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THICK LISSENCEPHALY WITH POSTERIOR–ANTERIOR GRADIENT AND AGYRIA–PACHYGYRIA PATTERN: A CASE REPORT IN AN ADOLESCENT GIRL WITH BREAKTHROUGH SEIZURES

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Abstract

Lissencephaly (LIS) represents a spectrum of malformations of cortical development due to disrupted neuronal migration, resulting in a smooth cerebral surface. The condition may present in complete or incomplete forms, often associated with intellectual disability and seizures. Classification is now based on severity, cortical thickness, gyral pattern, and associated malformations rather than the outdated Type 1 and Type 2 distinction.

We report a case of a 17-year-old girl with a history of developmental delay and seizures beginning at age 2. She was on antiepileptic treatment until age 10, after which therapy was discontinued. She now presents with breakthrough seizures. Her antenatal and perinatal histories were unremarkable. MRI revealed features of thick lissencephaly, incomplete form, with a posterior-to-anterior gradient—showing agyria in the parieto-occipital region and pachygyria in the frontotemporal areas—consistent with an agyria–pachygyria pattern.

MRI demonstrated cortical thickening with a smooth outer contour, broad gyri, and shallow sulci. The abnormal cortex followed the gray matter signal on all sequences. No subcortical band heterotopia was observed in this case.

This case illustrates the incomplete form of thick lissencephaly with a posterior–anterior gradient and agyria–pachygyria pattern in an adolescent presenting with recurrent seizures. Recognition of characteristic imaging patterns is critical for diagnosis, classification, and management planning, especially in patients with a history of early-onset seizures and developmental delay.

Introduction

Lissencephaly (LIS) with subcortical band heterotopia represents a spectrum of malformations of cortical development due to disrupted neuronal migration, resulting in a smooth cerebral surface.

The condition may present in complete or incomplete forms, often associated with intellectual disability and seizures.

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It is characterized by cortical thickening with gyral abnormality ranging from agyria to pachygyria. Previously, lissencephaly has been classified as type 1 (classic lissencephaly) and type 2 (cobblestone lissencephaly). It has been observed that type 2 has a completely different pathophysiology, so this classification has been discontinued. The current classification is based on severity, cortical thickness, gradient of gyral malformation and other associated malformation[1].

MRI features include agyria in the complete form, while the incomplete form shows agyria in parietooccipital region with pachygyria in frontotemporal region; however, any gradient occurs.

Agyria was defined as cortical regions with sulci >3 cm apart, pachygyria as abnormally wide gyri with sulci 1.5–3 cm apart, and subcortical band heterotopia (SBH) as longitudinal bands of gray matter located deep to the cerebral cortex and separated from it by a thin layer of normal appearing white matter[2].

Differential diagnoses include Tubulinopathies, often associated with basal ganglia dysplasia (e.g., fused striatum), internal capsule abnormalities, and a range of cortical malformations[3]. Microlissencephaly (a severe form of cortical malformation with microcephaly and thickened, smooth cortex). Microcephaly with a simplified gyral pattern, which shows reduced sulcation and normal cortical thickness, usually as an isolated anomaly[4].

Case presentation

Clinical Presentation

A 17-year-old female was referred to the psychiatry clinic for evaluation of global developmental delay and recurrent seizures. The patient had a history of developmental delay with seizure onset at 2 years of age. She had been receiving antiepileptic therapy until the age of 10 years, after which treatment was discontinued. She subsequently presented with breakthrough seizures in adolescence.

The antenatal and perinatal histories were unremarkable, with no reported complications during pregnancy or delivery. There was no family history of epilepsy, neurodevelopmental disorders, or consanguinity.

Clinical Examination

On examination, the patient exhibited global developmental delay. She demonstrated poor head control and absence of purposeful hand movements, consistent with severe neurodevelopmental impairment. Based on these findings, neuroimaging was pursued to identify an underlying structural abnormality.

Neuroimaging Findings

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Magnetic resonance imaging (MRI) of the brain was performed using standard sequences.

Three-dimensional T1-weighted images (Fig 1and 2) demonstrated marked cortical thickening predominantly involving the bilateral parietal and posterior temporal lobes. The cortex appeared smooth, with broad gyri, shallow sulci, and blurred gray–white matter differentiation, suggestive of a cortical malformation.

