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## Relentless Placoid Chorioretinitis

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**R**elentless placoid pigment epitheliopathy as an entity was first described by B Eric Jones et al<sup>1</sup>.

It is a condition affecting young individuals predominantly males. The lesions in the acute stage of the disease is characterized by yellow to grey lesions involving mid peripheral and peripheral retina usually not affecting the macula and the posterior pole at first presentation. Macula is involved later and there are accompanying lesions in the periphery which may have already healed. There is minimal vitritis. There is presence of posterior vitreous cells upto++. There is no disc involvement in most cases. Acute lesions are usually resistant to usual treatment to cortico steroids and it requires treatment with immunosuppressant. If treated early in the course of the disease the visual acuity can be maintained though there is usually a reduction in the contrast sensitivity of the affected eyes and a subnormal color vision.

Visual fields also show a reduction in the sensitivity in the affected areas. With the field affection matching the areas of involvement. Even though the vision may be maintained. The main characteristic of the lesion as the name suggests is relentless and has a prolonged course before the disease gets controlled finally after treatment. It may require continuation of the immunosuppressant to keep the activity of the disease under control. A constant follow up of the patient to titrate the dose of immunosuppressant is necessary. RPC is a definite indication of starting Immunosuppressant early as it can keep the disease under control with good visual outcome.

### Materials and Methods

Here we describe eight cases of relentless placoid pigment epitheliopathy in Table 1. Treatment received by the patients are given in Table 2.

**Table 1: Description of eight cases.**

Case	Age /Sex	Laterality	Periphery	Posterior Pole	Macular	Systemic Disease
1	12/F	Bilateral	Involved	Spared	Spared	Nil
2	26/M	Bilateral	Involved	Involved	Spared	Nil
3	18/M	Unilateral	Involved	Involved	Involved	Nil
4	20/M	Unilateral	Involved	Involved	Spared	Nil
5	26/M	Bilateral	Involved	Involved	Involved	Nil
6	31/M	Bilateral	Involved	Involved	Involved	Nil
7	23/F	Bilateral	Involved	Involved	Involved	Pregnancy
8	37/M	Bilateral	Involved	Involved	Spared	Cmv Hsv Igm +Ve

**Table 2: Treatment received**

Case	Bcva Initial	Bcva Final	Treatment	Duration of Fup (Months)	Clinical Features
1 Od	6/9	6/6	Immuran+	4	
1 Os	6/9	6/6	Prednisolone++		
2od	6/9	6/6	Immuran	7	
2os	6/6	6/6	Prednisolone		
3od	6/6	6/6	Ivmp	19	Fvp & Trd
3os	6/60	6/6	Prednisolone		
4od	6/6	6/6	Immuran Prednisolone	17	
4os	6/12	6/9	Acyclovir		
5od	3/60	6/36	Immuran	23	Subretinal Fibrosis
5os	6/6(P)	6/6	Prednisolone		
6od	6/24	6/18	Immuran	15	Os Scar
6os	6/9	6/12	Prednisolone		
7od	6/9	6/12	Immuran	96	Scleritis
7os	6/24	Fc 1mt	Prednisolone		Macular Lesion
80d	2/60	3/60	Immuran Tricort Inj	9	Od Scar
80s	6/6	6/6	Prednisolone		Healed Macula

BCVA: Best corrected visual acuity; FUP: Follow up ; FVP: Fibro vascular proliferation ; TRD: Tractional retinal detachment. IVMP: intravenous methylprednisolone

+Tab Immuran was given as 50 mg three times a day and the dose was tailored according to the activity of the choroidal lesions.

++Tab Prednisolone was given at 1mg/kg /day and tapered weekly.

