njretina®
An affiliate of PRISM Vision Group
June // 2022 // njretina.com

Physicians

Nneka O. Brooks, MD
Nicholas D. Chinskey, MD
Rishabh C. Date, MD
Lekha K. Desai, MD
Leonard Feiner, MD, PhD
Howard F. Fine, MD, MHSc
Eric S. Friedman, MD
Luis A. Gonzalez, MD, MPH
Jonathan P. Greenberg, MD
Paul Hahn, MD, PhD
Vincent Y. Ho, MD
Bruce J. Keyser, MD
David Y. Kim, MD
Jennifer M. Krawitz, MD
Marisa K. Lau, MD
Steven A. Madreperla, MD, PhD
Akosua Nti, MD
Alexander D. Port, MD
Jonathan L. Prenner, MD
Daniel B. Roth, MD
Christopher M. Seery, MD
Sumit P. Shah, MD
Harris C. Sultan, MD, MS
Elizabeth O. Tegins, MD
Vinod B. Voleti, MD
H. Matthew Wheatley, MD

Locations

North Jersey

Belleville
973-450-5100

Elizabeth
908-409-4900

Morristown
973-630-7700

Ridgewood
201-445-6622

Teaneck
201-837-7300

Union City
201-867-2999

Vauxhall
908-349-8155

Wayne
973-633-9898

Central Jersey

Bridgewater
908-218-4303

Eatontown
732-389-2333

Edison
732-906-1887

Lakewood
732-363-2396

Lawrenceville
609-896-3655

Monroe
609-655-8301

New Brunswick
732-220-1600

Toms River
732-797-3883

Birdshot Retinochoroidopathy – diagnosis and treatment

Uveitis is a sight-threatening disease that accounts for approximately 30,000 new cases of legal blindness per year in the United States.[1-5] It is considered one of the leading causes of total blindness in our country.[1-5] Uveitis is the inflammation of the uveal tissues, and it can be limited to a segment of the eye (i.e., iris and ciliary body, pars plana, choroid, and retina) or affect its entirety. It can be associated to infectious processes such as syphilis, tuberculosis, toxoplasmosis, herpes viruses, and other pathogens. However, it is more typically associated with non-infectious, autoimmune disorders - either systemic or limited to the eye. About 30% of cases of uveitis are idiopathic and do not have a definite etiology.[5] All patients with recurrent and/or severe uveitis must undergo a full work-up to diagnose infectious, autoimmune or masquerade (e.g., lymphoma, leukemia) underlying pathology.

The relevance of diagnosing non-infectious uveitis is the availability of therapy to prevent complications associated with chronic ocular inflammation that frequently lead to irreversible blindness. In certain cases, prompt diagnosis and aggressive initial therapy may arrest the inflammatory process and preserve the patient's vision.

Birdshot retinochoroidopathy (BSRC) is a bilateral, chronic idiopathic posterior uveitis characterized by mild vitritis and multiple creamy, hypopigmented lesions resembling impacts from shotgun pellets. (Figure 1). The term was coined by Dr. Ryan and Dr. Maumenee in 1980, but the disease was first described in the 1940s.[6] Although it is relatively infrequent it represents approximately 6-8% of cases of posterior uveitis.[7-9] It typically affects Caucasian females in their fourth decade of life.[7-9] The etiology is unknown (idiopathic) but it has a strong correlation with the human leukocyte antigen (HLA) A29 serotype (especially with HLA-A*2902 subtype). This relationship is the strongest known association between an HLA antigen and any disease.[9,10]

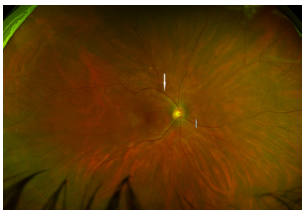


Figure 1a

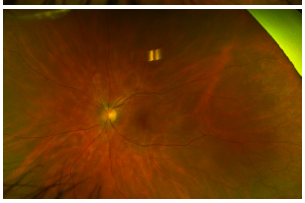


Figure 1b

Figures 1a-1b: Ultra-widefield fundus images of a patient newly diagnosed with Birdshot Retinochoroidopathy.Patient has 20/20 visual acuity with mild posterior pole retinal vasculitis (solid white arrow) and subtle multifocal oval shaped lesions nasal to the optic nerve (solid blue arrow) in his right eye. Notice the subtlety of the oval shaped lesions in the fellow eye, more marked nasal to the optic disc. The left eye also has retinal vasculitis.

