Original Article

Clinical Features and Differential Diagnosis of Acute Idiopathic Blind Spot Enlargement Syndrome

Xiaocui Liu, Bing Chen, Maonian Zhang, Houbin Huang*

Department of Ophthalmology, Chinese PLA (People's Liberation Army) General Hospital, Beijing 100853, China

Abstract

Purpose: To study the clinical manifestations and the diagnostic and differential diagnostic characteristics of acute idiopathic blind spot enlargement syndrome (AIBSES).

Methods: Six patients diagnosed with AIBSES underwent complete eye examinations including fundus photography, fundus fluorescein angiography(FFA), indocyanine green angiography (ICGA), optical coherence tomography (OCT), electroretinogram (ERG), and visual field examinations.

Results: All patients had enlarged blind spots of variable sizes and densities. Three eyes had mild swelling of the optic disc and one eye had peripapillary scarring that corresponded to the permanent field defect. Two patients who underwent FFA had fluorescein leakage of blood vessels around the optic disc and ICGA highlighted diffuse, small hypofluorescent spots scattering throughout the posterior pole. OCT showed that the inner and outer segment (IS/OS) line were absent in five patients and the middle cone outer segment tip line was absent in the nasal macular area in one eye.

Conclusion: AIBSES is a rare outer retinopathy. Visual field examination and OCT are the most important means of detection. ICGA and FAF can determine the range of lesions earlier, and the progress of the disease should be taken into account when making a diagnosis.(***Eye Science 2014; 29:143–150***)

Keywords: retinal disease; perimetry; optical coherence tomography; indocyanine green angiography; fundus autofluorescence

Introduction

Acute idiopathic blind spot enlargement syndrome (AIBSES) is a rare outer retinopathy found mainly in middle-aged female subjects. It is characterized primarily by an acute monocular onset dark shadow accompanied by diminished light perception. Fundus examination reveals no abnormality and perimetry shows blind spot enlargement, while optical coher ence tomography (OCT) and electrophysiological examination reveal abnormal signs. At present, the etiology and pathogenesis of AIBSES remain elusive. Diagnosis is likely to be missed or the condition misdiagnosed because of a lack of specific pathological changes during the early stages.

Fletcher et al[1]. were the first to report a case of AIBSES. Since then, nearly 20 relevant studies have been reported abroad whereas no typical cases have appeared in China. In this study, six consecutive cases diagnosed with AIBSES as outpatients at our hospital were enrolled and their clinical data were comprehensively analyzed, providing clinical evidence for the early diagnosis and clinical staging of AIBSES.

Materials and methods

General data

Between June 2011 and September 2013, 6 patients were diagnosed with AIBSES by repeated examination as ophthalmology outpatients of the General Hospital of the People's Liberation Army. The subjects were 4 females and 2 males, aged from 10 to 41 years, 26 years on average. All cases were unilateral onset with courses of disease ranging from 1 week to 4 months. Myopia was found in 3 eyes, but no systemic diseases were present.

Ocular symptoms

All 6 patients presented with a black shadow in front of the eyes or slightly decreased visual acuity, accompanied by photopsia; a severe decline in visu-

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* **Corresponding author:** Houbin Huang, E-mail: huanghoubin@hotmail.com

Table 1 Basic clinical data of 6 patients with acute idiopathic blind spot enlargement syndrome

No.	Gender	Age	Chief complaints	Corrected visual acuity	Fundus examination
1	Female	22	Visual acuity (OS) decreased for 1 month	0.8	Mild swelling of optic disc (OS) and yellow–white macular focus
2	Male	10	Visual field defects (OS) accompanied by blurry vision for 1.5 months	0.1	Mild swelling of optic nerve and surrounding nerve fiber (OS)
3	Female	23	Blind spots in the frontal visual acuity for 1 week (OS)	1.0	High myopia, fundus alterations and peripapillary retinal white opacity (OS)
4	Female	41	Dark shadow in the left eye for 4 months	0.5	No obvious abnormality (OS)
5	Female	32	Dark shadow in the right eye for 1 month	1.0	High myopia, fundus alteration, peripapillary ring–like and temporal topical scars (OD)
6	Male	29	Visual field loss accompanied by micropsia for 2 weeks (OS)	0.4	Mild optic nerve swelling (OS)

al acuity was observed in only 1 eye, as illustrated in Table 1.

