Acute Idiopathic Blind Spot Enlargement Syndrome

A Review of 27 New Cases

Nicholas J. Volpe, MD; Joseph F. Rizzo III, MD; Simmons Lessell, MD

Objective: To describe the clinical findings in patients with acute idiopathic blind spot enlargement (AIBSE).

Methods: Medical record review of 27 patients with AIBSE (without sufficient optic nerve head swelling to cause blind spot enlargement) seen in 2 academic neuro-ophthalmology units.

Results: All patients were women aged between 19 and 53 years. Twenty-three patients reported positive visual phenomena. Visual acuity was normal in 16 patients. All patients had enlarged blind spots of variable size and density. Dyschromatopsia and afferent pupil defects were prevalent. Ophthalmoscopic features included uveitis, mild optic nerve swelling, granularity of macular pigment, subretinal white dots, and peripapillary pigment disturbances. Twelve of the 13 patients who underwent fluorescein angiography had optic disc staining and 5 had retinal pigment epithelial lesions with late staining. Full-field electroretinogram results were normal in 8 of 9 patients, although focal electroretinogram results were abnormal in 8 of 9 patients. Photopsia always decreased but visual fields did not improve. Six patients experienced recurrence.

Conclusions: The clinical features of AIBSE include photopsia, visual field defects, abnormal findings from fundoscopic and fluorescein angiography, and abnormal results of focal electroretinography. The disease affects the peripapillary retina and may cause an afferent pupillary defect. The striking predilection for the peripapillary retina suggests a local etiologic factor and distinguishes AIBSE from the multiple evanescent white dot syndrome. Unlike patients with multiple evanescent white dot syndrome, recovery of visual field did not occur in patients with AIBSE.


The classification of the acute idiopathic blind spot enlargement syndrome (AIBSE) among various other fundus diseases remains controversial. Our review of 27 previously unreported cases of this disorder might not only offer insights into the nosology, but also contribute to the semiology of AIBSE. Our series suggests a spectrum of peripapillary retinal disease in women with abnormal parafoveal electroretinography (ERG) results, some evidence of optic neuropathy, and limited recovery.

RESULTS

All 27 patients were woman aged between 19 and 53 years, 11 (41%) of whom were taking birth control pills at the time they developed symptoms. The correct diagnosis was not made by the referring physician in any patient. Optic neuritis and ophthalmic migraine were common misdiagnoses. Twenty-five patients complained of decreased vision (Table 1). Twenty-three reported experiencing visual phenomena: in 5 cases the photopsia preceded the onset of visual loss by several weeks. Pain was reported by only 2 patients and was described as an “ache” not exacerbated by eye movement.

Results of vision testing are presented in Table 2. Visual acuity was normal in 16 patients (20/25 to 20/50 in 10 and 20/200 in 1). Nine patients had dyschromatopsia and 8 had afferent pupil defects. All patients had enlarged blind spots. Blindspot enlargement, present in all patients, was highly variable in terms of size, although all defects shared the common feature of steep margins (Figure 1). Only 8 patients had completely normal anterior segment and ophthalmoscopic examination results. Ten patients had more than 1 finding on examination (Table 3). The most common abnormalities were mild disc swelling (not commensurate with the blind spot size) or hyper-
SUBJECTS AND METHODS

All 27 patients were examined at the Massachusetts Eye and Ear Infirmary (Boston) or the Scheie Eye Institute (Philadelphia, Pa) by one of us and diagnosed with AIBSE from 1989 to 1997. The results are based on a retrospective review of their records. Each patient had symptomatic, acute onset of a visual disturbance and demonstrated blind spot enlargement on visual field testing. In none of these cases was there disc edema sufficient to explain the blind spot enlargement. The patients had been referred for neuroophthalmic evaluation by a comprehensive ophthalmologist or retinal specialist when a diagnosis could not be established. All patients had a complete neuroophthalmic examination including measurement of Snellen visual acuity, color vision (Ishihara test plates), pupillary examination, dilated funduscopy, and either Goldmann or automated (Humphrey) perimetry. Thirteen patients also had full-field photography with fluorescein angiography. Full-field and focal ERGs were recorded in 9 patients. The study conformed to the policies outlined by the institutional review board of studies involving human subjects at the University of Pennsylvania School of Medicine and the Harvard Medical School.

