

*Clinical & Refractive Optometry* is pleased to present this continuing education (CE) article by Dr. Brian Atkinson and Dr. Nathan A. Whitaker entitled **Ocular Manifestations of Birdshot Retinochoroidopathy: Case Report and Clinical Review**. In order to obtain a 1-hour Council of Optometric Practitioner Education (COPE) approved CE credit, please refer to page 158 for complete instructions.

## **Ocular Manifestations of Birdshot Retinochoroidopathy: Case Report and Clinical Review**

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### **ABSTRACT**

**Birdshot retinochoroidopathy is a form of posterior uveitis with a strong link to the human leukocyte antigen A-29 (HLA A-29) molecule. The attendant inflammation is chronic with acute exacerbations and associated with characteristic findings including vitritis, vasculitis, and creamy-white spots or retinal depigmentation that extends from the optic nerve to the equatorial retina. The progressive nature of the disease subsequently results in minimal to severe choroidal and retinal damage causing varying degrees of visual dysfunction. Herein, we report a case of profound visual loss associated with this unique disorder.**

### **CASE REPORT**

A 77-year-old Caucasian gentleman complained of vision loss that had gradually deteriorated during the preceding four years. Subjectively, he indicated that he was experiencing problems with photophobia, glare, nyctalopia, difficulty with depth perception, changes in his peripheral vision, adaptation problems associated with changes in illumination, and problems with bright lights. Even with the assistance of magnifiers, his visual reduction was such that he was no longer able to read. His medical diagnoses included hypertension, hyperlipidemia, osteoporosis, and hearing loss. His ocular history was remarkable for multiple bouts of retinal and choroidal inflammation.

Best-corrected visual acuity measured 10/140 OD and 10/200 OS. Pupil and muscle testing, as well as anterior segment findings, were unremarkable OU. Intraocular pressure measured 11 mmHg in each eye.

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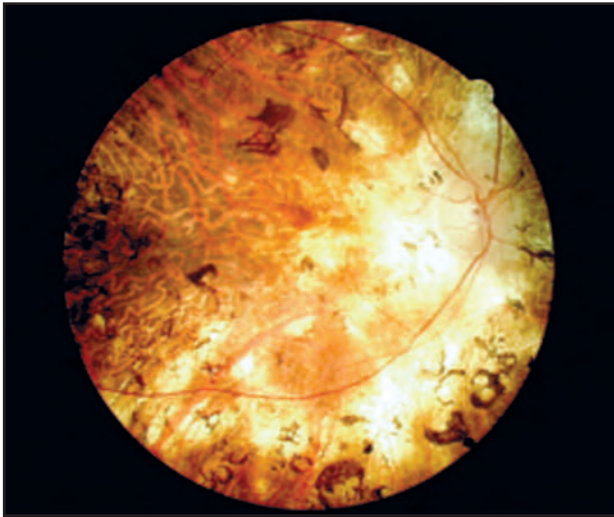
Dilated fundus examination revealed well-centered, clear, posterior chamber implants with moderate vitreal condensation and debris OU. Diffuse optic nerve pallor was evident OU and each macula demonstrated diffuse geographic atrophy. Evaluation of the peripheral retinae revealed extensive oval, creamy, hyperpigmented chorioretinal lesions 360 degrees extending into the mid-periphery (Figs. 1, 2).

A review of our patient's medical record indicated that he had been tentatively diagnosed with birdshot retinochoroidopathy in January 1993. An electroretinogram (ERG) followed and demonstrated a reduction in the b-wave amplitude, confirming the diagnosis. Over time, despite multiple therapeutic interventions with cyclosporine and prednisone, his disease progressed. Presently, low vision training and rehabilitation are ongoing.