**Results**

The patients were aged from 12 years to 37 years pointing towards a trend of younger people getting involved. Out of 8 patients 6 were male and 2 females pointing towards a male preponderance. Medical histories were not consistent with any single disease. Case 3 was diagnosed to have tuberculosis in the past and was treated for the same. Case 6 had a high ESR. Case 8 had a positive Toxoplasmosis immunoglobulin. One patient had corneal involvement and also had an episode of episcleritis, this same patient was pregnant in the course of the disease with activation of her lesions in the postpartum period necessitating stopping of her breast feeding as she had to be treated with high doses of systemic steroids. 6 had bilateral involvement over a period of time,

some had simultaneous involvement with severity more in one eye. Others had old healed lesions in the fellow eye. This indicated that the disease is bilateral with asymmetrical onset. All patients exhibited whitish lesions at the level of the RPE. While many of these lesions developed pigmented chorioretinal atrophy within weeks all patients had long clinical courses of activity with persistent lesions for few years in few cases after diagnosis. FFA showed early hypo fluorescence with late hyperfluoresence in the form of staining of the placoid lesions. One case had a lowered contrast sensitivity tested on FACT. The acute phase had a drop in vision which often returned back after treatment if the macula was not involved. All cases were severe and had prolonged course. All patients were treated with systemic immunosuppressant except

one who was given a trial of IVMP treatment. All patients required additional cover with oral steroids. Even when macula was involved in the acute stages with treatment the vision improved to even 6/6.

### Discussion

Serpiginous choroiditis is usually bilateral, presenting as a unilateral decrease in central vision, metamorphopsia, or scotoma. Anterior segment of the eye is typically normal. However, non-granulomatous anterior uveitis in patients with serpiginous choroiditis was observed in one study,<sup>2</sup> and fine pigmented cells in the vitreous humor has been described in up to 50% of eyes in some series.<sup>3,4</sup> The lesions are typically not multifocal as seen in our series. The active disease begins with peripapillary patches of grayish or creamy yellow sub-retinal infiltrates progress in an irregular serpentine fashion centrifugally. The overlying retina is usually edematous and occasionally a serous retinal detachment may occur.<sup>5</sup> The active lesions will resolve over 6–8 weeks, with or without treatment, leaving an area of atrophy involving both the choriocapillaris and the overlying retinal pigment epithelium (RPE). Multiple lesions in different stages of resolution are typical of the disease and may be observed in the affected eye. Recurrences usually, occur at the edges of previous atrophic scars.

APMPPE is a disease affecting age group between 20 to 50 years, with no sex predilection. It onset is abrupt and recurrences are, rare. Presentation symptoms are blurred vision, photopsia, scotomas. There usually are few vitreous cells mild. Fundus shows multifocal, flat, gray – white placoid lesions at the level of RPE it is usually at the posterior pole, there may be disc swelling.

The lesions described were different from APMPPE or Serpiginous choroiditis in that they

had a distinctive retinal distribution with a prolonged relapsing course. Our patients had lesions in the mid and far periphery unlike APMPPE or Serpiginous Choroiditis. In some cases peripheral lesions predated posterior pole lesions. The relapsing nature of the disease left the fundus with more than 50 lesions scattered throughout the fundus. The systemic workup and clinical manifestations and clinical course were not consistent with any of the above diagnosis. The best treatment of the disease has yet to be determined. Responses to treatment in our series were anecdotal and not consistent. It was observed that with treatment the visual acuity also improved in most patients unless the macula was involved. Most patients required immunosuppression for the lesions to reduce and also to keep the scarring to minimum. Only one patient had sub retinal fibrosis, there was no case of inflammatory CNV as seen with Serpiginous choroiditis. This condition like APMPPE and Serpiginous is of unknown origin and there is no single diagnostic test to confirm with certainty of any of the diagnosis.

**Differential Diagnosis:** (Apart from APMPPE and Serpiginous choroiditis) 1) multifocal choroiditis, 2) Hardas disease, 3) Bird shot chorioretinitis, 4) primary or secondary metastasis to the choroids and 5) granulomatous diseases like syphilis, tuberculosis, and sarcoidosis.

