



MANAGEMENT OF BIRDSHOT CHORIORETINOPATHY

Academic Advisory Committee
South African Vitreoretinal Society (SAVRS)
2024

Editorial

This is a revised Clinical Practice Guidelines (CPG) - Original version 2013: Dr Raoul Scholz

The main changes with this revision are:

- Updated to standard CPG format for society guidelines according to OSSA
- Updated treatment regimen with flow diagram

Key Points

- Birdshot chorioretinopathy is a rare, sight-threatening posterior uveitis
- Multimodal imaging is important to establish a diagnosis, determine disease activity, and monitor response to treatment
- The mainstay of treatment is initial high-dose systemic corticosteroids with early introduction of systemic immunosuppressive agent(s)

Scope and Purpose

- Guidelines on the management of birdshot chorioretinopathy, aimed at ophthalmologists and funders

Description of stakeholder involvement

- This guideline was developed by the Academic Advisory Committee of the SAVRS (South African Vitreoretinal Society), which consists of ophthalmologists from both the private and public sector.
- Input from other ophthalmologists in South Africa with an interest in uveitis was also sought.

Editorial Independence

- No funding or sponsorship was received for the publication of this clinical guideline
- The views of medical aids, government bodies and manufacturers of therapeutic agents have not influenced the content of this guideline
- The members of the group who developed this guideline have no competing interests

Adoption of recommendations from other guidelines

Flow diagram 1 was adopted from a proposed algorithm published in a recent review article on the management of Birdshot chorioretinopathy and was then adjusted to a South African context.¹

Evidence-based methods (= AGREE II Rigour of Development)

- A systematic google scholar search was conducted for original articles on the management of Birdshot chorioretinopathy. Recent review articles on the topic were also evaluated.^{1,2}
- As this condition is rare, there are no randomized, controlled trials on its management. Evidence is mostly from retrospective and prospective case series. The best levels of evidence were selected in formulating these recommendations.
- The guideline was primarily written by Dr Jonel Steffen (public sector) and Dr Raoul Scholz (private sector). It was then also reviewed and approved by all the members the Academic Advisory Committee of the SAVRS.

CLINICAL ASPECTS

Condition Background

- Birdshot Chorioretinopathy (BSCR)
- Rare, chronic, bilateral posterior uveitis with characteristic, widely distributed choroidal spots

Diagnosis

Diagnostic criteria for BSCR were recently published by the SUN working group (*see appendix 1*).³

History and examination

- Mostly middle-aged Caucasian adults with slight female predominance
- Usually present with flashing lights, floaters and decreased vision

Examination

- Bilateral posterior uveitis with characteristic widely distributed round/oval yellow-white choroidal spots (“birdshot spots”). Lesions may be extremely subtle early in the course of the disease
- Absent to moderate vitritis
- May have diffuse retinal vasculitis and cystoid macular oedema (CMO)

Multimodal imaging and visual field testing

While BSCR is diagnosed clinically, the signs early in the disease may be subtle. Hence multimodal imaging plays an important role in establishing the diagnosis, assessing severity of disease activity, and monitoring response to treatment.

- Fluorescein angiogram (FFA): Retinal vascular leakage, optic disc leakage and cystoid macular oedema
- Indocyanine angiography (ICG): Useful in identifying birdshot lesions that are not visible clinically. Unfortunately, not widely available in South Africa
- Macular OCT: Macular oedema; retinal thinning, loss of ellipsoid zone and choroidal thinning in later stages
- Visual field testing: Different patterns of field loss, including peripheral constriction, enlarged blind spot, and central/paracentral scotoma

- Other tests may include blue field autofluorescence, OCT-angiography, and electrophysiological tests such as ERG

Special investigations

- HLA-A29 (positive in more than 95% of cases)
- Exclude differential diagnoses, especially syphilis and sarcoidosis (may include syphilis serology, chest X-ray, serum ACE, etc.)
- Baseline workup before initiation of immunosuppressive agent (may include full blood count, urea and electrolytes, HIV test, liver function tests, hepatitis B and C serology)

