokde AL, Bromberg U. Incomplete hippocampal inversion: a comprehensive MRI study of over 2000 subjects. Frontiers in neuroanatomy. 2015 Dec 22;9:160.
13. Knezović V, Kasprian G, Štajduhar A, Schwartz E, Weber M, Gruber GM, Brugger PC, Prayer D, Vukšić M. Underdevelopment of the human hippocampus in callosal agenesis: an in vivo fetal MRI study. American Journal of Neuroradiology. 2019 Mar 1;40(3):576-81.

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