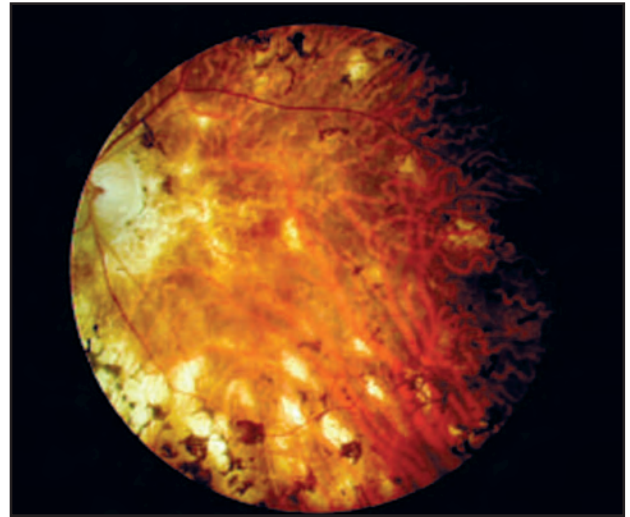
### **DISCUSSION**

Birdshot retinochoroidopathy, also referred to as BSRC or "birdshot," was first described in 1980<sup>1</sup> and represents a rare, potentially blinding form of posterior uveitis characterized by a pattern of retinal lesions that resemble birdshot scatter from a shotgun. BSRC is most often encountered clinically among Caucasian women in their fifth to seventh decade of life.<sup>2-4</sup>

Soon after BSRC was described, it was recognized that there was a strong association with the major histocompatibility complex antigen HLA-A29.<sup>5-7</sup> Subsequently, Priem demonstrated the presence of the HLA-A29 haplotype in over 95% of his patients diagnosed with BSRC and suggested that the risk among those with this antigen for developing birdshot was 200 times greater than it would be for an individual who did not carry the antigen.<sup>6</sup> The relationship between HLA-A29 and BSRC is recognized as the strongest HLA association with any known disease, yet we are still unaware of the exact mechanism by which this antigen confers risk for developing the disease.<sup>8</sup> Since most individuals who are HLA-A29 positive do not develop BSRC, it is obvious that other factors, such as an underlying infectious agent, are responsible for invoking an autoimmune response, possibly to a retinal protein,<sup>5</sup> and triggering disease onset.



**Fig. 1** OD. Late stage BSRC demonstrating retinal depigmentation, chorioretinal atrophy and optic atrophy.



**Fig. 2** OS. Late BSRC shows characteristic retinal lesions (with and without hyperpigmentation) that extend from the optic nerve to the retinal mid-periphery.

Reduced visual acuity and complaints of floaters represent the most common subjective findings among patients diagnosed with BSRC (Table I). Since birdshot represents a posterior segment inflammatory process, complaints of pain and photophobia are uncommon. In the later stages of the disease patients may report reduced color perception and difficulties in dim illumination or with their night vision.<sup>2</sup>

In the acute phase of the disease, fundus lesions appear bilaterally as flat, ovoid, creamy-yellow lesions with indistinct margins measuring 1/4 to 1 disc diameter in size extending from the optic disc to the equatorial retina. These findings most often occur in concert with a vitritis and vasculitis. Gass referred to this entity as vitiliginous chorioretinopathy due to the similarity in appearance of these areas of choroidal depigmentation to those occurring on the skin of individuals with vitiligo.<sup>9</sup> In the chronic phase, these lesions may coalesce to involve the macula and individual spots will generally evolve into more sharply defined areas of atrophy with or without secondary hyperpigmentation.<sup>2,3,9,10</sup> On occasion, the retinal and choroidal lesions common to BSRC develop after an initial bout of uveitis. Cases have been known to present initially as a vitritis and vasculitis without the characteristic fundus findings, only to develop these lesions years after the initial episode of inflammation.<sup>11</sup>

Chronic vitreal inflammation, a distinguishing feature of BSRC, will generally wax and wane. Cystoid macular edema occurs in 50% of patients and represents the most common complication associated with the

disease.<sup>2,3</sup> Associated conditions including serous macular detachment, choroidal neovascular membranes, ischemic optic neuropathy, and optic atrophy represent additional sight-threatening sequelae.<sup>12,13</sup> In advanced cases, chronic bouts of inflammation ultimately culminate in diffuse chorioretinal atrophy and varying degrees of visual loss. After following 28 affected patients for an average of 81.2 months, Kiss recorded the most common long-term complications resulting from BSRC and/or immunomodulatory therapy for treatment of this disorder as: cataracts (53.6%), cystoid macular edema (35.7%), glaucoma (21.4%), epiretinal membranes (10.7%), and retinal detachment (3.6%).<sup>14</sup> Optic disc edema, hemorrhaging, and exudation are also known to manifest in moderate to severe cases. Differential diagnoses are included in Table II.

Early reports suggested that visual stability was the norm once the initial bout of inflammation resolved.<sup>12,15</sup> However the conclusion that BSRC is self-limiting and benign was based on visual acuity results from studies that covered short follow-up periods. Other investigators suggested that the disorder follows a slower, progressive and relentless course. Oh et al,<sup>12</sup> demonstrated that the loss of retinal function initially occurs outside of the macula and that visual acuity alone is not an adequate gauge of disease stability. After prolonged follow-up, his cohort demonstrated extensive, progressive visual field loss and diminished electroretinogram (ERG) indices, with visual acuity being preserved until late in the course of the disease.

