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Schizencephaly: A Case Report and Review of Literature

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Abstract

Schizencephaly is a rare congenital malformation of the brain that could present with repeated seizures. We report a case of a 17-year-old boy who presented with status epilepticus. Further radiological evaluation revealed unilateral open lip schizencephaly. Seizure was well controlled with anti-epileptic drug and there was no need for surgical intervention. This case highlights the need for prompt radiological evaluation of patients with seizures, especially in resource-limited settings where the high cost and non-availability of such facilities might be a major impediment.

Keywords

Open Lip Schizencephaly, Status Epilepticus, Seizure

1. Introduction

Schizencephaly is a congenital malformation of the central nervous system (CNS) characterised by the presence of anomalous gray matter-lined cleft in the cerebral hemisphere that can enable communication between the subpial space and the ventricle [1] [2] [3] [4]. It was first described in 1946 by Yakovlev and Wadsworth as hemispheric clefts with infolding of gray matter along the cleft and associated cerebral malformations. They eventually coined the term Schizencephaly [4]. It is a rare condition and the global Incidence has been put at 1.5 in 1,000,000 live births and 1:1650 among children suffering from epilepsy [5] [6]. There is no gender predilection, but young maternal age (<20 yrs) is a risk factor [5] [6]. There have been few reported cases in Nigeria and there is no data on the incidence or prevalence in the country. Radio-imaging is required for its diagnosis, but this is beyond the reach of an average patient in our locale. Therefore, we report this case to highlight the need for prompt radiological evaluation of pa-

tients with intractable seizures, especially in resource-limited settings.

2. Case Report

A 17-year-old boy presented to children's emergency room with complaints of fever of 5-day duration and multiple convulsions which started 8 hours before presentation. The body was just warm and present most time of the day. He developed generalised tonic clonic convulsions 5 days after onset of the fever. He had 4 episodes within 8 hrs of onset without regaining consciousness in between the last 2 episodes. The last episode lasted about 40 minutes before it was aborted at presentation with IV Diazepam. This was the first episode of seizure in life time and no family history of epilepsy. Of note prior to this illness was history of forgetfulness, poor academic performance and emotional lability which were ignored by the parents as they were considered non-medical problems. Antenatal period was not adversely eventful and delivery was via spontaneous vertex. He reportedly cried immediately after birth and there was no other neonatal problem. No delay in achieving the various developmental milestones. He had finished senior secondary school and preparing intensely for university entrance examination prior to the onset of this acute phase of the illness.

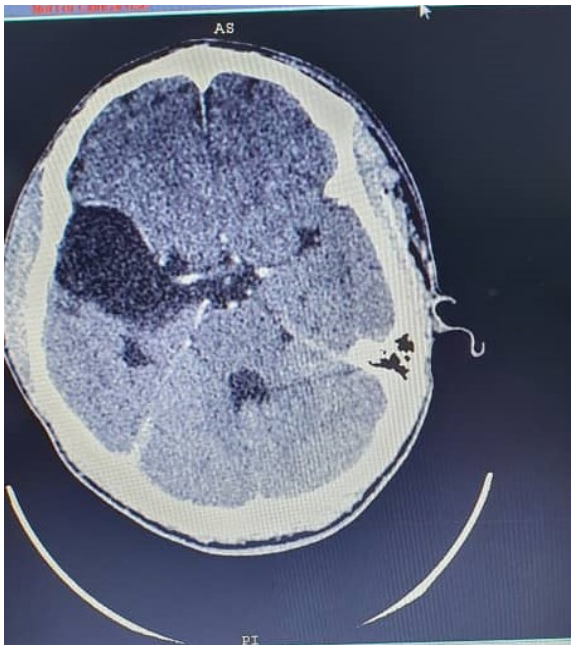
At presentation, his temperature was normal and had a Glasgow coma score of 12. He had macrocephaly (Head circumference of 60 cm), there were no lateralizing signs or features of meningeal irritation. Other systemic examination findings were not remarkable. Cerebrospinal fluid (CSF) biochemistry and microscopy were normal. The CSF culture yielded no growth. Other investigations like FBC, RBG, ESR and serum calcium (**Table 1**) were essentially normal. A Preliminary assessment of Meningitis with status epilepticus was made. He was commenced on IV Phenytoin and IV Ceftriaxone at meningitic dose.

