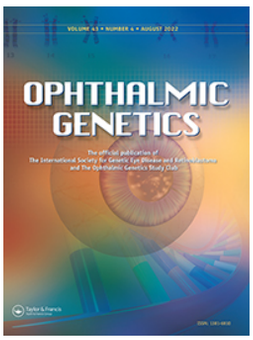

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CASE REPORT

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Septo-optic dysplasia presenting with nystagmus, pseudo-disc edema, and fovea hypoplasia

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ABSTRACT

Background: Septo-optic dysplasia (SOD) is a condition that affects the early development of the brain and eyes. It presents with a combination of optic nerve hypoplasia, brain midline structure abnormalities, and pituitary gland hypoplasia.

Methods: This is a case report of a 4-year-old male who presented with low amplitude horizontal nystagmus and decreased visual acuity 20/60 OU. Further imaging and electrophysiology were conducted to classify the ocular presentation.

Results: No iris transillumination was noted, but foveal hypoplasia and disc edema were evident on fundus examination. This prompted neurology consultation and MRI imaging. The MRI was consistent with the diagnosis of SOD showing hypoplasia of the optic nerves, chiasm, and tracts and an absent septum pellucidum, but with normal pituitary development and function. Lumbar puncture and intracranial pressure were normal. Genetic testing identified one pathogenic variant in the SLC45A2, indicating carrier status for oculocutaneous albinism type 4 (OCA4). Flash Visual Evoked Potentials (VEPs) were consistent with chiasm dysfunction or hypoplasia rather than the chiasmal misrouting of OCA.

Conclusion: This case report further elaborates the phenotypic variation of SOD, with the finding of blurred disc margins, in the absence of the typical optic nerve double ring sign and with normal intracranial pressure. The findings of fovea hypoplasia and blond fundi lead to the suspicion of OCA either as a separate diagnosis with a second pathogenic variant in SCL45A2 not yet identified or in association with SOD. This case highlights the importance of electrophysiology to help distinguish chiasmal hypoplasia or dysfunction from OCA misrouting.

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KEYWORDS
Septo-optic dysplasia; blurred disc margin; nystagmus; foveal hypoplasia

Introduction

Septo-optic dysplasia (SOD), also referred to as de Morsier syndrome, is a condition in which the early brain and eyes are underdeveloped. The signs and symptoms of SOD vary, but characteristics of the disease include a combination of hypoplasia of the optic nerve, abnormal formation of structures along the midline of the brain, mainly the septum pellucidum, and pituitary gland hypoplasia. Approximately one-third of people diagnosed with SOD have all three features of the disease; however, most affected individuals display at least two of the three signs (1). In rare cases, SOD may also be associated with more severe presentations of epilepsy, delayed development, persistent fetal vasculature, retinal detachment, and gastroschisis (2).

The incidence of SOD is 1 in 10,000 live births, with boys and girls affected equally (3). The etiology is unclear, though SOD has been associated with a younger maternal age and environmental factors may play a role (4). Some of these environmental risk factors that may contribute to malformations typical of SOD include drug consumption, viral infections, and maternal diabetes (4). The underlying genetic mechanisms are still being worked out, and common genetic abnormalities include common pathogenic gene variants in two genes: *HESX1* and *SOX2* (5). The *HESX1* homeobox gene functions as a transcriptional repressor and is responsible for pituitary organogenesis (6). The *SOX2* gene has been linked as a critical component in the proper development of the pituitary gland, forebrain, and eye during human embryogenesis (7). Other genes including *SOX3* and *OTX2* have also been identified in some cases of SOD (8).

The interesting aspect of people with SOD is its immense phenotypic variation. There are wide variations in the severity of clinical features and their associated diagnoses that do not follow a clear-cut pattern (9). The emergence of SOD can either occur at birth, along with other presenting congenital abnormalities, or later when the child displays growth delays and visual abnormalities (10). The diagnosis of SOD should be suspected in newborns with hypoglycemia, jaundice, a microphallus with or without descended testes, and nystagmus with or without associated midline abnormalities (9).

In terms of the ophthalmological examination, there are a few components that need to be assessed when determining a diagnosis of SOD. The first includes the presence of strabismus or nystagmus and whether its presentation is unilateral or bilateral. The next includes looking for signs of optic nerve hypoplasia (ONH), which includes a double-ring sign and

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a pale or small optic discs/neuroretinal rim area. Other indications of SOD can present with microphthalmia, coloboma, or optic nerve dysplasia. The final examination is to determine the degree of visual impairment. Further analysis of MRI brain imaging with pituitary functioning can be useful in the diagnosis of SOD.

Case

A 4-year-old male born full term presents with decreased vision in both eyes (OU) and horizontal nystagmus noted by his mother at the age of 2. The patient's mother states that his vision is blurry, even with glasses on. There was no history of patching, and he is sensitivite to bright light with squinting.

On review of systems, his mom stated her child to be hyperactive and occasionally complains of headaches but not eye pain.

There is no significant family history of other individuals with features of SOD. Maternal ancestry is of German, Swedish, and other European descent. Paternal ancestry is of Irish, German, and other European descent. No consanguinity is reported.

His past medical history includes newborn jaundice and ADHD. His mom denies a history of prematurity. With regard to the patient's development, his mother reports that he learned to walk around 16 months. The parents cannot recall when his first word was but reports that he was a quiet child until age 2.5 years. Current medications include ibuprofen, acetaminophen, and melatonin as needed.

