

Acute idiopathic blind spot enlargement syndrome (AIBSES) with retinal vasculitis

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ABSTRACT

Purpose: To report the clinical and anatomical features of an unusual case of acute idiopathic blind spot enlargement syndrome (AIBSES) with retinal vasculitis.

Observations: A 39-year-old patient, who was a known case of chronic headache with nonspecific visual symptoms for nine years, developed scotomas in her right eye. She was initially diagnosed with AIBSES which had been stable, but later worsened with symptoms of subsequent blind spot enlargement and photopsia on the left eye a year later. Increase in the size of the blind spot over the left eye and stability of the blind spot enlargement over the right eye was documented on Humphrey visual field (HVF) testing. Due to the rapid onset and severity of symptoms, an inflammatory etiology was entertained and this prompted referral to our clinic. At initial presentation, fluorescein angiogram (FA) revealed moderate diffuse vasculitis and disc leakage in the left eye, which existed alongside the enlarged blind spot. Corticosteroid treatment was suggested and initiated. The patient was found to have a reduction in the size of her blind spot and a decrease in severity of retinal vasculitis a month later. Unfortunately, the patient was then lost to follow up and had stopped steroid treatment of her own accord. After nine months without treatment, the patient's blind spot increased to a larger size than her initial presentation, as documented on HVF, with recurrence of vasculitis in the left eye.

Conclusion and Importance: This is an unusual case of AIBSES which presented with vasculitis and rapid progression and has responded to steroids. Though monocular AIBSES has been shown to later affect the contralateral eye, concurrent vasculitis with AIBSES has not previously been reported. Furthermore, the response to treatment with reduction in blind spot enlargement is unusual for AIBSES. These findings stress the need for regular monitoring in cases of AIBSES.

1. Introduction

Acute idiopathic blind spot enlargement syndrome (AIBSES) is an acute outer retinopathy of unknown origin. In previous reports, it typically presents in middle-aged Caucasian women with a unilateral enlarged blind spot and photopsia. Fundus examination may reveal no abnormalities with documented retinal findings being nonspecific including: optic nerve swelling, peripapillary retinal pigment epithelium (RPE) or choroidal defects, white dots, peripheral RPE changes and macular pigment mottling.^{1–3} The use of various imaging modalities is often essential for diagnosis. Visual field testing is pivotal in order to

establish enlargement of the blind spot to make the diagnosis. Though the size of the blind spot enlargement may be variable, it presents with steeply identifiable margins on testing.¹ Fluorescein angiography (FA) typically shows peripapillary hyperfluorescence during the early stage. Optical coherence tomography (OCT) displays defects in the IS/OS junction and the cone outer segment tip (COST) line involving the peripapillary region extending towards the macula.^{4–6} Finally, multifocal electroretinography (mf-ERG) may be employed and shows attenuated responses around the area of the normal blind spot.^{1,2,5}

The etiology of AIBSES remains unclear, but it may be associated with disruption of the ellipsoid zone (EZ), which can be identified on

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OCT.⁴ The theory that EZ disruption may be linked to AIBSES is strengthened by a recent case report that showed clinical improvement in a case of AIBSES, which corresponded with recovery of the peripapillary to perifoveal EZ on OCT.⁴ There is currently no consensus on the recommendation for treatment for AIBSES.

In this report, we present an unusual case of AIBSES that presented with worsening blind spot enlargement as well as posterior pole inflammatory findings that was responsive to anti-inflammatory therapy.

1.1. Case report

A 39-year-old female presented in August 2018 for evaluation of ocular symptoms involving a scotoma associated with photopsia in the left eye (OS) for 3–4 weeks as well as complaints of floaters OS which had persisted for over 2 months. The patient's past medical and surgical history included incidences of deep vein thrombosis, cholelithiasis, and migraine, as well as past LASIK and hysterectomy. The patient had also been on topiramate intermittently for chronic migraine since 2011.

