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# Unilateral Closed Lip Schizencephaly with Focal Cortical Dysplasia

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## Abstract-

*Schizencephaly is a rare congenital malformation of the central nervous system, characterized by abnormal clefts or slits in the cerebral cortex. Both genetic and non-genetic factors, such as prenatal infections or ischemia, have been implicated in its etiology. Clinically, schizencephaly presents with varying degrees of developmental delay, motor impairments (such as hemiparesis), and seizures. It is often associated with* ***focal cortical dysplasia (FCD)****, absent* ***septum pellucidum****, and dilated lateral ventricles. Magnetic resonance imaging (MRI) is the diagnostic modality of choice, allowing for detailed visualization of these structural abnormalities. Schizencephaly is typically diagnosed at birth, with symptoms presenting in early childhood. Early and accurate diagnosis is crucial to guide appropriate management and avoid unnecessary or incorrect treatments. In this report, we describe a rare case of* ***unilateral closed-lip schizencephaly*** *with coexisting focal cortical dysplasia in a child who presented with* ***generalized tonic-clonic seizures****.*

**Keywords*****: Focal cortical dysplasia, magnetic resonance imaging, closed-lip schizencephaly, generalized tonic-clonic seizures, developmental delay.***

Introduction-Schizencephaly is a rare congenital malformation of the central nervous system, characterized by a cleft extending through the cerebral hemisphere from the pial surface to the lateral ventricle, lined by heterotopic gray matter. The anomaly represents a neuronal migration disorder that develops between the second and fifth months of gestation.[1] It is most often identified during the evaluation of children or young adults presenting with epilepsy, neurodevelopmental delay, or as an incidental finding. The precise pathogenesis remains unclear,

though both antenatal environmental insults and genetic causes have been implicated.[2,3] Schizencephaly may occur in isolation, in association with other cerebral malformations, or as part of a multiple congenital anomaly syndrome.[4]

The malformation was initially described by Wilmarth in 1887,[5] and the term “schizencephaly” was later introduced by Yakovlev and Waldsworth in 1946.[6,7] They categorized the anomaly into two types: type I (closed-lip), in which the cleft walls are fused, thereby preventing cerebrospinal fluid (CSF) passage, and type II (open-lip), characterized by a wide cleft allowing CSF communication between the ventricular cavity and subarachnoid space. Schizencephaly may occur unilaterally or bilaterally, in any region of the cerebral hemispheres. Bilateral clefts are typically symmetric in location, though they may differ in size.

Among the malformations commonly associated with schizencephaly, focal cortical dysplasia is frequently observed. Evidence from both anatomical and clinical studies suggests that schizencephaly and focal cortical dysplasia may share a common pathologic mechanism.[8] According to Barkovich and Kjos,[8] involvement limited to the superficial cortical layers results in focal cortical dysplasia, whereas disruption across the full thickness of the hemisphere leads to a cleft extending from the subarachnoid space to the lateral ventricle. In this report, we present a pediatric female patient with unilateral right-sided closed-lip schizencephaly associated with focal cortical dysplasia and provide a brief review of the literature.

## Case report-

A 10-year-old female patient presented in out patient department of pediatrics with chief complaint of yellowish discoloration of the skin for the past 7-8 days, accompanied by vomiting and abdominal pain for the last 6-7 days. The patient also had a history of **right-sided weakness**, which was noted to be a sequel of **left-sided hemiparesis** present since birth. Additionally, she complained of **headaches** over the past 2 years, which were alleviated by oral medications. The patient was a known case of **seizure disorder**, having been on antiepileptic medications levetiracetam (40mg/kg/day) for the past 2 years but with **poor compliance**.(discontinued 2 month back without consultation). Upon further inquiry, the patient's mother reported a history of **bleeding per vaginum** during the first trimester of pregnancy and was on strict bed rest throughout