Examination by an outside ophthalmologist noted the patient to have full ductions, a non-accommodative bilateral alternating esotropia, and a low amplitude, intermittent horizontal nystagmus. No significant refractive error was noted, and his anterior and posterior exams were unremarkable.

One year later, the parents were concerned that his eyes were getting worse, turning in, and constantly moving. The patient was referred to the University of Minnesota Medical Center for a second opinion.

Results

External appearance revealed fair skin and blond hair. The best corrected VA was 20/60 OU. His refraction was −0.75 OD and −1.00 left eye OS. The pupils were equal, round, and reactive to light, although slightly sluggish. The extraocular movement was full in both eyes, and there was a non-accommodative bilateral alternating esotropia. A horizontal intermittent low amplitude nystagmus was also noted. The nystagmus did not appear to decrease with convergence. His slit-lamp examination was unremarkable. No transillumination defects were noted. His fundus examination revealed flat macula and the optic nerve disc margins were blurry and slightly elevated. The periphery had a blond appearance (Figure 1).

The optical coherence tomography (OCT) showed decreased foveal contour consistent with foveal hypoplasia of both eyes (Figure 2a–d). A retinal nerve fiber layer thickness (RNFL) OCT image of the disc was not performed in our

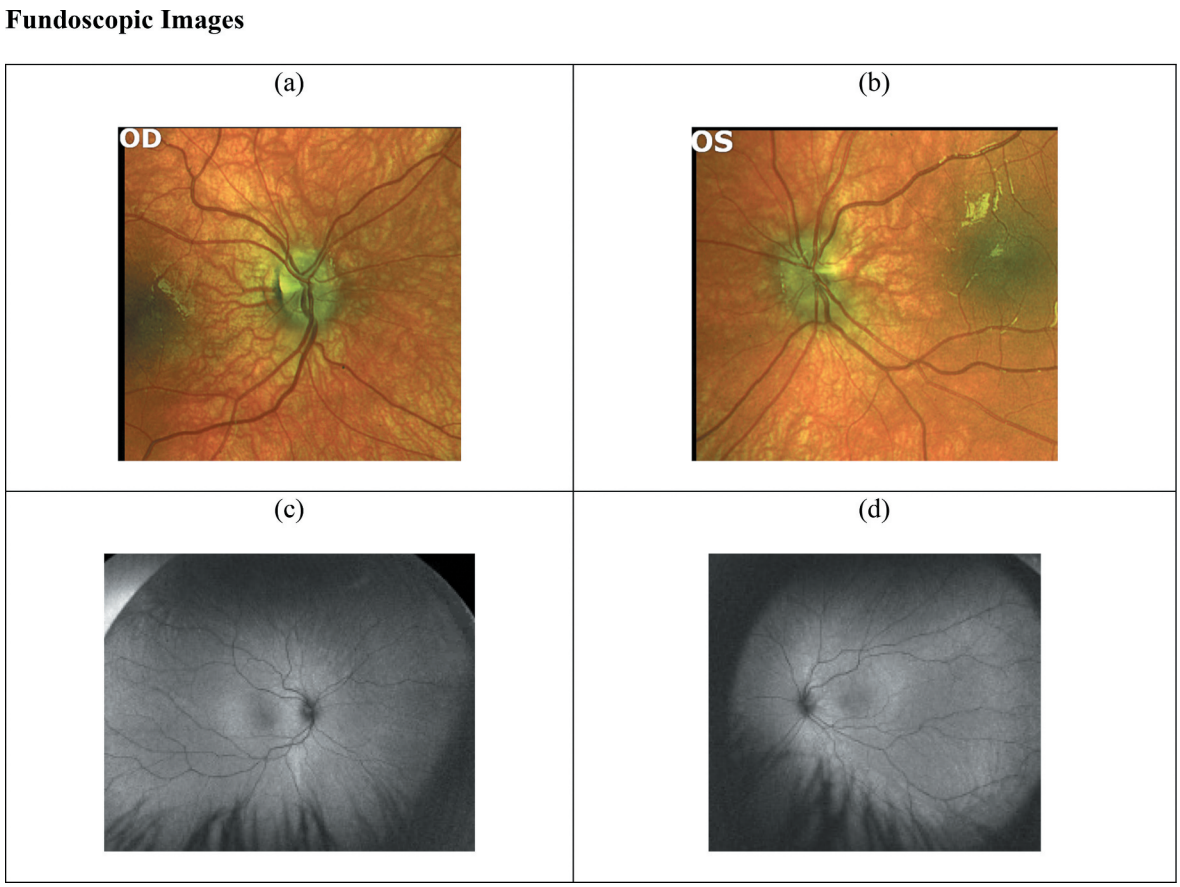


Figure 1. (a, b) Slightly blurred optic nerve disc margins, and blond peripheral appearance (c, d) normal fundus autofluorescence of both eyes.

patient, but the RNFL is not apparent in the axial slice in contrast to a different child who has foveal hypoplasia and a clear RNFL (Figure 2e,f). Fundus autofluorescence was normal. An ultrasound revealed elevated optic nerve head without optic nerve drusen (Figure 3).

A full-field electroretinogram (FFERG) using LKC RetEVAL® was conducted to exclude any retinal cone dystrophy associated with nystagmus (Figure 4). The FFERGs were compared to the manufacturer's normal reference age range values for the patient. Overall, mild rod system amplitude reduction was noted in both eyes, but with normal b:a configuration. The patient, however, was under anesthesia using propofol. Anesthesia can reduce scotopic ffERGs more than photopic responses and can also delay peak times. Previous reports have shown approximately 50% reduction in the isotopic ERG amplitudes (11).