Computerized tomography scan of the brain (**Figure 1**) revealed a large un-enhancing lesion arising from the pre-pontine cistern to the right temporal lobe/sylvian fissure with an appearance of associated hypoplasia of the right temporal lobe. The lesion is lined by grey matter. There is no shift of midline brain structures nor communication with the ipsilateral lateral ventricle. There are hypodense collections within the right ethmoidal and maxillary sinuses. These features are consistent with the diagnosis of unilateral right open lip schizencephaly. Further evaluation for congenital infections and genetic examination were not done due to limited resources in our locale.

Seizures stopped within 24 hours of admission and regained full consciousness by the 3rd day with no motor deficit. He was commenced on oral Levetiracetam at 500 mg q12hr. Completed 7 days of IV antibiotics and was discharged. EEG done on follow up showed focal activity with secondary generalization. The dose of Levetiracetam was increased to 750 mg q12hr after 2 weeks of commencement. He had poor seizure control despite good compliance. Therefore, the Antiepileptic drug was changed to Sodium Valproate which eventually achieved good seizure control and patient doing well on follow up.

Table 1. Investigation results.

Investigation	Result
Total WBC	5200/μL
Lymphocytes	2500/μL
Neutrophils	2300/μL
Monocytes	400/μL
Haematocrit	37.8%
Mean Corpuscular Volume	85 fL
Mean Corpuscular Haemoglobin	30 pg
Mean Corpuscular Haemoglobin Concentration	36.2 g/dL
Platelet (/μL)	160,000
ESR	17 mm/hr
Serum Calcium	8.2 mg/dl
CSF Protein	10 mg/dl
CSF Glucose	63 mg/dl
Concomitant RBG	70 mg/dl
Serum Urea	15 mg/dl
Serum Creatinine	0.6 mg/dl
Serum Sodium	136 mg/dl
Serum Chloride	104 mg/dl
Serum Potassium	3.6 mg/dl
Serum HCO_3	20 mg/dl



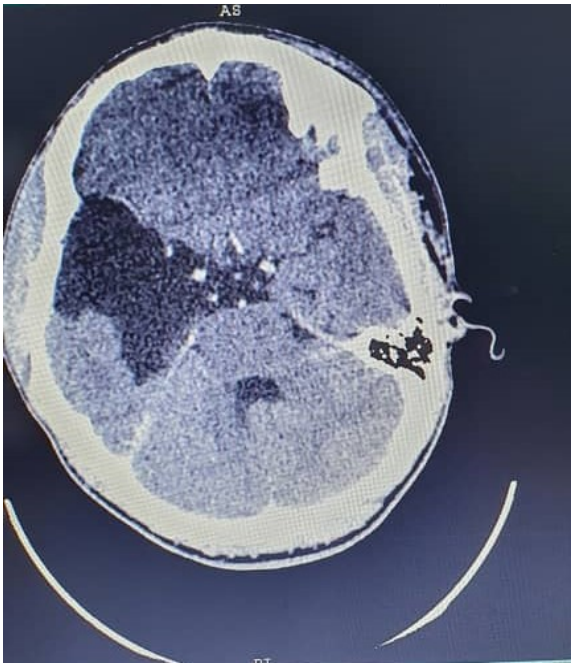


Figure 1. CT scan of the brain.

