Schizencephaly

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Abstract

Schizencephaly is a rare cortical malformation characterized by a full-thickness gray matter-lined cleft extending from the pial surface to the ventricular wall. This defect is frequently associated with other intracranial abnormalities, including absence of the septum pellucidum, optic nerve hypoplasia, corpus callosum dysplasia, hydrocephalus, arachnoid cysts, and cerebellar malformations. While increasingly diagnosed antenatally, many patients present later in life with seizures, intellectual disability, or psychomotor delay. Clinical severity is closely related to the size and location of the cleft. Management is symptom-based and may include medical treatment for seizures, shunt placement for hydrocephalus, and supportive therapies for developmental and motor impairments.

Keywords: brain, congenital, genetic

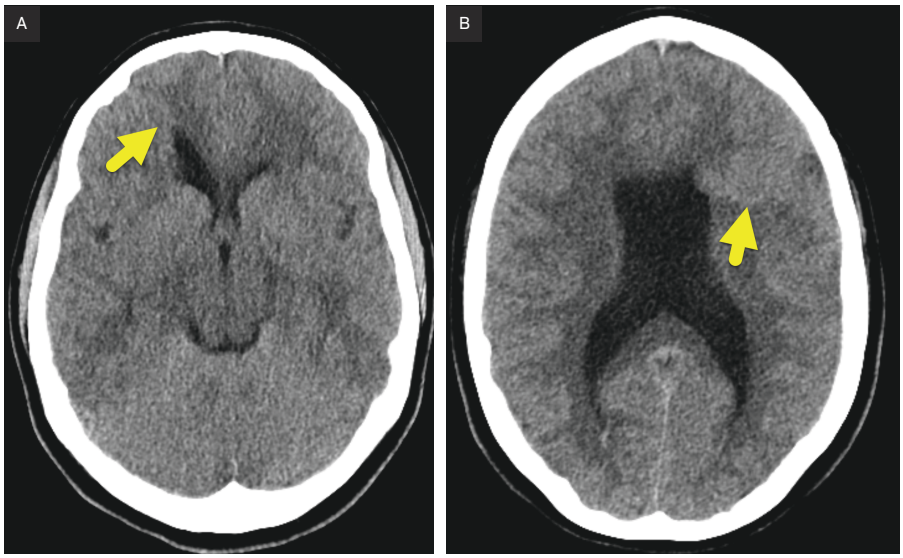
Case Summary

An adolescent, who was a restrained passenger in a motor vehicle collision, presented to the emergency department following a brief loss of consciousness. On examination, her Glasgow Coma Scale score was 15. Notably, the patient did not have a history of seizures.

Imaging Findings

Initial head CT (Figure 1) showed no traumatic findings. Instead, the study showed the absence of the septum pellucidum, closed-lip schizencephaly in the inferior right frontal lobe with mild distortion of the adjacent lateral ventricle, and closed-lip schizencephaly and polymicrogyria in the left frontal lobe. Subsequent MRI (Figure 2) confirmed these findings.

Figure 1. Axial CT images at the level of (A) the frontal horns of the lateral ventricles and (B) the body of the lateral ventricles showing the absence of the septum pellucidum and bilateral closed-lip schizencephaly (arrow) with gray matter lining each cleft.



Diagnosis

Schizencephaly.

The imaging differential diagnosis for schizencephaly includes porencephaly, heterotopic gray matter, gliosis, focal cortical dysplasia, polymicroglia, arachnoid cysts, and septo-optic dysplasia.

