

Case report

Acute idiopathic blind spot enlargement syndrome following influenza vaccination



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ABSTRACT

Purpose: To report a case of acute idiopathic blind spot enlargement syndrome (AIBSES) following influenza vaccination.

Observations: A 57-year old woman presented with a one-month history of photopsia, temporal visual field disturbance on the right eye, 11 days following the administration of the influenza virus vaccine. Visual acuity was 20/30, and color vision remained normal. Examination revealed mild venular dilation at the edge of the right optic disk and was otherwise unremarkable. Visual field testing revealed enlargement of the right physiological blind spot. Medical workup, including brain CT scan, brain MRI, RPR, *Treponema pallidum* antibodies, Chest X-Ray, ANA, and PPD testing, was found within normal limits. Ancillary testing was compatible with an assessment of AIBSES secondary to influenza virus vaccination.

Conclusions and Importance: Although direct causation may not be absolutely established by a single report, our case suggests that the influenza virus vaccine may serve as an immunological trigger for some cases of AIBSES. Thoughtful vaccination history is of the utmost importance when evaluating patients with AIBSES, as it may help elucidate the underlying precipitating factor. To our knowledge, this is the first reported case of AIBSES following influenza virus vaccination.

1. Introduction

Acute idiopathic blind spot enlargement syndrome (AIBSES) is a rare outer retinopathy first reported in 1988 by Fletcher et al. as a clinical entity presenting with acute monocular shadow or scotoma and photopsia, on an otherwise normal fundus.¹ It is characterized by an enlarged blind spot that can occur either as an isolated finding or as part of several other chorioretinopathies, such as acute zonal occult retinopathy, acute macular neuroretinopathy, multiple evanescent white dot syndrome (MEWDS), and multifocal inner choroiditis.²⁻⁴ The current belief is that these entities are a spectrum of primary inflammatory choriocapillaropathy (PICCP) that, regardless of etiology, may result in overlapping clinical features.^{5,6}

These disorders are most common in young adult myopic women, and each may be associated with visual field loss and abnormalities on electroretinograms.^{7,8} Optical coherence tomography (OCT) studies show a loss or irregularity of the photoreceptor ellipsoid zone in areas

corresponding to the visual field defects.⁸ The predilection for the peripapillary retina suggests a local etiologic factor and distinguishes AIBSES from MEWDS and other similar PICCPs.³

The etiology of AIBSES remains unknown.^{3,9} There have been numerous case reports of PICCPs following vaccination, including influenza, but to our knowledge, only one case of AIBSES was reported following the measles, mumps, and rubella (MMR) vaccine.⁹⁻¹¹ We report this case of a 57-year-old female with AIBSES after influenza vaccination to highlight vaccination as an important consideration in the medical history for the differential diagnosis of chorioretinal inflammatory syndromes.

1.1. Case report

A 57-year-old Hispanic woman presented to the neuro-ophthalmology service complaining of a 1-month history of photopsia, more pronounced on the temporal half of the right visual field, where

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she also noted seeing a “black spot.” She also complained of mild pain on extraocular movements, which emerged after the onset of her symptoms. She had received the influenza virus vaccine (Afluria Preservative Free, 2017–2018, 0.5 cc) 11 days before initial visual symptoms. Her past medical history was remarkable for type-2 diabetes mellitus. Review of systems, medical, social, and family history were otherwise unremarkable.

On examination, best-corrected visual acuity was 20/30 in the right eye (OD) and 20/20 in the left eye (OS) with a manifest refraction of +1.75–1.50 × 90 OD and +1.00–0.50 × 105 OS. A trace 0.3 log afferent pupillary defect (APD) was seen on the right eye. Color vision, by the Ishihara color test, was normal in both eyes. Extraocular movements revealed full ductions and versions. Intraocular pressure and anterior segment examination by slit lamp were unremarkable bilaterally. The vitreous was clear of cells and debris on both eyes. The fundus exam was remarkable for mild venular dilation at the edge of the right disk; otherwise, there was no disk edema or any evidence of posterior uveitis on either eye.