Examination methods

All 6 patients underwent a best corrected visual acuity test, slit-lamp examination, fundus examination, fundus photography, fundus autofluorescence (FAF), fluorescein fundus angiography (FFA), indocyanine green angiography (ICGA), OCT, and multifocal electroretinography (mfERG).

Results

Fundus condition

The onset time in 1 eye was 1 week, which was characterized as peripapillary white retinal opacity (Figure 1A), and 2 weeks in another eye presenting with mild swelling of the optic nerve revealed by

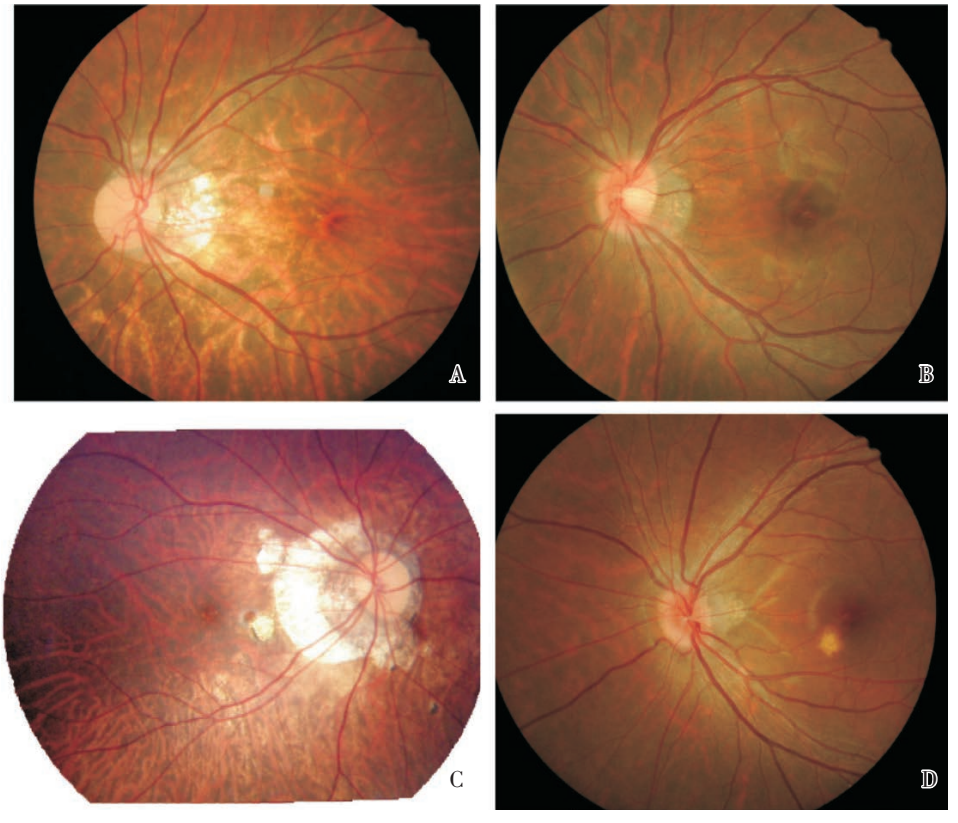

Figure 1 A.Fundus imaging of case 3 revealed mild white opacity in the peripapillary retina (OS); B.Fundus imaging of case 6 showed slight optic disc swelling (OS); C. Fundus imaging of case 5 revealed peripapillary ring-shaped and temporal topical scars (OD); D. Fundus imaging of case 1 showed mild optic disc swelling (OS) and yellow-white macular lesions.

fundus examination (Figure 1B). The onset time was 1–1.5 months in 3 eyes. Fundus examination revealed the signs of peripapillary ring-like and tempo ral focal scarring(Figure 1C), mild optic disc swelling and yellow-white macular focus in 1 eye (Figure 1D), and slight swelling of the optic nerve and surrounding nerve fiber. The onset time was 4 months in 1 eye, while no abnormality was detected by fundus examination.