The patient's ocular history dated back to 2011, when she first developed symptoms of migraine and nonspecific blurring of vision. At that time, the patient was diagnosed with pseudotumor cerebri, but underwent a lumbar puncture, which had a normal opening pressure and no significant findings. The patient was then lost to follow-up for multiple years.

In April of 2017, the patient visited an ophthalmologist with complaints of a scotoma in her right eye (OD) accompanied with photopsia. There was observed afferent pupillary defect (APD) and optic nerve head swelling at the time. A diagnosis of acute idiopathic blind spot enlargement syndrome (AIBSES) was established in September of 2017 based on Humphrey visual field (HVF) testing. The symptoms were initially stable, but later she experienced worsening with new symptoms of a blind spot OS, as documented by HVF in July 2018, along with photopsia and migraine. The patient was restarted on topiramate for migraine and referred to our clinic to rule out a possible inflammatory component.

On examination, the patient's best corrected visual acuity (BCVA) was 20/20 in both eyes (OU). Pupils were round and reactive to light with no APD and intraocular pressure was within normal limits OU. Slit-lamp examination demonstrated unremarkable anterior chamber findings with no evidence of current or previous inflammation OU. Dilated fundus examination revealed no abnormalities OD but showed 1+ vitreous cells and 0.5+ vitreous haze with mild optic disc edema and blurred disc margins OS. In addition, perivascular sheathing was observed OS. Clinical findings were documented using wide field imaging (Fig. 1).

Fluorescein angiography (FA) showed granular peripapillary

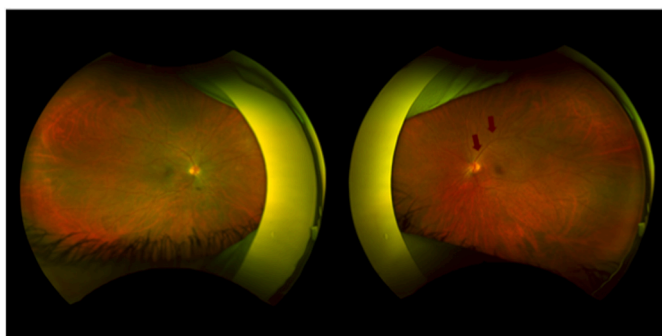


Fig. 1. Wide field fundus images were taken at presentation. No abnormalities OD. Image taken OS shows mild disc edema, blurred disc margins and perivascular sheathing (red arrows). Description based on clinical findings. Angiographic evidence of disc and vascular leakage supports wide-field images and clinical findings. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

staining extending nasally and inferiorly to the mid-periphery with no vascular leakage OD, and mild optic disc staining and leakage as well as diffuse leakage from venules in the posterior pole and periphery OS. No leakage was observed in the macula OU (Fig. 2-A). These findings were consistent with retinal vasculitis OS. Fundus autofluorescence (FAF) images revealed peripapillary hypo-autofluorescence involving 360° around the disk in OD, and peripapillary patchy hyper-autofluorescence nasal, inferior, and temporal to the disc OS (Fig. 3). Optical coherence tomography (OCT) was unremarkable OD, but displayed peripapillary and perifoveal outer retinal irregularities involving the photoreceptors OS (Fig. 4). Humphrey visual field (HVF) testing showed moderate blind spot enlargement and superotemporal depressions OD and a substantially enlarged blind spot extending inferiorly OS (Fig. 5-A). Full-field electroretinograms (ff-ERG) were performed on both eyes and showed decreased a-wave amplitudes in combined rod and cone responses OU. Multifocal ERG (mf-ERG) was also performed on both eyes and showed reduced responses in the nasal fields OU. mf-ERG findings were

