

# Article ▶ Clinical Findings and Management of Septo-Optic Dysplasia

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## ABSTRACT

**Background:** Septo-optic dysplasia is a congenital condition involving optic nerve hypoplasia, an absent septum pellucidum, and thinning of the corpus callosum. Endocrine dysfunctions may also be present. While only 30% of patients have a triad of optic nerve hypoplasia, absence of the septum pellucidum, and pituitary dysfunctions, early diagnosis of this disorder is important.

**Case Report:** A six-year-old male presented with a history of failing a school vision screening. The entering acuities, and subsequently the best-corrected visual acuities, were 20/500 OD, 20/20 OS. An afferent pupillary defect was present OD. Cup-to-disc ratios were 0.45H/0.50V OD, 0.30H/0.35V OS. Optical coherence tomography confirmed OD to be smaller in size than OS. Magnetic Resonance Imaging (MRI) revealed a hypoplastic optic nerve OD and partial absence of the septum pellucidum, consistent with the diagnosis of septo-optic dysplasia.

**Conclusion:** This case outlines the presentation of the patient, diagnostic testing, appropriate referrals, and management available for patients with septo-optic dysplasia.

**Keywords:** amblyopia, optic nerve hypoplasia, septo-optic dysplasia, septum pellucidum, endocrine dysfunction

## Introduction

Septo-optic dysplasia, also known as DeMorsier Syndrome, is a congenital condition involving optic nerve hypoplasia (ONH), an absent septum pellucidum, and thinning of the corpus callosum. Endocrine dysfunctions may also be present. Septo-optic dysplasia can present with multiple variations. As primary eye care providers, the diagnosis of septo-optic dysplasia, its management, and proper referrals are essential in getting this type of patient the proper care.<sup>1</sup> This case report will outline the diagnosis and management options for a six-year-old African-American male who presented with septo-optic dysplasia.

## Case Report

A six-year-old African-American male presented for a comprehensive eye exam due to failing a school vision screening the prior year. The parent also reported that she noticed that the patient's right eye turned out occasionally. The patient had no significant medical or family history and was born full term. The child was taking no medications and had no allergies to any medications.

Entering distance visual acuity without correction was OD: 20/500, OS: 20/20. The patient was unresponsive to near visual acuity testing OD; near acuity OS was 20/25. Extraocular motilities were full without pain or diplopia reported. Cover test revealed orthophoria at distance and near. No nystagmus was noted. Visual fields were assessed with finger counting; right eye and left eye confrontation visual fields were assessed as grossly full. Pupils were equal, round, and reactive to light with a grade 1+ relative afferent pupillary defect in the right eye. Retinoscopy revealed

OD: +0.50DS and OS: +1.00DS, with no change in visual acuity. Anterior segment was unremarkable, with IOP being 14mmHg OD and 13mmHg OS with the iCare tonometer.

Differential diagnoses included:

- Optic atrophy
- Megalopapilla
- Tilted disc
- Unilateral optic nerve hypoplasia
- Asymmetric, bilateral optic nerve hypoplasia

Upon dilation, the right eye was positive for a double ring sign, consistent with optic nerve hypoplasia. Cup-to-disc ratio was observed at 0.45H/0.50V OD. All findings were normal OS, with the cup-to-disc ratio being 0.30H/0.35V. Normal vasculature was observed with no tortuosity present. Optical coherence tomography (OCT) confirmed the small size of the right optic nerve relative to the left (Figure 1).

The patient was diagnosed with optic nerve hypoplasia OD, and the parent was educated about the condition. The patient was prescribed low plus polycarbonate protective glasses. Magnetic resonance imaging (MRI) of the brain was ordered to rule out any midline cranial anomalies. The MRI revealed a hypoplastic optic nerve OD and partial absence of the septum pellucidum, consistent with the diagnosis of septo-optic dysplasia. During a phone consultation with the parent, the findings were discussed. The importance of follow-up examination was stressed, and the patient was scheduled to come back in three months. The patient was to be monitored for the development of endocrine dysfunction but was lost to follow-up.