Visual field examination

Blind spot enlargement was detected in all patients by perimetry (Figure 2A). A visual field defect was observed within the region from the temporal side to beneath the nose in 1 case (Figure 2B); a 60 degree visual field revealed a large scotoma at the temporal side involving with the area within central 5 degrees and outside central 50 degrees from the temporal side (Figure 2C). The patient had a visual acuity of 0.1 due to scotoma involvement with the central area, and this was restored to 1.0 after 4 months.

Fundus angiography

The onset time was within 2 weeks in 2 eyes. FFA revealed peripapillary fluorescence leakage during early stage (Figure 3A). ICGA showed many weak fluorescence spots adjacent to the optic disc during later stage (Figure 3B). FAF revealed enhanced peripapillary autofluorescence (Figure 3C). The onset time was 1 month in 2 eyes. FFA revealed optic disc staining during the advanced stage in 1 eye and somewhat strong peripapillary fluorescence. ICGA showed a weak fluorescence spot in the corresponding focus during the advanced stage. FAF revealed peripapillary autofluorescence enhancement (Figure 3D). ICGA showed weakly fluorescent spot scattering surrounding the optic disc and macular scarring (Figure 3E). The onset time was 1.5 months in 1 eye. FAF revealed enhanced peripapillary autofluorescence (Figure 3F). FFA revealed a large quantity of fluorescent spots within the region surrounding the optic nerve to the subretinal upper posterior polar area (Figure 3G). The onset time was 4 months in 1 eye. No abnormal changes in autofluorescence were observed (Figure 3H).

OCT and mfERG

OCT examination revealed pathological changes in the outer layer of the retina in all 6 patients. The onset time was 2 weeks in 1 eye and IS/OS defects were observed on OCT (Figure 4A). The onset time was 1 month in another eye. The IS/OS defects were seen. A bulky mass was observed between the outer layer of the temporal photoreceptors and the retinal pigment epithelium (RPE) and partial Bruch's membrane rupture was seen, as shown in Figure 4B. The onset time was 1.5 months in 1 eye. Peripapillary retinal IS/OS and COST defects were observed by OCT and outer membrane and outer nuclear layer atrophy were found (Figure 4C). The onset time of another eye was 4 months. Only macular COST defects were observed on OCT (Figure 4D). The mfERG revealed a lower macular intensity of response in the

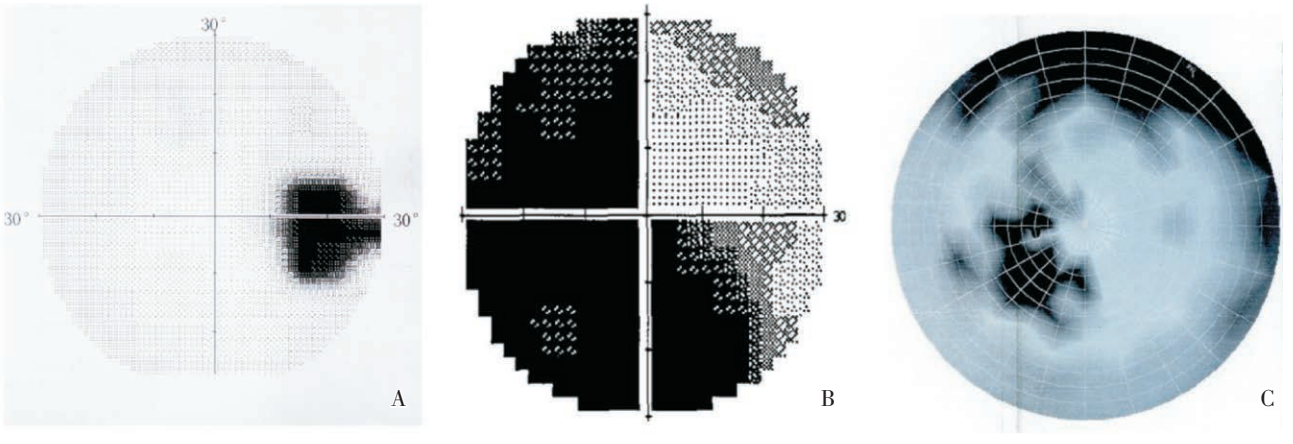

Figure 2 A. Perimetry of case 5 revealed blind spot enlargement; B. A visual field defect was observed within the region from the temporal side to beneath the nose (case 2, OS); C. A 60° visual field revealed a large scotoma at the temporal side involving with the area within central 5° and outside central 50° from the temporal side (case 2).

