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De Morsier plus syndrome: A rare congenital disorder presenting with adult onset seizure

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Abstract

De Morsier syndrome, also known as septo-optic dysplasia (SOD), describes a triad of optic nerve hypoplasia, hypothalamic-pituitary dysfunction and midline abnormalities such as absent septum pellucidum or dysgenesis of the corpus callosum. It is a rare congenital disorder that an estimated incidence of 1/50,000 was recorded. This disease has a variety of clinical symptoms, which include visual manifestations (85-90%), intellectual delay (42.5-60%), seizures (27.5-55%) and endocrine abnormalities (50-55%). However, those patients with symptoms of global developmental delay and motor deficits could not be explained by the corpus callosum hypoplasia alone and were noted to manifest other underrecognized cortical malformations such as schizencephaly and polymicrogyria, hence termed De Morsier plus syndrome. In the Philippines, the existence of De Morsier plus syndrome with a lack of developmental disorders detected during adulthood is uncommon with no reported case yet. This report is a case of a 24-year-old, male, who presented with adult-onset seizure with associated eye symptoms. Cranial magnetic resonance imaging revealed bilateral schizencephaly in both parietal lobes with absent septum pellucidum, polymicrogyria, agyria-pachygyria and optic nerve atrophy. On electroencephalogram, epileptiform discharges were noted in the left parietal area. This case was managed under anti-seizure medication with no seizure recurrence and a good outcome.

Keywords: De morsier plus syndrome, septo-optic dysplasia, schizencephaly

INTRODUCTION

De Morsier syndrome, also known as septo-optic dysplasia (SOD), was first reported in 1956 by a Swiss neurologist George de Morsier describing a triad of optic nerve hypoplasia, hypothalamic-pituitary dysfunction and midline abnormalities such as absent septum pellucidum or dysgenesis of the corpus callosum.[1] It is a rare congenital disorder with an estimated incidence of 1/50,000.[2] The causes of this early brain midline dysembryogenesis are still under investigation, but the most frequently suggested etiologies relate to embryonic vascular insult usually in the 6th -7th week of embryogenesis, bleeding during the first trimester of pregnancy, primiparity and young maternal age, maternal alcoholism as well as maternal drug abuse.[3] Although most of the cases are sporadic, less than 1% of cases have been associated with mutations in the following genes: HESX1, SOX2, SOX3, or OXT2.[4]

This syndrome has a wide spectrum of clinical symptoms and the most frequently described manifestation include visual manifestations (85-90%), intellectual delay (42.5-60%), seizures (27.5-55%) and endocrine abnormalities (50-55%).[5,6] A multicenter study across Association of Southeast Asian Nation (ASEAN) countries only listed 48 cases with SOD and symptoms were detected at a mean age of 33 to 39 months with profound eye abnormalities such as nystagmus (54%) and poor vision (35%), developmental delay (16.2%) and various endocrine abnormalities such as hypothyroidism (35%), growth hormone insufficiency (29%) and diabetes insipidus (19%), all leading to early mortality.[6] However, those patients with symptoms of global developmental delay and motor deficits could not be explained by the corpus callosum hypoplasia alone and were noted to manifest other underrecognized cortical malformations such as schizencephaly and polymicrogyria, hence De Morsier plus syndrome was suggested by Miller in 2000.[1]

A previous case series of 17 patients with De Morsier syndrome or SOD in Canada by Alt, *et al*, found that 6% of patients met the criteria for the classic syndrome, 76% with De Morsier plus or SOD plus syndrome, and 18% with SOD-like syndrome, those with normal septum pellucidum

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and corpus callosum in absence of any cortical abnormalities.[7,8] Nearly one-half of patients with SOD has schizencephaly.[9] Barkovich *et al*, classified SOD into two distinct anatomic subsets, one included patients with schizencephaly, normal size ventricles, a remnant of the septum pellucidum and normal-appearing optic radiations.[10] The second group of patients had no schizencephaly but did exhibit a complete absence of the septum pellucidum and diffuse white matter hypoplasia that resulted in ventriculomegaly.[6]

