

Septo-Optic Dysplasia in a Newborn Presenting with Bilateral Dilated and Fixed Pupils

Mehnaz Jabeen, MD¹ Amber Hairfield, DO¹ Leonard E. Swischuk, MD² Sunil K. Jain, MD¹

¹Department of Pediatrics, University of Texas Medical Branch, Galveston, Texas

²Department of Radiology, University of Texas Medical Branch, Galveston, Texas

Address for correspondence Sunil K. Jain, MD, Department of Pediatrics, University of Texas Medical Branch, 301 University Blvd, 6.104 Waverley Smith Pavilion, Galveston, TX 77555-0526 (e-mail: skjain@utmb.edu).

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Abstract

Keywords

- ▶ septo-optic dysplasia
- ▶ dilated and fixed pupils

Introduction We describe a newborn female infant with septo-optic dysplasia (SOD) presenting with bilateral dilated and fixed pupils.

Conclusion Our report is unique because the incidental finding of bilateral dilated and fixed pupils on the newborn exam was the only clinical finding which led to a prompt work-up and eventual diagnosis of SOD.

Septo-optic dysplasia (SOD) is a rare congenital syndrome affecting 1 in 10,000 live births.¹ It occurs equally in both genders. It is diagnosed by the presence of two or more of the following: optic nerve hypoplasia (ONH), midline neuro-radiological abnormalities, and pituitary dysfunction.² One-third of the cases present with this classic triad.³ Other common presentations involve developmental delay, visual abnormalities, and pituitary dwarfism.⁴ In the absence of endocrine dysfunction (40% of the patients),³ the first clinical sign is usually strabismus or nystagmus in early infancy.

We present a unique case of SOD which presented with bilateral fixed and dilated pupils as the only clinical finding. To our knowledge, this is the first reported case of initial presentations being these findings.

Case Report

A term female infant was born to a 20-year-old primigravida mother by cesarean section due to failure to progress with rupture of membranes 9 hours prior to delivery. Apgar scores were 4 and 7 at 1 and 5 minutes, respectively. Moderate meconium staining was noted. Initial respiratory distress resolved spontaneously. Prenatal course and antenatal ultrasounds were unremarkable except for chorioamnionitis which was treated with ampicillin and gentamicin. Mother used marijuana and alprazolam during pregnancy.

Newborn physical exam revealed that both her pupils were dilated and fixed at 5 mm with no response to light. A fundal

exam revealed pale optic discs with a “double ring” appearance (▶ **Fig. 1A**). Magnetic resonance imaging of the brain revealed hypoplastic optic nerves (▶ **Fig. 1B**), absent septum pellucidum (▶ **Fig. 1C**), and open lip schizencephaly (▶ **Fig. 1D**) on the right. Schizencephaly may be seen in association with SOD (hypoplastic optic nerve, absent septum pellucidum).

Complete blood count, basic metabolic panel, blood glucose, and urinalysis were unremarkable. Urine drug screen was positive for tetrahydrocannabinols. Growth hormone, cortisol, thyroid-stimulating hormone, and T4 were within normal limits. Karyotyping and electroencephalogram were normal. Other than fixed and dilated pupils, her postnatal course was unremarkable.

Discussion

We are presenting the first case of isolated bilateral fixed and dilated pupils secondary to SOD. Nonreactive dilated pupils and hypoplastic discs (▶ **Fig. 1A**), and on imaging, bilateral hypoplastic optic nerves with surrounding pallor, small optic nerves in absence of other optic tract abnormalities, and absent septum pellucidum confirmed the diagnosis of SOD.

The most common cause of fixed and dilated pupils in neonates is administration of mydriatic agents for fundoscopic exam for retinopathy of prematurity. Third nerve palsy due to tumors or aneurysms can present similarly but is usually unilateral. Rarer causes include congenital third nerve palsy, iris abnormalities⁵ and a syndrome with patent ductus

