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CASE SERIES

Lissencephaly with seizures: A case series of 3 children of under 5 years

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ABSTRACT
Lissencephaly is a rare neuronal migration defect that results in a smooth cerebral surface, mental retardation, and seizures. It is diagnosed primarily by correlating clinical manifestations with MRI findings. MRI typically shows features of lissencephaly and subcortical band heterotopia, which are crucial for diagnosis. Lissencephaly is associated with gene mutations. Treatment focuses on anti-seizure medications and physiotherapy to reduce seizures and improve motor skills. This case series highlights the importance of promptly diagnosing the LIS/SBH spectrum by MRI. Early diagnosis and intervention are critical for managing severe developmental outcomes.
Keywords: Lissencephaly, Subcortical band heterotopia, Magnetic resonance imaging (MRI)

INTRODUCTION

Lissencephaly (LIS) is a rare neuronal migration disorder characterized by a smooth cerebral cortex [1], leading to developmental delay, intellectual disability, and seizures. It can occur as part of the Lissencephaly/Subcortical band heterotopia (LIS/SBH) spectrum, often diagnosed via MRI, which shows a thickened cortex with absent gyration,hypoplasia of the corpus callosum [2] and abnormal subcortical bands. Lissencephaly can be congenital or caused by genetic mutations, particularly in the LIS1 gene, and is categorized into classical (type 1) and cobblestone (type 2) forms. [3]. A case series (consisting of 3 cases)of 1 day, 3 months & 4 years old respectively with their relevant clinical features are presented here, diagnosed via 3 Tesla MRI machine,highlighting MRI features of Lissencephaly.

CASE SERIES

CASE 1

A 1-day-old female was referred for lethargy, poor feeding, and hypotonia. The delay in feeding was first noticed shortly after birth, with poor suck and Moro reflexes. She was born via normal vaginal delivery at term without complications and is the first child in the family. On examination, she had generalized hypotonia but no dysmorphic features, and her weight and length were appropriate for age. Laboratory investigations were normal, and a cranial ultrasound showed no immediate abnormalities. Family history was unremarkable. After admission, she was advised MRI of the brain.

MRI revealed Cortical thickening with poor sulcation and smooth broad gyrus involving bilateral cerebral cortex (Fig 1A & 1B), suggestive of lissencephaly-pachygyria spectrum.