The MRI brain was consistent with the diagnosis of septo-optic dysplasia, with features of hypoplasia of the optic nerve, optic chiasm, and tracts. The patient's coronal retrobulbar optic nerve diameter measured 1.8 mm (OS) and 2.3 mm (OD). Reference range for a child aged 2–6 yo is 2.27 ± 0.12 (12)) (Figure 5f). The septum pellucidum was absent, and the fornices are fused and low-lying. There were no signs of pituitary gland atrophy or focal abnormality. There were no signs of hydrocephalus, mass effect, or midline shift intracranially

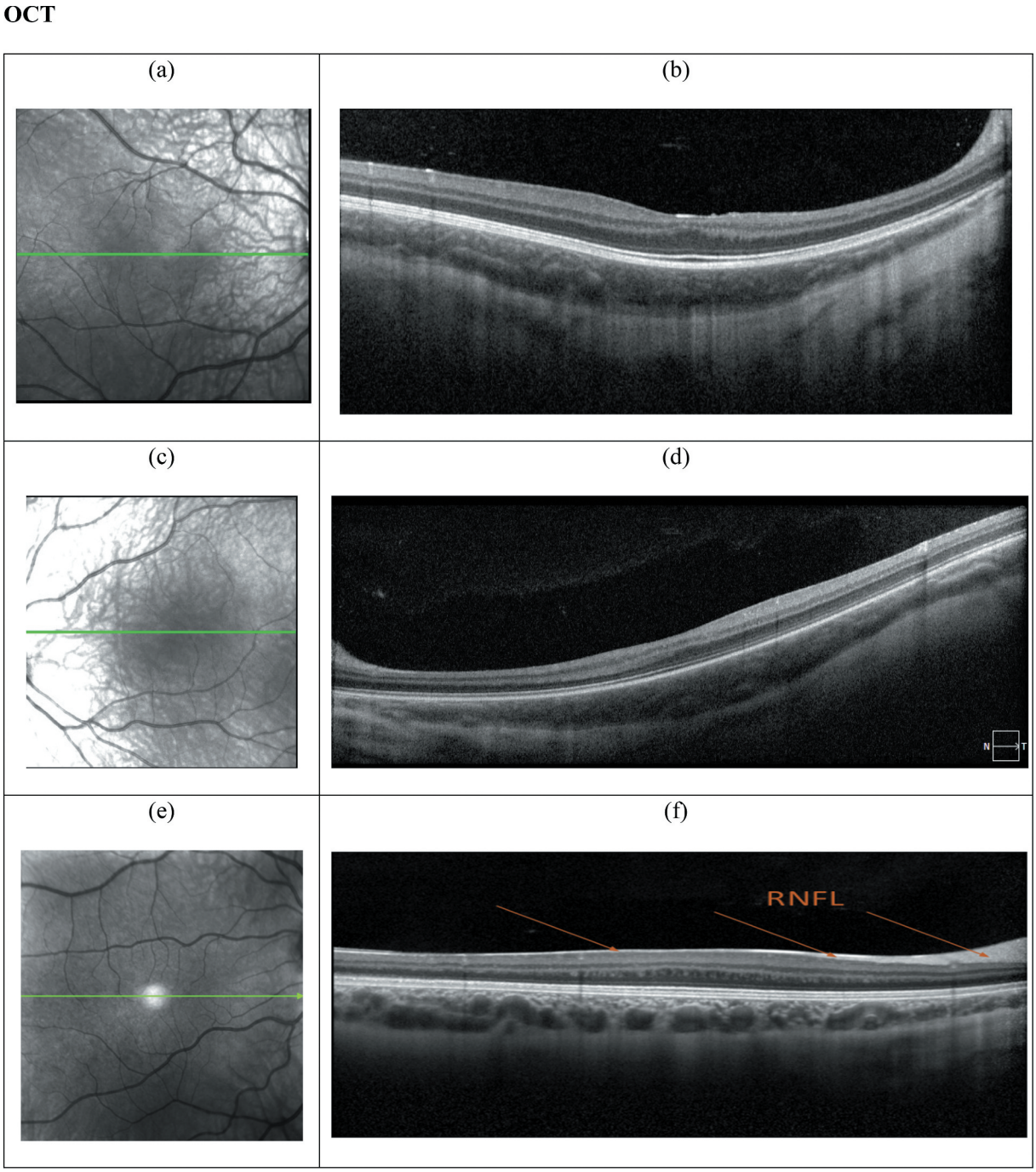


Figure 2. (a, c) Infrared image with a green line noting the single macula scan. (b, d) OCT showing decreased foveal contour in both eyes. (e, f) Example of a separate child with foveal hypoplasia and with RNFL evident.