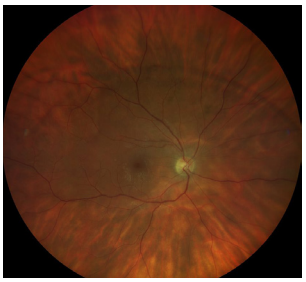


Figure 2a

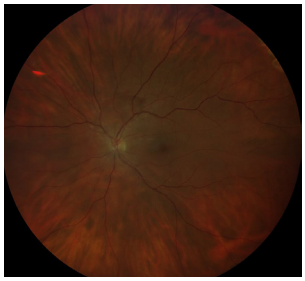


Figure 2b

Figures 2: Widefield fundus photographs of a patient diagnosed with Birdshot Retinochoroidopathy after persistent floaters and mild retinal vasculitis. Notice the oval shaped creamy lesions resembling shotgun pellets.

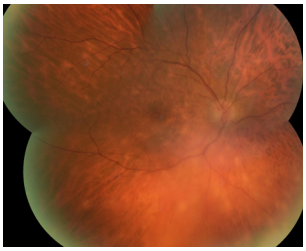


Figure 3a

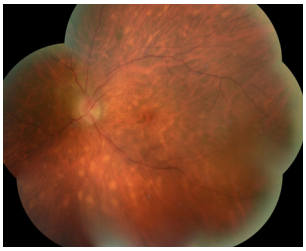


Figure 3b

Figures 3a-3b Fundus photographs of a 70-year-old male, asymptomatic with chronic fundus findings of multiple creamy lesions. Patient underwent extensive uveitis work up, which was unremarkable. HLA-A29 negative. The demographics and findings are atypical for a patient with BSRC. Also note the white spread more circular shaped lesions and absence of vasculitis. Patient is currently being worked up for secondary intraocular lymphoma, which can mimic BSRC. Patient with advanced birdshot retinochoroidopathy.

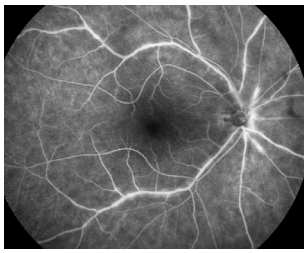


Figure 4a

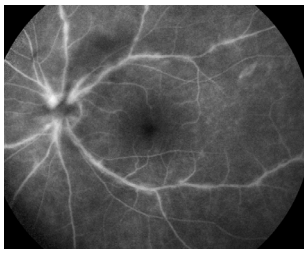
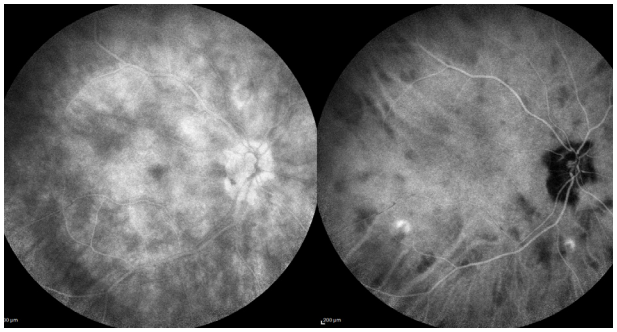


Figure 4b

Figures 4a-4b: Heidelberg fluorescein angiogram in a patient with newly diagnosed BSRC. Severe vascular leakage affecting the posterior pole is noted even in the face of a visual acuity of 20/20. Left untreated, inflammation will lead to irreversible retinal dysfunction.



Figures 5: Heidelberg fluorescein and indocyanine angiogram in a patient with end stage BSRC. Note the hypo lucent spots in ICG angiogram. Of note, the left eye has unrelated retinal arterial microaneurysm diagnosed prior to her uveitis.

Patients usually present with vague complaints of floaters, haziness or other nonspecific symptoms. On exam, there is mild vitritis with or without retinal vasculitis limited to the posterior pole (mild). Figure 2. A minimal anterior chamber reaction may be present but less than 1+ cells and there is never evidence of posterior synechiae or severe anterior inflammation. The most typical finding is the abnormal multifocal oval shaped lesions, especially nasal to the optic nerve, though these are more visible in the late stages of the disease. Ocular findings in BSRC can be easily overlooked as the inflammatory response is usually mild. The presence of dense vitritis, severe anterior uveitis or peripheral retinal vasculitis suggest another etiology as the cause of uveitis. The diagnosis is clinical, but laboratory work up is required to rule out other causes of multifocal choroiditis with vasculitis. It is not recommended to obtain routine HLA-I typing in all patients with uveitis. However, it is especially useful in patients with posterior uveitis and multifocal choroiditis (e.g., white dot syndromes). Although not essential for the diagnosis, its absence almost always rules out the diagnosis of BSRC and makes a workup mandatory for BSRC-like disorders (secondary lymphoma, metastasis, lymphoid hyperplasia).Figure 3.