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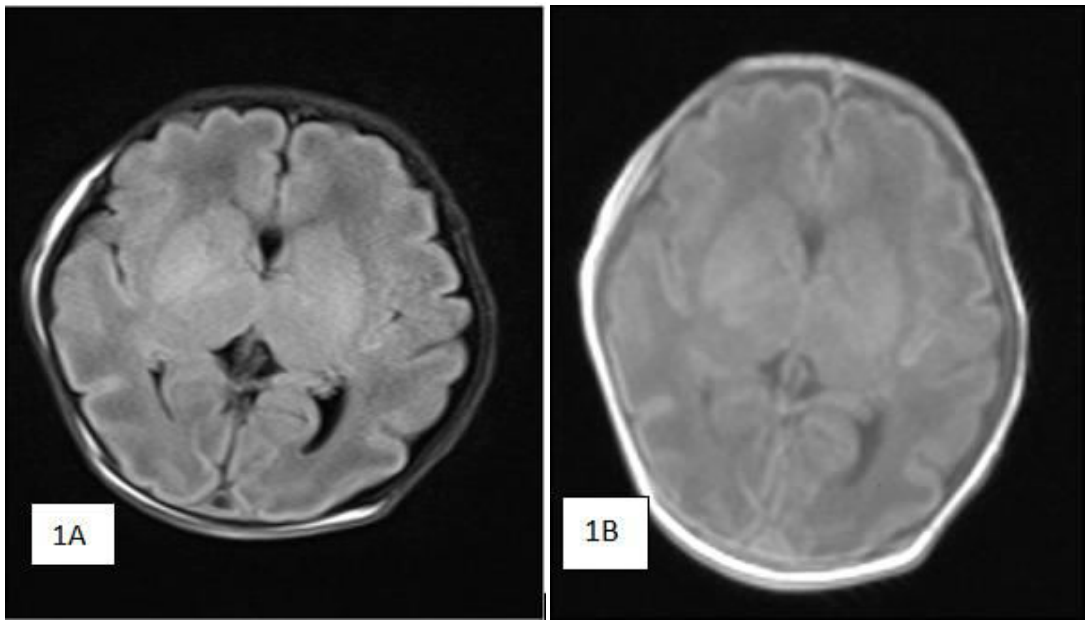
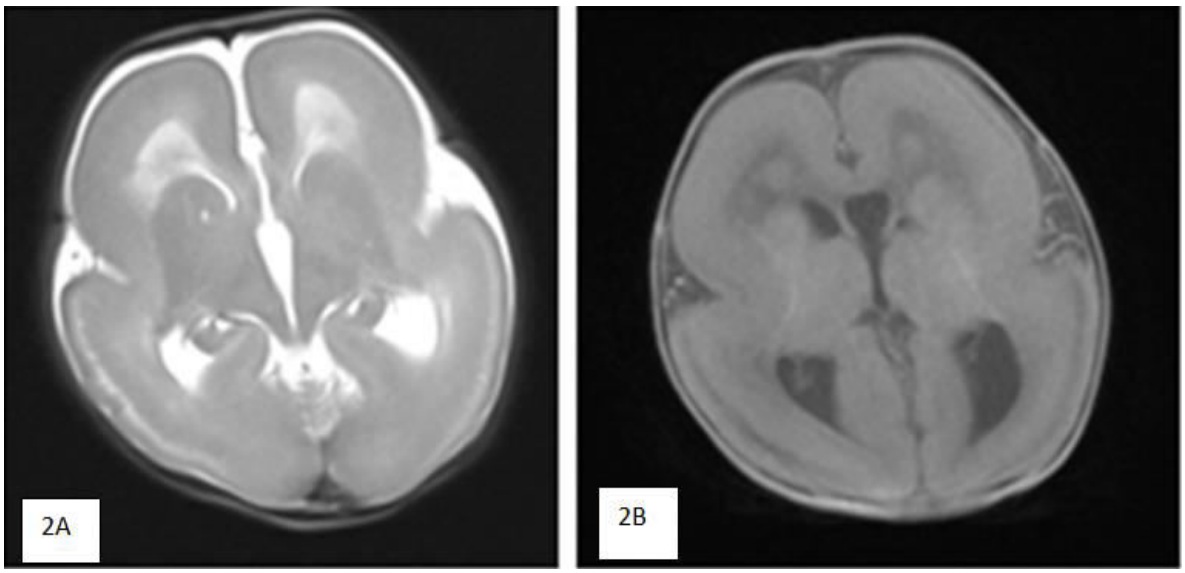


Images of case 1: Fig 1A & 1B. – Axial T2 FLAIR & T1 W images show thickened cortex, broad gyri with poor sulcation.

CASE 2

A 3-month-old male was referred for developmental delay and recurrent seizures. The delay was first noticed at 2 months when the infant exhibited poor head control. At 2.5 months, he started having focal seizures, initially not associated with fever but later triggered by mild febrile illnesses like upper respiratory infections. He was born via normal vaginal delivery with no complications and is the first child in the family. On examination, he had hypotonia but no dysmorphic features, and his weight and length were appropriate for age. Laboratory investigations were normal, and EEG showed mild cerebral slowing. Family history was unremarkable for neurological disorders. After admission, he was advised MRI of brain.

Magneticresonance imaging (MRI) revealed absence of cortical sulci and gyri, consistent with a smooth brain appearance, associated shallow bilateral Sylvian fissures (Fig. 2A & 2B). Posteriorhorns of bilateral lateral ventricles were dilated (Fig. 3). Diffuse and symmetric subcortical band heterotopias was noted (Fig. 4). The corpus callosum appeared flattened and hypoplastic. Additionally, the cerebral cortex was thickened, with poorly formed gyri in the temporal lobes. Based on these findings, the diagnosis of Lissencephaly (type 1) was established.



Images of case-2: Fig 2A & 2B. – MRI T2W & T1W images show lack of cortical sulci and gyri i.e. smooth brain with shallow bilateral sylvian fissures.