Ultrasound

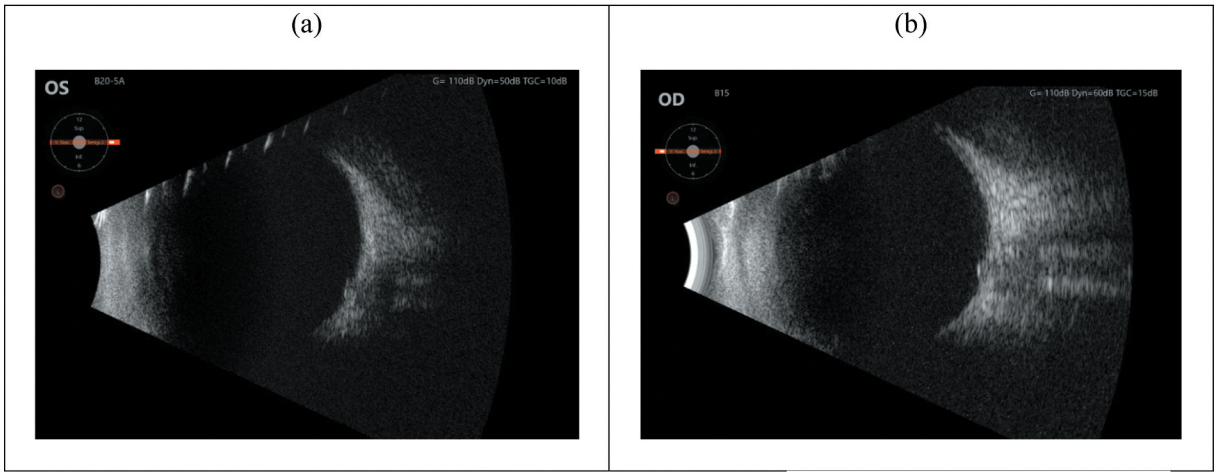
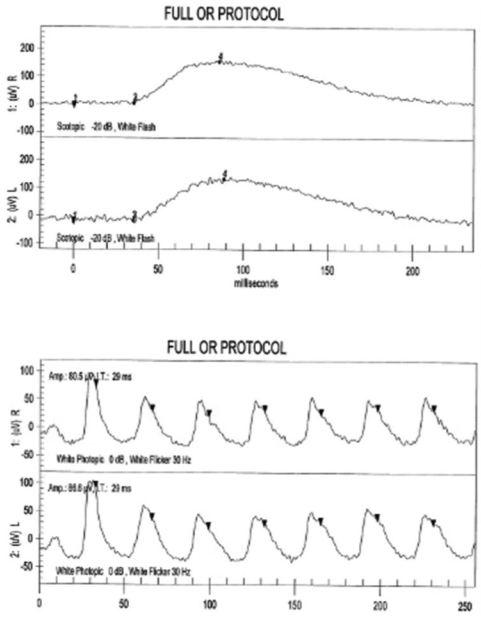


Figure 3. Ultrasound of the left (a) and right eye (b) showing mildly elevated optic nerve head without optic nerve drusen.

FFERG



ALL AVERAGED

Data for Full-Field ERG	Right Eye		Left Eye
DARK-ADAPTED	**Patient**	**Normal**	**Patient**
Rod response amplitude (μv)	**95**	159-347	**100**
Rod response implicit time (ms)	**91**	not avail	**95**
Maximal response a-wave amplitude (μv)	**124**	160-435	**120**
Maximal response a-wave implicit time (ms)	**19**	19-23	**26**
Maximal response b-wave amplitude (μv)	**229**	321-682	**253**
Maximal response b-wave implicit time (ms)	**49**	42-53	**51**
Brighter maximal response a-wave amplitude (μv)	**172**	not avail	**177**
Brighter maximal response a-wave implicit time (ms)	**16.5**	not avail	**14**
Brighter maximal response b-wave amplitude (μv)	**236**	not avail	**270**
Brighter maximal response b-wave implicit time (ms)	**53**	not avail	**53.5**
Oscillatory Potentials		present	
LIGHT-ADAPTED			
30-Hz Flicker amplitude (μv)	**81**	56-150	**87**
30-Hz Flicker implicit time (ms)	**29**	23-30	**29**
Single cone flash a-wave amplitude (μv)	**23**	not avail	**32**
Single cone flash a-wave implicit time (ms)	**16.5**	not avail	**18**
Single cone flash b-wave amplitude (μv)	**135**	84-198	**141**
Single cone flash b-wave implicit time (ms)	**30**	27-32	**30**

---- = residual to non-measurable
xxxx = not tested

Figure 4. The FFERG using LKC® shows that there is mild asymmetry of the responses between both eyes. In dark adapted conditions, the rod-specific b-waves have reduced amplitudes in both eyes. In light adapted conditions, the 30-Hz flicker response has a normal amplitude, and the implicit time is normal in both eyes.