Discussion

Schizencephaly is a rare malformation of the cerebral cortex occurring with a prevalence of 1.54 per 100,000

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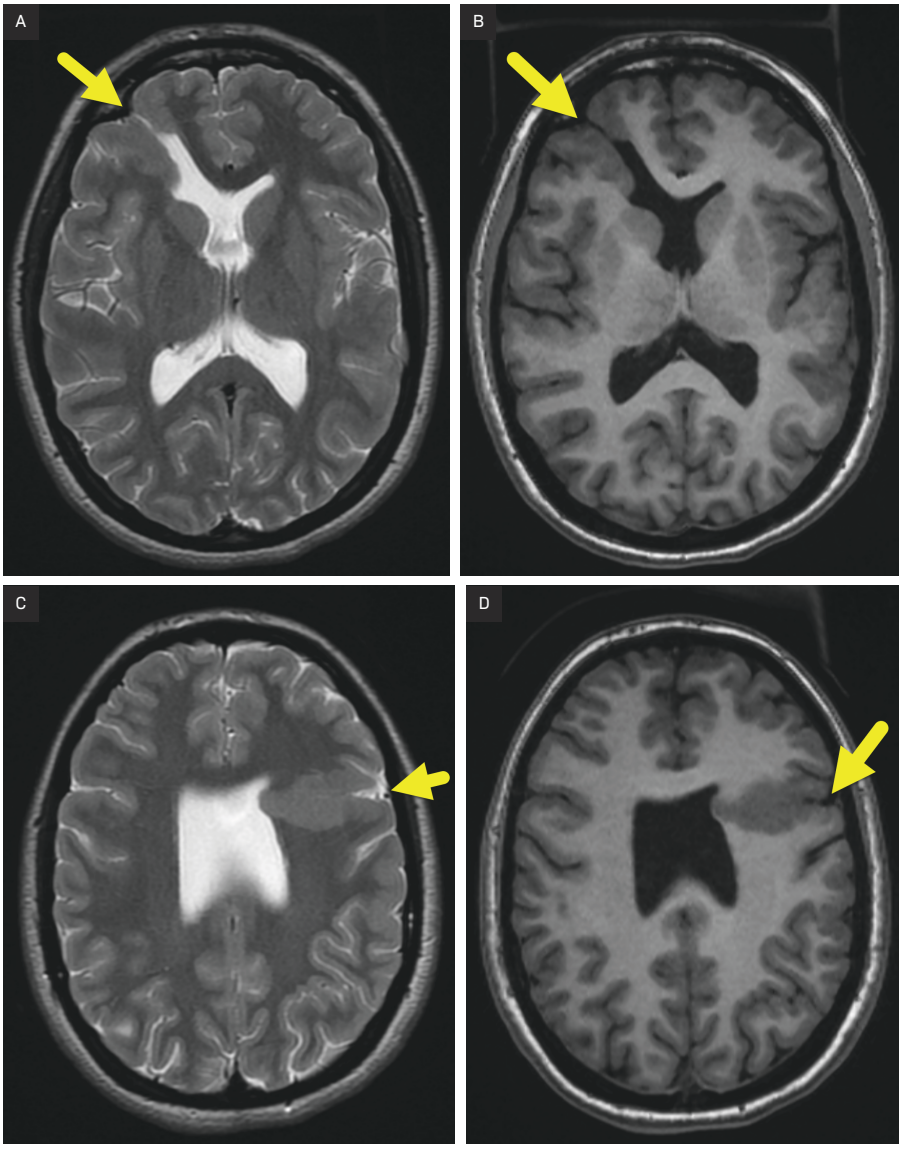
Figure 2. (A) Axial T2-weighted and (B) T1 FLAIR images at the level of the frontal horns of the lateral ventricles and (C) axial T2-weighted and (D) T1 FLAIR images at the level of the mid body of the lateral ventricles showing the absence of the septum pellucidum and bilateral closed-lip schizencephaly (arrow) with gray matter lining each cleft. Polymicrogyria is present at each cleft.



births.[1] It is characterized by a full-thickness gray matter-lined cleft that extends from the pial surface to the ventricular wall. The cleft's gray matter lining distinguishes it from other cortical abnormalities.[2] Schizencephaly typically occurs sporadically. Only a few familial cases have been described.[3] However, it has been occasionally associated with mutations in the *EMX2* and *COL4A1* genes, as well as with Vici syndrome, a disorder caused by *EPG5* gene mutations and characterized by agenesis of the corpus callosum, cardiomyopathy, albinism, and immune deficiency.

