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Case Report

Septo-optic dysplasia PLUS syndrome in a 23 years old patient: A case report ☆,☆☆

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ABSTRACT

Septo-optic dysplasia (SOD) is a rare malformation defined by septum pellucidum abnormalities and hypoplasia of the optic nerves and chiasm. It can be associated with cortical development malformations such as schizencephaly, which is then called septo-optic dysplasia plus. It usually manifests at birth, although it may not be diagnosed until childhood, or rarely, adolescence. We report the case of a 23 years old patient, with a history of epilepsy since early childhood never labeled, which was diagnosed with SOD-PLUS with brain MRI in our department.

Introduction

Septo-optic dysplasia (SOD) is a rare brain malformation that links hypoplasia of the optic nerves and chiasm with an absent or rudimentary septum pellucidum. It may be revealed by visual or olfactory disturbances, as well as hypothalamic-pituitary dysfunction (also known as De Morsier syndrome) [1]. This entity can be associated with cortical development disorders like schizencephaly, which is then called septo-optic dysplasia PLUS [2].

It is important to note that there are hardly any epidemiological studies of SOD which makes its prevalence uncertain, and our report all the more intriguing.

While a study from England study acknowledged a prevalence of 5.4 per 100,000 births, another one reported an incidence of 3.5 per 100,000 births [3,4]. We report a clinical case of a 23-year-old patient who had undiagnosed childhood epilepsy. Her MRI revealed closed-lip left schizencephaly with an absent septum pellucidum as well as bilateral optic nerves atrophy. Furthermore, it showed cortical malforma-

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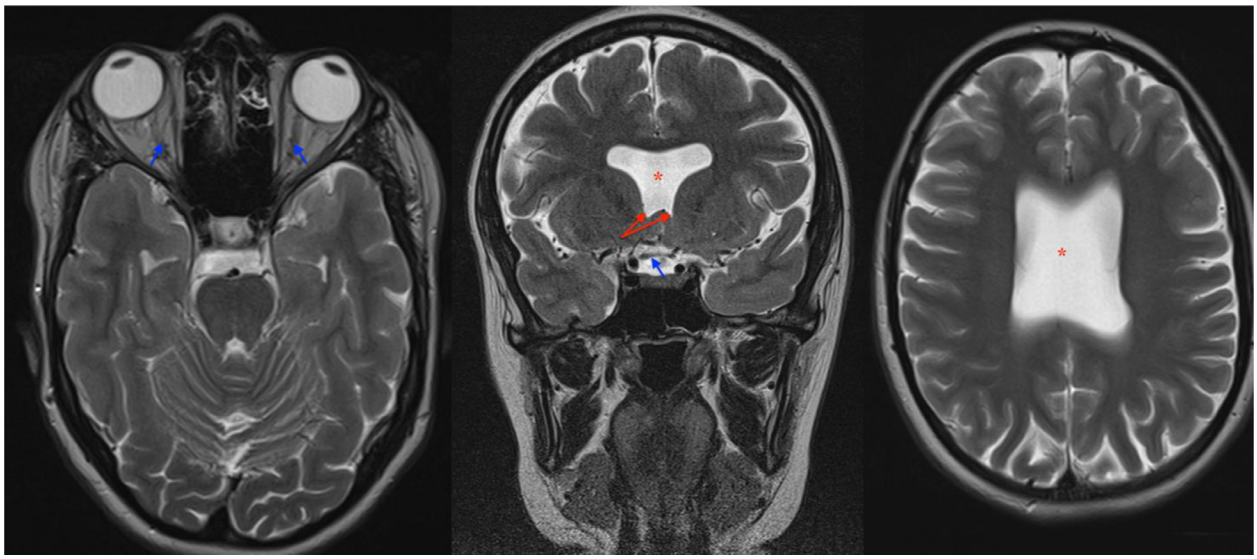

Fig. 1 – T2 WEIGHTED sequences (axial and coronal) showing: optic chiasm and bilateral optic nerves atrophy (blue arrows), an absent septum pellucidum (red asterisk) with the peculiar box-like or "squared-off" appearance of the frontal horns pointing inferiorly (red arrows).

tions which combined the criteria for diagnosing septo-optic dysplasia PLUS syndrome.

Case report

A 23-year-old female presented with a history of tonic-clonic generalized seizures starting since childhood and never labeled. According to her parents, the patient had cross-left eye esotropia since birth but never consulted an ophthalmologist. There was no history of anosmia or neurodevelopmental delay signs.

