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Ocular Manifestations of Septo-optic Dysplasia

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Ocular Manifestations of Septo-optic Dysplasia

Abstract

Background: Septo-optic dysplasia (SOD) is a congenital deformity of the brain which can result in neurologic, systemic, and physical malformation.Due to the proximity of these deformities to the optic chiasm and optic nerves, ocular manifestations are common.

Case Report: A 28-year-old male with a long-standing history of reduced vision presented for a routine eye examination. Upon examination he was found to have an afferent pupillary defect, bilateral optic nerve pallor with corresponding nerve fiber layer thinning by optical coherence tomography. Humphrey visual field testing revealed a bi-temporal visual field defect. Neurological imaging was obtained with a subsequent diagnosis of Septo-optic dysplasia (SOD).

Conclusion: Our patient had bilateral optic nerve hypoplasia and an absent septum pellucidum without endocrine abnormalities. This case reiterates the importance of accurate diagnosis of amblyopia only in the absence of ocular and neurological disease. This review also highlights the importance of imaging in instances of unexplained optic atrophy.

Keywords

septo-optic dysplasia, optical coherence tomography, Humphrey visual field, magnetic resonance imaging, amblyopia

Cover Page Footnote

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INTRODUCTION

Septo-optic dysplasia (SOD) is a rare, congenital deformity of the brain causing midline cerebral malformations that can result in neurologic, systemic, and physical malformation. Due to the proximity of these deformities to the optic chiasm, ocular manifestations are common.[1] Up to 90% of these patients will have some level of visual impairment due to the risk of optic nerve hypoplasia (ONH) in SOD.[2] Given the high variability of findings, SOD is difficult to diagnose without neuroimaging. This case will show how optical coherence tomography (OCT), visual field testing, and neuroimaging were used to diagnose SOD in a patient previously misdiagnosed as amblyopic. This case report reviews the neurologic, hormonal, and ocular manifestations of SOD, as well as demonstrates the ocular findings through clinical ancillary testing. Appropriate treatment, testing, and monitoring for patients with SOD will be included in the discussion.

CASE SUMMARY

A 28-year-old Caucasian male presented to our clinic for a comprehensive eye examination. The patient reported poor vision in his left eye since birth that was unable to be corrected with glasses. His ocular history was positive for strabismus and amblyopia OS, diagnosed at three years of age. He reported receiving his first pair of glasses at three years of age and intermittent patching until 10 years of age. The patient did not recall further evaluation or treatment being performed other than being told he had an "eye turn" and "lazy eye." He denied any history of diplopia, ocular surgeries, or injuries. He denied maternal gestational alcohol or drug use and reported no known forceps injury during birth. His developmental history was negative for any learning disabilities or known developmental delays. As a child, he was treated with methylphenidate HCL for attention deficit hyperactivity disorder. His medical history was significant for vitamin D deficiency for which he took vitamin D3 2,000-unit supplementation. He reported no significant family history.

Entering unaided visual acuities were 20/15 in the right eye and 20/100 in the left eye. There was no improvement in visual acuity of the left eye with the use of a pinhole. Manifest refraction yielded +0.50 -0.25 x 018 OD and +1.50 -5.50 x 120 OS, without change in visual acuity. Pupils were equal, round, and reactive to light with a 3+ relative afferent pupillary defect of the left eye. His extraocular motility was significant for both upgaze and downgaze deficits of -2 in the left eye, without nystagmus**.** Cover test at distance revealed a left hypertropia that was neutralized with 14 prism diopters of base down prism as well as a component of exotropia that was neutralized with 12 prism diopters of base in prism. Confrontation visual fields

were full to finger count in both eyes. Intraocular pressures measured with a Tono-Pen were 17 mm Hg in each eye.

A slit lamp examination of the anterior segment demonstrated normal and healthy physical structures including normal eyelids, clear corneas, open angles by Van Herick, and deep and quiet anterior chambers. His eyes appeared normal in size (no microphthalmia) and irides were flat and intact. A dilated fundus exam revealed clear vitreous and a flat and dry macula in each eye with a notably absent foveal light reflex in the left eye. Retinal vasculature was enlarged. The retinal periphery was flat and intact in both eyes. Additional pertinent findings included small optic discs in both eyes with slightly asymmetric cup-to-disc ratios OS>OD. Additionally, sectoral temporal optic nerve head pallor versus a "double ring" sign was noted in the left eye (Figure 1).