Table I Common symptoms of birdshot retinochoroidopathy	
Symptoms	Comments
Floaters	-Variable depending on severity of vitritis
Reduced visual acuity	-Caused by moderate to severe vitritis -Due to cystoid macular edema (50% of cases) -Due to chorioretinal atrophy in late stages -Central Snellen acuity is preserved until late
Photophobia	-More likely if inflammation is severe and involves anterior segment
Visual field loss	-Progressive -Requires periodic monitoring and therapeutic intervention considered if worsening
Nyctalopia*	
Reduced color vision*	

\* Electrodiagnostic testing assists in determining the cause for these symptoms. In the early stages the electroretinogram (ERG) may be normal, but in time demonstrate a reduction in the b-wave amplitude, a classic finding in BSRC. With advancing disease both the a-wave and b-wave indices are diminished indicating dysfunction in all retinal layers.

Since the HLA-A29 is positive in 80% to 95% of patients, HLA typing becomes an important component of the work-up when attempting to establish a diagnosis of BSRC. Because of this strong association, when HLA typing is negative, other diagnoses should be considered or the test repeated if clinical suspicions are high. Optical coherence tomography (OCT) is useful in identifying cystoid macular edema and monitoring the efficacy of treatment.<sup>2</sup> Intravenous fluorescein angiography (IVFA) demonstrates no characteristic findings unique to BCRS, although delayed retinal arterial-venous circulation time and reduced fluorescence of the vessels during the angiography have been described.<sup>15,16</sup> IVFA is most beneficial when monitoring macular edema, evaluating the severity of vasculitis, or when searching for vascular leakage in those cases where the visual acuity or patient symptoms are inconsistent with what may be observed by ophthalmoscopy alone.<sup>2,4</sup> The electroretinogram (ERG) is a key component for both diagnosing and following BSRC. Early in the course of the disease the ERG may appear normal but in time will classically demonstrate reduced b-wave amplitudes.<sup>17-19</sup> As the disease progresses, both the a-wave and b-wave indices are reduced, suggesting functional loss in all retinal layers.

A previous strategy employed in managing patients with BSRC was to treat only the acute exacerbations of inflammation or any secondary complications that might develop, such as cystoid macular edema. However, since episodic treatment does not appear to sufficiently slow the course of the disease, more aggressive long-term immunosuppressive therapy may be offered to affected patients. Since central Snellen visual acuity is spared until late in the disease, periodic visual field testing and

Table II Differential diagnoses for birdshot retinochoroidopathy
Pars planitis
Panuveitis
Presumed ocular histoplasmosis syndrome
Fungal endophthalmitis
Sarcoidosis
Intraocular lymphoma
Acute posterior multifocal placoid pigment epitheliopathy (APMPPE)
Multifocal choroiditis
Multiple evanescent white-dot syndrome (MEWDS)

electrodiagnostic evaluations have been recommended to evaluate for functional stability outside of the macula.<sup>4,12</sup> If evidence of disease progression is apparent, therapeutic intervention is warranted. Treatment options for BSRC vary depending on the severity of the inflammation. Mild inflammation may be controlled with intraocular corticosteroid injections, whereas more severe inflammation could require systemic dosing. Due to the complications associated with chronic steroid use, long-term administration of these medications is not recommended. The immunosuppressant cyclosporine, in low-doses, has proven to be effective in reducing vitreal inflammation and improving or stabilizing visual acuity without the major side-effects of hypertension and nephrotoxicity.<sup>20</sup> When the anti-fungal ketoconazole is combined with cyclosporine, further reductions in the cyclosporine dose can be used to achieve and maintain long-term therapeutic control of intraocular inflammation with the added benefit of fewer systemic side effects.<sup>21-23</sup>

## CONCLUSION

Birdshot retinochoroidopathy represents a chronic posterior uveitis that is characterized clinically by the presence of a vitritis, depigmented spots that radiate from the optic nerve to the retinal mid-periphery, and varying degrees of vasculitis. Primary eye care providers should familiarize themselves with this potentially blinding condition in order that timely and appropriate referral can be made to physicians who are familiar with the treatment and management of these patients. If evidence of disease progression manifests, either by progressive visual field loss or diminished electrodiagnostic indices, low vision needs should be assessed and rehabilitation initiated. □

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