Humphrey 30–2 visual field test showed enlargement of the right physiological blind spot (Fig. 1A). An intravenous fluorescein angiogram (IVFA) of the right fundus performed 3 days before presentation revealed late, disk, and perivascular hyperfluorescence with leakage, in the peripapillary region (Fig. 2). A computerized tomography (CT) scan of the head, as well as a brain and orbit magnetic resonance imaging (MRI) scan, which had been ordered by the referring ophthalmologist, were both unremarkable. A medical workup, including complete blood count, electrolytes, urinalysis, erythrocyte sedimentation rate, rapid plasma reagin (RPR), *Treponema pallidum* antibodies, anti-nuclear antibody (ANA), purified protein derivative (PPD), and a chest x-ray, was ordered and found within normal limits.

Based on clinical findings and ancillary test results, a presumptive diagnosis of AIBSES was made. Treatment was started with oral prednisone at a dose of 60 mg daily. At the one-week follow-up visit, the patient had noted the subjective improvement of her vision. However, the patient had developed uncontrolled glycemia, and a decision was made to start tapering the oral prednisone prior to the complete resolution of symptoms. The prednisone was gradually tapered over 11 weeks. At the one-month follow-up visit, the patient had subjective improvement of the photopsia, the APD of the right eye had resolved, BCVA was 20/25, and Humphrey visual fields showed slight improvement (Fig. 1B). Multifocal electroretinogram (mERG) analysis of the

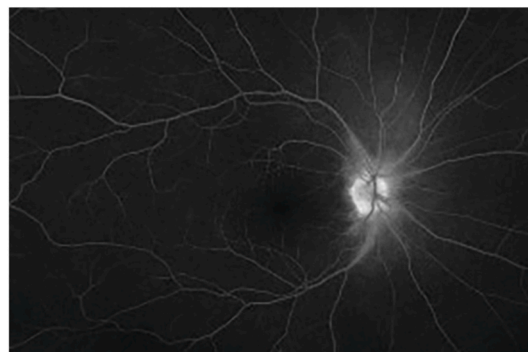


Fig. 2. Fluorescein angiogram of the right fundus, late views (10 min post dye injection), revealing disk and perivascular hyperfluorescence with leakage in the peripapillary region.

right eye performed 3 months after the onset of symptoms revealed reduced wavelet amplitudes in areas corresponding to scotoma (Fig. 3). OCT images of the right optic nerve and macula, 4 months after presentation, revealed disruption of the ellipsoid zone in the parafoveal and peripapillary locations along with loss of regularity of the photoreceptor inner segment/outer segment (IS/OS) line, in areas corresponding to the visual field defect (Fig. 4). Five months after presentation, the fundus revealed peripapillary retinal pigment epithelium changes, which correlated with a well-demarcated area of hypoautofluorescence (Fig. 5 A and B). This area of hypoautofluorescence was surrounded by a zone of hyperautofluorescence that extended further temporally to the nasal perifoveal region. At the 1-year follow-up visit, the patient’s visual acuity remained stable, and the photopsia had resolved; however, no significant improvement was noted on her visual field examination (Fig. 1C).

2. Discussion

AIBSES most commonly occurs in young to middle-aged females, but there are numerous cases in the literature of older age women and males.^{1,12,13} Central scotoma and photopsia are the classic symptoms, both of which were present in our patient presented since the initial visit.^{1,3} The examination of patients with AIBSES usually reveals normal