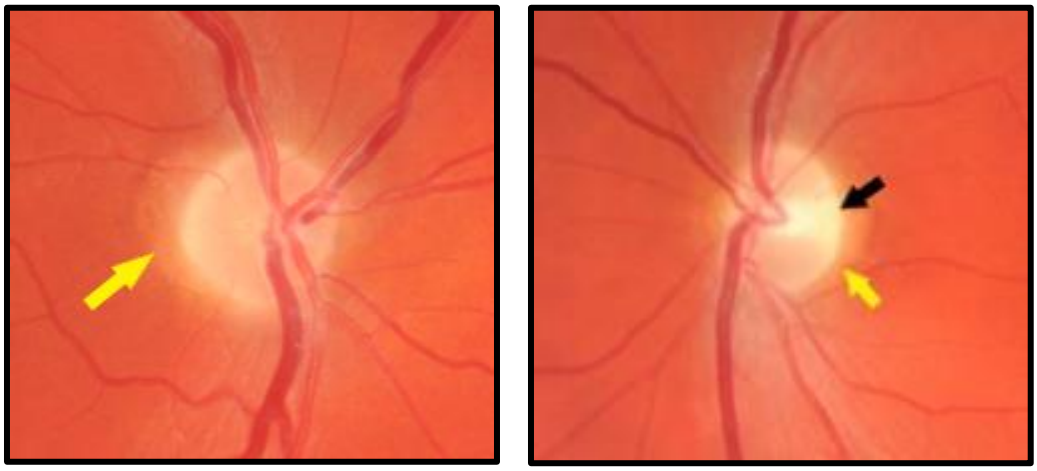


Figure 1: Colored fundus photos of the optic nerve head, OD (left image), OS (right image). Small, asymmetric cup-to-disc ratios, by color, with circumferential hypo-pigmentary changes (yellow arrows). Possible optic atrophy (black arrow).

To further elucidate the clinical findings, OCT of the macula and retinal nerve fiber layer (RNFL) were obtained the same day. The OCT of the macula revealed normal macular architecture and retinal layers in the right eye. In the left eye, a lack of foveal umbo was noted with intact retinal pigment epithelium and photoreceptor layers. Also notable on the macular scan of the left eye was a lack of diminution of the inner retinal layers (Figure 2).