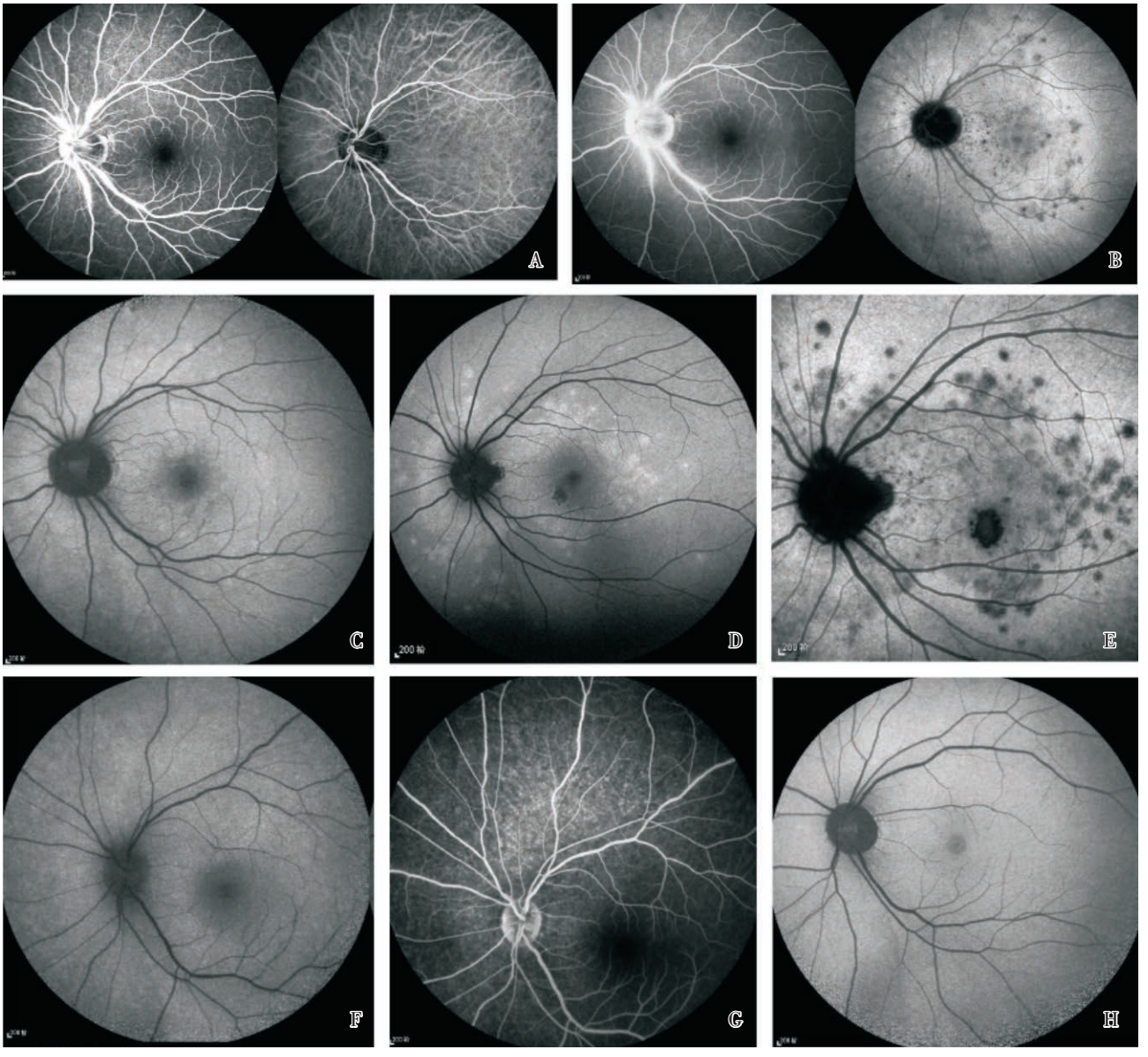

Figure 3 A. FFA of case 6 revealed peripapillary fluorescence leakage during early stage. B. ICGA of case 6 showed a bulk of weak fluorescence spots adjacent to the optic disc during late stage. C. FAF of case 6 revealed peripapillary autofluorescence enhancement; D. FAF of case 1 showed peripapillary autofluorescence enhancement; E. ICGA of case 1 revealed peripapillary diffusive weak fluorescence spots and macular scars during late stage; F.The onset time of case 2 was 1.5 months; FAF revealed mild peripapillary autofluorescence enhancement; G. FFA of case 2 revealed a large quantity of fluorescence spots within the region surrounding the optic disc to the subretinal upper posterior polar area; H. The onset time of case 4 was 4 months and no autofluorescence abnormality was observed.

affected eyes than in the fellow eyes (Figure 5).

Discussion

AIBSES is a rare ocular disease with an onset age between 10 and 57 years. It is consistently accompanied by moderate to high myopia, has a mainly unilateral onset, and occurs more frequently in females. Caucasians have a higher incidence of this disease compared with their Asian counterparts. It is not correlated with contact with felines or other animals[2,3]. The patients have a slight reduction in central visual acuity or even a decline below 0.1. In the present study, the patients' visual acuity ranged from 0.1 to 1.0, with an average of 0.6.