Table 1. Initial Symptoms of 27 Patients With Acute Idiopathic Blind Spot Enlargement Syndrome

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of vision</td>
<td>25</td>
</tr>
<tr>
<td>Blurring</td>
<td>9</td>
</tr>
<tr>
<td>Awareness of darkened area or missing vision</td>
<td>9</td>
</tr>
<tr>
<td>Spots in vision</td>
<td>3</td>
</tr>
<tr>
<td>“Looking through film”</td>
<td>4</td>
</tr>
<tr>
<td>Positive visual phenomena</td>
<td>23</td>
</tr>
<tr>
<td>Photopsia (sparkles, flashes, flickering)</td>
<td>16</td>
</tr>
<tr>
<td>Swirling</td>
<td>1</td>
</tr>
<tr>
<td>Movement within scotoma</td>
<td>3</td>
</tr>
<tr>
<td>Colored light</td>
<td>1</td>
</tr>
<tr>
<td>After “flash bulb”</td>
<td>2</td>
</tr>
</tbody>
</table>

Ten patients had more than 1 finding. RPE indicates retinal pigment epithelium.

Table 2. Measured Visual Dysfunction in 27 Patients With Acute Idiopathic Blind Spot Enlargement

<table>
<thead>
<tr>
<th>Examination Finding</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual acuity</td>
<td></td>
</tr>
<tr>
<td>20/20</td>
<td>16</td>
</tr>
<tr>
<td>20/25-20/50</td>
<td>10</td>
</tr>
<tr>
<td>20/200</td>
<td>1</td>
</tr>
<tr>
<td>Dysechromatopsia</td>
<td>9</td>
</tr>
<tr>
<td>Afferent pupil defect</td>
<td>8</td>
</tr>
<tr>
<td>Visual field defects (largest diameter of scotoma, degrees)</td>
<td></td>
</tr>
<tr>
<td>&lt;15</td>
<td>12</td>
</tr>
<tr>
<td>15-30</td>
<td>12</td>
</tr>
<tr>
<td>&gt;30</td>
<td>3</td>
</tr>
</tbody>
</table>

One patient had normal full-field and focal ERG results. Full-field ERG amplitudes were within normal limits in all patients but 1, whose ERG showed mildly reduced amplitudes. In 4 patients, intereye differences were noted, and the full-field ERG amplitudes were slightly less in the affected eye. However, nasal parafoveal focal ERG amplitudes were abnormal in 8 of the 9 patients who had ERGs. The nasal parafoveal response was not recordable in 1 patient, and a reduction in amplitude or delayed implicit time was found in the others.
One patient demonstrated dysfunction of the nasal parafoveal retina compared with normal temporal parafoveal retinal responses.

Although all but 1 of the patients with reduced visual acuity improved, there was no improvement of the enlarged blind spot in the 10 patients who were followed up. Photopsias always decreased. In 6 patients, either a recurrence was noted on our follow-up examinations or the current episode was thought to be a recurrence based on the history. These episodes occurred between

Figure 2. The spectrum of ophthalmoscopic findings in acute idiopathic blind spot enlargement. A and B, Mild optic nerve head swelling and peripapillary pigmentary changes were the most common findings. C, Peripapillary atrophy and focal, deep pigment changes in a patient. D, A peculiar grayish-yellow peripapillary halo (arrow) was seen in 4 patients.