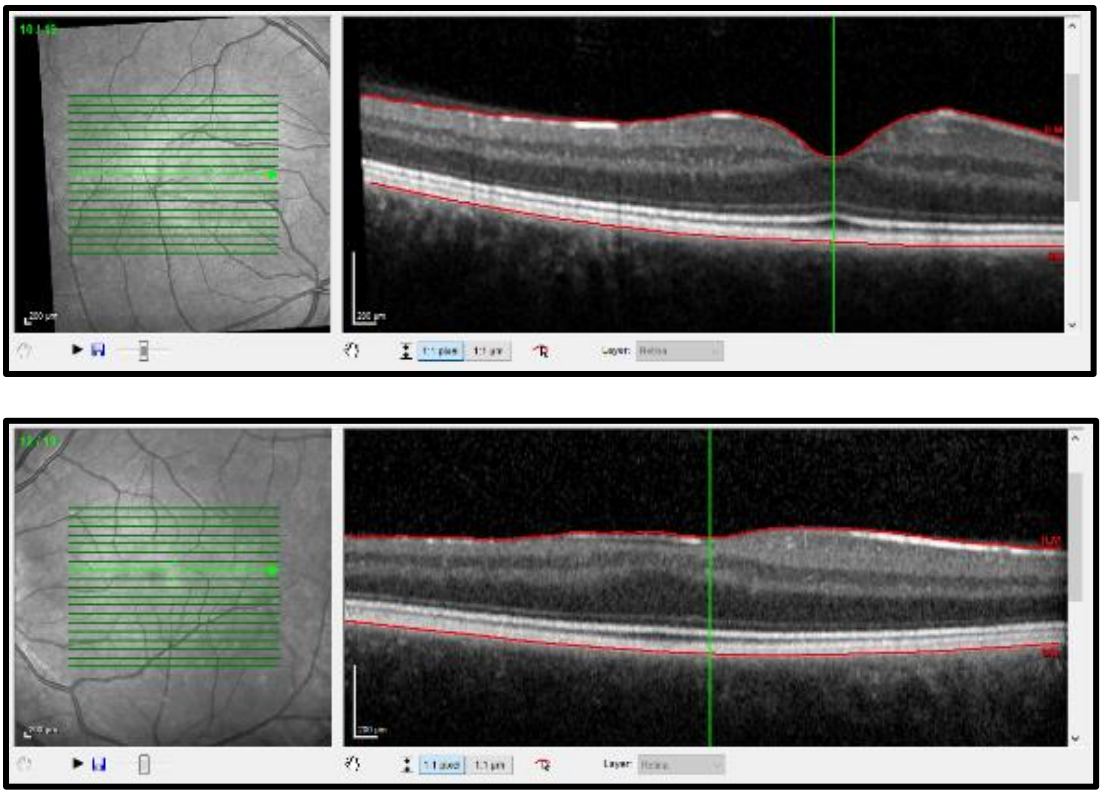
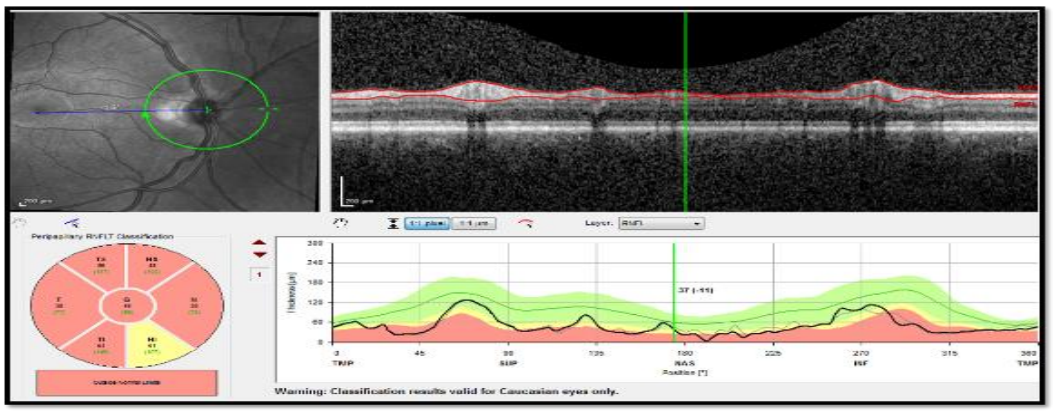


Figure 2. Heidelberg OCT macula of the right eye (top image) and left eye (bottom image). The macula of the right eye demonstrates normal foveal contour with mild ILM changes. The macula of the left eye demonstrates a flattened foveal umbo with lack of diminution of the inner retinal layers as well as mild ILM changes. The retinal pigment epithelium and photoreceptor layers are intact.

The OCT RNFL revealed extensive, diffuse thinning of the retinal nerve fiber layer in both eyes. Also notable were a "double ring" sign, small overall disc size OD>OS and enlarged retinal vasculature (Figure 3).