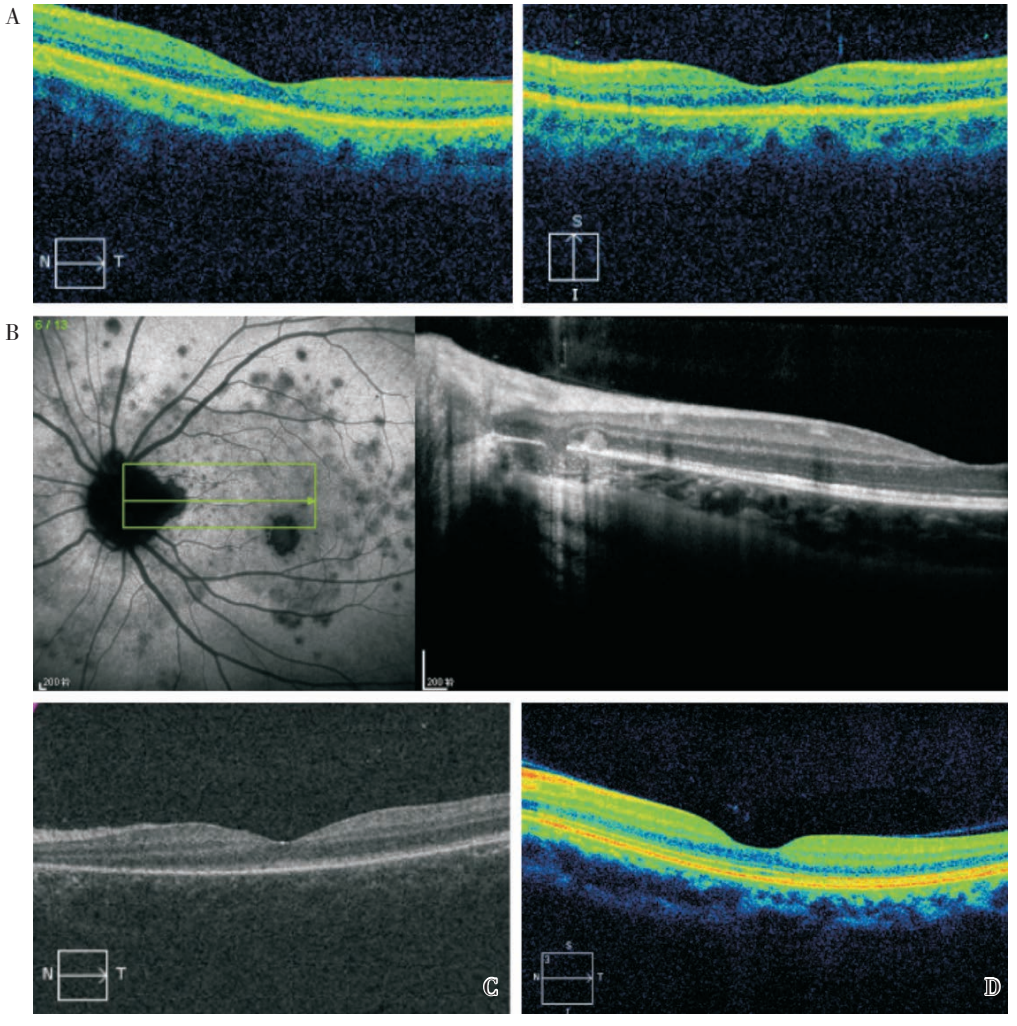

Figure 4 A. The onset time of case 6 was 2 weeks. OCT showed IS/OS defects; B. The onset time of case 1 was 1 month. OCT revealed IS/OS defects, a bulk of mass was observed between the outer layer of temporal photoreceptors and RPE and partial Bruch´s membrane rupture; C. The onset time of case 2 was 1.5 months. OCT revealed peripapillary retinal IS/OS and COST defects, outer membrane and outer nuclear layer atrophy; D. The onset time of case 4 was 4 months. OCT only showed macular COST defects.

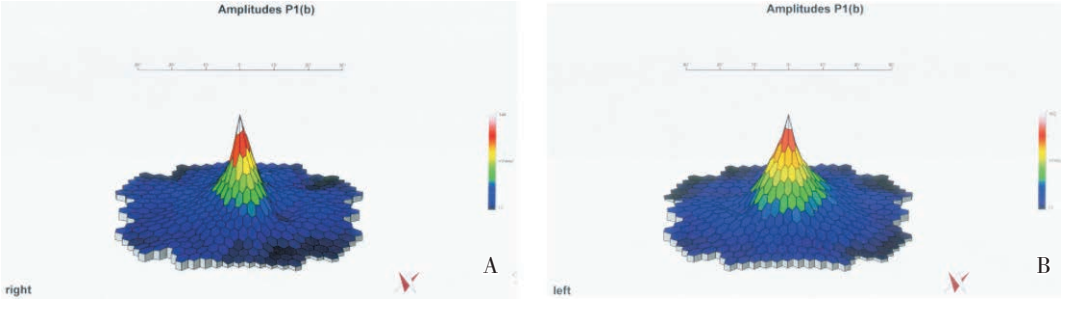

Figure 5 The mfERG of case 5 revealed a lower macular intensity of response in the right eyes than in the left eyes.

Fundus pathological changes during early stage AIBSES

Fundus examination revealed almost no abnormality. During the early stage, the following specific manifestations may occur: ① Some patients had optic disc swelling and bulging, and mild swelling in

Table 2 Special test results of 6 patients diagnosed with acute idiopathic blind spot enlargement syndrome

No.	Visual field test	FFA/ICGA test	Autofluorescence	OCT
1	Blind spot enlargement (OS)	ICGA found weak fluorescence spots scattering surrounding the optic disc and macular scarring (OS)	FAF revealed peripapillary autofluorescence enhancement (OS)	IS/OS defects, a bulk of mass was observed between the outer layer of temporal photoreceptors and RPE and partial Bruch's membrane rupture was seen.