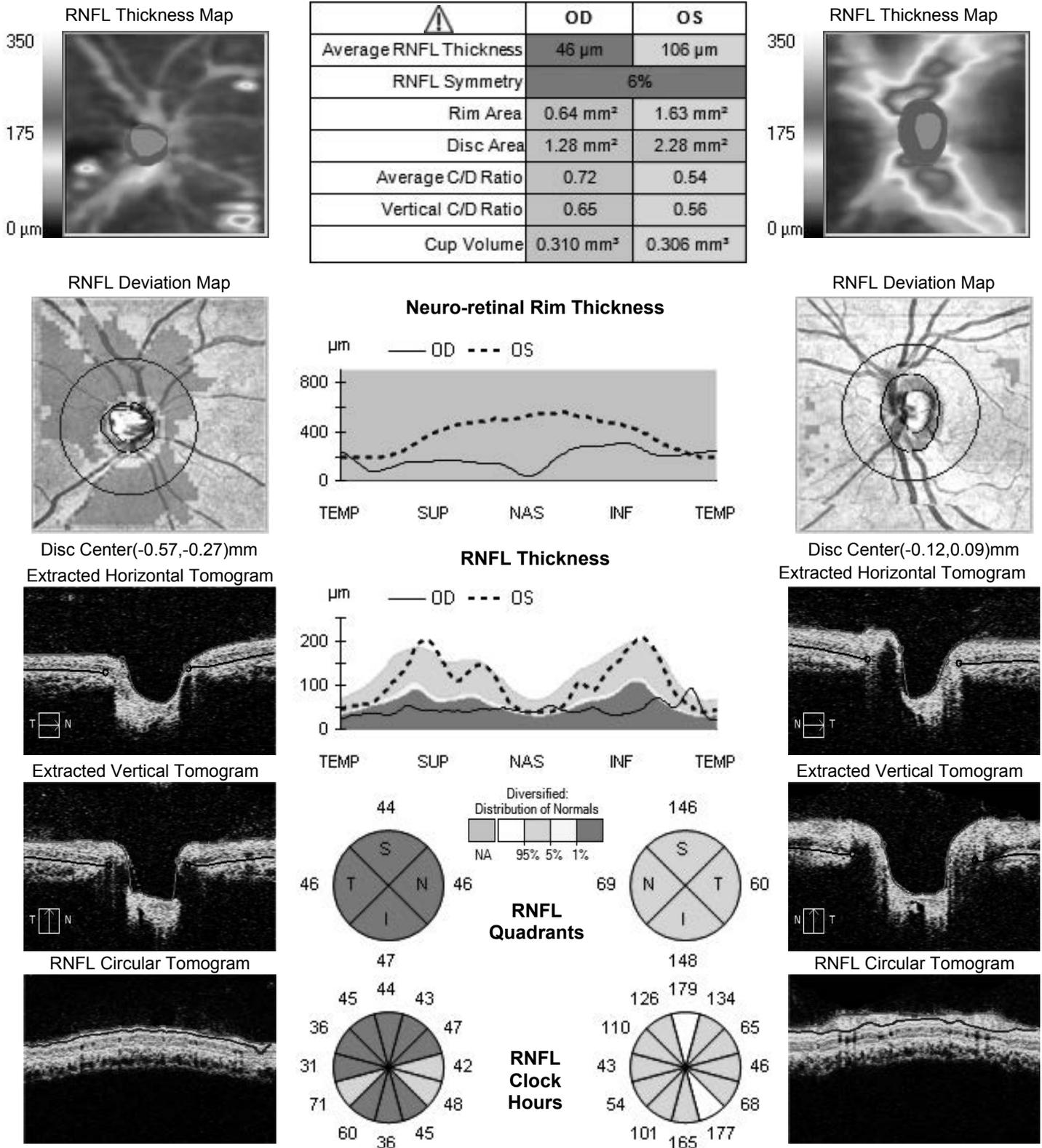


Figure 1. Optical coherence tomography (OCT)

## Discussion

Septo-optic dysplasia is a common congenital neurological anomaly in children. While multiple health concerns can manifest in these patients, ocular symptoms are common. Septo-optic dysplasia consists of ONH, an absent septum pellucidum, thinning of the corpus callosum, and possible endocrine dysfunction. Each aspect of the condition, its presentation, diagnosis, management, and prognosis will be discussed.