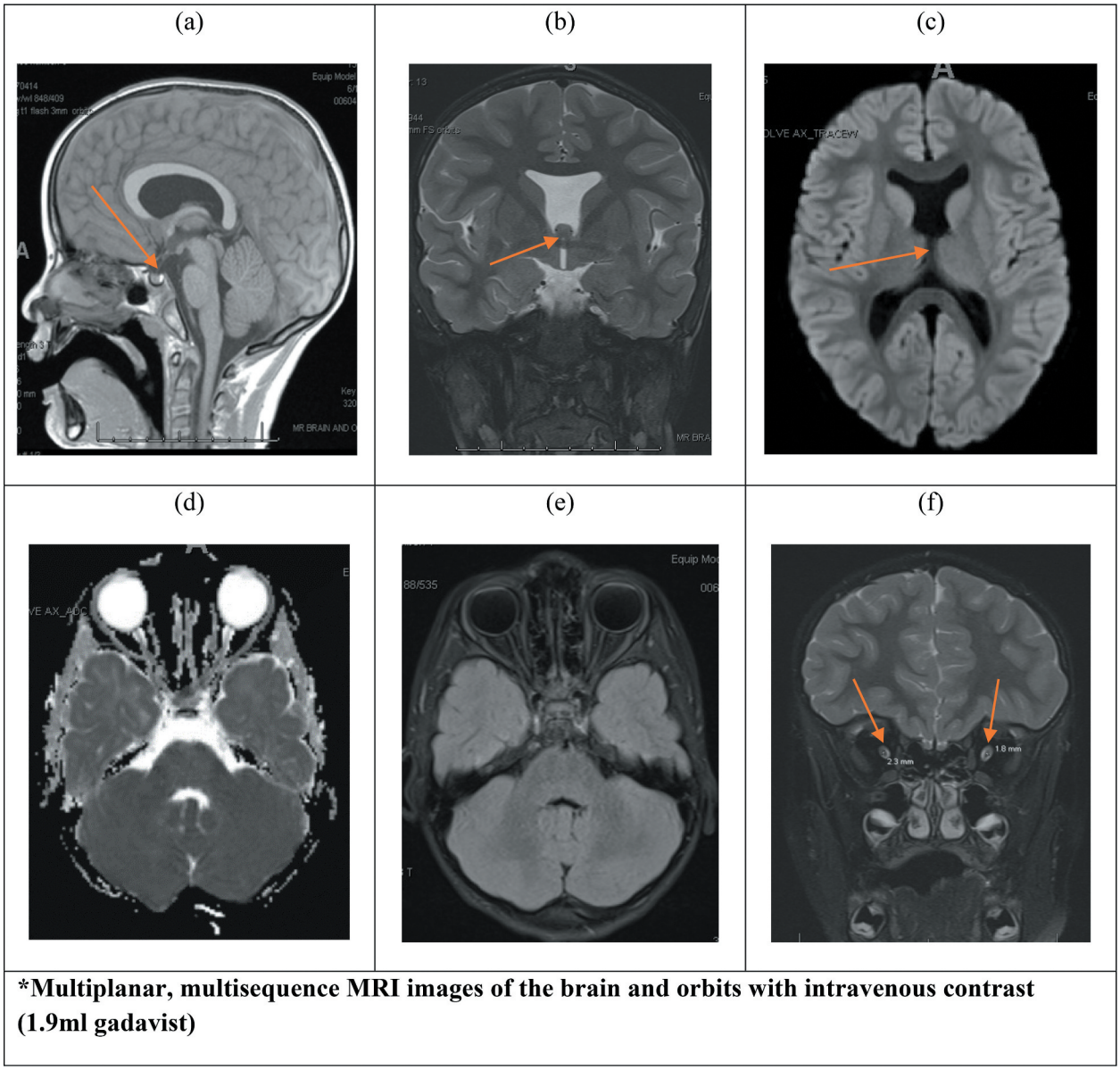
(Figure 5). Additional SOD-specific related gene panel, including GLI2, HESX1, OTX2, PAX6, PROP1, SOX2, SOX3, and TAX1BP3 genes, was negative.

Monocular flash VEP tests produced larger amplitudes on the occiput ipsilateral to the stimulated eye. These findings were consistent with chiasmal dysfunction or hypoplasia (Figure 6). Although the amplitude of the patient's flash VEP is low compared to the albino example, flash VEPs can show high inter-individual variability in size and waveform.

Paediatric neurology and endocrinology were followed up. Pediatric neurology agreed with the diagnosis of SOD. The risks of seizures were discussed but deemed to be relatively low. Pediatric endocrinology ordered lab values for Insulin-Like Growth Factor, IFG Binding Protein 3, TSH, Free T4, BMP, ACTH, and Cortisol and reported normal per mom.

In parallel, the child had a 293 gene panel for genes associated with inherited retinal disorders and nystagmus (Invitae Laboratory). This testing identified one pathogenic variant and one variant of uncertain significance in the *SLC45A2*. The SCL45A2 gene is associated with autosomal recessive oculocutaneous albinism type 4 (OCA4). The c.987del (p.Ala330Profs*68) pathogenic variant and the c.987C>G (p.Thr329Arg) variant of uncertain significance were confirmed to be on the same chromosome (in cis). Therefore, this individual is a carrier for autosomal

MRI



***Multiplanar, multisequence MRI images of the brain and orbits with intravenous contrast (1.9ml gadavist)**

Figure 5. (a) Normal pituitary gland atrophy as shown by the arrow. (b) Low-lying fused fornices as shown by the arrow with no midline shift or hydrocephalus. (c) Absence of a septum pellucidum as shown by the arrow. (d, e) Hypoplastic optic chiasm, nerves, and tracts. (f) Diameter measurement of the optic nerves exemplifies hypoplasia as shown by the arrows.

recessive SLC45A2-related conditions. Additionally, the patient did have sequencing and deletion/duplication analysis of the OCA2 gene included on his IRD panel and no variants in OCA2 were identified. Testing for Angelman syndrome and Prader–Willi syndrome was not performed as there was no clinical suspicion for these conditions at the time of evaluation. It should be further addressed that the patient can verbalize and carry out a conversation. This would also contribute against the suspicion for Angelman syndrome.

Discussion

The clinical presentation and eventual diagnosis of septo-optic dysplasia in this child was complex. The family history of "lazy eye" and parental concerns regarding infantile esotropia and nystagmus triggered further ophthalmological examination. The patient's fair skin and light-colored hair, blond fundi, and decreased foveal contour (although no transillumination defects) led to suspicions of oculocutaneous albinism to explain the child's development of nystagmus, strabismus, and mild photophobia.

