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Schizencephaly Presenting for the First Time in a Previously Healthy Adult Male

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Case Report

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ABSTRACT

As is true for any human tissue, normal cellular differentiation and migration in the central nervous system is crucial for normal functioning of the body. Any defects in the neuronal migration can be disastrous, and can potentially lead to devastating disability. Amongst the spectrum of various neuronal migration defects within the brain, schizencephaly is the most severe form and is an extremely rare clinical entity. Schizencephaly can pose different health related problems to the affected child. Refractory seizure disorder and developmental delay are amongst such issues. Although; normally, schizencephaly presents during the 1st decade of life, rarities do exist. We report one such rare presentation of bilateral closed lip schizencephaly in a previously healthy 35 years old gentleman who was admitted with new onset generalized seizures, unmasked by a urinary tract infection. This is possibly the first ever case of bilateral schizencephaly, presenting for the first time in the fourth decade of life.

INTRODUCTION

Schizencephaly is an extremely rare clinico-radiological diagnosis. The overall prevalence of this disorder has been estimated to be around 1.54 per 100,000 population [1-4].

The cause of schizencephaly is thought to be, the defective neuronal migration, and differentiation during brain formation and maturation [3-5]. Any problem encountered during neuronal growth, maturation and migration may lead to a variety of problems within the brain. The spectrum of these disturbances ranges from mild gyral abnormalities, i.e., alterations in the designing and formation of the cerebral cortex and its surface, to more severe cerebral defects, such as a total focal agenesis of an entire region of the cerebral cortex, as in schizencephaly [2,4,6].

Usually, schizencephaly presents during childhood and rarely during teen age. The common presentations include, developmental problems, failure to thrive, swallowing and breathing problems, protracted seizures, mental retardation and so forth [3,5,7]. Such affected children very rarely survive into their third decade of life, as they succumb to a variety of complications like aspiration pneumonia, and infected bed sores [3-7]. It must be noted that although, it is extremely rare for schizencephaly to present during adult life, we present one such case in a previously fit and well 35 year old laborer, who presented with new onset seizure disorder, triggered by a urinary tract infection (UTI).

CASE PRESENTATION

A 35 year old unmarried Pakistani male was admitted in the department of medicine of Khyber Teaching Hospital (KTH), Peshawar, Pakistan, for the management of new onset generalized tonic clonic seizures. The seizures lasted for 10 min. Associated clinical features included loss of consciousness, tongue bite and urinary incontinence.

He was previously fit and well. By profession, he was a laborer. He was delivered through a normal vaginal delivery, and had achieved all his developmental mile stones normally. He was never hospitalized in the past, and was not on any regular medications. His parents were related. However, he did not have any family history of epilepsy. His two sisters and three brothers were all normal. The patient denied any use of recreational drugs. Moreover, the patient reported dysuria, urinary frequency and urgency, left sided flank pain and high grade continuous fever for the preceding seven days before his current admission. Rest of his history was unremarkable.

On clinical assessment he was pyrexial and tachycardiac. Rest of the vital signs including blood pressure (BP), respiratory

rate (RR) and oxygen saturations were normal. He had a 3/5 power in both his lower limbs and a 4/5 power in the upper limbs, bilaterally. He had generalized hypertonia and hyper-reflexia. The plantar reflex was extensor on the right side and equivocal on the left. Both, the spinal and cranial nerves examinations were normal. Examination of the chest, cardiovascular and gastrointestinal system was unremarkable. His slit-lamp ophthalmologic examination was within normal limits. His performance on neuropsychiatric tests, namely; mini mental state examination (MMSE), mental state examination (MSE) and cognition assessment tests was satisfactory.

His base line investigations are shown below in **Tables 1 and 2.** Urinalysis was consistent with urinary tract infection (UTI). Urinary culture grew E-Coli which were treated with a seven days course of intravenous ciprofloxacin, given at a dose of 500mg every 12 h. He had unremarkable serology, and polymerase chain reaction (PCR) for both cytomegalovirus and herpes simplex viruses, respectively.

Table 1. Results of baseline biochemical and endocrine panels of our patient.