the remainder of the pregnancy. There were no postnatal complications, and the child did not exhibit any global developmental delay **Family history** and **birth history** were largely unremarkable. Other histories were non contributory. Vital signs at the time of presentation were stable and within normal limits. On examination, patient had icterus positve and hepatomegaly . Rest examination were within normal limits. A thorough workup, including blood tests and other laboratory investigations, was performed to rule out metabolic and other potential causes of the seizure. Liver function tests (LFT) and viral markers were advised in view of icterus positive for Hepatitis A, B , C ,E and and Hepatitis A came as positive confirming the diagnosis of Acute Viral Hepatitis. Bilirubin , Liver enzymes were raised . The patient's condition gradually improved with the supportive treatment as per our unit protocol, with decreasing trend in liver enzymes. However, on day four of hospitalization, the patient developed a single episode of **generalized tonic-clonic seizure**, which lasted for approximately 90 seconds. Antiepileptic treatment with **IV Phenytoin** was initiated as bolus dose and maintenance were continued .No further seizure episodes were observed there after

**Neuroimaging** was conducted using **brain MRI**, which revealed the following findings:

- A **grey matter-lined cleft** extending through the right fronto-temporal region, reaching up to the right periventricular area.
- The cleft was **non-communicating with the right lateral ventricle**, with the cleft walls apposing in places, exhibiting **thickened and irregular grey matter** along its edges.
- An **absent septum pellucidum** with **mildly dilated bilateral lateral ventricles**, and a **wavy, irregular margin** of the right lateral ventricle.
- **Focal T2 and FLAIR hyperintense signals** observed in the **right parietal region**, posterior to the cleft, suggestive of **focal cortical dysplasia**.

These findings are consistent with **unilateral closed-lip schizencephaly**, with associated **focal cortical dysplasia**.