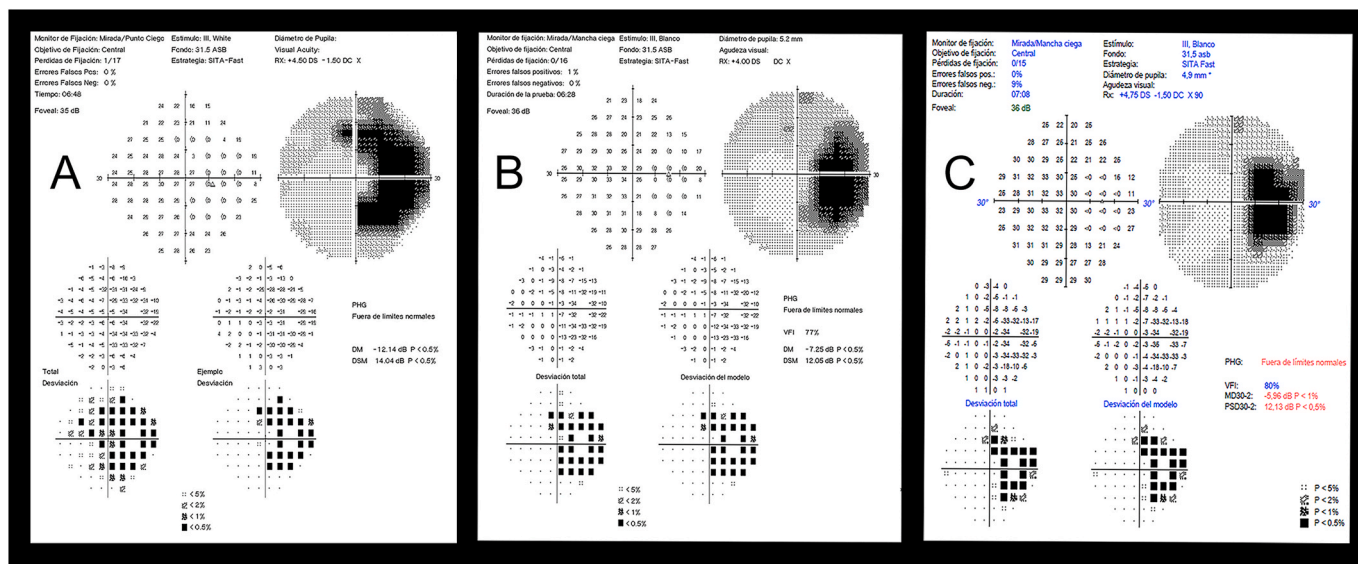


Fig. 1. Right eye visual field (Humphrey, Central 30-2 Threshold Test, Stimulus III, White, SITA-FAST). A. Upon presentation, there is an enlargement of the physiological blind spot. Mean deviation: -12.14 dB, P < 0.5% B. One-month post-presentation shows a mild improvement of the visual field defect and the mean deviation. Mean deviation: -7.25 dB, P < 0.5% C. At 1-year follow-up, there is the persistence of the abnormal scotoma. Mean deviation: -5.96 dB, P < 1%.