### Optic Nerve Hypoplasia

ONH is a non-progressive developmental disorder that is a major cause of blindness in children.<sup>2</sup> ONH results in a decrease in optic nerve fibers and the ganglion cell layer.<sup>3,4</sup> It shows no preference for a unilateral or a bilateral presentation and can have a wide impact on the patient's visual acuity.<sup>1,5</sup> Distinguishing factors typically dictate when the patient will present to the clinic, as severely affected patients present before those only mildly affected by the condition. A patient with unilateral ONH will commonly present around school age, once they have failed a school screening. Some present sooner due to an eye turn that can be secondary to unilateral ONH. Unilateral ONH patients may present later in life due to normal vision in the unaffected eye. Bilateral ONH patients normally present earlier in life due to poor vision in both eyes and the presence of nystagmus.<sup>1</sup> This is commonly a pendular nystagmus due to poor vision in both eyes.<sup>6</sup>

The development of ONH is typically idiopathic. External factors that may contribute to the development of ONH include a young maternal age, maternal diabetes, congenital cytomegalovirus, the mother using anticonvulsant medication, quinine, smoking, or alcohol. It is also linked to preterm birth complications.<sup>1,6-8</sup>

The patient can present with a wide range of visual acuity, from 20/20 to no light perception in the affected eye.<sup>4,5,8,9</sup> Typically, a patient with ONH will have a poorer visual acuity of count fingers to no light perception.<sup>5</sup> These patients generally have a high spherical refraction with large amounts of astigmatism.<sup>1</sup> Refractive correction will usually not improve visual acuity in the affected eye significantly. Strabismus is present in 50% of cases with unilateral ONH. Esotropia of the affected eye is most common.<sup>8</sup>

When the patient has esotropia, high refractive error, and reduced visual acuity, the additional diagnosis of amblyopia should be considered.<sup>8</sup> The reduction in vision needs to be explored in order to determine whether the reduction is due to the optic nerve hypoplasia or is secondary to an amblyogenic factor. Any improvement in visual acuity should be attempted, and twelve weeks of amblyopia therapy is recommended to see whether any improvement is achieved.<sup>8,10</sup> Since no amblyogenic factor was present for this patient, no amblyopia therapy was initiated.

Relative afferent pupillary defect (RAPD) commonly presents in unilateral cases of ONH.<sup>10</sup> Due to the damage of

the nerve fibers in the optic nerve, less stimulation is received to the Edinger-Westphal nucleus when light is directed into the affected eye. This absence of stimulation will result in the absence of a simultaneous bilateral pupil constriction.<sup>11</sup> The degree of the RAPD is dependent upon the amount of damage to the optic nerve. An objective grading scale is listed below. A practitioner may also use neutral density filters to quantify an RAPD. The neutral density filters range from 0.3 log to 1.8 log in 0.3 steps. Bilateral ONH typically does not present with an RAPD, unless the damage is asymmetric.

Grading Scale: RAPD

- Grade 1+: A weak initial pupillary constriction followed by greater redilation
- Grade 2+: An initial pupillary stall followed by greater redilation
- Grade 3+: An immediate pupillary dilation
- Grade 4+: No reaction to light – Amaurotic pupil (<http://bit.ly/1W1CBfj>)

Color vision can also be affected in patients who have ONH.<sup>4,8,10</sup> Optic nerve abnormalities typically produce red-green defects. Early macular or outer retinal disease may result in blue-yellow defects.

Fundus evaluation is essential in the diagnosis of ONH. The affected optic nerve will appear small in size and pale in color.<sup>5</sup> The appearance of the disc will be very crowded since the disc may only be one-third to one-half its normal size.<sup>4,10</sup> There will be an inner pigment ring present that will stop at the border of the nerve; this pigment is from migrating pigment epithelial cells.<sup>10</sup> The disc is then surrounded by a yellow/white ring, which shows the normal size of the optic nerve. This yellow/white ring is the junction between the sclera and the lamina cribrosa.<sup>1,10</sup> The appearance of the nerve with an outer ring is described as a “double ring sign.”<sup>1,5,7,10</sup> However, this double ring sign can be absent in ONH.<sup>8</sup>

Contrary to what was previously thought, the size of the disc does not correlate to the visual acuity.<sup>1,9</sup> Yanoff and Duker state that visual acuity is dependent upon the damage to the papillomacular nerve fiber bundle.<sup>9</sup> The papillomacular bundle consists of fibers from the macular area.<sup>11</sup> The macular fibers take up one-third of the disc and make up the temporal wedge of the optic nerve.<sup>11</sup>