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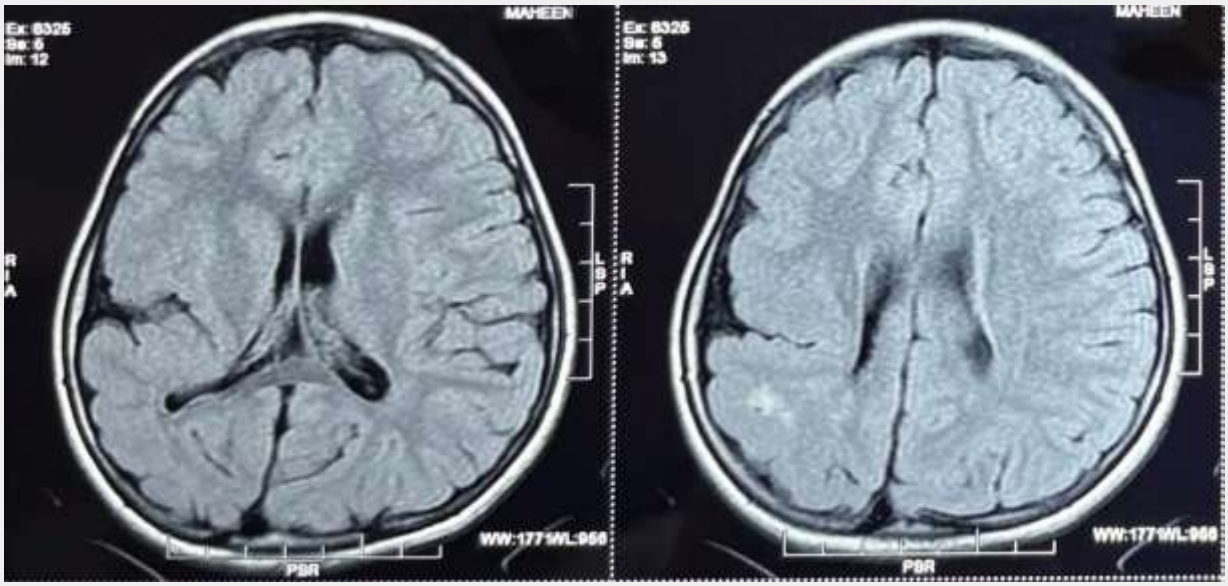
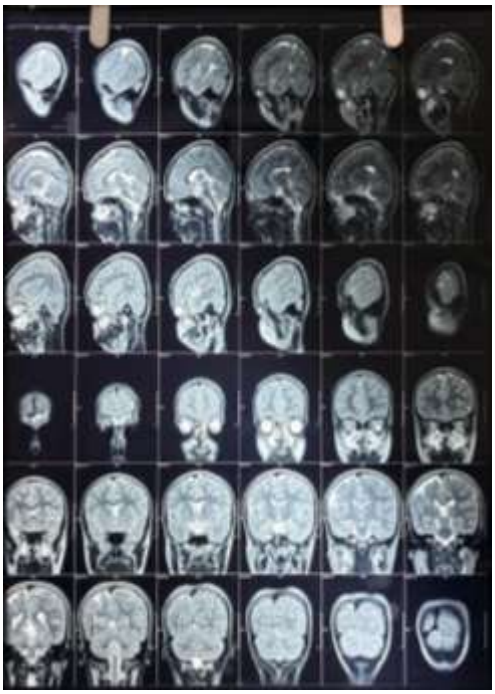
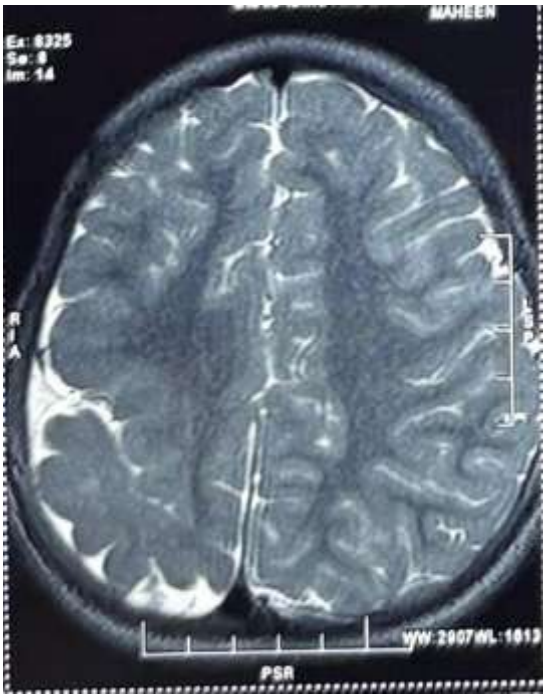



Figure 1





The above figure 1, 2 and 3 depicts:

- Gray matter lined cleft extends though the right fronto-temporal region & reaching up to right periventricular region & cleft is not communicating with right lateral ventricle, sides of cleft in places appose to each other with thickened & irregular gray matter along the cleft.
- Absent septum pellucidum with mildly dilated bilateral lateral ventricles and wavy irregular margin of right lateral ventricle.
- Focal T2 & FLAIR hyperintense signals in the right parietal region, posterior to cleft--?Focal Cortical Dysplasia.

***All findings in radioimaging confirmed the diagnosisSuggest unilateral Schizencephaly - close***

The patient was managed as per nit protocol with iv fluids , antibiotics and Anticonvulsant . IV Phenytoin was gradually taperd and stopped before discharge and tab levetiracetam was continued..On follow up the patient was asymptomatic and at the time of writing patient was asked to follow up after one month.

## Discussion

Schizencephaly is defined as a cerebrospinal fluid (CSF)-filled cleft lined with dysmorphic gray matter, extending medially from the subarachnoid space to the lateral ventricle. It results from injury involving the full thickness of the developing hemisphere during cortical organization. In some cases, gray matter may extend into the lateral ventricle in the form of subependymal heterotopias. The cleft may be small or large, unilateral or bilateral, and is classified into two types: closed-lip (type I), where the gray matter-lined lips are in contact, and open-lip (type II), in which the lips are separated with a CSF-filled cleft extending to the ventricle.[8] These clefts are most commonly located in the perisylvian region, with the surrounding cortex typically polymicrogyric.[9]

The incidence of schizencephaly has been estimated at approximately 1 per 100,000 live births.[20] In a large cohort study of 4 million births, the prevalence of isolated schizencephaly was reported as 1.06/100,000, while schizencephaly with at least one additional extracranial

malformation occurred in 0.49/100,000 births, yielding a combined prevalence of 1.54/100,000.[21] Interestingly, young parental age (<20 years) was identified as a significant risk factor, with a fourfold increased risk for isolated schizencephaly and a threefold increased risk for non-isolated cases. No gender predilection has been demonstrated.