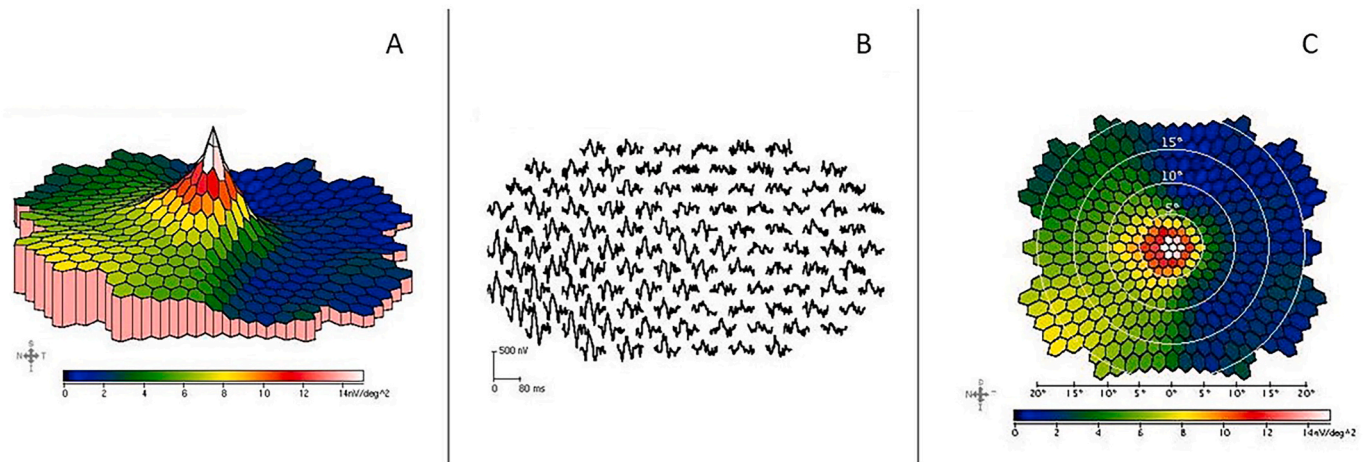


Fig. 3. Multifocal ERG of the right eye, 3 months after the onset of symptoms, revealing decreased wavelet amplitude in the macular regions corresponding to the existing scotoma. A. Field View B. Traces distribution. C. Response density tomography.

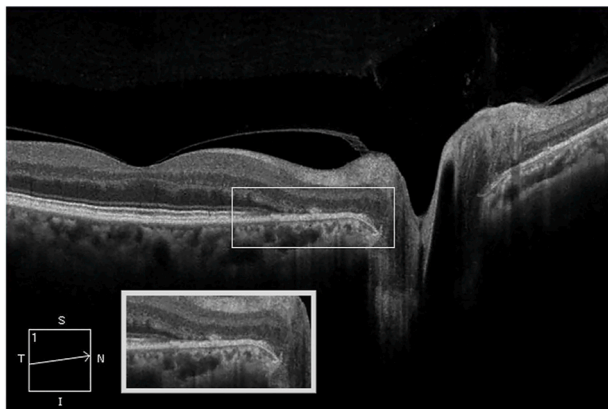


Fig. 4. High Definition OCT, encompassing the right optic nerve and macula, four months after the initial presentation. The images reveal disruption of the ellipsoid zone and loss of regularity of the photoreceptor inner segment/outer segment (IS/OS) line in the peripapillary region (box).

fundus and optic disc and, seldom instances, intraocular inflammation.^{1,3,8,9} However, as was the case with our patient, some may show mild optic disc swelling and peripapillary vascular changes.^{3,7-9}

The diagnosis of AIBSES may be challenging or easily missed as the condition lacks explicit changes in the early stages of the disease.^{1,3,8,9} In our case, the initial referral was due to suspected optic neuritis due to her complaint of painful eye movements. However, the characteristic visual field defect and OCT findings and normal color vision and negative MRI findings and abnormal mERG suggested otherwise. As expected, visual field testing in AIBSES shows blind spot enlargement.^{1,3,8,9} Furthermore, OCT may reveal loss of regularity of the photoreceptor IS/OS line, and IVFA may show peripapillary leakage.⁸ Moreover, mERG tends to be abnormal, more frequently than full-field ERG.⁸ All the aforementioned characteristic changes seen in AIBSES were present in our case.

Vaccination has been cited to be a potential precipitating cause for other PICCPs.¹²⁻¹⁷ While MEWDS's etiology remains unknown, some authors hypothesize an immune basis as there have been multiple reports following vaccination.¹²⁻¹⁶ Excessive lymphocyte activation, cytokine expression, and molecular mimicry have been considered as mechanisms that may explain the rare autoimmune phenomena that have been observed following vaccinations.¹⁷ MEWDS and AIBSES share a very similar presentation; both syndromes cause photopsia and

blind-spot enlargement.^{3,7} MEWDS may present with a flu-like viral prodrome before the onset of ocular symptoms.⁷ Characteristic yellow-white fundus lesions disappear within a few weeks.^{7,14} There is speculation that AIBSES and MEWDS are the same entity, with AIBSES presenting as a late manifestation.⁷