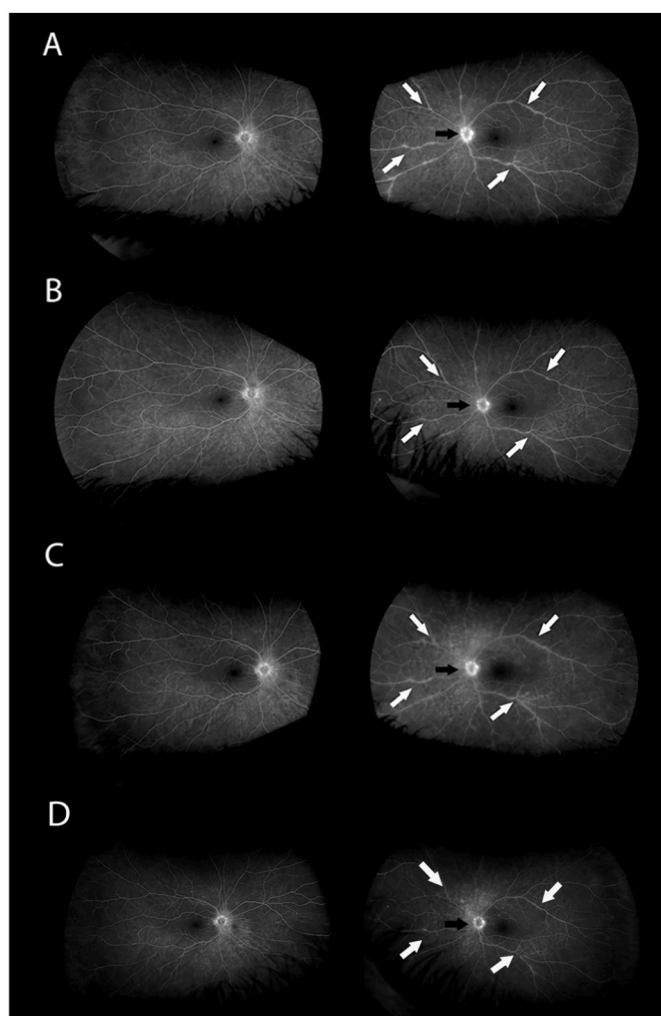


Fig. 2. Late phase fluorescein angiographs (FA) were taken in August 2018 before steroid therapy (A), September 2018 with steroid therapy (B), July 2019 after loss to follow up (C), and September 2019 after IV pulse steroid therapy (D). There is stability of right eye findings. The left eye, however, shows leakage of the optic disc (black arrows) as well as moderate diffuse retinal vasculitis (white arrows). Findings were improved with corticosteroid therapy (B). Unfortunately, a loss to follow up and cessation of treatment led to recurrence of symptoms with late stage FA of the left eye assuming a similar appearance to the initial presentation (C). Post IV pulse steroid therapy, there is noted improvement and reduction in leakage from the optic disc (black arrows) and the retinal vasculitis (white arrows).

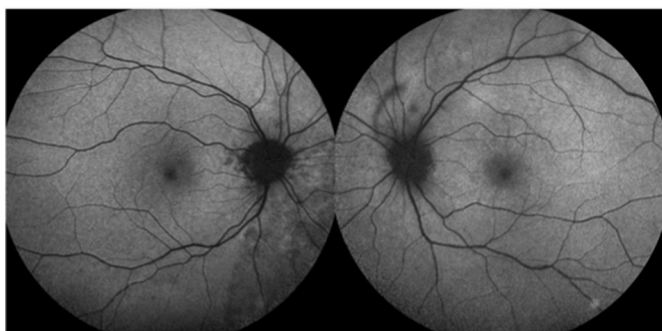


Fig. 3. Fundus autofluorescence (FAF) images showing peripapillary hypo-autofluorescence involving 360° of the disk OD. There is observable peripapillary patchy hyper-autofluorescence nasal, inferior, and temporal to the disc OS. There is also focal vitreous opacity visualized near the disc of the left eye, likely a vitreous floater as it was not pertinent clinically.