The etiology of schizencephaly remains unclear. Proposed mechanisms include intrauterine infections and early vascular disruptions.[1] One hypothesis suggests that intracranial insults occurring before neuronal migration (4-6 months gestational age) result in schizencephaly, while injuries after this period produce defects not lined by gray matter, such as porencephaly (without gliosis) or encephalomalacia (with gliosis).[4] Additional risk factors include young maternal age (under 20 years), prenatal exposure to toxins or teratogens, and maternal trauma.[3]

Schizencephaly can be distinguished from other intracranial abnormalities, such as porencephaly, by the presence of a gray matter lining along the cleft. Porencephaly refers to a cystic cavity within the cerebral hemisphere that communicates with the ventricular system or subarachnoid space. These cavities are typically surrounded by gliosis, lack a gray matter lining, and are usually the result of acquired brain injury. While antenatal US is increasingly capable of detecting schizencephaly in utero, MRI remains the preferred imaging modality due to its ability to clearly visualize the gray matter lining.[3]

Schizencephaly is typically classified into 2 types: type 1 (closed-lip) and type 2 (open-lip). In open-lip schizencephaly, the cleft walls are separated and filled with cerebrospinal fluid. In contrast, closed-lip schizencephaly is characterized by direct apposition of the cleft walls without intervening fluid. More recent literature proposes an expanded classification that includes a third variant: a column of heterotopic gray matter without a visible cleft. In this system, type 1 represents isolated gray matter heterotopia, type 2 corresponds to closed-lip schizencephaly, and type 3 to open-lip schizencephaly.[1,4]

Open-lip schizencephaly is the most common form, seen in approximately 80-85% of patients, while closed-lip accounts for the remaining 10-15%. Schizencephaly may be unilateral or bilateral, with bilateral involvement slightly more frequent. Among patients with bilateral clefts, 60% have bilateral open-lip defects, and 20% have mixed defects. Of those with unilateral clefts, 60% have open-lip defects.[4]

Between 50% and 90% of patients with schizencephaly have additional intracranial anomalies. The most common

associated abnormality is absence of the septum pellucidum, seen in approximately 70% of patients. Other frequent findings include optic nerve hypoplasia (30%), corpus callosum dysplasia (30%), and hydrocephalus, which occurs in about 30% of patients with open-lip clefts.[3-5] Additional associations include arachnoid cysts and cerebellar malformations.[3]

When schizencephaly is not detected on antenatal imaging, it is often identified later in childhood during evaluation for psychomotor delay or seizures. In patients with a unilateral cleft, seizures may originate from the contralateral hemisphere, often in regions of polymicrogyria.[5] The severity of symptoms and overall prognosis correlates with the size and location of the cleft. Larger or bilateral defects are associated with more significant motor and cognitive impairments, including hemiparesis or quadriparesis, intellectual disability, language deficits, and global developmental delay.[1,6] Frontal or perisylvian clefts may also be associated with behavioral disturbances or characteropathies.[3]

In contrast, unilateral schizencephaly may be asymptomatic and is sometimes discovered incidentally in adulthood, often after the onset of seizures in individuals with otherwise normal development.[7] Treatment is symptom-directed and may include antiepileptic medications, ventriculoperitoneal shunting for hydrocephalus, and supportive therapies such as occupational and physical therapy to address cognitive and motor impairments.[1,8]

Conclusion

Schizencephaly is a rare cortical malformation characterized by a full-thickness gray matter-lined cleft extending from the pial surface to the ventricular wall. This defect is frequently associated with other intracranial abnormalities, including the absence of the septum pellucidum, optic nerve hypoplasia, corpus callosum dysplasia, hydrocephalus, arachnoid cysts, and cerebellar malformations. While increasingly diagnosed antenatally, many patients present later in life with seizures, intellectual disability, or psychomotor delay. Clinical severity is closely related to the size and location of the cleft. Management is symptom-based and may include medical treatment for seizures, shunt placement for hydrocephalus, and supportive therapies for developmental and motor impairments.

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