



## Acute zonal occult outer retinopathy-like presentation secondary to scleral buckle

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### ABSTRACT

**Purpose:** To describe a case of acute zonal occult outer retinopathy-like (AZOOR-like) presentation following scleral buckle surgery for rhegmatogenous retinal detachment.

**Observations:** A 48-year-old man underwent successful scleral buckle with cryotherapy for repair of a left eye inferior macula-on rhegmatogenous retinal detachment. Five years later he presented with a six-month history of left peripheral field restriction. Fundus autofluorescence and optical coherence tomography demonstrated degeneration of the photoreceptors in a ring pattern around the left macula. Humphrey visual fields showed functional loss correlating with the imaging, with a paracentral ring scotoma. Electrophysiology demonstrated a delayed 30 Hz flicker latency in the left eye confirming cone system dysfunction.

**Conclusion and Importance:** Scleral buckling surgery for repair of a rhegmatogenous retinal detachment may be associated with a late AZOOR-like presentation.

### 1. Introduction

Acute zonal occult outer retinopathy (AZOOR) is a rare idiopathic disease predominantly characterised by an acute loss of photoreceptor function.<sup>1</sup> Symptoms include an acute onset of photopsia and progressive scotoma in one or both eyes, and the majority of patients affected by AZOOR are young Caucasian females.<sup>2</sup> Although the cause of AZOOR is still unclear, a viral illness or autoimmune response are the most likely associations. An AZOOR diagnosis is usually confirmed with abnormalities on electroretinography, characterised by a delayed implicit time of the 30 Hz cone flicker response.<sup>3</sup>

Scleral buckling is a surgical technique used either as a primary or adjunctive treatment for rhegmatogenous retinal detachments for over 60 years.<sup>4</sup> Herein, to our knowledge we present the first case of AZOOR-like presentation possibly triggered by scleral buckle surgery for repair of a rhegmatogenous retinal detachment.

### 2. Case report

A 48-year-old Indian man presented with a five-day history of a left

superior scotoma. His ocular history was unremarkable apart from mild myopia and astigmatism. Past medical history included chronic myelogenous leukemia (CML) for which he has been taking imatinib for the past nine years prior to presentation. Best-corrected visual acuity (BCVA) was 6/6–2 and 6/7.5 in the right and left eye respectively, while intraocular pressures were 18 and 14 mmHg.

Anterior segments were normal. In the left eye there was an inferior macula-on rhegmatogenous retinal detachment with a horseshoe tear at the six o'clock position and posterior vitreous detachment (Fig. 1A and B). An urgent left eye scleral buckle and cryotherapy was performed on the same day. A Number 5 silicone scleral buckle (MIRA®) was encircled posterior to all recti and connected superonasally with a Number 70 silicone sleeve. The surgery was uncomplicated and at 7 months follow-up the retina was re-attached with BCVA 6/9.5 + 2 in the left eye (Fig. 1C and D). Nine months post-operatively the patient's BCVA was 6/7.5–1 but he developed delayed-onset post-operative cystoid macular edema (CME). Fluorescein angiography did not demonstrate any other cause for the CME such as retinal vein occlusion. The CME resolved over the next 10 months with topical steroids (g. dexamethasone, Maxidex® 0.1%), topical non-steroidal anti-inflammatories (g. Ketorolac,