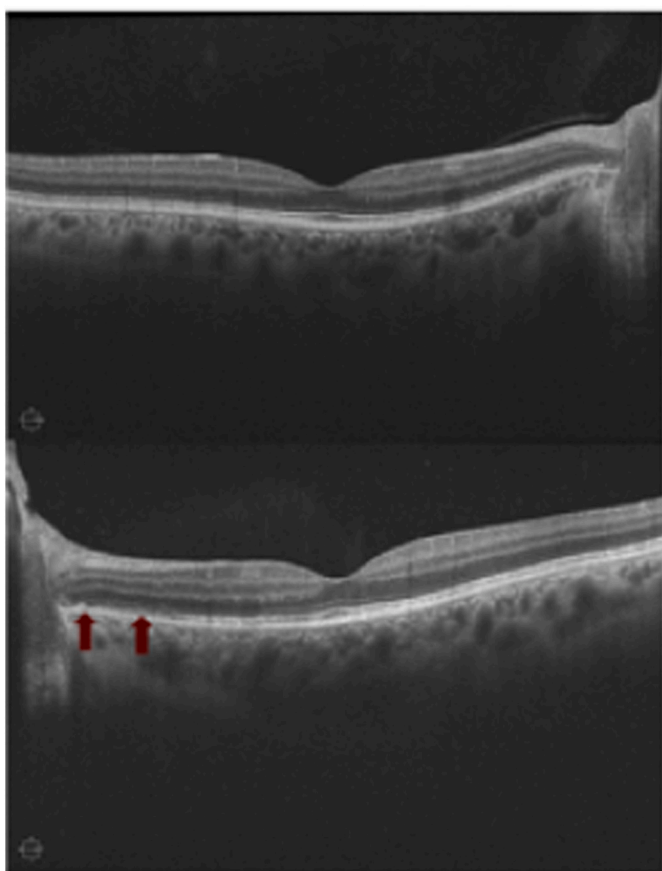


Fig. 4. Optical coherence tomography (OCT) taken at presentation is unremarkable OD. Images display peripapillary and perifoveal outer retinal irregularities including cone outer segment tip (COST) line OS.

compared with previous testing done in 2017 and had similar findings in the right eye, but newly found deficits in the left eye. Pattern-reversal visual evoked potential (VEP) showed a delay in P100 peak latencies OU.

Ancillary laboratory testing was done including complete blood count, comprehensive metabolic panel, liver function test, erythrocyte sedimentation test, C-reactive protein, angiotensin converting enzyme, lysozyme, lupus anticoagulant, antinuclear antibodies, anti-dsDNA antibodies, anti-neutrophil cytoplasmic antibodies and urine analysis. These tests were performed to rule out other potential systemic