Investigation	Results	References
Hemoglobin (Hb)	14 g/dl	14-18 g/dl
White blood cells (WBCs)	7000/mm^3	4000-11000/mm^3
Platelets	200,000/mm^3	150,000-400,000/mm^3
Alanineamino transferase (ALT)	30 IU/L	<40 IU/L
Aspartateamino transferase (AST)	33 IU/L	<40 IU/L
Alkaline phosphatase (ALP)	200 mg/dl	70-265 mg/dl
Serum creatinine	0.8 mg/dl	0.8-1.2 mg/dl
Serum Urea	30 mg/dl	20-40 mg/dl
Serum fasting glucose	94 mg/dl	Upto 70-110mg/dl
Lactate (venous)	2.2 mmol/L	0.6-2.4 mmol/L
Serum TSH	1.9 IU/L	0.5-4.5 IU/L
Serum Cortisol (morning)	560 mmol/L	450-700 mmol/L

Table 2. Results of serum electrolytes and arterial acid & base balance.

Investigation	Results	References
Serum sodium	139 mmol/L	135-145 mmol/L
Serum potassium	4 mmol/L	3.5-5.5 mmol/L
Serum chloride	100 mmol/L	95-105 mmol/L
Serum calcium	9.98 mg/dl	9-11 mg/dl
Serum magnesium	0.90 mmol/L	0.75-1.05 mmol/L
Bicarbonate (arterial)	26	24-30 mmol/L
pH (arterial)	7.41	7.35-7.45

Magnetic resonance imaging (MRI) of the brain showed bilateral closed lip schizencephaly in the fronto-parietal region **(Figures 1-3).** MRI brain demonstrated dilatation of subarachnoid spaces and pachygyria **(Figure 4).** Electroencephalography (EEG) demonstrated an epileptic focus in the left fronto-parietal region. Furthermore, bodies of the lateral ventricles were dilated and irregular. Rest of the scan was normal. Other investigations including abdominal ultrasound, chest x-ray, MRI of the spine, lumbar puncture, antinuclear factor (ANF), ECG and Echocardiogram were unremarkable.

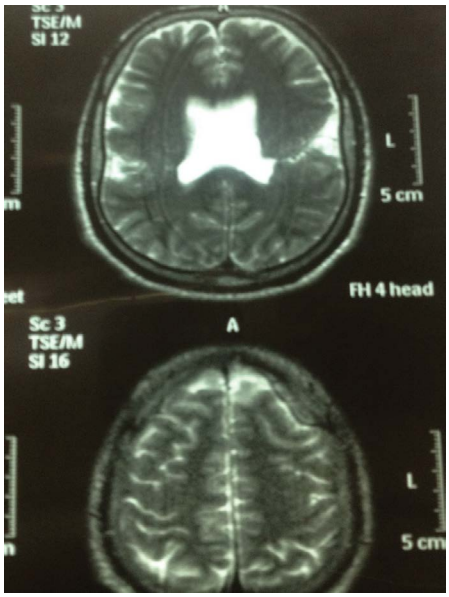

Figure 1. T2 weighted image on MRI brain showing CSF intensity clefts in the fronto-parietal areas bilaterally.

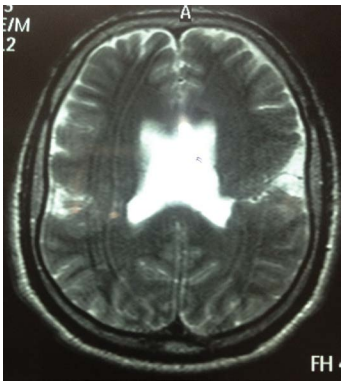

Figure 2. A magnified view of bilateral schizencephaly on T2 weighted MR imaging of the brain.

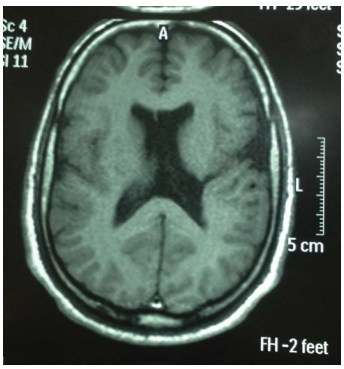

Figure 3. T1 weighted imaging of MR brain showing schizencephalic cleft (more on the left hand side).

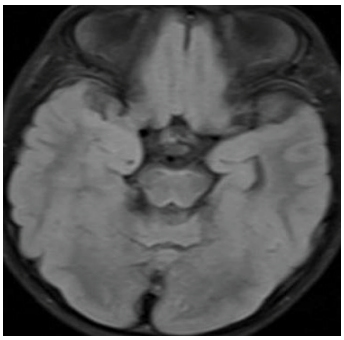

Figure 4. MRI FLAIR sequence showing evidence of Pachygyria.

