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Protocol for Management of Birdshot Chorioretinopathy

I have been requested by Discovery Health medical aid to assist with the development of a protocol for the management of Birdshot Chorioretinopathy. I have reviewed many articles and spoken to world experts, ophthalmologists, (Profs. Stephen Foster, U.S.A., Janet Davis, U.S.A., William Ayliffe, U.K.) who have managed many cases. In addition, I have canvassed opinions from my local colleagues actively involved in managing cases. (Dr. Karin Lecuona, Uveitis Clinic, Groote Schuur Hospital, Dr. Joanne Miller, Medical Retina specialist, Johannesburg and Dr. Rizwana Amod, SA Vitreoretinal Society). This is a rare disease, and while we manage only a handful of cases in South Africa, Foster and Ayliffe have managed hundreds. I have previously forwarded opinions from Foster and Ayliffe to Discovery Health.

I refer you to articles in:

1) International Ophthalmology Clinics 2006 Kiss, Anzaar, Foster. Birdshot Retinochoroidopathy.
2) Current Opinion in Ophthalmology 2006 17: 545-550.
3) BJO April 2013 Combination Therapy in Birdshot Chorioretinopathy.

This is not a review article on this disease, as the details will be found in the above articles. The aim is to assist funders and colleagues with management issues.

This condition is a rare but sight threatening condition and ideal treatment is not known. In my experience, in the early stages of the disease, the diagnosis is often missed, and thus patients often have sight threatening well established disease when diagnosed. Thus there is a need to initiate urgent immunosuppressive therapy. In addition, the activity of the disease is difficult to monitor, and thus delayed action of therapies would make management more difficult. The response to treatment is not always predictable with any one drug and thus treatment needs to be modified based on treatment response.

My suggested management is thus:

1) Confirm diagnosis. (Symptoms, signs, angiography, HLA A29+).
2) Exclude/investigate for other causes of chorioretinal inflammation and vasculitis.
3) Confirm active inflammation. (Angiography and Electroretinogram).
4) Make decision whether treatment is indicated or not.
5) Decide on follow-up management to monitor disease activity and drug side effects.
6) Initiate medical therapy. Co-manage with a physician.

Suggested medical therapy: Assistance from Physician, Rheumatologist or Renal Physician, with the use of drug management sheets and regular blood tests as indicated per drug management sheets.

1) Oral Prednisone 0.5 to 1.0mg/kg/day, decrease over a few weeks, but maintain until other immunosuppressive and steroid sparing drugs have been started.
2) Initiate Cyclosporine therapy, lower dose than is generally required for graft rejection, from 2mg increasing to 5mg/kg/day in two divided doses, depending on response and side effects. Serum trough levels (blood taken before morning dose) not as critical as in graft rejection, as lower doses generally used to control disease. Peak levels done 2hrs after dose.

The above drugs are used to initiate remission, giving one time to initiate testing, discussion and insurer/funder motivation, and these drugs are also used to control relapses.

3) Urgent introduction of steroid sparing agent in the form of Mycophenolate Mofetil (CellCept), up to 2g to 3g per day, in two divided doses, depending on response and side effects. Taper and stop the steroids. CellCept works quickly, effectively and with good patient tolerance.
4) Cyclosporine and CellCept are used to maintain remission for a two year period, and doses are altered depending on tests for activity, patient symptoms, and side effects.
5) After two years in remission one can taper doses slowly, 6 weekly, over a period of one year, monitoring for relapse. Increase doses again if relapse, or add steroid again (oral, subtenons triamcinolone, intravitreal triamcinolone, or Ozurdex dexamethazone implant).

Monitoring for activity of disease:
Baseline: Fluorescein angiography (vascular leakage, cystoid macular edema, birdshot spots may only be evident later). Repeat twice a year or as necessary. Baseline and annual visual fields. Baseline and annual ERG (electroretinogram), very sensitive for monitoring activity, 30Hz B wave implicit time prolongation, reduced amplitudes. Patient symptoms are important.

Alternative medications as mentioned by experts and authors:
1) Azathioprine, may substitute CellCept, but less effective, slower response (see comments above), liver breaks it down in some patients, enzyme test for this. 1mg to 3mg/kg/day. 4-6 weekly blood monitoring liver function and blood counts.
2) Triamcinolone or Ozurdex as discussed above. Former has higher incidence of cataract and glaucoma and is section 21 application MCC, the latter longer duration/effect, registered.

3) Alternative immunosuppressives and biologics may need to be considered.

The numbers of patients with this disease in South Africa are very low, and as we appreciate the need for cost containment but also effective medication with fewer side effects, we request that this protocol be accepted, for a disease that is potentially blinding if not managed effectively.

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