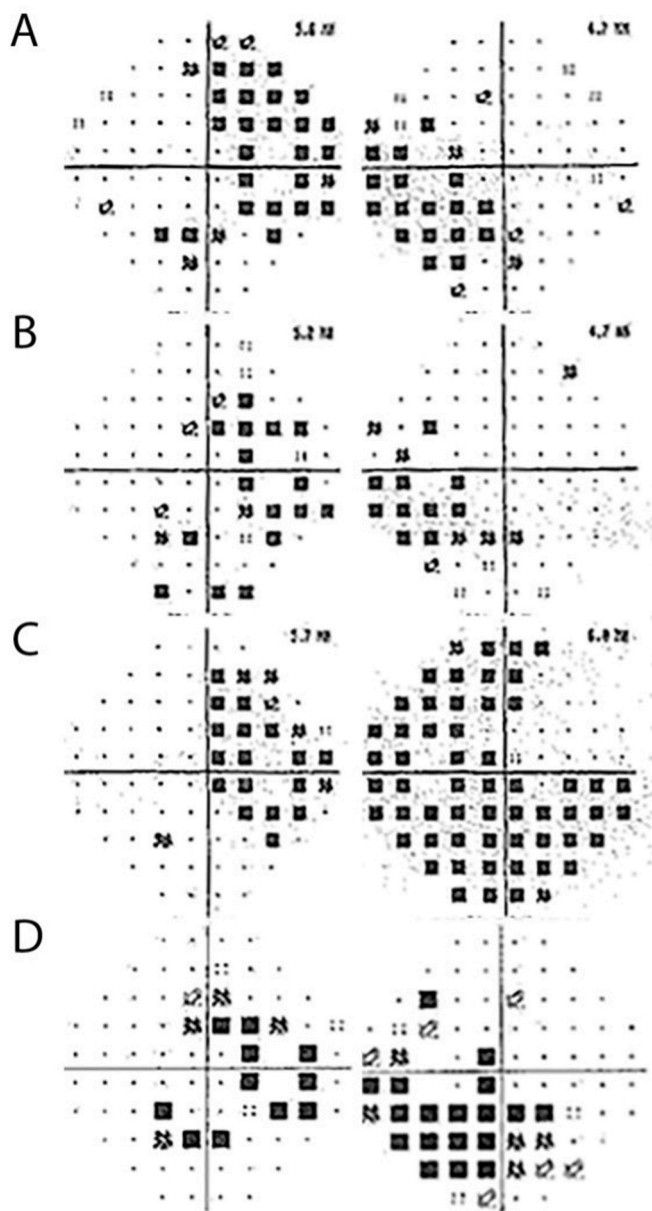


Fig. 5. Corrected pattern deviations in Humphrey Visual Fields (HVF) taken in August 2018 before steroid therapy (A), September 2018 with steroid therapy (B), July 2019 after loss to follow up (C), and September 2019 after IV pulse steroid therapy (D). There is an enlarged blind spot over the right eye which has remained relatively stable. The left eye, however, shows fluctuations in areas of visual field loss. There appeared to be minimal improvements post steroid therapy (B). However, after being lost to follow up, the patient developed severe progression of visual field defects (C) which have since shown improvement following IV pulse steroid therapy (D).

etiologies, such as systemic vasculitic conditions as well as infections that present with similar symptoms, to avoid missing any comorbid causes for the ocular manifestations. All were within normal limits. Additionally, testing for syphilis, Lyme disease, and tuberculosis were negative. No tests were performed to rule out retinal dystrophy, as there was no strong clinical suspicion or significant family history.

Based on the history of the patient, negative lab evaluations and abnormal ERG findings associated with the scotoma, initial diagnosis of AIBSES was made. The presence of a new onset scotoma which was worsening in addition to retinal vasculitis, however, led to the suggestion of starting the patient on oral steroids, which was initiated by the referring physician at 60mg daily on a rapid taper.

Follow-up testing was done in September 2018. FA performed after treatment showed clear improvement in the peripapillary and perivascular leakage associated with vasculitis (Fig. 2-B). HVF testing done after treatment also showed improvement in the previously noted visual field defects (Fig. 5-B).

The patient was then lost to follow-up for 9 months. During this time, she received no treatment for ocular issues and had discontinued steroids of her own accord but claimed that symptoms had initially been stable. Worsening of symptoms OS prompted the patient to return in early July of 2019. FA revealed that vasculitis, which had previously improved following prednisone treatment, had worsened, appearing similar to its initial severity (Fig. 2-C). HVF testing showed worsening of the blind spot OS, enlarging to cover most of her visual field (Fig. 5-C). The patient was placed on high dose IV pulse corticosteroid therapy.

In September 2019, the patient followed up after receiving three cycles of the steroid therapy. She noted improved vision in her left eye. FA showed substantial decrease in both disc leakage and retinal vasculitis in the left eye (Fig. 2-D). HVF likewise demonstrated improvement in the visual field of the left eye (Fig. 5-D).