3. Discussion

In schizencephaly, there is a cleft that extends through the entire cerebral hemisphere from the ependymal surface of the ventricle to the pial surface of the brain. The cleft is characteristically lined with dysmorphic grey matter [1] [2] [3] [7]. Two types of Schizencephaly have been identified. Type 1 or closed lip, in which the walls of the cleft are closely apposed thus obliterating the CSF space within the cleft [2] [8]. Conversely, in the most common type which is Type 2 or open lip, the cleft walls are separated with CSF filling the cleft and extending from the ventricle to the subarachnoid space [1] [6] [8]. The cleft could be bilateral or unilateral and it commonly occurs in the parietal and frontal lobes. Our patient had unilateral open lip schizencephaly in the right temporal lobe. Schizencephaly is often associated with other CNS malformations including absent septum pellucidum, polymicrogyira, heterotopias and septo-optic dysplasia [2] [6]. The patient presented here did not have any of the aforementioned associations but had hypoplastic temporal lobe.

The pathophysiologic mechanism of schizencephaly remains unknown. However, it is hypothesized to result from the arrest of neuronal migration. At about 7^{th} to 8^{th} week gestation, neuroblasts migrate from the germinal matrix along the radially oriented glia cells to the cerebral cortical region. Any significant vascular insult at this watershed area could lead to failure of neuroblast migration thus resulting in cleft formation [5]. Intrauterine Cytomegalovirus (CMV), Zika virus and Herpes Simplex virus (HSV) infections have been associated with schizencephaly through disruption of the germinal matrix vascular supply [9]. Some Familial cases of schizencephaly have also been identified; the genetic basis for this has not been fully understood. The heterozygous mutations

of the EMX2 gene shown to be associated with schizencephaly by Granata *et al.* [10] have been refuted while WDR62 and COL4A1 genes have been recently identified to play a role in its development [1] [11] [12].

Clinical manifestations vary depending on the level of brain tissue involvement. It ranged from asymptomatic cases to those with severe neurological disabilities. Common features include seizures, motor deficit, delayed milestones, cognitive impairment, microcephaly and others based on associated anomalies [13] [14]. Patients with closed lip type are more likely to have milder forms of neurologic deficit when compared to those with open lip type.

Recent systematic review of all published cases of schizencephaly over a period of 40 years by Braga *et al.* [2] identified a total of 734 patients that met the inclusion criteria. Motor impairments ranging from hemiparesis to tetraplegia constitute the most frequent and debilitating disabilities in Schizencephaly (about 90% of the patients reviewed). Neurocognitive impairment is the second most common disability with 77.5% of patients having it. Bilateral clefts are associated with more severe neurocognitive impairments. Early diagnosis at age < 4 years is associated with motor and neurocognitive impairments.

The third most frequent clinical manifestation is epilepsy occurring in 67.5% of the patients reviewed. Lopes *et al.* [15] found that open lip type is more associated with treatment resistant epilepsy. However, the occurrence of epilepsy is similar in both types of schizencephaly.

In this our case, the main clinical feature is epilepsy with no motor deficit. Even though he presented at 17 yr, he has been showing features of neurocognitive impairment much earlier which were dismissed by the parents.

Magnetic resonance imaging (MRI) is the neuro-imaging of choice in the evaluation of schizencephaly as it is more sensitive and able to differentiate between gray and white matter when compared to Computerized tomography (CT) scan. The pathognomonic finding is the presence of gray mater lined cleft in the cerebral cortex [1] [14] [16]. The drawback is the high cost which makes the use of CT scan an alternative. In our patient, CT scan was done due to the high cost and non-availability of MRI in our facility. However, it was able to demonstrate the gray matter lined large un-enhanced lesion.

Management of schizencephaly is mainly conservative. It involves rehabilitation for the motor deficits and mental retardation as well as use of antiepileptic drugs to control seizures. Surgical intervention is indicated when there is concomitant hydrocephalus and intracranial hypertension, in which case a ventricular shunt is typically inserted [3] [8]. In our patient, seizure was controlled with antiepileptic drug and no need for rehabilitation as motor deficit was absent.

4. Conclusion

A case of schizencephaly in an adolescent presenting for the first time with status epilepticus was highlighted to underscore the need for prompt radiological investigation in the evaluation of patients with intractable seizures, especially

in resource-limited settings where it is not routinely done.

Patient Consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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