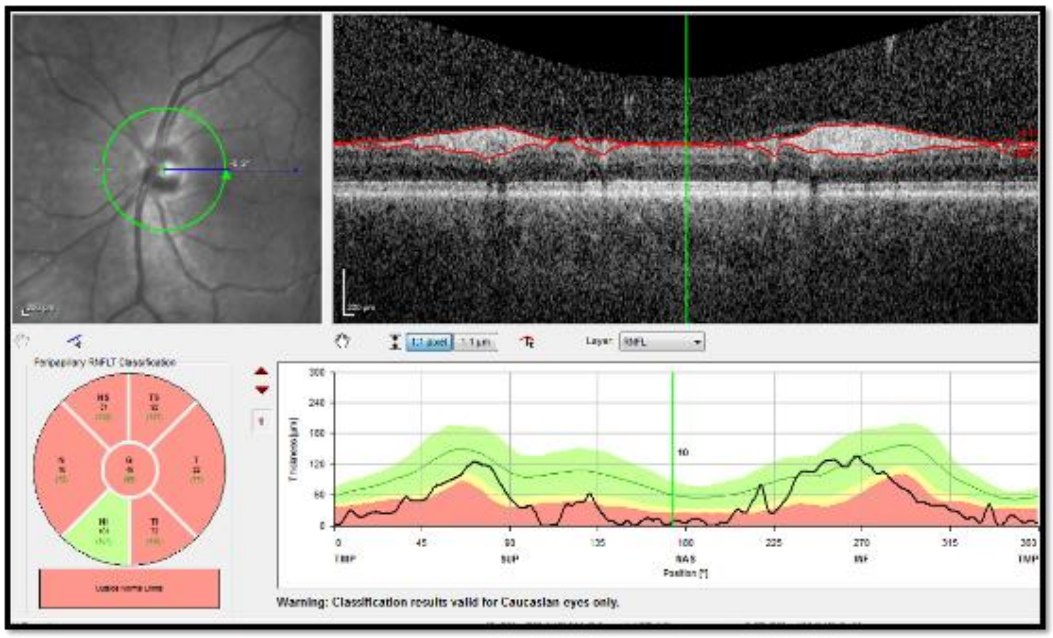


Figure 3. Heidelberg OCT RNFL of the right eye (top image) and left eye (bottom image) demonstrating diffuse retinal nerve fiber layer thinning OU. Note the overall small disc size OD>OS as well as the enlarged vasculature and "double ring" sign OU.

At the conclusion of the initial vision assessment, our patient was diagnosed with optic nerve hypoplasia (ONH) in both eyes. Optic atrophy versus a "double ring" sign was noted in the left eye, as well as strabismus. He was educated on the exam findings and asked to return for threshold visual field testing given the association of ONH and optic atrophy with visual field deficits. Magnetic Resonance Imaging (MRI) of the brain and orbits was concurrently ordered to evaluate for any brain malformation or space occupying lesion. Given his functionally monocular status, he was prescribed spectacles with polycarbonate lenses and recommended to wear them full time for protection.

On the follow up examination, his vision, preliminary tests, and anterior segment findings remained stable. A Humphrey visual field 30-2 was completed and revealed a dense, incomplete bitemporal hemianopsia OS>OD (Figure 4). Considering the bitemporal defects that respected the vertical meridian, this further raised concern for possible chiasmal compression versus anatomic malformation. Since the MRI was still pending at this visit, efforts were made to get this imaging scheduled as soon as feasible.

