Septo-optic dysplasia syndrome with schizencephaly and sudden visual loss. *A new observation*

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Septo-optic dysplasia (SOD) is diagnosed clinically by a variable combination of absence of the septum pellucidum, optic nerve hypoplasia, and hypopituitarism.[1] The SOD phenotype is consequently, highly variable, with approximately 30% of cases manifesting complete symptoms, 62% manifesting hypopituitarism, and 60% manifesting absence of the septum pellucidum.[1] We report the case of a child with SOD that was missed until the age of 13 years, when he presented with signs of increased intracranial pressure and sudden visual loss.

The patient is a 13 year-old male. He was born at term, weighed 2.64 kg, and was the first part of a twin that died at 5 days of age due to neonatal sepsis. Postnatally, the patient had progressive increase in head circumference for which a ventriculo-peritoneal shunt was inserted in the neonatal period. There was no asphyxia or known episodes of hypoglycemia, and he was lost to follow-up since then. He exhibited neither developmental delay nor poor visual acuity, and he had no school difficulties. At the age of 13 years, he started to complain of progressive headache over 2 weeks associated with vomiting and poor appetite. He was afebrile. Ten days after the onset of the headache, he developed a squint followed by blurred vision that deteriorated to complete loss of vision over several days, with signs of early papilledema. He had no other associated neurological deficits. His brain CT on admission revealed chronic subdural fluid collection in the right frontoparietal region with ventriculoperitoneal shunt tip in the right parietal parenchyma. Due to absence of previous brain CT scan and unfamiliarity with the type of shunt, the neurosurgeon evacuated the collection by doing right frontal burr hole. The CSF analysis and culture were normal. Five days later, he developed a subgaleal collection with recurrence of symptoms; revision of the proximal end of shunt was carried out. The intra ventricular pressure measured during the operation was normal. After surgery the headache disappeared, however, he continued to have persistent visual loss. A brain MRI revealed an absent septum pellucidum, atrophic optic chiasm and optic nerves, schizencephaly, and dilated ventricles. The presence of schizencephaly allowed the subdural fluid collection in the right frontoparietal region, and thus signs of acute hydrocephalous due to shunt dysfunction were absent on neuroimaging. The initial eye examination showed normal disc size in both eyes with no evidence of disc hypoplasia. Later, with the resolution of disc swelling, optic disc hypoplasia became apparent in both eyes, with development of bilateral optic disc atrophy (**Figure 1**). Follow up of his condition after 8 weeks revealed improvement in his visual acuity. Unfortunately, there was no formal medical evaluation for his visual acuity prior to this episode of acute deterioration. All endocrine work up was normal. Vitamin B12 level was low, 129 pg/ml (normal 179-1162 pg/ml) and he was treated with vitamin B12. The level normalized upon follow up. Genetic analysis for SOD was not carried out because it is not available in Jordan.

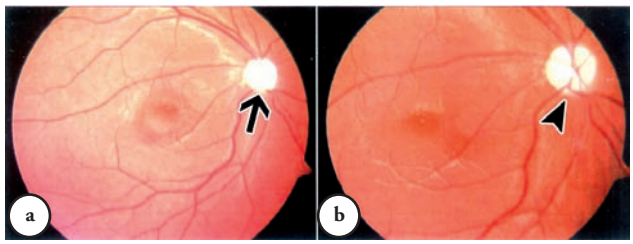

Figure 1 - Right fundus photo showing **a)** normal optic disc size with clear margins (arrow). **b)** Right fundus photo after resolution of high intracranial pressure showing optic disc hypoplasia with secondary disc atrophy (arrowhead).

The findings in our patient are consistent with the diagnosis of SOD. The brain MRI in SOD typically shows a constellation of lesions with at least 2 distinct magnetic resonance appearances.[2] The first group has a high incidence of malformations of cortical development (including schizencephaly, heterotopia, and the partial absence of the septum pellucidum). The second group has a complete absence of the septum pellucidum and hypoplasia of the white matter, but a normal cerebral cortex.[2] A potential third group of patients with septo-optic dysplasia have posterior pituitary ectopia,[2] while a fourth subset has been reported as having hypogenesis of the corpus callosum.[3,4] Based upon the aforementioned classification, the brain MRI findings in our patient constitute a combination of the first group (partial absence of septum pellucidum and schizencephaly) and the fourth group (agenesis of corpus callosum), in addition to hydrocephalus. The findings in our patient extend the variability and overlap between the groups based on MRI findings.

The brain MRI in our patient did not show signs of active hydrocephalus although the patient had signs of early papilledema; this is mostly related to shunt malfunction with an excessive fluid collection in the subdural regions in the presence of an open lip schizencephaly. Although the papilledema was mild and of short duration, the patient exhibited sudden deterioration of visual acuity over a few days, which

is not the usual presentation in SOD. Although the pathogenesis of SOD is unknown, theories suggest a developmental defect. Any insult arising at an early stage, between 4-6 weeks of gestation, has the potential to produce failure of ganglion cell formation with subsequent hypoplasia of optic nerves and chiasm and lack of commissural or septal formation.[1] In addition, a familial form of septo-optic dysplasia has been described in association with a homozygous mutation in the HESX1 locus.[3]

Based on the aforementioned proposed pathogenesis theories, the optic atrophy and the visual deficit in SOD would be non-progressive. Nevertheless, our patient showed progressive deterioration in his visual acuity. This sudden deterioration in visual acuity could be the consequence of an increase in intracranial pressure on already vulnerable nerves. An additional possible factor is the low serum level of vitamin B12, which has also been reported to cause optic atrophy.[5] The progressive deterioration in visual acuity observed in our patient might indicate that even in patients with apparently normal or mildly hypoplastic optic nerves, even minor insults might lead to deterioration in the actual visual status. This also leads us to hypothesize that microscopic findings might be more helpful in understanding the pathogenesis of SOD than the macroscopic findings currently used.

In conclusion, urgent evaluation of any visual complaint in patients with SOD is necessary to prevent further possible damage, even in patients with apparently normal or mildly hypoplastic optic nerves.

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