Axial T2-weighted images (Fig 3 and 4) revealed multiple radially oriented subcortical hyperintensities, which were suppressed on corresponding FLAIR sequences, consistent with prominent perivascular spaces.

Coronal T2-weighted images (Fig 5) showed periventricular radially oriented hyperintensities, further supporting the presence of dilated perivascular spaces.

On coronal T1 inversion recovery (IR) sequences (Fig 6), the thickened cortex demonstrated alternating hypo- and hyperintense bands, producing a striated appearance within the abnormal cortex.

The abnormal cortex follows signal of cortex on all sequences.

Diffusion-weighted imaging (DWI) showed no evidence of restricted diffusion, and the apparent diffusion coefficient (ADC) maps were unremarkable. Gradient-echo (GRE) sequences did not demonstrate blooming artifacts to suggest haemorrhage or calcification.

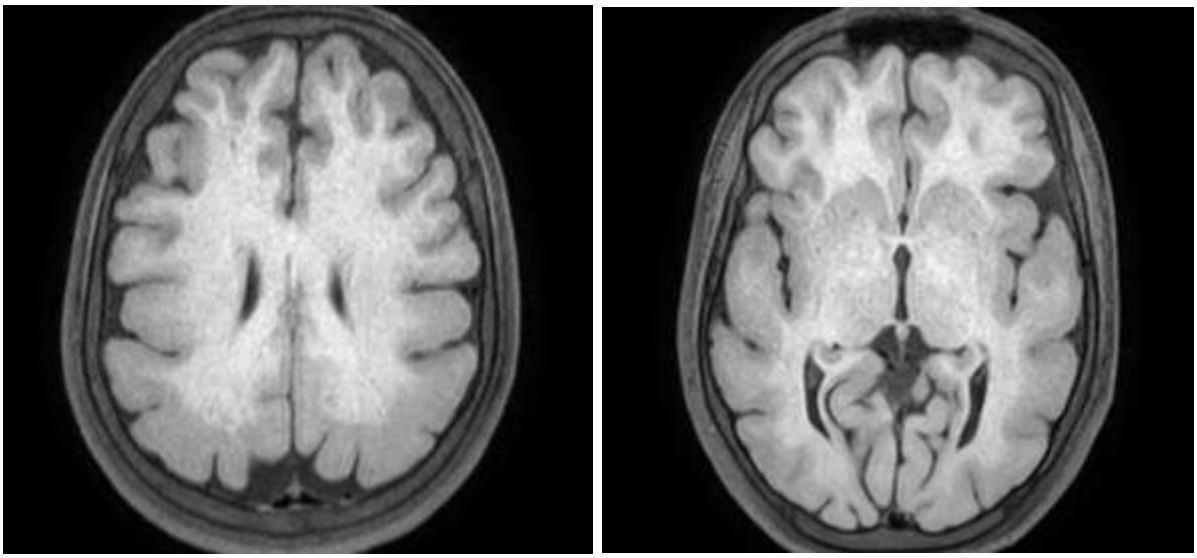

Figure 1&2: Axial 3D T1-weighted MR images show marked cortical thickening of predominantly bilateral parietal (black tringles) and posterior temporal (black arrow) lobes associated with broad gyri and shallow sulci, blurred grey white matter differentiation and smooth cortical surface