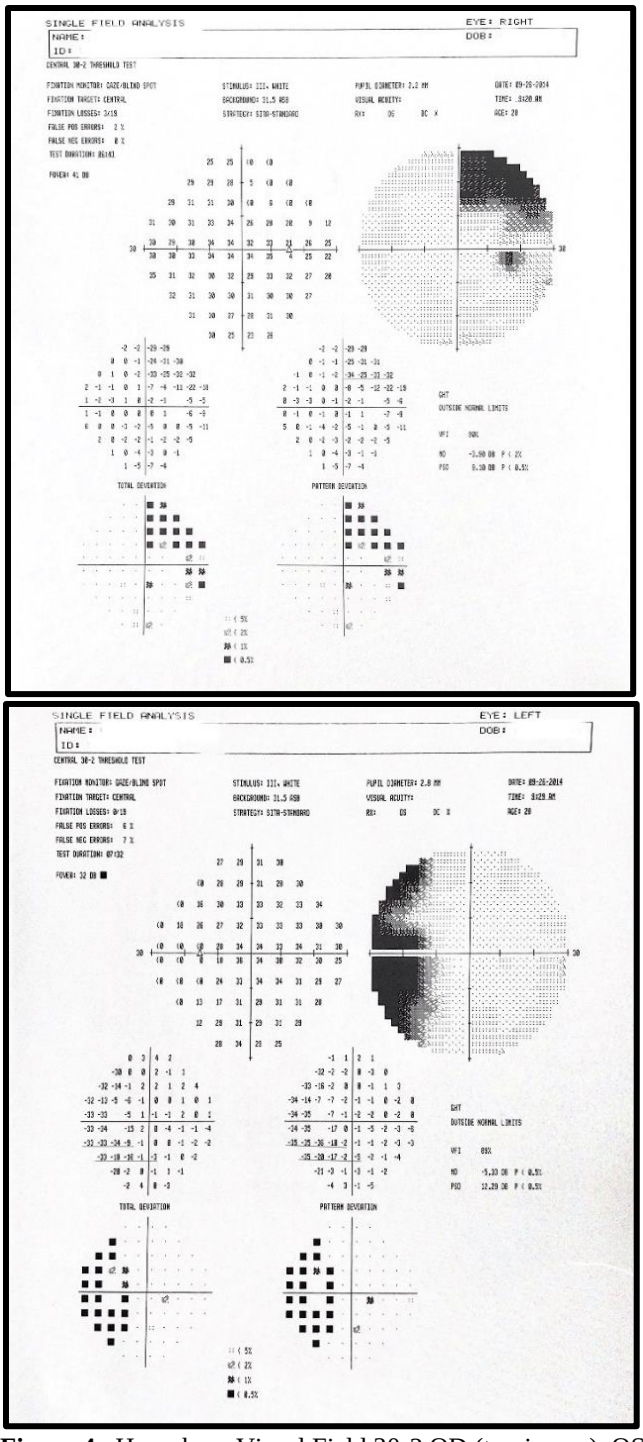


Figure 4. Humphrey Visual Field 30-2 OD (top image), OS (bottom image) demonstrating an incongruous, bi-temporal hemianopsia with good reliability indices.

The MRI showed marked, symmetrical optic nerve atrophy of both eyes. There was no compressive lesion; however, an absence of the septum pellucidum was noted (Figure 5). The pituitary gland was reported as normal radiologically. A diagnosis of septo-optic dysplasia was made based on the presence of optic nerve hypoplasia as well as the lack of a septum pellucidum. These results were discussed with the patient and lab work was ordered to rule out any associated hormonal deficiencies. Lab work was subsequently completed and yielded normal thyroid stimulating hormone, T_3 and T_4 levels, cortisol, and growth hormone levels. The patient was advised of these lab results.

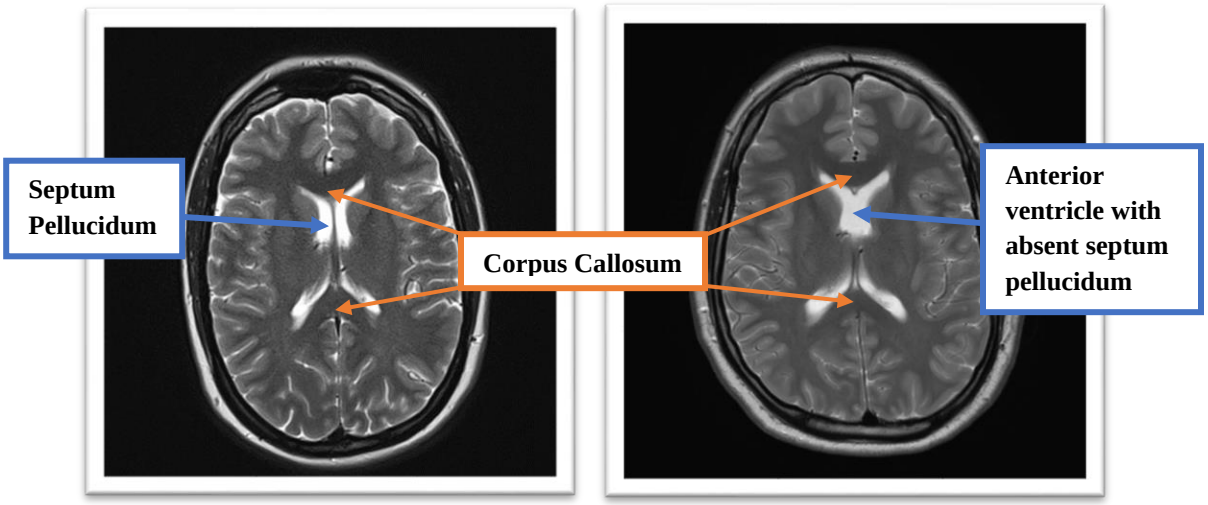


Figure 5. Left image: Normal MRI brain, axial view, demonstrating a normal septum pellucidum (blue arrow) and corpus callosum (orange arrows). Right image: MRI brain image, axial view, of our patient lacking the septum pellucidum (blue arrow). While absent or deformed corpus callosum are common in this condition, it was normal for our patient (orange arrows).