The natural history of BSRC consists in multiple inflammatory episodes with few periods of remission. Without treatment, this condition eventually progresses to blindness – most frequently due to chronic cystoid macular edema and diffuse retinal dysfunction.[11,12] One of the typical features of BSRC is that central vision is often preserved in early stages. Patients usually complain of progressive, debilitating visual symptoms (nyctalopia, floaters, decreased blue-yellow color discrimination or decreased contrast) even when scoring 20/20 in the reading charts. To make the diagnosis more difficult, BSRC seldom has frank vitritis or angiographic leakage in the early stage. Figure 4 In this situation, electroretinogram, visual field and contrast sensitivity testing are extremely helpful in monitoring the disease. Indocyanine green angiography is also helpful in diagnosing the abnormal hypo lucent spots in the choriocapillaris, not otherwise seen with other testing techniques. Figure 5 The 30Hz flicker scotopic response in the ERG is valuable in monitoring response to therapy and recurrent inflammation.[19,20,31] Serial ERG testing is important to assess the progression of deterioration of retinal function and to support clinical decision making in treating patients with BSRC.[12,20]

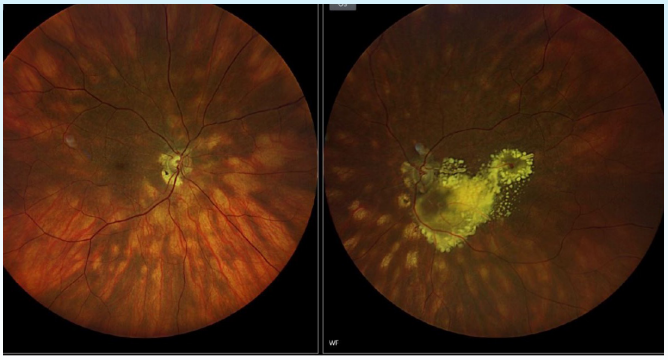
Once the diagnosis is established it is imperative to start therapy as soon as possible to preserve visual function. Corticosteroid monotherapy has proved to be ineffective in preventing progression and blindness.[6,13-18] Therefore, it is recommended to start immunomodulatory therapy (IMT) early on to halt the progression of the disease. Several IMT regimens have been explored in efforts aimed at achieving durable remission without the risks of long-term steroid therapy.[11,14,22-28] However, there is no published consensus providing a guideline for BSRC treatment.

Immunosuppressive agents such as cyclosporine, mycophenolate mofetil, azathioprine, and methotrexate have been studied as monotherapy with different success rates.[29] For example, cyclosporine monotherapy is highly effective at induction of remission, but patients require high doses and years of treatment rather than achieving durable remission or cure with discontinuation of therapy.[31] The use of combined IMT allows to use immunosuppressive agents at low-dose and decreases the incidence of side effects, which are directly proportional to the dose[30.31] Combination of mycophenolate mofetil with cyclosporine at low-dose is highly successful in inducing durable remission with a relatively safe profile.[31] In a large series of patients with BSRC, 92% achieved control of inflammation within one year and were able to maintain remission off any kind of corticosteroids after one year of follow-up with this combined regimen.[31]

Other therapeutic agents include the biologic response modifiers, these agents are extremely effective in inducing durable remission in patients with aggressive vasculitis or that have failed to standard IMT. Both infliximab and adalimumab have been successfully used in patients with BSRC.[29] In patients that fail to these agents or in those in which uveitis is uncontrollable, stubborn, or rapidly progressive, the use of more aggressive therapies such as intravenous immunoglobulin G with rituximab, daclizumab, alkylating agents (i.e., cyclophosphamide, chlorambucil) is warranted.

Although corticosteroid monotherapy is inadequate in these patients to achieve control of inflammation, the local use of steroids may be helpful as an adjuvant in the management of cystoid macular edema and inflammation. Dexamethasone and fluocinolone intravitreal implants and suprachoroidal triamcinolone injection have all been approved for the use in uveitic CME. It is important to emphasize that intermittent treatment with corticosteroid alone has been proved not to prevent vision loss in patients with BSRC.[17] Moreover, early initiation of IMT is more effective in reducing the risk of developing CME in these patients than corticosteroid therapy alone.[18] Thus, corticosteroids should be adjuvant to IMT to achieve rapid inflammatory control, after which they should be tapered and discontinued.[31] Figure 6