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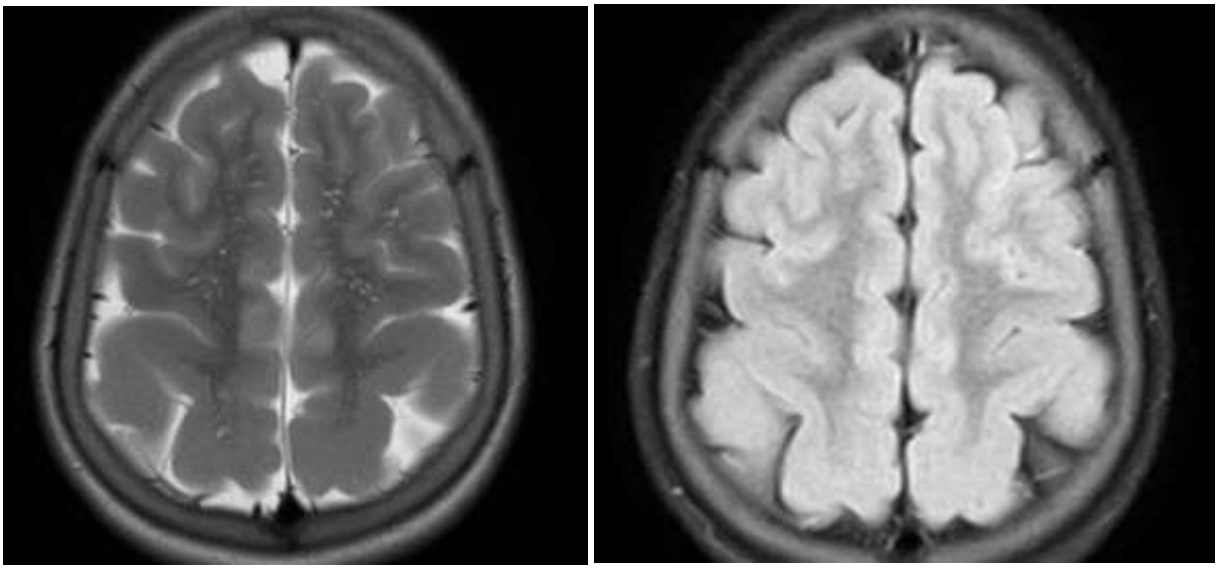

Figure 2&3: Axial T2W and FLAIR images multiple radiating subcortical hyperintensities (white arrows) suppressed on corresponding FLAIR image representing perivascular spaces

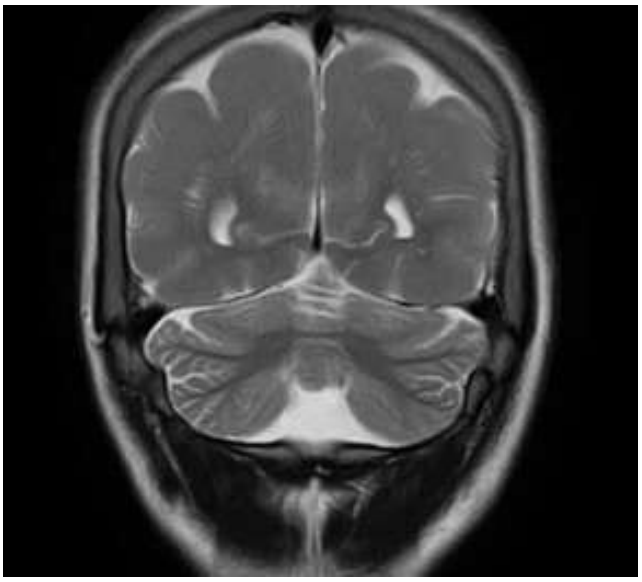

Figure 5: Coronal T2W image shows periventricular radiating hyperintensities representing perivascular spaces

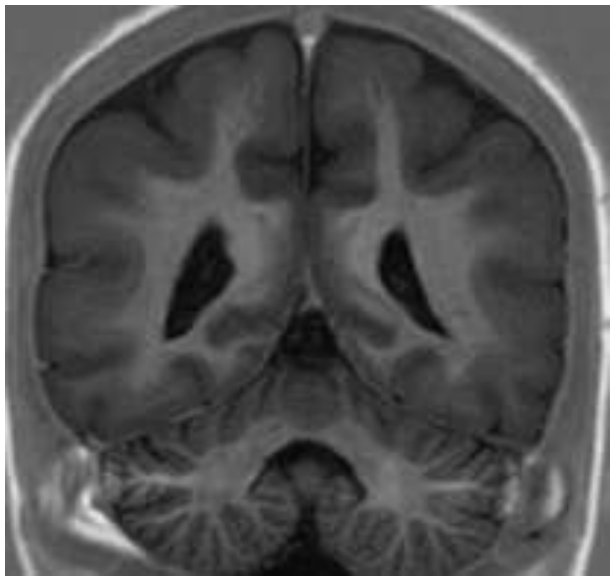

Figure 6: Coronal T1IR (F) sequence shows alternative hypo and hyperintense bands in the thickened gyri (star).