Considering excellent visual acuity in the right eye and the non-progressive nature of SOD, no further treatment or evaluation was recommended from an ocular standpoint. The patient was urged to wear protective eyewear and told to return for annual eye examinations. His visual acuity, fundus examination, and OCT RNFL have remained stable at subsequent visits. His primary care physician was advised of the diagnosis of SOD, recent laboratory findings, and the association of SOD with hormonal deficiencies. The PCP was asked to consider an endocrine consultation. The patient was advised to continue to follow up with his primary care physician for continued hormonal monitoring and treatment if deficiencies occur. He was further advised of the possibility of needing to see an endocrinology specialist in the future.

DISCUSSION

Septo-optic dysplasia, formerly known as de Morsier syndrome, is a rare, congenital condition causing imperfect development of the corpus callosum or septum pellucidum.[3] The syndrome has equal predilection for males and females. The etiology of SOD is most often sporadic, though genetic and environmental causes have been suggested. SOD typically occurs in 1 in 10,000 births but has been documented as high as 53 in 100,000 births in areas of high teenage pregnancy and maternal alcohol or drug abuse.[1,4,5] Signs of SOD can vary in severity, but diagnosis is ultimately made when two or more components of a clinical triad are present: optic nerve hypoplasia, pituitary hormone abnormalities, and midline brain defects.[3,4]

Neurologic manifestations of SOD may include seizures, cerebral palsy, and developmental delay.[4] Developmental delay occurs more frequently in the presence of bilateral optic nerve hypoplasia compared to unilateral optic nerve hypoplasia.[3]

Concurrent hypothyroidism and corpus callosum hypoplasia, which are common among SOD patients, are strongly correlated to developmental delay, though poor visual function may contribute to further delays. Pituitary hormone deficits may develop in up to 66% of patients with SOD.[1,3] These hormonal deficiencies may occur even when the pituitary gland is deemed normal radiologically, as is the case of our patient.[6] Hormonal deficiency may cause early puberty, hypothyroidism, hypoglycemia, and short stature, among other sequelae.[4]

Ocular findings of SOD may include optic nerve coloboma, strabismus, nystagmus, microphthalmia, anophthalmia, and optic nerve hypoplasia.[3,7] Optic nerve hypoplasia, part of the SOD triad, is a non-progressive underdevelopment of the optic nerve head and its axons. Typically, the affected optic disc may be 50-70% smaller than a normal optic disc.[2] The presence of ONH may be determined by evaluating the distance from the center of the optic disc to the center of the fovea and comparing that to the optic disc diameter. A ratio greater than 3:1 is considered smaller than normal; however, this is not considered pathognomonic for ONH.[6] Additionally, this ratio varies with gender, age and race.[6] Other characteristic findings of ONH may include a disc that is pale or gray, the presence of a "double-ring" sign, arteriolar or venous tortuosity or straightening, and thinning of the nerve fiber layer. [2,4,5,7] The "double-ring" sign can be identified by the presence of a circumferential halo around the disc. This circumferential halo is thought to arise histologically by the proliferation of retina pigment epithelial cells surrounding the disc.[8]

Bilateral optic nerve hypoplasia accounts for over 70% of ONH cases in SOD.[9] ONH is thought to be a leading cause of juvenile visual impairment and blindness in the United States.[10] Vision ranges from normal visual acuity to no light perception.[9] Visual acuity and resultant visual impairment varies but does not correlate with the size of the optic nerve.[9,11]Instead, visual acuity is determined by the integrity of the papillomacular bundle rather than the overall size of the optic disc.[2] Recent evidence suggests a correlation between the severity of the RNFL thinning and the reduction in visual acuity.[6] With the advent of OCT RNFL and a normative database, RNFL thickness is now measurable and ONH is more identifiable in "subtle" cases.[11] The macular structure in patients with ONH has been found to be correlated with visual acuity; notably the continuation of the inner retinal layers at the foveal pit, which can be seen on the OCT, is related to poor visual acuity.[11] Afferent pupillary defects are common among patients with optic nerve hypoplasia; therefore, careful pupillary assessment is warranted.[7] Visual field defects are variable in presentation and may result in afferent pupillary defects, even in the presence of normal visual acuity.[7]