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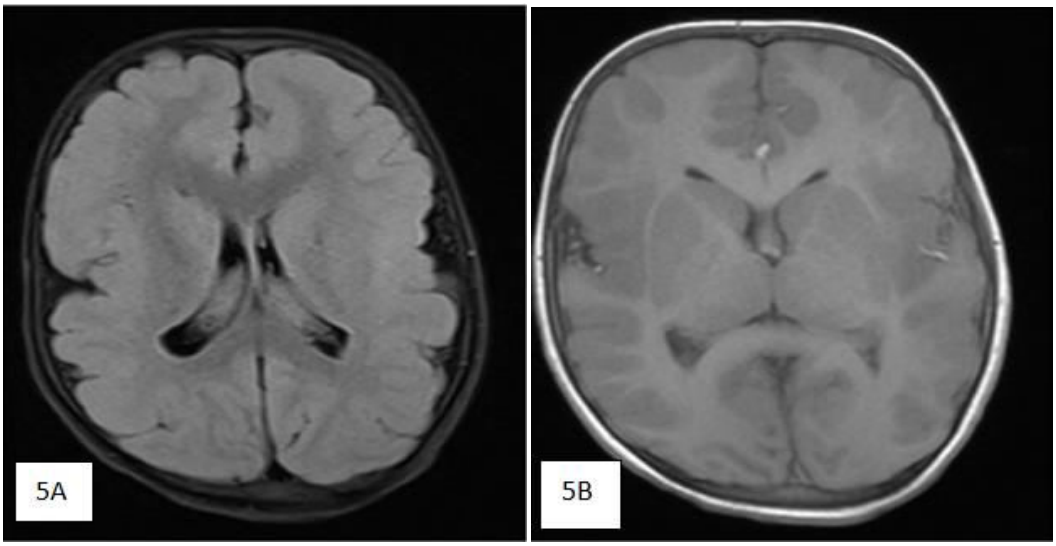
CASE 3

A 4-year-old male was referred for global developmental delay and behavioural concerns. The delay was first noticed at 18 months when the child failed to meet motor milestones. He had poor coordination, speech delay, and exhibited temper tantrums. He was born via normal vaginal delivery with no complications and is the first child in the family. On examination, he showed hypotonia but no dysmorphic features, and his weight and length were appropriate for age. Laboratory investigations were normal, and EEG showed mild focal abnormalities. Family history was notable for a maternal uncle with learning difficulties. After admission, he was advised MRI of the brain.

MRI revealed Irregular cortical surface with thickened and over folded cortex, sparse sulci, and irregularity at the grey-white interface (Fig. 5A & 5B). Multiple hyperintense signal areas on T2-weighted images in the periventricular and subcortical white matter involving the right fronto-parietal lobe, suggestive of lissencephaly (Type I).



Images of case-3: Fig 5 A & 5B. – Axial T2 FLAIR & T1 W images show irregular cortical surface with thickened and over folded cortexirregularity at the grey-white interface

DISCUSSION

Lissencephaly is a rare cortical disorder that can be classified into Type 1 (classic) and Type 2. Type 1 is characterized by absent or hypoplastic sulci and is often associated with subcortical band heterotopias [4]. Type 2, also known as "cobblestone lissencephaly," involves over migration of neurons and is linked to conditions like Walker-Warburg syndrome and Fukuyama congenital muscular dystrophy [5].

In Type 1 lissencephaly, infants present with hypotonia, developmental delay, feeding difficulties, and seizures, often starting as infantile spasms. Seizures, often starting as infantile spasms, occur in up to 90% of children before 6 months and progress to more severe forms [6] such as Lennox-Gastaut syndrome. Patients typically experience microcephaly by age 1, with severe developmental impairments.

MRI of our patient revealed a thickened cortex, shallow sulci, and enlarged ventricles, consistent with Type 1 lissencephaly. The clinical features, including delayed motor milestones and recurrent seizures, align with the radiological findings and further support this diagnosis. [7]

The prognosis for lissencephaly is generally poor, with most children experiencing refractory epilepsy and severe developmental delays. Treatment focuses on managing seizures with antiepileptic drugs, but survival beyond childhood is uncommon, with many affected individuals passing away by adolescence.

CONCLUSION

Lissencephaly and subcortical band heterotopia (LIS/SBH) are rare neurodevelopmental disorders that require early identification for improved outcomes. Early diagnosis, through imaging like MRI, and genetic testing can guide effective management, including physiotherapy to enhance developmental milestones. Healthcare providers in low-resource settings should consider LIS/SBH in cases of developmental delays and seizures. Early intervention improves the quality of life and prognosis, emphasizing the need for awareness and timely care to avoid misdiagnosis and improve long-term outcomes.

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