Discussion

Malformations of cortical development (MCDs) comprise a heterogeneous group of congenital brain anomalies resulting from disturbances in neuronal proliferation, migration, or cortical organization during embryogenesis. These disorders are a well-established cause of epilepsy,

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global developmental delay, hypotonia, and cognitive impairment, as demonstrated in the present case[5,6]. Advances in neuroimaging and genetics have refined the understanding and classification of MCDs, emphasizing the importance of early and accurate diagnosis[7].

The MRI findings in this patient are characteristic of a lissencephaly spectrum disorder, most consistent with pachygyria. Hallmark imaging features—including marked cortical thickening, broad gyri, shallow sulci, and blurred gray–white matter differentiation, predominantly involving the bilateral parietal and posterior temporal lobes—are typical of abnormal neuronal migration occurring between the 12th and 24th weeks of gestation[5,6,8] . The smooth cortical surface further supports impaired cortical folding and maturation. Recent literature emphasizes that regional predilection and severity of cortical involvement correlate with clinical outcome and seizure burden[7].

A notable imaging feature in this case is the presence of alternating hypo- and hyperintense bands within the thickened cortex on T1 inversion recovery sequences, reflecting abnormal cortical lamination. Such laminar disorganization has been described in neuronal migration disorders and corresponds histologically to incomplete or disrupted cortical layering[8-10]. Contemporary reviews highlight that recognition of laminar abnormalities on advanced MRI sequences improves diagnostic confidence in complex cortical malformations[7].

Additionally, the presence of radially oriented perivascular spaces, seen as T2 hyperintensities with suppression on FLAIR images, represents an important ancillary finding. Prominent perivascular spaces have been reported in association with cortical malformations and may reflect altered cortical architecture and abnormal white matter organization, rather than a primary pathological process[10,11]. Their identification has been increasingly recognized as supportive, though nonspecific, imaging evidence in malformations of cortical development[7].

Clinically, patients with pachygyria commonly present with early-onset seizures, hypotonia, and severe developmental delay, with seizure onset typically occurring in infancy or early childhood[9,11]. The recurrence of seizures in adolescence in this patient may be attributable to discontinuation of antiepileptic therapy, highlighting the chronic epileptogenic potential of cortical malformations. The presence of microcephaly and severe motor impairment is associated with an unfavorable neurodevelopmental prognosis[11,12]. Recent studies emphasize the need for long-term neurological follow-up in such patients due to evolving seizure patterns across the lifespan[7].

The imaging differential diagnosis includes polymicrogyria, cobblestone lissencephaly, and subcortical band heterotopia. Polymicrogyria is characterized by an excessively folded cortex with an irregular cortical–white matter junction, unlike the smooth, thickened cortex seen in this case. Cobblestone lissencephaly is usually associated with brainstem and cerebellar abnormalities, which were absent. Band heterotopia typically demonstrates a discrete subcortical gray matter band, not observed in the present study[5,6,8]. Thus, the imaging findings most closely favor a

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pachygyria-predominant lissencephaly spectrum disorder, consistent with current classification systems[7].

Although genetic testing was not performed, lissencephaly and pachygyria are frequently associated with mutations in genes such as LIS1 (PAFAH1B1) and DCX, among others. Identification of a genetic etiology is valuable for prognostication, genetic counseling, and family planning, particularly in sporadic cases with severe phenotypic expression[5,13,14]. Recent guidelines underscore the role of genotype–phenotype correlation in refining diagnosis and counseling strategies[7].

This case underscores the critical role of MRI in adolescents presenting with long-standing developmental delay and epilepsy, particularly when seizures recur after a prolonged seizure-free interval. Accurate recognition of characteristic imaging patterns, supplemented by contemporary classification frameworks, is essential for definitive diagnosis, exclusion of mimics, and guiding long-term multidisciplinary management[5,7,10,12,].

Conclusion:

This case illustrates the incomplete form of thick lissencephaly with a posterior–anterior gradient and agyria–pachygyria pattern in an adolescent presenting with recurrent seizures. Recognition of characteristic imaging patterns is critical for diagnosis, classification, and management planning, especially in patients with a history of early-onset seizures and developmental delay.

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