In this case, the patient was examined by an ophthalmologist 4 days after the onset symptoms and noted to have normal fundus findings, rendering MEWDS an unlikely diagnosis. Our review of English language literature disclosed five cases of vaccine-related MEWDS: three following hepatitis vaccination, one with HPV and meningococcus vaccine, and one with the influenza vaccine.¹²⁻¹⁶ There are five cases of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) following vaccines; three with influenza vaccine, one with meningococcal C, and one with varicella vaccine.^{10,11,18-20} There is one reported case of multifocal choroiditis following simultaneous hepatitis A, typhoid, and yellow fever vaccination.¹⁷ We only found one case of AIBSES following vaccination, which was after measles, mumps, and rubella vaccination (MMR).⁹ To our knowledge, this is the only case reported of AIBSES following the influenza vaccine. AIBSES remains a rare syndrome, which shares features with other PICCPs, especially MEWDS.⁷ This case highlights the importance of obtaining a vaccination history in all patients with suspected PICCPs.

3. Conclusions

Although direct causation may not be absolutely established, PICCPs such as MEWDS and AIBSES may occur following the administration of a wide array of vaccinations. Accordingly, our case suggests that the influenza virus vaccine may serve as an immunological trigger of such conditions, particularly AIBSES. Thoughtful vaccination history is of the utmost importance when evaluating patients with PICCPs, as it may help elucidate the underlying precipitating factor.

Patient consent

Consent to publish this case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Declaration of competing interest

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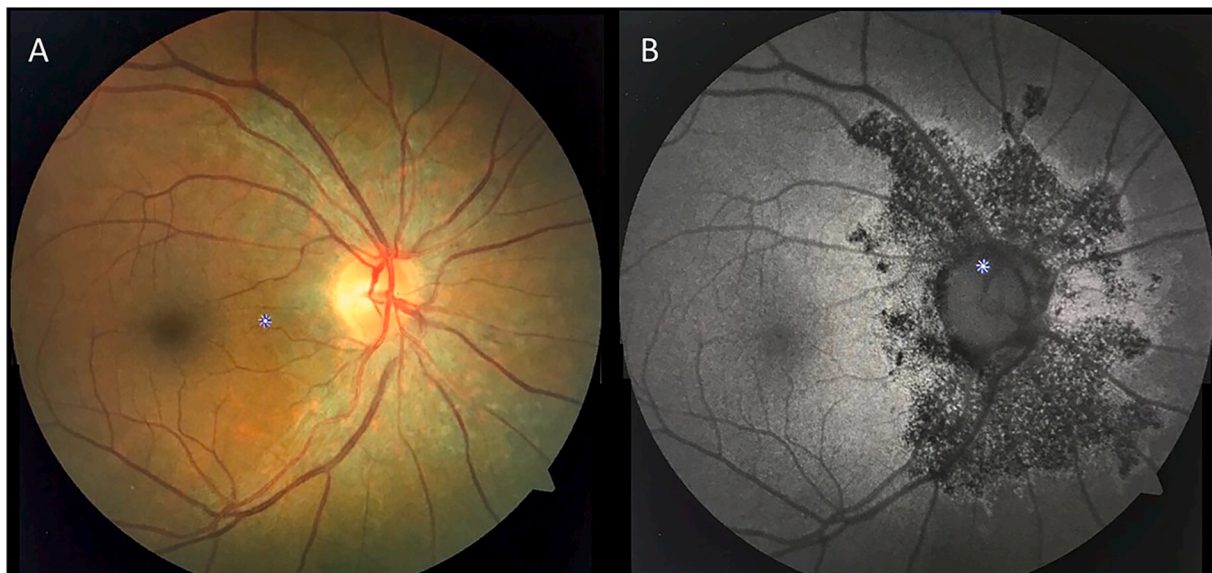


Fig. 5. Right eye fundus images obtained 5 months after presentation. A. Color photographs reveal mild peripapillary retinal pigment epithelium changes. B. Fundus autofluorescence images disclose a well-demarcated area of hypoa autofluorescence, which is surrounded by a zone of hypera autofluorescence, which extends further temporally up to the nasal perifoveal region. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Authorship.

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None.

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