In the Philippines, only 4 cases of De Morsier syndrome were recorded by David, J. and Collao, M. last 2017, however only one patient was reported to have De Morsier plus syndrome and that case was a 17-month-old male presenting with blurred vision demonstrated cerebral atrophy, open-lip schizencephaly, absent septum pellucidum with dilated ventricles and atrophic optic nerves leading to early mortality.[2] There was no noted literature on De Morsier plus syndrome with a lack of profound developmental disorder presenting with adult-onset seizures in our country.

CASE REPORT

This is a case of a 24-year-old, male, who sought consult due to stiffening of extremities described as upward rolling of eyeballs with jerky movements of both upper and lower extremities, occurring daily, approximately 1-2 minutes with regain of consciousness in between attacks and associated post-ictal confusion. There were no associated symptoms noted. The patient had no comorbidities with no family history of hereditary diseases as displayed in Figure 1. He was born from a G2P2 (2002) mother via normal spontaneous vaginal delivery without complication before, during and after pregnancy. The developmental milestone was at par with age and he was able to finish high school with honours.

Assessment

Upon consult, vital signs were normal with unremarkable physical examination findings. The patient was awake, oriented to three spheres and following commands. On Tagalog Mini-Mental State Examination, he scored 29/30 and on Montreal Cognitive Assessment-Philippines, he scored 24/30 which was normal. Cranial nerve examination noted visual acuity of 50/20 on his right eye. On fundoscopic examination, optic atrophy was noted with a temporal pallor of the disc on the right eye. The rest of the neurologic examinations were normal.

Laboratory work-up

Laboratory examinations such as complete blood count, electrolytes, coagulation studies, blood chemistries and hormonal studies were normal. Figure 2 (T2 axial view of the brain MRI) and Figure 3 (T1 sagittal view), showed bilateral closed-lip schizencephaly in parietal lobes with an absence of septum pellucidum. There was also noted associated polymicrogyria in the right temporal lobe and agyria-pachygyria in the left temporal lobe with incidental finding of an arachnoid cyst at the left middle cranial fossa as shown in Figure 4.

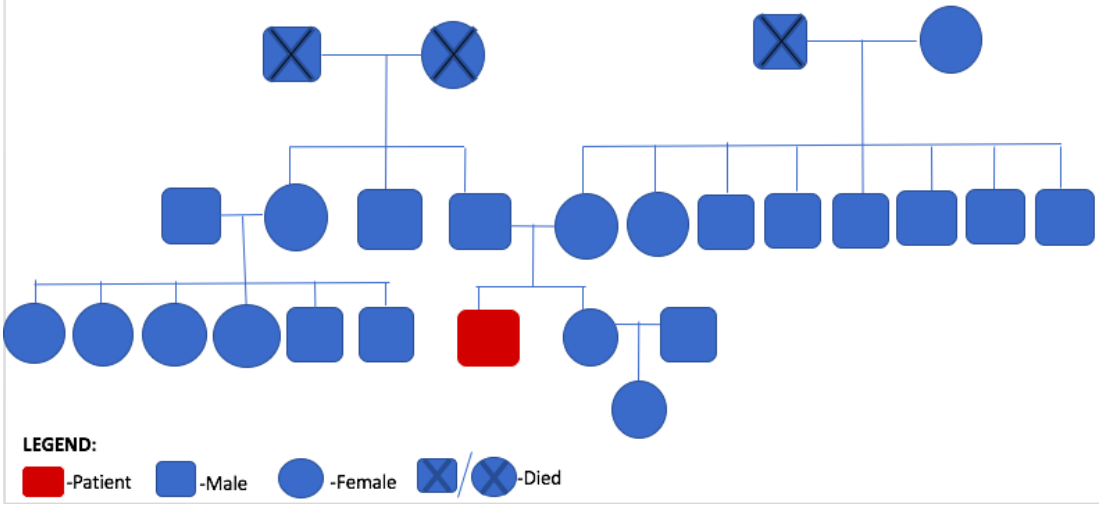

Figure 1. Family Genogram.