The intrauterine pathogenesis of schizencephaly is complex, involving both genetic and environmental factors. Developmental disturbances affecting the germinative zones and migrating neurons along radial glial fibers occur during the early stages of neuronal migration in the third month of gestation.[15–18] Mutations in the **EMX2** gene, a key regulator of neuronal migration, have been identified in some familial cases. Conversely, mutations in **LHX2, HESX1,** and **SOX2**, previously thought to be causative, have been refuted.[19] More recently, pathogenic variants in **WDR62** and **COL4A1** have been linked to schizencephaly.

Clinically, outcomes are highly variable. Granata et al. demonstrated that the severity of motor and cognitive impairments correlates with the extent of the anatomic defect, though no association was observed with the presence or severity of epilepsy.[10] Liang et al. (2002) further correlated neuroimaging findings with clinical features, concluding that imaging can aid in predicting developmental outcomes. The spectrum of phenotypes depends on the size of the cleft, laterality, and whether the anomaly is open- or closed-lip.[11]

Radiologically, CT has limited diagnostic value, especially in closed-lip cases, though subtle outpouchings at the ependymal surface may occasionally be seen. Secondary features such as hydrocephalus, heterotopia, polymicrogyria, subdural hygromas, and arachnoid cysts may also be present. Barkovich and Kjos,[12] as well as Packard et al.,[13] noted that schizencephaly and focal cortical dysplasia frequently occur in similar hemispheric locations.

Schizencephaly is also associated with other cerebral anomalies, including septo-optic dysplasia, gray matter heterotopia, agenesis of the septum pellucidum, and corpus callosum dysgenesis.[9] MRI is the imaging modality of choice, as it provides detailed visualization of cortical dysplasia, heterotopic gray matter, and the characteristic pial-to-ependymal cleft. Each sequence has specific diagnostic utility: T1-weighted images delineate cortical detail, sagittal T2-weighted sequences are particularly useful in assessing polymicrogyria, and FLAIR imaging is valuable for

characterizing clefts. The most common differential considerations are focal cortical dysplasia and heterotopic gray matter.

The key differential diagnosis includes subarachnoid cysts and porencephaly. Identification of the gray matter lining within the cleft is critical to distinguish schizencephaly from porencephaly. This distinction is not only diagnostic but also significant for genetic counseling, given that anomalies of cell migration have been reported in 5–20% of siblings of affected children.[14]

## 5. Conclusion-

Schizencephaly is a rare congenital malformation of the central nervous system resulting from neuronal migration defects and is associated with a wide spectrum of neurological and psychological dysfunction. Imaging plays a pivotal role in diagnosis, with prenatal ultrasonography and MRI enabling early identification of open- or closed-lip variants as early as 21 weeks of gestation. The precise number of reported cases worldwide remains unclear; however, the estimated prevalence is approximately 1 in 64,935 births.

While up to 10% of patients may remain asymptomatic, others may present later in adulthood with variable clinical manifestations. In the absence of reliable data on the true incidence of asymptomatic cases, imaging evaluation and management should be guided by predictors of adverse motor and psychomotor outcomes.

Therapeutic measures includes anti-seizures medications and developmental support to patient.Given its rarity, continued reporting of cases and advocacy for long-term follow-up studies are essential to improve understanding of the natural history of schizencephaly. Such efforts will be critical in shaping future imaging protocols, guiding management strategies, and ultimately optimizing patient outcomes.

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