The patient was loaded with 1000 mg of intravenous Phenytoin and then continued on maintenance dose of 100 mg eight hourly for the first 24 h. The patient was then switched to 500 mg of sodium valproate two times daily. After three days fit free stay in the hospital, he was discharged home on 1 g daily dose of sodium valproate.

The patient was reviewed in two months' time post-discharge. The patient did not have a recurrence of the seizure activity. However, he still had some weakness on the right side, with a degree of spastic gait. The patient was seen by the neurosurgeon who decided watchful waiting before consideration for any surgical intervention. The patient will be reviewed again in six months' time.

DISCUSSION

Schizencephaly is one of the rarest, but most severe congenital brain anomalies described for the first time by Haeschl in 1859 as a brain malformation. However, the term "schizencephaly" was coined by Yakovlev and Wadsworth in 1946 [7,8].

There are two types of this disorder. In type-1 or closed-lip schizencephaly, the defect is interrupted and lacks continuity with the lateral ventricular wall. In type-2 or open-lip scizencephaly, the cleft within the brain is in continuity with the lateral wall of the ventricle and is filled with cerebrospinal fluid (CSF) [9,10].

The clinical manifestations vary, but the most frequently encountered problems are; motor deficit, epilepsy, and mental retardation. Moreover, some patients have no neurological alterations [11]. It must be noted that type-2 schizencephaly is the more severe form, and usually, presents with mental retardation, severe developmental delay and intractable epilepsy. In contrast, type-1 is less severe anatomical defect within the brain parenchyma, and thus, has less severe clinical manifestations and a relatively, benign clinical course. Nevertheless, bilateral schizencephaly is more severe than unilateral form and usually, presents with quadriparesis and cognitive decline [9-13]. It is interesting to mention that our patient had bilateral closed lip cerebral clefts, but still had no such pre-existing clinical evidence. Moreover, he presented for the first time in 4th decade of life, with mild-

moderate focal neurologic deficit in all his limbs, and generalized seizure activity. The reasons as to why he presented so late, cannot be clearly stated.

Schizencephaly results from an abnormality of neuronal migration and maturation. The neuro-anatomical spectrum of schizencephaly as a group includes; unilateral or bilateral clefts within the brain, polymicrogyria, pachygyria and heterotopic gray matter [14,15]. Our patient had both bilateral schizencephaly and pachygyria.

The exact cause of schizencephaly is not known. However, hypothetical causes include any intra-partum infection, cytomegalovirus and herpes virus, maternal trauma of different types, teratogens, alcohol and drug abuse, warfarin, monozygotic twin interactions and so forth [16]. There is a possibility for mutations in EMX-2 gene. In our case, there was no identifiable etiology [17]. There is some growing evidence that shizencephaly might have a genetic component and can be transmitted to the offspring [18]. It is interesting to write that; although, the parents of our patients were related, they themselves, and their other kids were all normal, clinically.

MRI brain is diagnostic and is thus, the imaging modality of choice. MRI brain can precisely demonstrate the type, size and location of the anomaly. Moreover, it can guide regarding the treatment and the neurosurgical approach [17-20]. Although; less sensitive, computed tomography (CT) is widely used as a diagnostic and prognostic tool because of its lower cost, higher availability and ability to sufficiently demonstrate the anomaly [21]. The MRI brain of our patient precisely demonstrated the lesion and helped in excluding the alternative diagnoses.

The treatment of symptomatic schizencephaly depends upon the symptoms and their severity. Those with epilepsy need anti-epileptic medications; usually, in combination due to the refractory nature of the resulting seizure disorder. Rufinamide, which is a new antiepileptic medication recommended as adjuvant treatment in the management of seizures associated with Lennox-Gastaut syndrome, has been found to be a beneficial therapy in patients with schizencephaly [22]. Similarly, if epileptic focus is accurately identified and resected, the outcomes can be satisfactory. Intracranial electrocorticography (ECoG) is superior to conventional electroencephalography (EEG) in demonstrating the epileptic focus precisely [23]. The EEG in our case showed evidence of an epileptic focus within the left frontoparietal region. Moreover, we treated our patient with intravenous phenytoin acutely, and discharged him home with 1 g daily dose of sodium valproate with excellent results.

CONCLUSION

Scizencephaly is a rare congenital brain malformation. Although, it usually presents during childhood, atypical presentation in a previously healthy adult is possible. Sodium valproate alone can be used to treat such cases with a very good effect.

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