The patient was on anti-epileptic but kept presenting seizures, which had motivated a neurology consultation. She was also referred to an ophthalmic examination which revealed the visual acuity to be 8 out of 10 in the left eye and 9 out of 10 in the right eye. The visual fields were full to confrontation and fundus examination results were normal.

Interictal electroencephalogram (EEG) showed paroxysmal abnormalities of epileptic appearance in the left posterior temporal diffusing posteriorly and to the right.

The patient was then referred for brain MRI protocoled as follows: 3D FLAIR sequences, axial and coronal T2, diffusion weighted-images (DWI), SWI, coronal turbo inversion recovery (TIR), and sagittal T1 SE. It showed the absence of the septum pellucidum with chiasm and bilateral optic nerves atrophy (Fig. 1), as well as closed-lip left parietal schizencephaly (Fig. 2). It also revealed an abnormal left post and precentral sulcation as well as thickened adjacent cortex with a "bumpy" contour (Fig. 3). As for the hypothalamo-hypophyseal tract, there were no abnormalities to note (Fig. 4). The SODPLUS syndrome was then diagnosed. Strabismus correction was recommended for the patient as well as triple antiepileptic therapy.

Discussion

Septo-optic dysplasia (SOD) has been considered by some authors as being part of the holoprosencephaly (HPE) spectrum. Nevertheless, the disorder's heterogeneity and the lack of ventral midline fusion are more consistent with a distinct but connected midline abnormality. De Morsier first identified it in 1956, citing the absence of the septum pellucidum and hypoplasia of the optic nerves as its 2 cardinal pathologic features. The syndrome is called SOD PLUS if it co-occurs with other abnormalities such as schizencephaly or callosal dysgenesis [5]. Schizencephaly is also a rare congenital malformation that literally means "split-brain." It is a gray-matter-lined cleft extending from the ependyma of the ventricle to the pial cortical surface. Both schizencephaly and septo-optic dysplasia were believed to be embryological disorders of cortical development. However, schizencephaly can now be regarded as a disorder with heterogeneous causes such as destructive vascular lesions or infections occurring before the seventh week of gestation during early forebrain development [6].

Clinically, SOD has a variety of manifestations. It mostly depends on whether it is associated with schizencephaly, which allows identifying 2 forms of the entity. Firstly, the nonassociated to schizencephaly SOD, with its most common clinical feature being visual impairment. Nearly 60%-80% of patients also develop endocrine abnormalities from hypothalamic-pituitary dysfunction such as hypoglycemic seizures in the neonatal period, as well as growth hormone deficiency, hypothyroid, and rarely precocious puberty [7]. In the SOD form associated with schizencephaly (or SOD PLUS), the optic apparatus is usually less severely affected, and we may have other cortical development abnormalities such as polymicrogyria and cortical dysplasia. Epilepsy, psychomotor retardation, or spastic motor deficit can also be found [8].

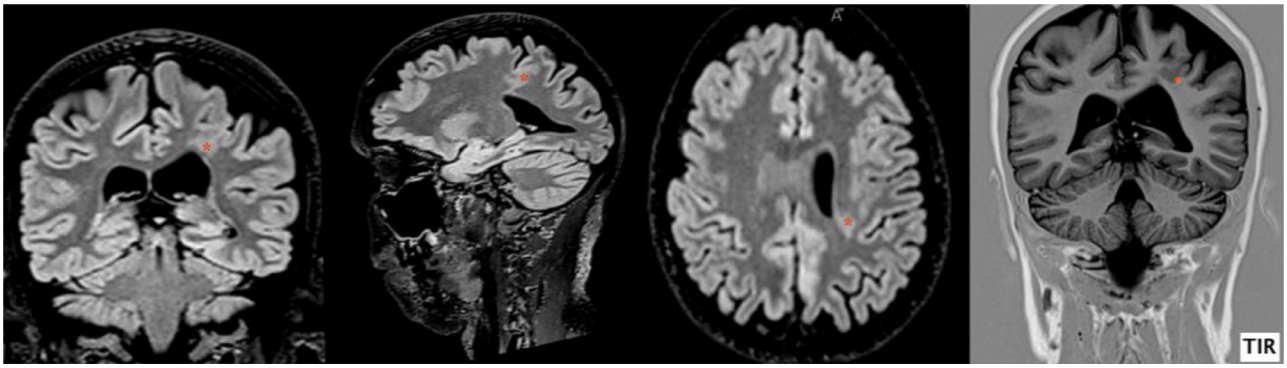

Fig. 2 – 3D FLAIR and TIR sequences showing abnormal grey matter (red asterisk) extending from ventricular to the outer surface of the brain, centered on the postcentral gyrus. No CSF cleft is visible, hence the classification as closed-lip schizencephaly (type 1).