2	Large scotoma at the temporal side involving with the area within central 5° and outside central 50° from the temporal side (OS)	FFA revealed a large quantity of fluorescence spots within the region surrounding the optic nerve to subretinal upper posterior polar (OS)	FAF revealed peripapillary autofluorescence enhancement (OS)	Peripapillary retinal IS/OS and COST defects were observed by OCT and outer membrane and outer nuclear layer atrophy was found
3	Blind spot enlargement (OS)	FFA revealed fluorescein leakage of blood vessels around the optic disc, ICGA highlighted a large bulk of peripapillary hypofluorescent spots	FAF revealed peripapillary autofluorescence enhancement (OS)	Retinal outer layer became thinner (OS)
4	Blind spot enlargement was located at the temporal side of the left eye, inferior temporal visual field defects with a maximal diameter >50°	No FFA abnormality (OS)	No abnormality (OS)	Macular COST defects (OS)
5	Blind spot enlargement (OD)	FFA revealed optic disc staining during advanced stage (OD), slightly strong peripapillary fluorescence. ICGA showed weak fluorescence spot in corresponding focus during late stage.	FAF revealed peripapillary autofluorescence enhancement (OD)	Retinal outer layer became thinner (OD)
6	Blind spot enlargement (OS)	FFA revealed fluorescein leakage of blood vessels around the optic disc, ICGA highlighted a large bulk of peripapillary hypofluorescent spots(OS)	FAF revealed peripapillary autofluorescence enhancement (OS)	IS/OS defects (OS)