Figure 3. Late-phase fluorescein angiography of 2 patients with acute idiopathic blind spot enlargement. A, Disc staining. Five patients had small isolated, bright deep (late staining) retinal lesions (arrows). B, The ring of peripapillary deep hyperfluorescence.
The phrase big blind spot syndrome has been used to designate several different entities (Figure 4). When associated with significant optic nerve head swelling, blind spot enlargement results from displacement of the peripapillary retina and refractive changes. In patients with inflammatory disease of the retina and choroid, blind spot enlargement corresponds to areas of retina and choroid that appear abnormal ophthalmoscopically. In 1988, Fletcher et al described a clinically distinct syndrome of blind spot enlargement in 7 patients who acutely developed photopsias and enlargement of the blind spot without optic disc swelling or choroiditis. In 1984, Jam- pol et al and Takeda et al described a similar condition, common in women, associated with scotomas and multiple evanescent white lesions at the level of the RPE (MEWDS). Subsequently it became clear that AIBSE and MEWDS share clinical features and perhaps represent different forms of the same disease, with some differences accounted for by the timing of the initial clinical examination. Interestingly, these clinical syndromes were not recognized in patients prior to the 1970s.

In our series, when all of the clinical findings were taken together (acute onset of positive visual phenomena, a visual field defect centered on an enlarged blind spot, and the absence of marked disc swelling), the diagnosis of AIBSE was relatively easily made. However, we found a high prevalence of misdiagnoses by the referring physician. The overlap with other common neuro-ophthalmic entities and the variability of clinical findings make AIBSE an important entity in neuro-ophthalmic differential diagnosis. Photopsia may be incorrectly ascribed to migraine. The abrupt onset of a visual field defect in a young patient might suggest optic neuritis. The presence of an enlarged blind spot and disc hyperemia might suggest papilledema or a temporal defect from a chiasmal lesion.

Acute idiopathic blind spot enlargement is a disease of the outer retina and therefore shares many features with MEWDS. Enlarged blind spots are often found in MEWDS. It is possible that the evanescent white dots of MEWDS are present but unrecognized or ophthalmoscopically obscure in some or all patients with AIBSE. Abnormalities in the indocyanine green angiography results have been demonstrated in patients with MEWDS who had no apparent white spots on ophthalmoscopy. Callanan and Gass suggested that MEWDS, AIBSE, multifocal choroiditis, acute macular neuroretinopathy (AMN), and acute zonal occult outer retinopathy (AZOOR) may be a single disease with variable presentation. Supporting the theory that these signs and symptoms all represent the spectrum of a single disease are reports of patients with AIBSE and MEWDS who developed lesions typical of AMN. Patients with MEWDS and AIBSE have also been reported to develop multifocal active or atrophic fundus lesions typical of multifocal choroiditis. The etiology of AIBSE and all of these other syndromes is unknown, although they all seem to result from photoreceptor outer segment dysfunction. It is not surprising that any condition (regardless of etiology) associated with dysfunction of the outer retina would have a similar presentation. These syndromes are characterized by acute, focal loss of outer retinal function associated with photopsias. They occur predominantly in young women, and initially there are minimal or no fundus changes. Abnormal ERG results are commonly identified.

Our findings suggest that AIBSE is distinct from MEWDS, AZOOR, AMN, and multifocal choroiditis. Unlike most patients with MEWDS, recovery of visual field did not occur in our patients with AIBSE. Fundus findings in addition to intraocular inflammation and disc swelling were common in our patients, including focal areas of peripapillary deep pigmentary changes that took the form of atrophic or discolored spots, or a grayish halo around the optic nerve head (Figure 2). In all of our patients, the extent of the visual field defects implied retinal dysfunction beyond any visible abnormalities of the disc or peripapillary retina. Although we did find a high incidence of funduscopic abnormalities, we agree with Jampol and Wiredu that these abnormalities are different from those seen in AMN, multifocal choroiditis, and AZOOR. Indeed, at the time of the initial visit, each of these entities had a highly variable appearance of the fundus. On the other hand, we did find that some patients with MEWDS could not be distinguished from patients with AIBSE. Five of our patients had ophthalmoscopically visible white dots that were consistent with MEWDS. However, macular pigment granularity, considered pathognomonic of MEWDS, was recognized in only 2 of our patients. Finally, features common to the series of patients with AZOOR reported by Gass and Jacobson et al, including progression of visual field loss during weeks or months, progressive ERG worsening, second eye involvement, chronic photopsia, and late RPE atrophy, were not prominent in our patients. The clinical courses of our patients were characterized by resolution of photopsia with stable, persistent visual field defects, suggesting that photoreceptor dysfunction is permanent but not progressive.