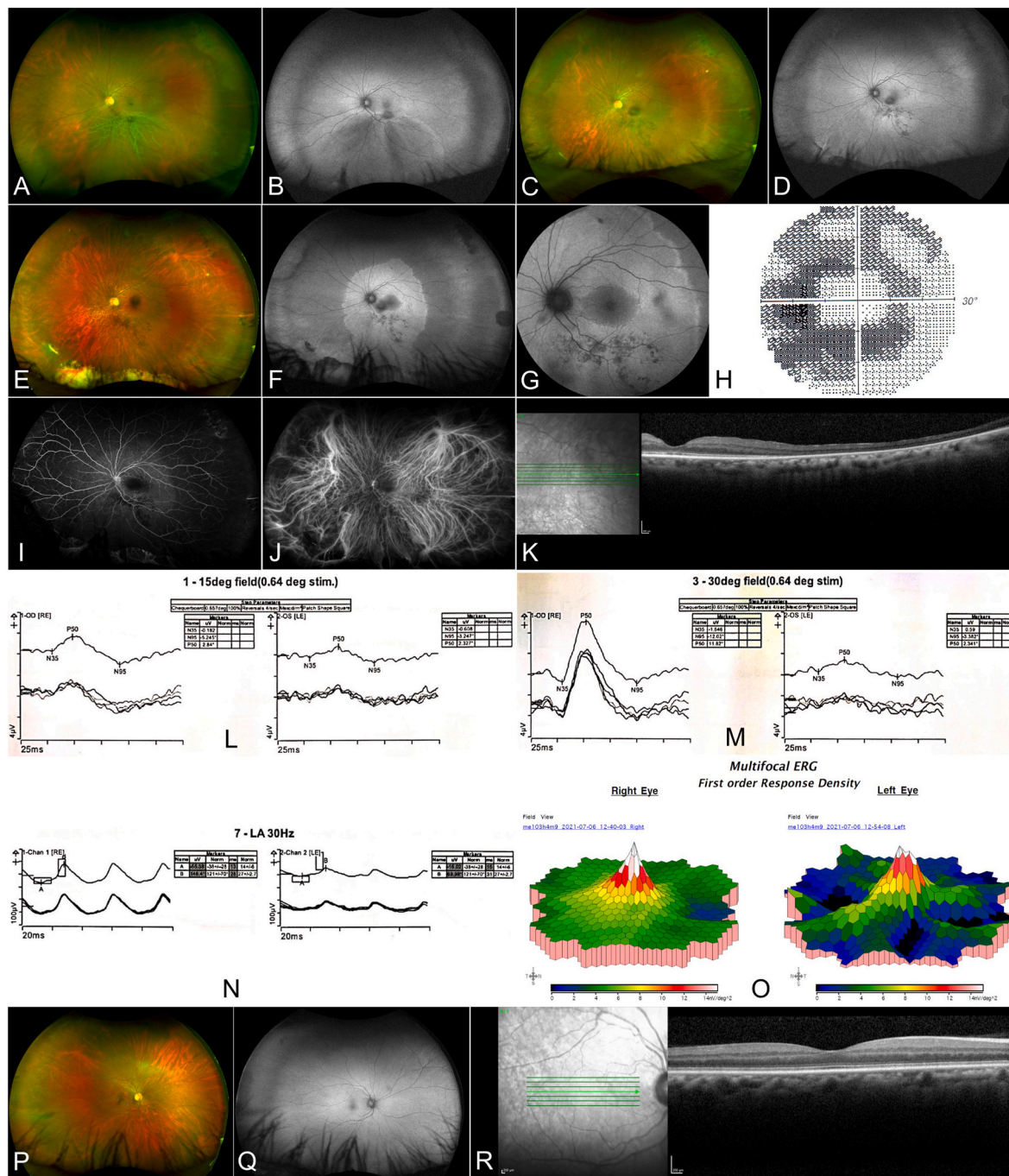
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ACULAR®), and intravitreal anti-vascular endothelial growth factor therapy (two bevacizumab and three aflibercept injections).

Five years after the scleral buckle surgery, the patient re-presented with a six-month history of left peripheral vision restriction. In addition to long-term imatinib for his CML, the patient had started taking

thyroxine for non-autoimmune hypothyroidism two years prior to this presentation. Best-corrected visual acuities were 6/4.8–2 and 6/9.5–2 in the right and left eyes respectively, while intraocular pressures were 16 and 13 mmHg. Although the left retina was still attached, fundus autofluorescence demonstrated a ring of hyperautofluorescence at the



**Fig. 1.** Wide-field color fundus photography (A) and autofluorescence (B) of left inferior macula-on rhegmatogenous retinal detachment at initial presentation. Ten months after scleral buckling with cryotherapy, the retina remained attached as shown in color fundus photography (C) and autofluorescence (D). Five years after surgery, the patient represented with a restriction in left peripheral field of 6 months duration. Color fundus photography (E) and autofluorescence (F, G) is once again performed, demonstrating a new ring of hyperautofluorescence at the posterior pole extending beyond the vascular arcades but sparing the fovea. Humphrey visual fields 30–2 of the left eye (H) demonstrated a corresponding ring-shaped scotoma in the mid-periphery. Early phase fluorescein angiography of the left eye (I) demonstrated a window defect corresponding to the ring lesion, but indocyanine green angiography (J) was normal. Optical coherence tomography (K) revealed loss of photoreceptors restricted to the area of hyperautofluorescence. Pattern ERG detected an appropriate doubling P50 response from the 15°–30° stimulus for the right eye, but not the left eye (L, M). Full-field ERG revealed a delayed 30 Hz flicker latency in the left eye which was consistent with cone system dysfunction (N). Multifocal ERGs were significantly reduced parafoveally in the left eye compared with the right eye (O). The right eye wide-field color fundus photography (P), autofluorescence (Q) and optical coherence tomography (R) has remained normal at all visits. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

posterior pole extending beyond the vascular arcades and to the periphery inferiorly but sparing the fovea (Fig. 1E and F). Humphrey visual field testing showed a ring-shaped scotoma in the mid-periphery, consistent with the ring of hyperautofluorescence (Fig. 1H). Fluorescein angiography demonstrated mild hyperfluorescence corresponding to the ring of hyperautofluorescence (Fig. 1I). Indocyanine green angiography was normal (Fig. 1J). Optical coherence tomography (OCT) scans through the area of hyperautofluorescence revealed a loss of outer retinal architecture (Fig. 1K). Electrophysiology including pattern, full-field and multi-focal electroretinogram (ERG) was performed. Pattern ERG detected an appropriate doubling P50 response from the 15°–30° stimulus for the right eye, but not the left eye (Fig. 1, L and M). Full-field ERG revealed a delayed 30 Hz flicker latency in the left eye which is consistent with cone system dysfunction (Fig. 1N). Multi-focal ERGs were significantly reduced parafoveally in the left eye (Fig. 1O). There were no abnormalities detected with the right eye on examination, functional studies or multi-modal imaging (Fig. 1, P-R).