The optic nerves did not have the double-ring sign that usually alerts to the possibility of SOD, instead the blurry disc margins, without any drusen on ultrasound imaging raised concerns about raised ICP and prompted an LP that was normal. It should be noted that prolonged ICP monitoring was not carried out and only a lumbar puncture was performed. MRI brain imaging showed 2 of the 3 MRI features consistent with the diagnosis of SOD, with hypoplasia of the left optic nerve, borderline hypoplastic right optic nerve (12), chiasm, and tracts and absent septum pellucidum, but he did

VEP

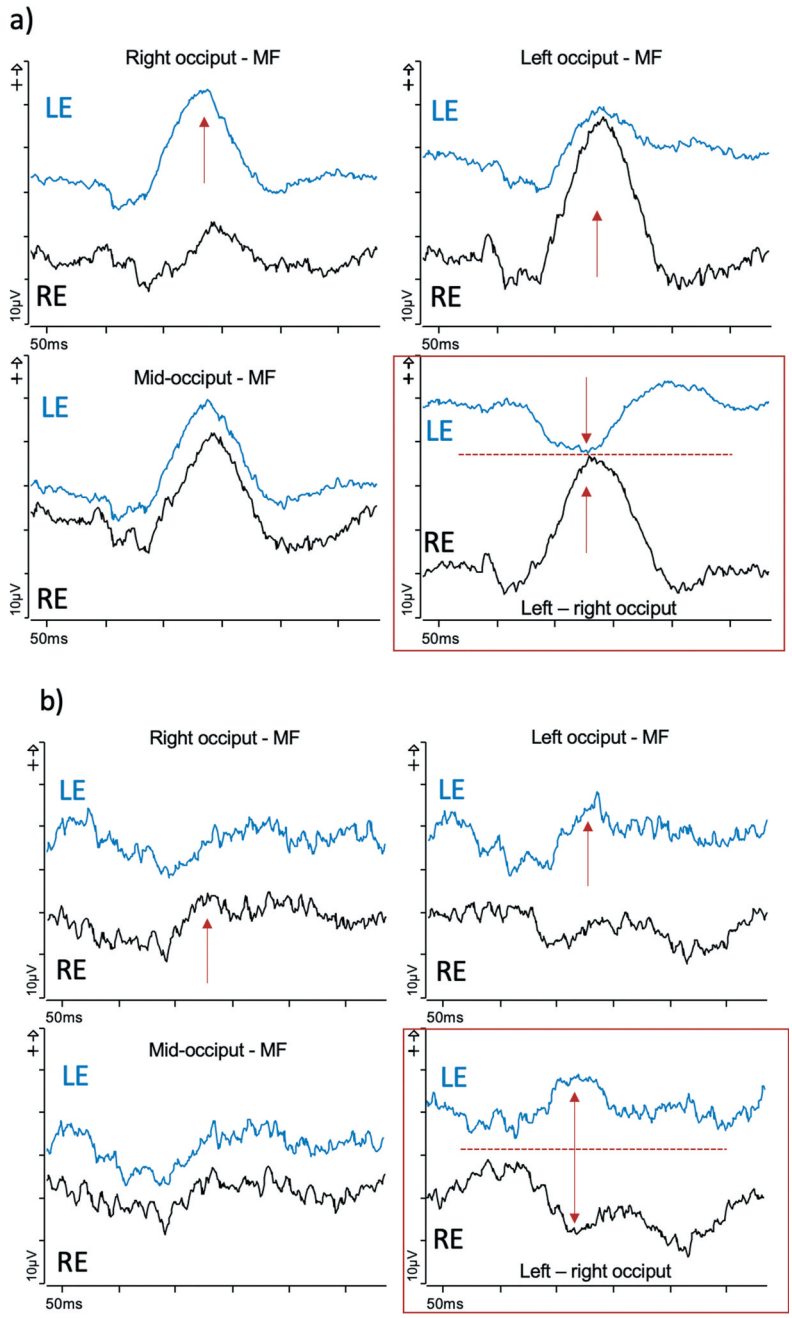


Figure 6. These are flash VEP recordings from two different patients. a) A child with albinism compared to b) our patient with chiasmal hypoplasia. The traces show flash VEPs recorded as they appear on electrodes placed over the right, mid, and left occiput. These active electrodes are referenced to the mid frontal electrode (mf). Traces from the OS/LE are shown in blue, from the OD/RE in black. In both patients, the mid occipital flash VEPs look similar from each eye, but on the lateral channels, the size of the VEP changes depending upon which eye is stimulated. This difference is enhanced by a subtraction of the right occiput from the left occiput displayed in the red boxes. The dotted line shows how the maximal response flips depending on eye stimulated termed a crossed asymmetry. The direction of the "flip" is opposite in case a) a child with albinism and case b) our patient who has chiasmal hypoplasia. In detail: (a) The trans-occipital distribution of monocular flash VEPs in a child with albinism is because too many RGC axons from OD/RE cross over at the chiasm to the contralateral left hemisphere. When the RE is stimulated, the largest VEP peak is on the left occiput. And vice versa for the LE. The difference of lateral channels shows a crossed asymmetry. The dotted red line simply highlights the flip of polarity. (b) Our patient has smaller amplitude flash VEPs and the VEP peaks are larger on the same occiput as the stimulated eye such as when the OD/RE is stimulated the largest VEP peak is on the right occiput. This provides an opposite pattern of crossed asymmetry (in red box) to case a). This indicates a paucity of chiasmal crossing fibers or achiasmia or chiasmal dysfunction. The trans-occipital distribution of flash VEPs in albinism compared to chiasmal hypoplasia

not have signs of pituitary atrophy. Due to the patient's unusual appearance/presentation, it should be emphasized that the diagnosis of SOD was delayed to the age of 4, despite previous ophthalmological examination.