Fluorescein angiographic findings in our patients were similar to those reported in patients with MEWDS (peripapillary hyperfluorescence from late RPE staining). However, we found a high incidence (12/13 patients) of disc staining compared with patients with MEWDS. While
disc staining may simply reflect an altered vascular permeability, it also raises the possibility of a simultaneous inflammation of the optic nerve. Dodwell et al reported optic nerve involvement in MEWDS. While extensive visual field loss on a retinal basis could cause a relative afferent pupil defect and dyschromatopsia, simultaneous retinal ganglion cell and photoreceptor dysfunction needs to be considered.

Focal ERG abnormalities were found in 8 of 9 of our patients studied. We suggest the use of focal or multifocal ERG to confirm the diagnosis of AIBSE. The use of focal ERG to diagnose AIBSE was first reported by Fletcher et al, and confirmed by Singh et al. Full-field ERG abnormalities in patients with MEWDS have also been recognized. Electoretinogram abnormalities along with photopsia suggest localization of the disease to the photoreceptors and pigment epithelium. Jacobson et al demonstrated full-field ERG abnormalities in AZOOR and identified a pattern of retinal dysfunction most compatible with outer segment disease.

Six of our patients had recurrences although none had a progressive condition. It is unusual for patients to experience recurrences, and therefore, an autoimmune condition, which typically relapses, would be a less likely explanation for the retinopathy than an environmentally triggered causative factor. Although Chung et al have reported elevated levels of serum immunoglobulins in patients with MEWDS, Jacobson et al were unable to demonstrate histochmical evidence of retinal antibodies in the sera of their patients affected with AZOOR. Since we did not encounter a single male patient with AIBSE during an 8-year period, it seems likely that hormonal or genetic factors contribute to the development of AIBSE. Borruat et al found a higher than expected prevalence of HLA-B51 in their patients with MEWDS. Patients with MEWDS and AZOOR have frequently been noted to have an antecedent flulike illness, suggesting an environmental trigger, but this did not seem to be true in our patients.

In addition to peripapillary retinal dysfunction in AIBSE, there may also be optic neuropathy. Features of peripapillary nasal retina (primarily involved in AIBSE), such as increased cone density, blood supply, and proximity to the optic nerve, indicate that it may be uniquely vulnerable to conditions that do not involve the remainder of the retina. In our patients with AIBSE, photopsia and abnormal focal ERG and disc staining results were the most consistent findings. With increasingly accurate diagnosis rates, more patients will be identified early and a pattern of findings will lead to an etiology or pathogenic mechanism for each or all of these conditions. Assigning a label to a collection of similar signs and symptoms will not further the cause of determining the disease etiology or etiologies. Therefore, until a single etiology cause is found for all of these conditions, it is reasonable to assume they are all distinct entities. Efforts should be made to try and determine an etiologic factor, and more extensive immunological testing of both sera and spinal fluid might prove to be helpful to further define the etiology of this condition. We offer the following definition of AIBSE: absolute symptomatic enlargement of the blind spot without commensurate swelling of the optic nerve head occurring in conjunction with presumed disease of the optic nerve and peripapillary retina.

Accepted for publication June 2, 2000.
Corresponding author and reprints: Nicholas J. Volpe, MD, Scheie Eye Institute, 51 N 39th St, Philadelphia, PA 19104 (e-mail: nickvolp@mail.med.upenn.edu).

REFERENCES