There is a decrease in the nerve fiber layer with ONH.<sup>1,4,5,8,10</sup> The nerve fiber layer will have a white appearance with a loss of striations.<sup>10</sup> Since there is damage to the nerve fiber layer, the foveal light reflex could be absent.<sup>1</sup> The damage to the nerve fiber layer can be assessed with the red-free light.<sup>1</sup> The loss of the nerve fiber layer could result in a visual field loss as well. Multiple types of field loss could be present; common types include central depressions, nasal and temporal wedges, inferior altitudinal loss, or generalized constrictions.<sup>1,6</sup>

The vasculature typically remains unaffected, but tortuosity of the vessels can occur.<sup>1,5,8,10</sup> The outer retinal layers

of the retinal pigment epithelium and the choroid are typically unaffected by ONH.<sup>4</sup>

Special testing can support or confirm the diagnosis of ONH when the appearance of the optic nerve is atypical. The use of retinal photos, Heidelberg retinal tomography (HRT), OCT, MRI, B-scan ultrasound, electroretinography (ERG), and visual-evoked potential (VEP) can all help confirm or dismiss the diagnosis of optic nerve hypoplasia.

Retinal photos are able to confirm the diagnosis of optic nerve hypoplasia by using the disc-macula distance to disc diameter ratio. This is calculated by measuring from the center of the disc to the center of the macula and then dividing by the disc diameter. A number greater than three is suggestive of ONH, while a number greater than four is definitive for ONH.<sup>1,6,8,10</sup> The normal disc diameter for most eyes is 1.5 millimeters (mm), while the average measurement for the distance between the center of the disc and macula is 4 mm.<sup>10</sup>

HRT has also been shown to be beneficial for the confirmation of ONH in relation to disc area. One ongoing study by Pang shows that the average disc area of the normal optic nerve using HRT is  $2.37 \pm 0.55 \text{ mm}^2$  in African-American children ages 4 to 18.<sup>8</sup> A case report by Pang and Frantz shows the value of HRT in diagnosing ONH. Their patient was positive for unilateral ONH with an HRT reporting the disc areas as  $1.545 \text{ mm}^2$  for the affected eye and  $2.52 \text{ mm}^2$  for the unaffected eye.<sup>8</sup>

The use of OCT can assist with the diagnosis of ONH. An OCT will allow assessment of the size of the cup as well as the retinal nerve fiber layer (RNFL). For this patient, an average RNFL was assessed at  $46 \mu\text{m}$  for the right eye and  $106 \mu\text{m}$  for the left eye. The average disc area for the right eye was  $1.28 \text{ mm}^2$ , while the left eye was  $2.28 \text{ mm}^2$ . The decreased disc area, along with the damaged RNFL, helped confirm the diagnosis of ONH.

MRI is a sensitive diagnostic tool that is able to detect subtle malformations and needs to be ordered with any patient suspected of ONH and septo-optic dysplasia.<sup>2</sup> MRI has been shown to be a great diagnostic tool in determining ONH by evaluating the size of the optic nerve and showing whether a small optic nerve is truly present.<sup>3</sup> Additionally, MRI of the brain and brainstem without contrast, along with scans of the orbit, face, and neck without contrast, will show whether there is an absence of the septum pellucidum and thinning of the corpus callosum. These brain malformations are also consistent with the diagnosis of septo-optic dysplasia.

The use of an ophthalmic B-scan ultrasound can also show the presence of a small optic nerve. Due to more easily accessible equipment, a B-scan was not ordered for this patient.

ERG testing could also help confirm ONH. A standard ERG measures electrical responses of various cell types in the outer retina.<sup>6</sup> The results of a standard ERG in a patient with ONH should be normal, since the outer layers of the retina are not affected.<sup>1,4</sup> The results of a pattern ERG and multifocal

ERG would be abnormal due to inner layers of the retina being affected.

A VEP would be reduced for patients with ONH but would show the potential achievable acuity.<sup>1,4</sup> A VEP could be beneficial as it predicts the potential acuity that could result after any amblyopia treatment is performed.<sup>4,8</sup> Since no amblyogenic factor was present for this patient, a VEP was not ordered.

There are no treatment options for patients with ONH. Fortunately, it is a stable, non-progressive condition. Polycarbonate or Trivex eyewear for protection is recommended. Low vision devices can also be beneficial for these patients. Depending on the severity of the condition and the age of the patient, specific low vision devices could aid those with bilateral ONH.