This patient contributes to the phenotypic diversity reported in SOD. The absence of pituitary atrophy suggests a less likely involvement of the *HEX1* and *SOX2* genes as seen in some SOD patients.

Blurred disc margins are a rare finding in SOD. There is one case reported on a 13-year-old male who presented with sudden vision loss and papilledema that was noted on fundus examination. The papilledema was mild and short in duration; however, he developed sudden deterioration of visual acuity over the span of a few days, which is not the typical presentation of SOD (13). There were no other associated neurological deficits. The papilledema of this patient was related to a shunt malformation with an excessive fluid collection in the subdural region in the presence of an open lip schizencephaly (13). It has been noted that there is an existence between schizencephaly and SOD. The relation is uncommon yet a known finding that may be related to the primary defect leading to schizencephaly (14). In our case, the lumbar puncture revealed normal intracranial pressure. The opening pressure was measured at pCO_2 at 30 kPA—12 cm of H_2O. The ultrasound ruled out optic nerve drusen that could have the appearance of optic disc edema. The MRI had the findings described for SOD, but Schizencephaly was not present. It is unknown why this patient did not have the typical double ring sign and why the optic nerves had blurred disc margins, with normal intracranial pressure and no ON drusen.

The patient also had foveal hypoplasia, along with ONH. A study conducted on 16 ONH patients found that more than 80% also had foveal hypoplasia (15). A subset of those patients were also found to have SOD. A case report on a 12-year-old female additionally found the strange coexistence of SOD with ONH, septum pellucidum agenesis, and fovea plana (16). Interestingly, ONH and fovea hypoplasia are commonly associated with other ophthalmic disorders, such as ocular albinism (17).

The monocular flash VEPs were consistent with chiasm dysfunction or hypoplasia with the largest positive peaks over the same hemisphere as the stimulated eye. This contrasts with the chiasmal misrouting of too many crossing fibres in albinism, which produces larger flash VEP amplitude on the occiput opposite to the stimulated eye, such as a larger OS VEP amplitude over the right hemisphere, and over the left hemisphere for the OD. It is worth noting, however, that the visual system and VEP components are still maturing at age 5 (Figure 5). In albinism, visual inspection of VEPs provides sensitivity of 86% and specificity of 81% (18), while mean sensitivity of 80% for detecting chiasmal causes of bitemporal hemianopia (19).

There was a high index of clinical suspicion that this child had oculocutaneous albinism, he scored 3.5/6 on a recently developed clinical albinism score (20) which encompasses six variables including the presence of nystagmus, iris transillumination defects, visual acuity, optic nerve anomalies, foveal hypoplasia (fundoscopy), and foveal hypoplasia (OCT). The clinical albinism score does not lead to a diagnosis, however, and a genetic analysis must be performed. Only a single pathogenic variant was identified in the *SLC45A2* gene. Parental genetic testing and examination were not performed. However, the genetic testing technology confirmed that the patient's pathogenic variant and VUS in SLC45A2 are on the same allele (in cis). Copy number variants (CNV) analysis via next-generation sequencing was performed for the *SLC45A2* gene and was negative for a variant on the second allele. While it is possible that the patient could have a second unidentifiable pathogenic variant on their other *SLC45A2* allele, at this time, the patient is considered a carrier of autosomal recessive SLC45A2-related disorders. The *SLC45A2* gene encodes a transporter protein that mediates melanin synthesis. Biallelic pathogenic variants in this gene are a cause of oculocutaneous albinism type 4, and polymorphisms in this gene are associated with variations in skin and hair color (21). Carriers of *SCL45A2*-related oculocutaneous albinism type 4 can exhibit lighter complexion and pigmentation than is typical for their ethnic group (22). In addition, some of the children showed severe hypopigmentation with white hair and blue eyes (22). Our patient does have lighter complexion and light hair, but whether this is due to being a carrier for oculocutaneous albinism type 4 or attributed to his ethnic background cannot be determined. In addition, a SOD-specific related gene panel did not show any variants in the genes specifically associated with SOD, though it is known that <1% have a genetic diagnosis.

Conclusion

Our case adds to our knowledge of the phenotypic spectrum of children with SOD with the finding of pseudo-disc edema, in the absence of the typical optic nerve double ring sign, normal intracranial pressure, and no optic disc drusen. The MRI was key in the diagnosis with findings of absence of the septum pellucidum, hypoplasia of optic chiasm, optic nerves, and tracts, but without pituitary abnormalities, which are often associated with SOD. In addition, the findings of foveal hypoplasia and blond fundus lead to the suspicion of OCA either as a separate diagnosis with a second pathogenic variant in *SCL45A2* not yet identified contributing to the patient's symptoms or in association with SOD. This case highlights the importance of electrophysiology to help distinguish chiasmal hypoplasia or dysfunction from OCA misrouting.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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References

1. Septo-optic dysplasia. Genetics home reference. 2010 Retrieved June 8, 2021, from March. http://ghr.nlm.nih.gov/condition/septo-optic-dysplasia.
2. Jordan M, Montezuma SR. Septo-optic dysplasia associated with congenital persistent fetal vasculature, retinal detachment and gastroschisis. Retin Cases Brief Rep. 2015;9(2):123–26. doi:10.1097/ICB.0000000000000113.
3. Patel L, and McNally RJ et al. Geographical distribution of optic nerve hypoplasia and septo-optic dysplasia in Northwest England. J Pediatr. 2006;148:85–88.