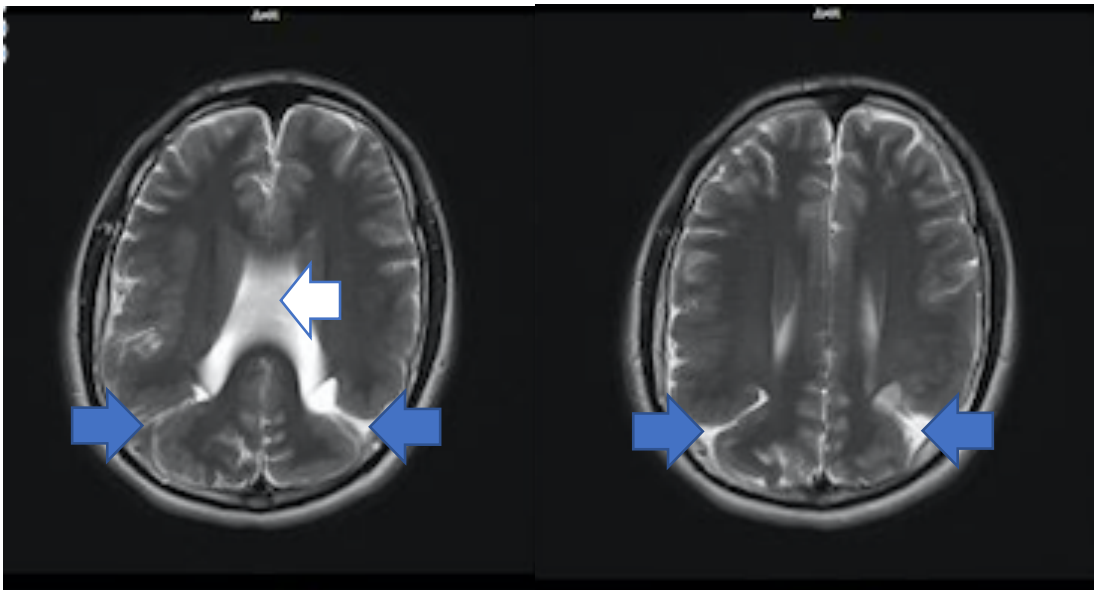

Figure 2. Cranial MRI on T2 axial view showing bilateral closed-lip schizencephaly on both parietal lobes indicated by the blue arrow and absent septum pellucidum indicated by the white arrow.

An electroencephalogram (EEG) was also performed to further localize and detect epileptiform discharges in the brain of the patient. A 30-minute 21-channel digital EEG recording performed using the standard international 10-20 system showed intermittent sharp and slow waves seen over the left parietal area maximal at P3.

Outcome

The patient was given levetiracetam 500mg tab 2x/day as home medication upon consult and was compliant. On follow up check-up, there was no recurrence of seizure noted. There were no noted changes in behaviour. He can do activities of daily living independently and is currently working.

DISCUSSION

De Morsier syndrome, also known as septo-optic dysplasia (SOD), describes a triad of optic nerve hypoplasia, hypothalamic-pituitary dysfunction and midline abnormalities such as absent septum pellucidum or dysgenesis of the corpus callosum.[1]