The patient is currently continuing high dose IV pulse corticosteroid therapy with plans of placing her on a steroid sparing agent if needed on future follow up.

2. Discussion

AIBSES was first described by Fletcher et al., in 1988. They presented a series of seven patients, predominantly female, who showed an enlarged blind spot with normal fundus exam findings or with juxta-papillary retinal pigment changes that were not severe enough to cause these visual symptoms.⁷ Since then, the diagnosis of AIBSES has been a controversial subject.

As early as 1991, blind spot enlargement has been linked to uveitis. Rosenberg was the first to report it in association with multifocal chorioiditis.⁸ In 1995, Jampol et al. proposed that AIBSES was a symptom of multiple evanescent white-dot syndrome (MEWDS).⁹ Gass et al. have postulated that AIBSES is a part of the acute zonal occult outer retinopathy (AZOOR) complex of diseases, which also includes MEWDS.¹⁰ On the other hand, Volpe et al. report AIBSES as a distinct entity due to the difference in presentation and outcome in AIBSES versus MEWDS and AZOOR.¹ AIBSES has also been reported linked to a history of inflammatory choroidal neovascular membrane in the contralateral eye.¹¹ Currently, diagnosis of AIBSES involves initially ruling out inflammatory conditions which may respond to targeted therapy. Blind spot enlargement in AIBSES is said to remain stable and is not usually treated. Cases of secondary AIBSES in patients with resolved incident of ocular uveitis has, however, been shown to respond to and improve after steroid treatment.¹²

Our patient presentation is very similar to those reported by Volpe et al. On initial presentation in August 2018, she presented with photopsia and an enlarging blind spot. The severity of her visual field deficits was out of proportion compared to ocular examination findings. Furthermore, the patient lacked many of the findings present in MEWDS, including white dots, macular pigment granularity, peripapillary pigment changes and recent flu-like illness. Likewise, she also lacked the findings found in AZOOR, which is characterized by progressive visual field loss, progressive ERG worsening, chronic photopsia and late RPE changes.¹ Additional laboratory examination was likewise nonrevealing for other infectious and noninfectious etiology. Because of these findings, the patient was diagnosed with AIBSES.

The presence of retinal vasculitis in our patient was a very interesting finding. To our knowledge, no cases of retinal vasculitis associated with AIBSES has been reported. In our patient, marked improvement of her retinal vasculitis OS was associated with regression of her enlarged blind spot.

Most patients with AIBSES have spontaneous resolution of photopsia with improvement in visual deficits. In our case, the patient had a

history of right eye visual complaints lasting nearly 10 years with a diagnosis of AIBSE OD which had been stable on monitoring for a year. Though it is known that AIBSE may affect the contralateral eye at a later date, the rapid worsening of vision accompanied by signs of posterior pole inflammation mentioned above, make the presentation unusual for AIBSES.⁷ This could represent two scenarios: either this is a case of AIBSES that increased in severity and presents with retinal vasculitis or this is a case of AIBSES with concurrent retinal vasculitis. Neither scenario has been reported in previous literature.

In addition, when treated with corticosteroids, the patient experienced improvement in her retinal vasculitis with reduction in the size of her blind spot OS. Moreover, when the patient ceased treatment with corticosteroids, ocular symptoms worsened. In the published literature, we could find no reported treatment of AIBSES, as generally photopsia resolved spontaneously and the blind spot remained enlarged, but stable.^{2,4}

Although there is no consensus on the standard method of AIBSES diagnosis, the use of multimodal imaging may assist in increasing the accuracy of the diagnosis and monitoring. Innovative methods for monitoring these patients continue to be pursued. A recent case report has demonstrated increased choriocapillary granularity around the optic disc on OCT angiography of an AIBSES patient, shedding some light on a possible new method to monitor the patients in whom using other modalities, such as FA, may not be feasible or may be contraindicated.¹³

This case illustrates the importance of regular monitoring of patients with AIBSES. Though the condition may be thought of as benign, regular monitoring may reveal subtle changes that may merit treatment. It is also important to address patient concerns as well as subjective worsening of scotomas that may be indicative of the development of worsening pathology. The diligence of the treating physician and the use of multimodal imaging may thus provide the AIBSES patient minimal discomfort, as well as prevent worsening either by the innate nature of this not well understood disease or by the development of secondary pathology which could potentially be left untreated otherwise.