In the pediatric population, optical and non-optical devices could be beneficial for patients with visual impairment. Some non-optical accommodations include 20/20 pens, bold lined paper, a slant board, and writing guides. Electronic tablets are also a great resource for the pediatric population with visual impairment. Some optical devices that would benefit the patient are a SmartLux Digital or a Ruby®, which are both handheld or stand video magnifiers. A 4x dome magnifier is a non-electronic optical device that could be helpful for near work. Most children are able to use a monocular telescope easily for distance targets. The telescopes come in a 2.5x-10x range, and the power needed is dependent upon the starting visual acuity and the desired visual acuity. Any patient with a visual acuity of 20/200 or worse could benefit from the use of a closed circuit television (CCTV). These small accommodations can go a long way in the classroom and in helping the child succeed in everyday activities.

### Brain Malformations

The malformations present with septo-optic dysplasia are the absence of the septum pellucidum and the thinning of the corpus callosum. The diagnosis is made by an MRI. The patient's MRI results show a partial absence of the septum pellucidum, consistent with the diagnosis of septo-optic dysplasia.

The absence of the septum pellucidum alone does not result in intellectual, neurologic, or behavioral dysfunction.<sup>10,12</sup> Studies have shown that ablation of the septum pellucidum in animals can affect their spatial orientation and suggests that intellectual and behavioral problems could arise.<sup>1,13</sup> Thinning of the corpus callosum has been associated with developmental delays in association with the Battelle Developmental Inventory.<sup>12</sup> This inventory assesses six developmental areas, including personal-social, adaptive, motor, communications, cognition, and overall development.<sup>12</sup> The corpus callosum was not affected in this patient. The parent reported that the patient had met all of his developmental milestones on time. The patient was doing well in school and did not exhibit behavioral problems.

## Endocrine Dysfunction

When a patient presents with optic nerve hypoplasia, septo-optic dysplasia and its side effects need to be considered. It is reported that 60% of patients with septo-optic dysplasia manifest with dysfunction of the hypothalamic-pituitary axis.<sup>13</sup> If the patient has been previously diagnosed with septo-optic dysplasia, endocrine function needs to be evaluated. Early indicators of an endocrine disorder can include neonatal jaundice, seizures, feeding problems, and lethargy.<sup>4</sup> Septo-optic dysplasia is also associated with an early onset of puberty, accelerated growth, skeletal maturation, and rapid sexual maturation.<sup>13</sup> It is recommended to order blood work evaluating the levels of growth hormone, cortisol, gonadotropin, serum prolactin, thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), and testosterone.<sup>12,13</sup> An MRI can also evaluate the appearance of the pituitary gland. The MRI of this patient showed a normal appearance of the pituitary gland.

A growth hormone deficiency is the most common hormone deficiency for patients with septo-optic dysplasia.<sup>4,9</sup> Children with septo-optic dysplasia and a deficiency of growth hormone will typically have normal growth until the third or fourth year of life.<sup>4</sup> This is due to the elevated levels of prolactin which stimulate growth.<sup>4</sup>

Pertinent history questions include the presence of abnormal thirst or frequent urination. While in office, the height and weight of the patient should also be evaluated.<sup>1</sup> This can be charted on a growth chart to see the development and to make comparisons for their age group.

While this patient was lost to follow-up, due to his age and sex, blood work that would have been ordered would have included T4 and TSH for thyroid function, cortisol, insulin-like growth factor (IGF-1) as a screening for growth hormone problems, ACTH, and prolactin.

Patients with septo-optic dysplasia need to be followed for endocrine changes. Early diagnosis is important as replacement therapies can be started and normal development can occur.<sup>1</sup> If an endocrine deficiency is found, parents should be educated on the changes that can occur and the signs and symptoms that could pose serious problems.<sup>14</sup> Sudden death is possible if endocrine dysfunctions are left untreated.<sup>3,14</sup>

## Conclusion

Septo-optic dysplasia can have multiple effects on a patient and his or her development. This case illustrates the importance of proper diagnostic testing and careful clinical examination in the diagnosis of septo-optic dysplasia. Optic nerve hypoplasia is present in septo-optic dysplasia, and the use of specialty testing is an important asset in diagnosing these cases. Septo-optic dysplasia can have many negative effects on a patient and his or her development. It is important for clinicians to insure proper management and that referrals are met. Endocrine dysfunctions need to be investigated and monitored as it is

essential for avoiding serious complications. Careful clinical examination is important in making the correct diagnoses of optic nerve hypoplasia and septo-optic dysplasia.

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