4. Ganau M, Huet S, Syrmos N, Meloni M, Jayamohan J. Neuro-ophthalmological manifestations of septo-optic dysplasia: current perspectives. Eye Brain. 2019;11:37–47. doi:10.2147/EB.S186307.
5. McCabe MJ, Alatzoglou KS, Dattani MT. 2011. Septo-optic dysplasia and other midline defects: the role of transcription factors: HESX1 and beyond. Best Pract Res Clin Endocrinol Metab. 25 (1):115–24. doi:10.1016/j.beem.2010.06.008.
6. McNay DE, Turton JP, Kelberman D, Woods KS, Brauner R, Papadimitriou A, Keller E, Keller A, Haufs N, Krude H, et al. HESX1 mutations are an uncommon cause of septo-optic dysplasia and hypopituitarism. J Clin Endocrinol Metab. 2007;92:691–97. doi:10.1210/jc.2006-1609.
7. Kelberman D, and de Castro SC , et al. SOX2 plays a critical role in the pituitary, forebrain and eye during human embryonic development. J Clin Endocrinol Metab. 2008;93:1865–73.
8. Saranac L, Gucev Z. New insights into septo-optic dysplasia. Pril (Makedon Akad Nauk Umet Odd Med Nauki). 2014;35(1):123–27. PMID: 24802313.
9. Webb EA, Dattani MT. 2010. Septo-optic dysplasia. Euro J Hum Genet. 18(4):393–97. doi:10.1038/ejhg.2009.125.
10. Hellstrom A, Aronsson M, Axelson C, Kyllerman M, Kopp S, Steffenburg S, Strömland K, Westphal O, Wiklund L, Albertsson Wikland K, et al. Children with septo-optic dysplasia – how to improve and sharpen the diagnosis. Horm Res. 2000;53(Suppl1):19–25. doi:10.1159/000053200.
11. Pennesi ME, and Stover NB , et al. Abstracts: XLVII ISCEV international symposium. Documenta Ophthalmologica. 2009;119(S1):17–92. doi:10.1007/s10633-009-9182-9.
12. Al-Haddad CE, Sebaaly MG, Tutunji RN, Mehanna CJ, Saaybi SR, Khamis AM, Hourani RG. Optic nerve measurement on MRI in the pediatric population: normative values and correlations. AJNR Am J Neuroradiol. 2018 Feb;39(2):369–74. doi:10.3174/ajnr.A5456. Epub 2017 Dec 7. PMID: 29217740; PMCID: PMC7410600.
13. Masri AT, Abu-Libdeh AM, Ababneh OH, Al-Hadidy AM. Septo-optic dysplasia syndrome with schizencephaly and sudden visual loss. A new observation. Neurosciences (Riyadh). 2011 Jul;16 (3):281–82.PMID: 21677624.
14. Fadakar K, Dadkhahfar S, Esmaeili A, Keyhanidoust Z. A case of schizencephaly and septo-optic dysplasia presenting with anterior encephalocele. Iran J Child Neurol. 2012;6(4):47–50.
15. Pilat A, Sibley D, McLean RJ, Proudlock FA, Gottlob I. 2015. High-resolution imaging of the optic nerve and retina in optic nerve hypoplasia. Ophthalmology. 122(7):1330–39. doi:10.1016/j.ophtha.2015.03.020.
16. Keles A, Ilhan C, Teke MY, Tekin K. Septo-optic dysplasia with fovea plana: a case report. Eur J Ophthalmol. 2020;30(5):NP36–NP40. doi:10.1177/1120672120934961.
17. Garcia-Filion P, Borchert M. Optic nerve hypoplasia syndrome: a review of the epidemiology and clinical associations. Curr Treat Options Neurol. 2013;15(1):78–89. doi:10.1007/s11940-012-0209-2.
18. Soong F, Levin AV, Westall CA. 2000. Comparison of techniques for detecting visually evoked potential asymmetry in albinism. J AAPOS. 4(5):302–10. doi:10.1067/mpa.2000.107901.
19. Handley SE, Šuštar M, Tekavčič Pompe M. 2021. What can visual electrophysiology tell about possible visual-field defects in paediatric patients. Eye (London, England). 35(9):2354–73. doi:10.1038/s41433-021-01680-1.
20. Dorey SE, Neveu MM, Burton LC, Sloper JJ, Holder GE. 2003. The clinical features of albinism and their correlation with visual evoked potentials. Br J Ophthalmol. 87(6):767–72. doi:10.1136/bjo.87.6.767.
21. Sengupta M, Chaki M, Arti N, Ray K. SLC45A2 variations in Indian oculocutaneous albinism patients. Mol Vis. 2007;13:1406–11.
22. Hayashi M, and Suzuki T. Oculocutaneous albinism type 4. In: Adam MP, and Ardinger HH et al., editors. GeneReviews® [Internet]. Seattle: University of Washington, Seattle;2005 Nov 17 Updated 2017 Sep 7. p. 1993–2021.