Ocular morbidity associated with chronic uveitis is well-known and its prevention must be one of the primary goals of managing patients with uveitis. In BSRC, one must monitor vitreous inflammation, CME, retinal angiographic leakage, blue-on-yellow visual fields, and electroretinogram. Visual acuity is not the best parameter to monitor in these patients, as they usually preserve good visual acuity until late stages of the disease. The presence or severity of floaters is particularly helpful as a subjective measure of disease activity.[31] However, objective tests are the standard of care (e.g., fluorescein and indocyanine green angiogram, electroretinogram, visual fields). In patients with chronic sight-threatening uveitis, such as BSRC, zero tolerance for even mild inflammation is mandatory to preserve visual function in the long term. In these patients, it is the presence of intraocular inflammation rather than an arbitrary visual acuity measurement what dictates the use of immunomodulatory therapy.



Figures 6: Widefield fundus photograph of a patient with advanced stage of BSRC. The oval shaped lesions are prominent and spread throughout the fundus. Patients with BSRC retained good central visualacuity until late stages; however, there is significant decline in their retinal function as measured by ERG.

References:

1. *Acharya NR, Tham VM, Esterberg E, et al. Incidence and prevalence of uveitis: results from the Pacific Ocular Inflammation Study. JAMA Ophthalmol. 2013;131:1405–1412.*
2. *Nussenblatt RB. The natural history of uveitis. Int Ophthalmol. 1990;14:303–308.*
3. *Suttorp-Schulten MS, Rothova A. The possible impact of uveitis in blindness: a literature survey. Br J Ophthalmol. 1996;80:844–848.*
4. *Darrell RW, Wagener HP, Kurland LT. Epidemiology of uveitis. Incidence and prevalence in a small urban community. Arch Ophthalmol. 1962;68:502–514*
5. *González MM, Solano MM, Porco TC, et al. Epidemiology of uveitis in a US population-based study. J Ophthalmic Inflamm Infect. 2018;8(1):6.*
6. *Ryan SJ, Maumenee AE. Birdshot retinochoroidopathy. Am J Ophthalmol 1980;89(1):31-45.*
7. *Gass JD. Vitiliginous chorioretinitis. Arch Ophthalmol 1981;99(10):1778-87.*
8. *Kaplan HJ, Aaberg TM. Birdshot retinochoroidopathy. Am J Ophthalmol 1980;90(6):773-82.*
9. *Rodriguez A, Calonge M, Pedroza-Seres M, et al. Referral patterns of uveitis in a tertiary eye care center. Arch Ophthalmol 1996;114(5):593-9.*
10. *Nussenblatt RB, Mittal KK, Ryan S, et al. Birdshot retinochoroidopathy associated with HLA-A29 antigen and immune responsiveness to retinal S-antigen. Am J Ophthalmol 1982;94(2):147-58.*
11. *Priem HA, Kijlstra A, Noens L, et al. HLA typing in birdshot chorioretinopathy. Am J Ophthalmology 1988;105(2):182-5.*
12. *Rothova A, Berendschot TT, Probst K, et al. Birdshot chorioretinopathy: long-term manifestations and visual prognosis. Ophthalmology 2004;111(5):954-9.*
13. *Sobrin L, Lam BL, Liu M, et al. Electroretinographic monitoring in birdshot chorioretinopathy. Am J Ophthalmol 2005;140(1):52-64.*
14. *Opremcak EM. Birdshot retinochoroiditis. In: Albert DM, Jakobiec FA, eds. Principles and practice of Ophthalmology. Volume 1. Philadelphia:WB Saunders Company;1994:475.*
15. *Vitale AT, Rodriguez A, Foster CS. Low-dose cyclosporine therapy in the treatment of birdshot retinochoroidopathy. Ophthalmology 1994;101(5):822-31.*
16. *Priem HA, Oosterhuis JA. Birdshot chorioretinopathy: clinical characteristics and evolution. Br J Ophthalmol. 1988;72:646-59.*
17. *Fuerst DJ, Tessler HH, Fishman GA, et al. Birdshot Retinochoroidopathy. Arch Ophthalmol, 1984;102:214-219.*
18. *Oh KT, Christmas NJ, Folk JC. Birdshot Retinochoroiditis: long term follow up of chronically progressive disease. Am J Ophthalmol 2002;133(5):623-9.*
19. *Thorne JE, Jabs DA, Peters GB, et al. Birdshot retinochoroidopathy: ocular complications and visual impairment. Am J Ophthalmol 2005;140:45-51.*