The patient had bilateral optic nerve hypoplasia and an absent septum pellucidum without endocrine abnormalities, meeting two of the three components for the SOD triad. The diagnosis of optic nerve hypoplasia with secondary visual field defects in each eye and reduced vision in the left eye, is based upon the bilateral characteristically small optic discs with a "double ring" sign. The disc to fovea distance was compared to the disc diameter and found to be approximately 1:3.5. This ratio further supports the ONH diagnosis. The patient had an afferent pupillary defect in the left eye as well as concurrent optic nerve head pallor. These findings have been described elsewhere but may be more typical among patients with unilateral optic nerve hypoplasia or with asymmetric visual field defects.[6]

The patient had symmetrical nerve fiber layer thinning with the visual field defects greater in the left eye. He also had a constant (left) strabismus, another common finding in SOD. Additionally, he had notable continuation of the inner retinal layers and an absent foveal pit on the OCT of the macula (Figure 2). While ONH is associated with poor vision, recent evidence suggests vision correlates with the extent of nerve fiber layer thinning.[11] In our patient, the average nerve fiber layer thickness was similar in both eyes, but abnormally thin compared to normative values. However, visual acuity was asymmetric with best-corrected visual acuities of 20/20 OD and 20/100 OS. Certainly, the abnormal foveal architecture, commonly found in patients with ONH, could have contributed to his poor vision. Furthermore, the patient had a constant left strabismus and significant astigmatic anisometropia to cause amblyopia. The optic nerve hypoplasia and strabismus or refractive astigmatic anisometropia may all be contributing factors. Given that

patching was performed, we would expect the visual acuity to be better, which suggests optic nerve hypoplasia as the primary cause of reduced vision. However, it is possible that patching did improve this patient's visual outcome for the left eye.

Prior to visiting our clinic, our patient was thought to have amblyopia. Upon completion of his initial visit, he was diagnosed with optic nerve hypoplasia in each eye with confirmed bilateral nerve fiber layer thinning (Figure 3) and possible optic atrophy versus a "double-ring" sign in the left eye. Other authors have noted the challenge in distinguishing the surrounding hypo-pigmentary changes with optic atrophy which contributes to the misdiagnosis.[6,8] The presence of the afferent pupillary defect with a history of suspected optic atrophy of unknown etiology in such a young patient warranted further neurological work up.

The diagnosis of SOD should be shared with a patient's primary care physician. These patients may also benefit from a referral to endocrinology for close monitoring due to the risk of hormonal imbalance development. A treatment trial with patching is recommended among (young) patients with ONH and strabismic or refractive amblyogenic factors to treat any amblyopia that may be superimposed with the ONH. As these findings were present since birth, the patient was well adapted to his reduced vision; therefore, vision therapy and low vision services were deemed unnecessary. These services should always be considered in patients with reduced acuity who struggle with activities of daily living. The patient was educated on the diagnosis as well as the potential for hormonal deficits in the future. He was encouraged to continue follow up with his healthcare team. Repeat visual field testing may be considered annually or sooner with any change in the OCT RNFL or as deemed clinically indicated.

CONCLUSION

This case underscores the importance of an accurate diagnosis of amblyopia, only in the absence of ocular and neurological disease. SOD may not have been diagnosed in the patient's childhood because the findings were masked by the concurrent amblyopia diagnosis. Although SOD and amblyopia can both present with decreased vision, additional ocular findings can accompany SOD, including optic nerve hypoplasia, optic nerve coloboma, microphthalmia, anophthalmia, or nystagmus.[3,7] This case report highlights the importance of imaging in instances of unexplained optic atrophy to confirm suspected etiology. The role of OCT in assisting in the diagnosis of optic nerve hypoplasia and SOD was also demonstrated.

While ocular findings associated with SOD are non-progressive, the long-term complications of hypopituitarism could have significant health implications and should be monitored frequently by an endocrinologist or a primary care physician. The patient was advised to continue regular appointments with his primary care provider to monitor for any potential hormonal deficiencies that may develop. Annual dilated fundus examinations as well as OCT RNFL were recommended.

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