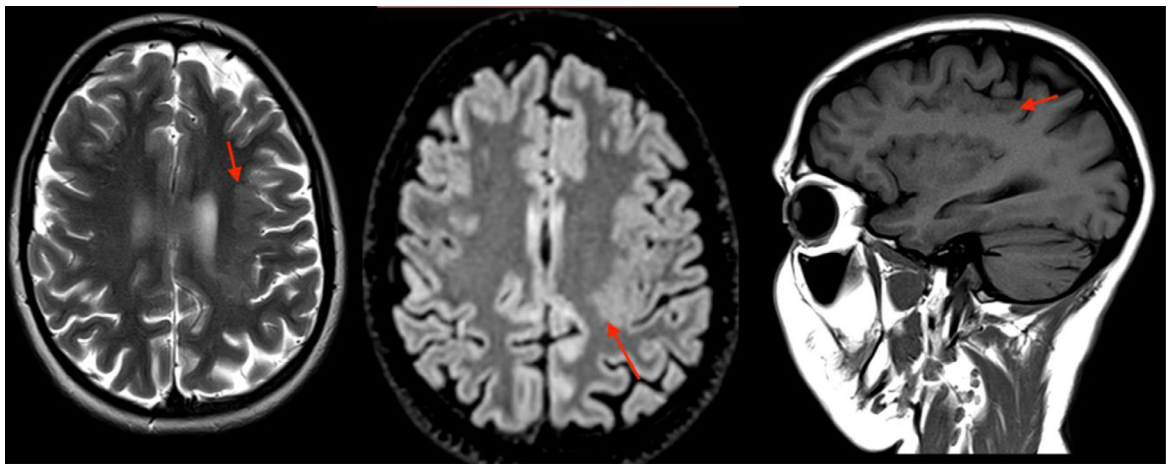

Fig. 3 – Axial T2 and FLAIR with sagittal T1 WIshowing abnormal brain cortex in the left frontoparietal area which is thickened and irregular representing polymicrogyria.

Normally, all imaging modalities that can bring out the septum pellucidum (ultrasound, CT, and MRI) will highlight its absence in SOD. However, CT can hardly visualize the optic apparatus, and may sometimes demonstrate small optic apparatus (best seen with coronal reformats), and small bony optic foramina, in addition to highlighting the enlarged lateral ventricles and an absent septum pellucidum [9].

To assess septo-optic dysplasia, MRI is considered as the modality of choice and 3 orthogonal planes are key to identifying the imaging findings. The absence of septum pellucidum appears on axial and coronal sections in both T1 and T2 weighted images. Sagittal sequences can show indirect signs with a low position of the fornix giving the lateral ventricles an "empty" appearance. On coronal images, the frontal horns of the lateral ventricular may show a "point down" appearance or box-like with distinct inferior pointing [2]. These imaging findings are associated with a small optic chiasm and optic nerves. MRI may also visualize a hypoplastic pituitary stalk as well as olfactory tract/bulb hypoplasia and incomplete hippocampal rotation.

Schizencephaly should be carefully looked for since its presence defines the SOD PLUS (Table 1). Its key imaging features are a CSF-filled defect that extends from the wall of the ventricle to the pial surface and a dysplastic gray matter lining the cleft. On MRI, the cleft follows CSF signal intensity on all sequences, and this modality delineates better the associated abnormalities, such as cortical dysplasia (polymicrogyria, pachygyria) and heterotopic gray matter. SOD PLUS can also be associated with thinning or even the absence of the corpus callosum [10].

The main differential diagnosis of SOD is well-differentiated lobar HPE. Some features may help in differentiating it such as the presence of olfactory bulbs. The cerebral anterior artery will have its course shifted anteriorly in lobar holoprosencephaly. Also, the optic chiasm is not expected to be hypoplastic. Finally, the cerebral hemispheres as well as basal ganglia are completely separated in SOD [11].