the peripapillary nerve fiber layer[4]. In this study, the onset time was 2 weeks in 1 eye presenting with slight optic disc swelling, and 1 month in 1 eye, where mild swelling was observed in optic nerve and peripapillary nerve fiber layer. ② Slight hyperemia and plump periphery optic disc tissues appeared together with redness; sometimes this was merely characterized as slight hyperemia and fullness in optic disc periphery tissues(such as the temporal side). ③ White opacity in periphery optic nerve retina was observed, corresponding to blind spot enlargement induced by outer retinitis. This may be one common feature of AIBSES, where it occurred during the early stage (approximately within 1 week) and then disappeared rapidly. One patient suffered from this disease for 1 week. Consequently, white opacity was seen in the peripheral optic nerve retina. ④ During the early stage, peripapillary nodular lesions or peripapillary scars might be observed in some patients, characterized as choroidal capillary atrophy. As the

disease progresses, most patients could present with peripapillary ring-shaped or temporal topical scars. In this study, peripapillary ring-shaped scars were detected in 1 patient.⑤ Slight venous dilation, and vitreous cell and macular scars were observed in some cases[2].

Watzke et al[2]. retrospectively analyzed 25 patients with blind spot enlargement. The presence of acute unilateral blind spot enlargement within 2 weeks was complicated by choroidal changes. After the acute stage, optic nerve hyperemia and swelling, periphery optic nerve retinitis, and white retinal opacity were all alleviated. Herbort et al[5]. also found posterior polar abnormality during the early stage of AIBSES, whereas retinal defects in the advanced stage could be gradually alleviated.

Auxiliary eye examination

FFA revealed normal findings: peripapillary fluorescence leakage occurred during the early stage, along with optic disc staining and strong peripapillary fluorescence. No optic disc staining was observed during the advanced stage of pathological changes[2]. ICGA showed weak scattered fluorescent spots surrounding the entire posterior polar area. However, these lesions were not detected by FFA[6]. Consequently, ICGA had a higher accuracy in locating the lesions. ICGA showed weakly fluorescent peripapillary spots during the late stage in patients with onset times within 1.5 months. FAF revealed peripapillary autofluorescence enhancement at the early stage, which gradually declined after 2–4 weeks, suggesting that ICGA and FAF could show the range of lesions occurring at the early stage.

OCT revealed pathological changes in the outer layer of retina.Peripapillary retinal IS/OS and/or COST defects were observed in AIBSES patients[7]. A bulky mass (probably inflammatory exudation) was observed between the outer layer of temporal photoreceptors and the RPE, confirming peripapillary choroidal inflammation in AIBSES. Severe inflammation may lead to Bruch's membrane rupture. All cases in this study presented with pathological changes in the outer layer of the retina. IS/OS defects were observed in all eyes except one that merely had COST defects. A bulky mass was observed between the outer layer of the temporal photoreceptors and the RPE of one eye. Full-field ERG revealed normal amplitude, whereas several reports found that ERG declined at early onset or progressive stages[3,4]. Patients had abnormal bilateral first- and second-order mfERG responses, even if they were diagnosed with unilateral onset by subjective symptoms and objective examinations, which hinted at a higher accuracy of mfERG in locating retinal injury. Even after visual field recovery, mfERG abnormality still existed[8]. Consequently, mfERG could identify retinal dysfunction in subclinical settings, which would not be detected by visual field examination.