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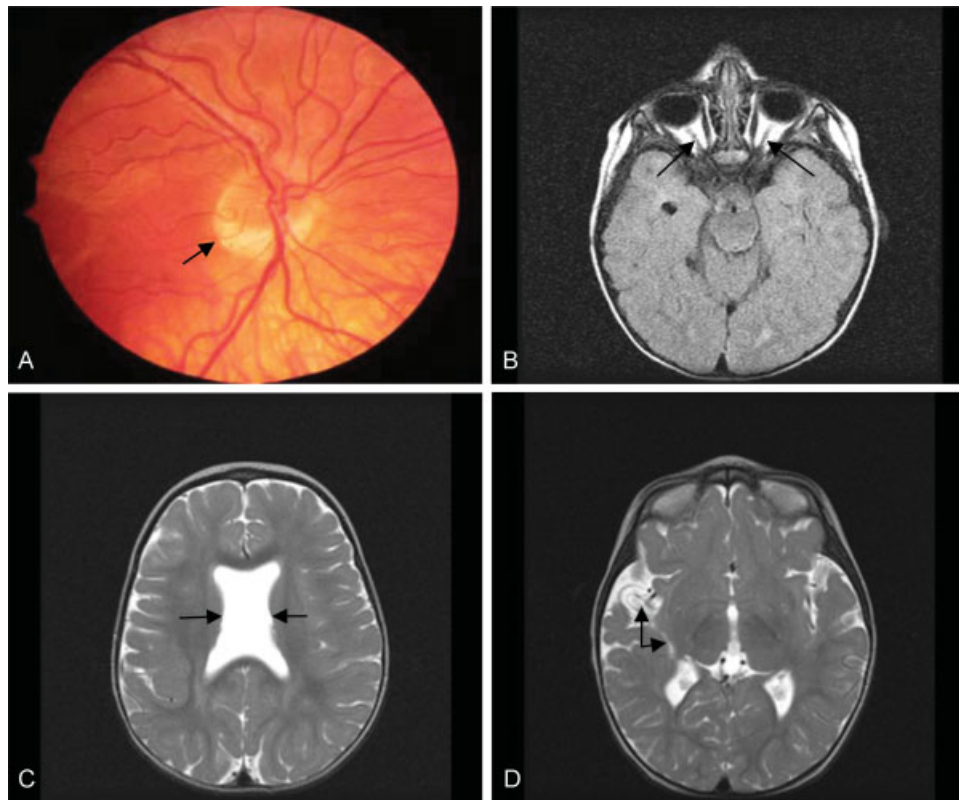


Fig. 1 Features of septo-optic dysplasia seen in the infant. (A) Hypoplastic optic discs with normal color, surrounded by a hypopigmented rim (arrow). (B) Hypoplastic optic nerves (arrows). (C) Absent septum pellucidum- typical ventricular configuration (arrow). (D) Open lip schizencephaly on right (arrow).

arteriosus, dilated pupils, and failure of accommodation.⁶ All these potential etiologies were ruled out in our patient.

The association of SOD with abnormalities of the forebrain reflects an insult around 5 weeks of gestation when the forebrain develops. This may be either during development or vascular disruption.⁷ Current understanding of the interplay of genetic and environmental etiologies is rudimentary.⁸ HESX1, SOX2, and SOX 3 mutations have been associated with SOD³; however, evidence suggests that patients with mutations in the EMX2, SHH, and SIX3 may have schizencephaly. Environmental factors include antenatal drug use, young maternal age (mean age of 22 years), and primigravida³

The age of presentation of SOD varies. No proven relationship exists between the severity of structural findings and the clinical manifestations. Major clinical findings include hypopituitarism (62–80%), visual impairment (23%), and developmental delay (32–57%).⁸ Deficiencies of growth hormone (70%), thyroid-stimulating hormone (43%), and adrenocorticotrophic hormone (27%) are common.⁹

Poor visual behavior may be the presenting feature of ONH.⁹ A total of 80% of the cases are legally blind.¹⁰ Bilateral ONH is more common than the unilateral ONH (88 vs. 12%)³ and poses a higher risk for pituitary dysfunction (81 vs. 69%) and developmental delay (78 vs. 39%).¹¹ Other neonatal presentations include hypoglycemia, microphallus, anophthalmia, microphthalmia, and cleft palate. Nystagmus and strabismus, typically esotropia, develops within infancy. Later

presentations include developmental delay, growth failure, obesity, precocious puberty, temperature instability, autism, and epilepsy.⁹ It is imperative to identify the disease early as untreated hormonal deficiencies place the child at risk of hypoglycemia, adrenal crisis, and subsequent death.

Work-up includes ophthalmological evaluation, brain imaging, and assessment of pituitary dysfunction. After diagnosis, follow-ups every 6 months by multidisciplinary teams involving the endocrinologist, ophthalmologist, neurologist, and physical and occupational therapists are required to monitor hormonal deficiencies, neurological abnormalities, and visual progression so that support can be initiated early in the disease for a child with neurodevelopmental and visual impairment.

Follow-Up of Our Patient

Our patient was discharged at 1 week of age with regular follow-ups with ophthalmology, endocrinology, neurology, and pediatric special services for chronic care. She is now 5 years old. The pediatric ophthalmologist is managing her for bilateral esotropia and poor vision. She has global developmental delay, greatest in the gross motor component. She received Early Childhood Intervention and is being co-managed by the chronic care team and pediatric neurologist. Her first seizure occurred at 4 years of age which is under control with antiepileptic medications. Repeat brain imaging remains unchanged. Her height and weight are both below the fifth

centile. Otherwise, endocrine work-up including cortisol, thyroid-stimulating hormone, and T4 were within normal limits except for insulin-growth-factor 1, level which was initially found to be low but then normalized.

Conclusion

This case report emphasizes the importance of a thorough physical exam because other than an incidental finding of abnormal pupillary findings, our patient had no other clinical manifestations of SOD. Early diagnosis with multidisciplinary team follow-up is the key to manage SOD.

Conflict of Interest

The authors declare no conflict of interest.

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