20. *Kiss S, Anzaar F, Foster CS. Birdshot retinochoroidopathy. Int Ophthalmol Clin 2006;46(2):39-55.*
21. *Zacks DN, Samson CM, Loewenstein J, et al. Electroretinograms as an indicator of disease activity in birdshot retinochoroidopathy. Graefes Arch Clin Exp Ophthalmol 2002;240(8):601-7.*
22. *Foster CS, Vitale AT. Diagnosis and Treatment of Uveitis. Philadelphia:WB Saunders;2002:731.*
23. *Becker MD, Wertheim MS, Smith JR, et al. Long-term follow-up of patients with birdshot retinochoroidopathy treated with systemic immunosuppression. Ocul Immunol Inflamm 2005;13(4):289-93.*
24. *Cassoux N, Goichot-Bonnat L, Karmochkine M, et al. Efficacy of intravenous immunoglobulin in the treatment of Birdshot retinochoroiditis. J Fr Ophtalmol, 2002;25(1):23-30.*
25. *Forooghian F, Gulati N, Jabs DA. Restoration of Retinal Architecture following Systemic Immunosuppression in Birdshot Chorioretinopathy. Ocul Immunol Inflamm 2010;18(6):470-1.*
26. *Leder HA, Galor A, Thorne JE, et al. Disappearance of classic birdshot spots after immunosuppression with tacrolimus and mycophenolate mofetil. Br J Ophthalmol 2008;92(2):291.*
27. *Sobrin L, Huang JJ, Christen W, et al. Daclizumab for treatment of birdshot chorioretinopathy. Arch Ophthalmol 2008;126(2):186-91.*
28. *Thorne JE, Jabs DA, Kedhar SR, et al. Loss of visual field among patients with birdshot chorioretinopathy. Am J Ophthalmol 2008;145(1):23-8.*
29. *Menezo V, Taylor SRJ. Birdshot uveítis: current and emerging treatment options. Clin Ophthalmol 2014;8:73-81*
30. *Trinh L, Bodaghi B, Fardeau C, et al. Clinical features, treatment methods, and evolution of birdshot chorioretinopathy in 5 different families. Am J Ophthalmol, 2009;147(6):1042-7,1047e1041.*
31. *Cervantes-Castañeda RA, Gonzalez-Gonzalez LA, Cordero-Coma M, Yilmaz T, Foster CS. Combined therapy of cyclosporine A and mycophenolate mofetil for the treatment of birdshot retinochoroidopathy: a 12-month follow-up. Br J Ophthalmol. 2013;97(5):637-43*
32. *Yamada Y, Sugita S, Tanaka H, et al. Timing of recurrent uveitis in patients with Behçet's disease receiving infliximab treatment. Br J Ophthalmol, 2011;95(2):205-8.*
33. *Levinson RD, Brezin A, Rothova A, et al. Research criteria for the diagnosis of birdshot chorioretinopathy: results of an international consensus conference. Am J Ophthalmol 2006;141(1):185-7.*
34. *Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol, 2005;140(3):509-16.*
35. *Nussenblatt RB, Palestine AG, Chan CC. Cyclosporin A therapy in the treatment of intraocular inflammatory disease resistant to systemic corticosteroids and cytotoxic agents. Am J Ophthalmol 1983;96(3):275-82.*
36. *LeHoang P, Cassoux N, George F, et al. Intravenous Immunoglobulin (IVIg) for the treatment birdshot retinochoroidopathy. Ocul Immunol and Inflamm 2000;8:49-57.*
37. *Shah KH, Levinson RD, Yu F, et al. Birdshot chorioretinopathy. Surv Ophthalmol, 2005;50(6):519-41.*

At the **forefront** of **clinical research**

NJRetina continuously conducts clinical trials at key locations. Our clinical research coordinators will be happy to discuss the inclusion/exclusion criteria or any other aspect of these studies with you or your patients. If you have any questions, please feel free to contact:

Joe Martinez - Teaneck: 201-837-7300, jmartinez@njretina.com
Joseph Portelli - Teaneck: 201-837-7300, jportelli@njretina.com
Zoe Etuke - Teaneck: 201-837-7300, zetuke@njretina.com
Dina Christodoro - Toms River: 732-797-3984 and Edison: 732-906-1887, dchristodoro@njretina.com
Andy Merino - Toms River: 732-797-3984 and Edison: 732-906-1887, amerino@njretina.com

Enrolling Studies:

Wet AMD

Edison

Opthea Coast: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Aflibercept, Compared with Aflibercept Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Toms River

Opthea Shore: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Ranibizumab, Compared with Ranibizumab Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

To read past issues of our newsletter, visit njretina.com.