Neurologically, one of the most feared complications is drug-resistant epilepsy, in which focal cortical dysplasia is frequently the cause [12]. Normally, endocrine findings are diag-

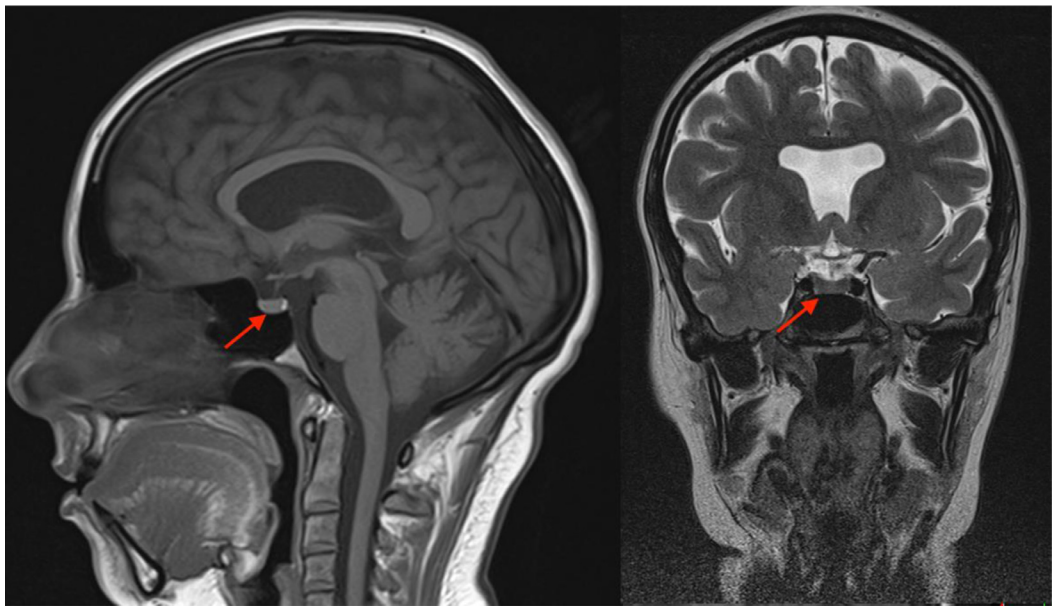

Fig. 4 – SagittalT1 and coronal T2 sequences showing the hypothalamo-hypophyseal tract (red arrow) perfectly shaped with no abnormalities.

Table 1 – A summary of the clinical and imaging features of both SOD and SOD-PLUS syndrome.

SOD	SOD PLUS
Clinical features - Visual or olfactory disturbances such as anosmia - Hormonal dysfunction (in neatly two-thirds) → Growth hormone deficiency → hypothyroidism → precocious puberty → Diabetes insipidus	*Clinical features* - Epilepsy - Neurodevelopmental delay - Spastic motor deficit
Cardinal pathologic features - Absence of septum pellucidum → "Squared-off" frontal horns, pointed inferiorly on coronal T2WI - Optic nerve/chiasma hypoplasia - Thin stalk, small gland, ectopic posterior pituitary	**In addition to the triad:** - Schizencephaly : → outpouching("nipple")fromlateral ventricle → CSF-filled cleft lined → Cleft lining follows cortex signal on all sequences - Look for: → Corpus callosum dysgenesis → cortical dysplasia (polymicrogyria, pachygyria) → heterotopic gray matter.

nosed at an early age, with central hypothyroidism and GH deficiency are commonly found. Secondary/tertiary adrenal insufficiency and central diabetes insipidus can also be present [7].

Therefore, the management of this entity needs a multidisciplinary team to assess and treat seizures, hormonal dysfunctions, loss of vision, autism as well as obesity (secondary to diabetes insipidus) [6].

Conclusion

Septo-optic dysplasia (SOD) is described with the triad of dysgenesis or absence of the septum pellucidum, hypoplasia/dysplasia of the optic nerve, and hypothalamic-hypophyseal dysfunction. Years after its first discovery, the term SOD-PLUS was introduced, describing a syndrome characterized by the original triad associated with other cortical malformations with schizencephaly being the most common. MRI remains the modality of choice to diagnose this entity.

Patient consent

Written informed consent was obtained from the patient for publication of this article, including accompanying images.

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