Management

See flow diagram in appendix 2

Treatment

First-line treatment

- The mainstay of treatment is initial corticosteroids with early introduction of immunosuppressive agents.
- Oral corticosteroids:
 - Prednisone 0.5-1mg/kg/day PO
 - Used for initial control of inflammation until immunosuppressive agent becomes effective
 - Slow taper over several weeks once inflammation inactive
 - Aim for long-term dose of ≤ 7.5 mg/day, and ideally stop if possible
 - Add Calcium and Vitamin D supplementation if on long-term Prednisone
- Intravenous corticosteroids:
 - Methylprednisolone 1g daily IVI for 3 days may be used prior to oral Prednisone as initial treatment for patients who present with profound sight-threatening disease or relapses
 - Usually inpatient hospital treatment
- Initial immunosuppressive agents
 - Early introduction of immunosuppressive agents is associated with better outcomes and less side effects relating to the long-term use of high dose corticosteroids
 - None of the immunosuppressive agents have been evaluated in controlled trials and there is no accepted optimal treatment protocol
 - Based on current evidence, we suggest using the following as initial immunosuppressive agent: Mycophenolate mofetil 1g bd PO

Second-line treatment options

- Initiate second-line treatment if inflammation remains inadequately controlled after 6 months of first-line therapy (refer to monitoring below). Consider earlier initiation in cases of severe uncontrolled inflammation, or if patients experience side effects or complications from first-line agents.
- Agent(s) choice will depend on disease severity, as well as experience of ophthalmologist/ rheumatologist/ physician with the different agents
- Switch to a different immunosuppressive agent
 - Options include Methotrexate, Azathioprine or Ciclosporin A
- Combine immunosuppressive agents:

- Ciclosporin 2mg/kg/day PO (can be increased to 5mg/kg/day) combined with Mycophenolate Mofetil
- Switch to a biologic immunosuppressive agent
 - Infliximab monthly IVI or Adalimumab monthly SC
 - Newer biologic agents are currently under investigation
- Intravitreal steroids
 - Indicated in patients with persistent macular oedema despite systemic therapy, or in patients who can't tolerate systemic therapy
 - Options include intravitreal Triamcinolone injections and intravitreal slow-release implant, e.g. Ozurdex

Discontinuation of immunosuppressive agent(s):

- Only consider discontinuation of immunosuppressive agent(s) once inflammation has been inactive for at least 2 years.
- Some patients may require long-term immunosuppression

Monitoring

- Monitoring disease activity requires regular multimodal imaging, which include macular OCTs, as well as 6-monthly FFA.
- Periodic visual field testing may be necessary.
- ICG and ERG may also be indicated if available.

Co-management with rheumatologist/physician

- These patients should ideally be co-managed with a rheumatologist/physician, especially to assist with immunosuppressive agent monitoring.
- Patients will require regular blood tests and/or blood pressure monitoring according to the immunosuppressive agent used and may require bone density scanning yearly if on long-term Prednisone.

Reference List

1. Bousquet E, Durauffour P, Debillon L, Somisetty S, Monnet D, Brézin AP. Birdshot Chorioretinopathy: A Review. *Journal of Clinical Medicine* 2022, Vol 11, Page 4772. 2022;11(16):4772. doi:10.3390/JCM11164772
2. Crowell EL, France R, Majmudar P, Jabs DA, Thorne JE. Treatment Outcomes in Birdshot Chorioretinitis: Corticosteroid Sparing, Corticosteroid Discontinuation, Remission, and Relapse. *Ophthalmol Retina*. 2022;6(7):620-627. doi:10.1016/J.ORET.2022.03.003
3. Classification Criteria for Birdshot Chorioretinitis. *Am J Ophthalmol*. 2021;228:65-71. doi:10.1016/J.AJO.2021.03.059

Appendix 1: Diagnostic criteria for birdshot chorioretinopathy³

Criteria ([#’s 1, 2, and 3] OR # 4)

1. Characteristic bilateral multifocal choroiditis on ophthalmoscopy
 - a. Multifocal cream-colored or yellow-orange, oval or round choroidal lesions (“birdshot spots”)

AND

2. Absent to mild anterior chamber inflammation
 - a. Absent to mild anterior chamber cells AND
 - b. No keratic precipitates AND
 - c. No posterior synechiae

AND

3. Absent to moderate vitritis

OR

4. Multifocal choroiditis with
 - a. Positive HLA-A29 test AND either (b. or c.)
 - b. Characteristic “birdshot” spots (multifocal cream-colored or yellow-orange, oval or round choroidal lesions) on ophthalmoscopy OR
 - c. Characteristic indocyanine green angiogram (multifocal hypofluorescent spots) without characteristic “birdshot” spots on ophthalmoscopy

Exclusions

1. Positive serologic test for syphilis using a treponemal test
2. Evidence of sarcoidosis (either bilateral hilar adenopathy on chest imaging or tissue biopsy demonstrating noncaseating granulomata)^a
3. Evidence of intraocular lymphoma on diagnostic vitrectomy or tissue biopsy

^aPossible sarcoidosis should be evaluated with chest imaging at a minimum.

Appendix 2: Management of birdshot chorioretinopathy