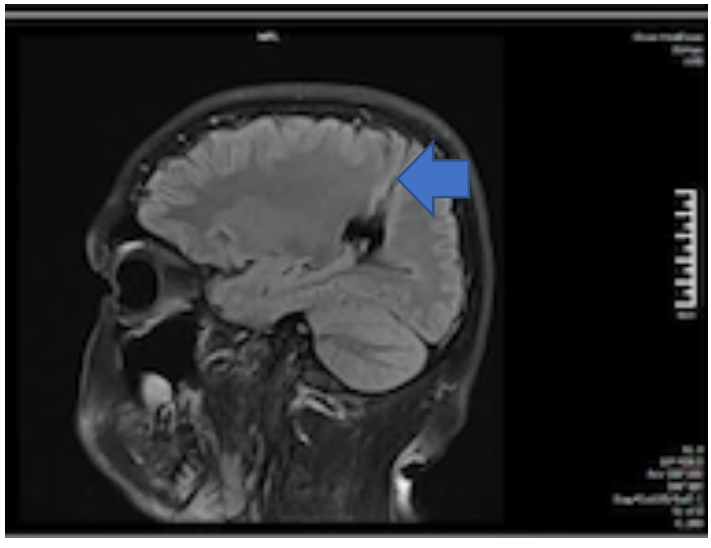

Figure 3. Cranial MRI on T1 sagittal view showing bilateral closed-lip schizencephaly on parietal lobe indicated by the blue arrow.

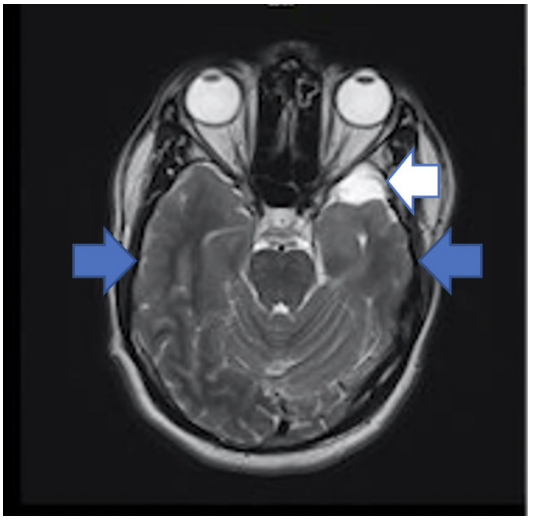

Figure 4. Cranial MRI on T2 Axial view showing polymicrogyria in the right temporal lobe, agyria-pachygyria in the left temporal lobe indicated by the blue arrow, and arachnoid cyst at left middle cranial fossa indicated by the white arrow.

It is a rare congenital disorder that an estimated incidence of 1/50,000 was recorded.[2] The most frequently suggested etiologies relate to embryonic vascular insult usually in the 6th -7th week of embryogenesis, bleeding during the first trimester of pregnancy, primiparity, young maternal age, maternal alcoholism as well as maternal drug abuse.[3] Further, less than 1% of cases have been associated with mutations in the following genes: HESX1, SOX2, SOX3, or OXT2.[4] This syndrome has a wide spectrum of clinical symptoms and the most frequently described manifestation include visual manifestations, intellectual delay, seizures and endocrine abnormalities. However, those patients with symptoms of global developmental delay and motor deficits could not be explained by the corpus callosum hypoplasia alone and were noted to manifest other underrecognized cortical malformations such as schizencephaly and polymicrogyria, hence termed De Morsier plus syndrome or SOD plus syndrome.

Our case is an uncommon type of this rare congenital disorder, De Morsier plus syndrome. It is a case of a bilateral closed-lip schizencephaly with absent septum pellucidum, polymicrogyria, agyria-pachygyria and optic atrophy. The findings were supported by the MRI brain and the EEG findings. The patient was managed with anti-seizure medication and was able to do activities of daily living independently with a good outcome.

In conclusion, we report a rare case of a 24-year-old, male who presented with adult-onset seizure with no known comorbidities and no family history of congenital anomalies or seizures. On examination and neuroimaging, a rare congenital disorder was noted, De Morsier plus syndrome, with bilateral schizencephaly, agyria-pachygyria, polymicrogyria, optic atrophy and absent septum pellucidum. Although reports of this condition have been reported in other countries, patients with symptoms such as seizures in adulthood with no developmental delay have not been reported in the Philippines.

DISCLOSURE

Ethical consideration: Consent from patient obtained for publication

Financial support: None

Conflicts of interest: None

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