3. Conclusion

In this report, we present a rare case of AIBSES with retinal vasculitis and worsening of the blind spot enlargement which has responded to steroid therapy. This presentation of AIBSES is atypical due to variability in the size of the patient's blind spot over time as well as associated posterior pole inflammation. This report highlights the importance of monitoring visual field defects and disease progression in AIBSES.

Patient consent

Patient consent was obtained, and the consent form is uploaded separately as a PDF file.

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Authorship

All authors attest that they meet the current ICMJE criteria.

Declaration of competing interest

The authors declare that there are no conflicts of interest related to this article.

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References

1. Volpe NJ, Rizzo 3rd JF, Lessell S. Acute idiopathic blind spot enlargement syndrome: a review of 27 new cases. *Arch Ophthalmol*. 2001;119:59–63.
2. Liu X, Chen B, Zhang M, Huang H. Clinical features and differential diagnosis of acute idiopathic blind spot enlargement syndrome. *Eye Sci*. 2014;29:143–150.
3. Watzke RC, Shults WT. Clinical features and natural history of the acute idiopathic enlarged blind spot syndrome. *Ophthalmology*. 2002;109:1326–1335.
4. Trese MGJ, Cohen SR, Besirli CG. Recovery of outer retina in acute idiopathic blind spot enlargement (AIBSE). *Am J Ophthalmol Case Rep*. 2016;1:13–15.
5. Piri N, Kaplan HJ, Sigford DK, Tezel TH. High-definition optical coherence tomography findings in acute idiopathic blind spot enlargement (AIBSE) syndrome. *Ocul Immunol Inflamm*. 2014;22:494–496.
6. Sugahara M, Shinoda K, Matsumoto SC, et al. Outer retinal microstructure in a case of acute idiopathic blind spot enlargement syndrome. *Case Rep Ophthalmol*. 2011;2:116–122.
7. Fletcher WA, Imes RK, Goodman D, Hoyt WF. Acute idiopathic blind spot enlargement. A big blind spot syndrome without optic disc edema. *Arch Ophthalmol*. 1988;106:44–49.
8. Khorram KD, Jampol LM, Rosenberg MA. Blind spot enlargement as a manifestation of multifocal choroiditis. *Arch Ophthalmol*. 1991;109:1403–1407.
9. Jampol LM, Wiredu A. MEWDS, MFC, PIC, AMN, AIBSE, and AZOOR: one disease or many? *Retina*. 1995;15:373–378.
10. Gass JD, Agarwal A, Scott IU. Acute zonal occult outer retinopathy: a long-term follow-up study. *Am J Ophthalmol*. 2002;134:329–339.
11. Macias-Murelaga B, Rodriguez-Agirretxe I, Bascaran L, Goni N, Mendicutie J. [Acute idiopathic blind spot enlargement syndrome associated with choroidal neovascularization]. *Arch Soc Esp Oftalmol*. 2013;88:450–452.
12. Jabbarpoor Bonyadi MH, Hassanpour K, Soheilian M. Recurrent focal choroidal excavation following multiple evanescent white dot syndrome (MEWDS) associated with acute idiopathic blind spot enlargement. *Int Ophthalmol*. 2018;38:815–821.
13. Gunasagaran HL, Waldie A, Xiao W, Moore P. Coarsening of choriocapillaris on optical coherence tomography angiography as a sign of acute idiopathic blind spot enlargement. *Am J Ophthalmol: Case Rep*. 2022;26, 101558.