Diagnosis and differential diagnosis

Watzke et al[2]. proposed well-recognized diagnostic criteria: scotoma at the temporal side and surrounding optic disc; onset time within 2 weeks; clinical and FFA revealing normal results; or mild optic nerve swelling or hyperemia and only FFA showing peripapillary vascular fluorescence leakage and staining. The time of the examination is extremely important. During the early stage, certain characteristics, such as peripapillary outer retinitis and specific manifestations revealed by FAF and ICGA, may rapidly disappear or still exist at 2–4 weeks after onset[2]. If admission was delayed, blind spot enlargement might be found. The absence of ICGA and FAF abnormalities complicate the explicit diagnosis of AIBSES.

The identification of multiple evanescent white dot syndrome (MEWDS) depended upon the following: pathological changes were mainly located at peripheral or central peripheral vascular arch, equally involved with the posterior polar area rather than surrounding the optic nerve. The lesions of AIBSES were distributed adjacent to the optic disc. Multiple white dots were observed at the central periphery area during the early stage, but none were seen in AIBSES patients. ICGA revealed that the pathological changes were mainly distributed in spots, while no diffusive peripapillary lesions were seen during the acute stage. AIBSES patients had peripapillary lesions and spot lesions, which were invisible on fundus images. FFA showed weak fluorescence in white dots during the early stage and strong fluorescence in the late stage. FFA revealed no explicit ab-

normality or merely slight optic disc staining in AIBSES patients.

Clinical staging and prognosis

AIBSES is considered a primary inflammatory choriocapillaropathy (PICCP). However, its pathogenesis remains elusive. Inflammatory responses are hypothesized to induce peripapillary choriocapillar occlusion. The outer layer of the retinal barrier may cause blind spot enlargement and scotoma in the visual field[5]. According to the clinical data of previous and present studies, the pathogenesis of AIBSES could be divided into 4 phases: ① An acute inflam matory phase(approximately within 2 weeks), where slight acute inflammation of the peripapillary choriocapillar causes mild fundus changes. Patients in this study presented with optic disc edema, mild peripapillary nerve fiber swelling, peripapillary opacity in the outer layer of retina, and peripapillary ring-shaped or temporal topical scars. FFA showed no obvious alterations or only mild peripapillary venous fluorescence leakage. ICGA revealed diffusive weak fluorescence. FAF showed diffusive autofluorescence enhancement. OCT showed slight defects in the outer layer of the retina, such as COST defects or ab sence; ② An involuting inflammatory phase in which acute choriocapillary inflammation was gradually alleviated. FFA revealed slight transparent fluorescence induced by RPE defects. In the present study, OCT showed IS/OS and outer membrane rupture or absence. ③ A chronic phase, where the lesions progressed. No obvious manifestations were revealed by FFA and ICGA, whereas OCT showed the loss or thinning of the outer layer of the retina. ④ A recovery phase where, at 3–4 months, OCT showed that the outer layer pathological changes were steadily repaired. The visual function of the patients also gradually improved.

Most AIBSES patients had recovered from their visual symptoms at 3–4 months; their visual acuity gradually improved and photopsia was alleviated. However, these symptoms persisted for a longer time in certain patients. Even in patients with no symptoms, blind spot enlargement accompanied with peripapillary scars might be observed. Visual field defects and ICGA abnormality were gradually alleviated after 4 weeks. Almost half of the patients with visual field defects progressed and 25% of them had a recurrence[8].

In summary, blind spot enlargement in AIBSES cases does not result from optic disc swelling or optic nerve diseases, but is probably due to a functional barrier in the retinal outer layer induced by peripapillary choriocapillar lesions. Not all cases of outer layer retinopathy accompanied by blind spot enlargement are AIBSES. Ophthalmologists should understand the basic clinical characteristics of AIBSES and take the course of the disease into account when making a diagnosis in order to avoid misdiagnosis and missed diagnosis.

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