Interferon-gamma release assay (IGRA) was positive for tuberculosis (TB-specific antigens CD4 1.92IU/ml (reference range <0.35), TB-specific antigens CD4/CD8 2.04IU/ml (reference range <0.35), however there were no respiratory symptoms and his chest X-ray demonstrated no abnormalities. Other blood tests including syphilis serology, angiotensin-converting enzyme, antinuclear antibodies and anti-neutrophil cytoplasmic antibodies were normal.

The above findings were thought to be consistent with an AZOOR-like presentation in the left eye. The clinical and multimodal imaging appearance in both eyes remain unchanged, 12-months after they were first detected.

### 3. Discussion

Since its first description in 1992 by Gass et al.,<sup>5</sup> a variety of examination and investigation findings have been proposed to diagnose AZOOR. Fundus examination may initially be unremarkable, however changes akin to retinitis pigmentosa may develop over time.<sup>2</sup> 40–61%<sup>2,6</sup> of patients with AZOOR present with unilateral involvement, but around three-quarters of patients will progress to bilateral involvement.<sup>2,6</sup> Multi-modal imaging including fundus autofluorescence, optical coherence tomography and fluorescein angiography can be useful in elucidating a diagnosis. These demonstrate a trizonal pattern of sequential involvement of the outer retina, retinal pigment epithelium and choroid.<sup>6</sup> Adaptive optics OCT can reveal early changes in retinal areas otherwise considered to be normal on conventional multi-modal imaging.<sup>7</sup> The pattern of visual field defects can be variable, with peripheral field defects and central field sparing most commonly exhibited.<sup>2</sup> A delay in the cone system derived 30 Hz flicker function on electrophysiology, in the above clinical setting, is required for the diagnosis.<sup>3</sup>

Our patient demonstrated several features consistent with AZOOR, including progressive scotoma, fundus hyperautofluorescence pattern, loss of outer retinal architecture on OCT, window defect on fluorescein angiography, and characteristic delay of 30 Hz flicker response on electrophysiology. However, he is not a healthy young female, as were Gass' original cohort and he did not have typical symptomatology of photopsias. A complete trizonal pattern with loss of retinal pigment epithelial cells could not be convincingly demonstrated on OCT. Thus, our patient appears to not have typical AZOOR but rather has an AZOOR-like presentation.

The etiology of AZOOR remains uncertain. Viral triggers have been suggested due to antecedent prodromes, while an autoimmune component has also been proposed due to the typical demographic affected and prevalence of autoimmune co-morbidities.<sup>2,3</sup> Nevertheless, immunosuppressive therapy have been met with mixed results, and prognosis remains highly variable.<sup>8</sup>

Our patient did not report an antecedent viral illness nor did he have any diagnosed autoimmune conditions. Of possible relevance is his

imatinib therapy for his CML as this has been shown to have potential immunostimulatory effects.<sup>9</sup> However, our patient had been taking imatinib for 14 years prior to his AZOOR-like presentation, and therefore this is unlikely to be causal. In addition, one would expect a systemic therapy to cause bilateral ocular involvement.

It is noted that our patient had a positive IGRA. Given his lack of respiratory symptoms and a normal chest X-ray, combined with his Indian background, he most likely has latent tuberculosis (TB). The possibility of latent TB causing his presentation is unlikely as his presentation does not fit with any of the described ocular manifestations of latent TB.<sup>10</sup> Specifically, there were no signs of anterior, intermediate or posterior uveitis, such as vasculitis or choroidal tubercles. Like imatinib, one would expect bilateral pathology if the cause was TB.

There are currently no reports of AZOOR associated with scleral buckling. The only difference between the two eyes was the previous retinal detachment and scleral buckle in the left eye. The AZOOR-like presentation is unlikely to be associated with the retinal detachment because fundus autofluorescence and OCT were both normal 7-months following resolution of the detachment, and only appeared 5 years later. In addition, the ring-like changes on fundus autofluorescence and OCT have a distribution parallel to the circumferential scleral buckle and do not correspond with the inferior retinal detachment. Hyperautofluorescence and patchy hypoautofluorescence at retinal detachment demarcation lines are often seen following scleral buckle surgery.<sup>11,12</sup> However, the hyperautofluorescent changes described in our patient are different to this.

It is uncertain how a scleral buckle might cause an AZOOR-like presentation. Possibilities include changes to retinal or choroidal perfusion, although this was not seen on our patient's fluorescein or indocyanine green angiography. Low-grade physical trauma from the scleral buckle indent could be contributory, but the ring of photoreceptor loss lies posterior the scleral buckle, rather than over it. An AZOOR-like presentation has been documented following a motor vehicle whiplash injury,<sup>13</sup> but there is no proven link between ocular trauma and AZOOR.

In summary, scleral buckling may be associated with a presentation showing some, but not all features consistent with AZOOR. More research is required to understand this poorly understood disease.

### Patient consent

The patient consented to publication of the case in writing.

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### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

### Declaration of competing interest

All the authors have no financial disclosures.

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