**Treatment:** The goal of any successful therapy would be the rapid control of the active lesions during recurrences, and the prevention of further recurrences. Therefore, to demonstrate the success of any therapeutic approach for relentless placoid chorioretinitis, a long follow-up with serial fundus photography and angiography to show non-progression is required. Final visual acuity, although obviously important, does not provide an objective measure of non-progression in cases where extra-foveal

recurrences continue to affect the eye and cause more scarring. Even if central visual acuity is preserved, the ensuing scotoma caused by the atrophic parafoveal lesions can be debilitating.<sup>6</sup> Based on our experience with treatment for serpiginous following modalities could be used.

#### **A. Corticosteroids**

Systemic corticosteroids and retrobulbar steroidal injections were effective in controlling the active lesions and shortening the duration of active disease.<sup>7</sup> However, corticosteroids had no effect on the prevention of recurrences. Patients often relapse during tapering or after discontinuation of steroid therapy.<sup>8</sup> Hence short-term treatment with corticosteroids does not alter the natural course of the disease and the final visual outcome remains unsatisfactory in the long run. Choroiditis. Intravitreal steroid, like systemic and periocular, will likely be efficacious in the treatment of the acute lesions, but will probably not prevent the recurrences unless it is administered on a continuous basis and for a prolonged duration such as a long-acting steroid implant.

#### **B. Cyclosporine A, Azathioprine, And Mycophenolate Mofetil**

The results with cyclosporine A mono-therapy for serpiginous choroiditis have been mixed. There were initial reports on treatment failure with cyclosporine A,<sup>9</sup> and there were subsequent reports with treatment success.<sup>10, 11</sup>

Araujo et al reported favorable results with 7 patients (14 eyes) treated with oral cyclosporine A (3–5 mg/kg/day) for a duration ranging from 1.3–5 years (median 3 years).<sup>10</sup> Five out of seven patients achieved remission and had no recurrences while on therapy. One patient, refractory to treatment, was switched to FK506 and mycophenolate mofetil and one patient relapsed on low-dose cyclosporine A. Secchi

et al also reported favorable results with 7 patients treated with oral cyclosporine A (4–7 mg/kg/day). Nine out of 14 eyes had improvement in visual acuity whereas the remaining 5 were unchanged.<sup>11</sup> Christmas et al reported 4 out of 6 patients with serpiginous choroiditis treated with 2–40 months of immunosuppressive drugs, such as cyclosporine A, azathioprine, or mycophenolate mofetil, successfully discontinued their therapy without recurrences.<sup>8</sup> Akpek et al reported that 2 out of 4 patients with serpiginous choroiditis who were

treated with cyclosporine alone or combined with azathioprine experienced a recurrence while on therapy.<sup>12</sup>

#### **C. Triple-Agent Therapy**

Combination therapy consisting of cyclosporine A, azathioprine, and prednisolone was first described by Hooper and Kaplan to control inflammation rapidly and promoted visual recovery in 5 patients with bilateral serpiginous choroiditis.<sup>13</sup> The therapy was administered for 8 weeks and tapered. Two patients relapsed during tapering and the remaining patients were in remission while they were maintained on low-dose triple immunosuppressive therapy or azathioprine and prednisolone. Another study of four patients maintained on low dose triple agent therapy for 12–69 months (median 39 months) reported a similarly favorable outcome. Three out of four patients achieved drug-free remission.<sup>12</sup> Munteau et al also reported satisfying results with triple-agent therapy on 34 patients with serpiginous choroiditis.<sup>14</sup> Further studies using the triple-agent therapy also demonstrated good control of inflammation with minimal side effects.<sup>15</sup>

#### **D. Alkylating Agents and Anitmetabolites**

Laatikainen reported visual improvement in 2 patients with sight-threatening disease treated

with cytosine arabinoside combined with azathioprine.<sup>16</sup> In later reports, alkylating agents, such as cyclophosphamide and chlorambucil, appeared to be effective in rapidly controlling the inflammation and producing a long-term drug-free remission in patients with serpiginous choroiditis. Alpek et al reported the use of alkylating agents (cyclophosphamide or chlorambucil) in 9 patients with active vision-threatening serpiginous choroiditis which progressed despite initial conventional steroid and triple-agent therapy (2 patients).<sup>17</sup>

All patients had no recurrences while on the therapy and had preservation of vision. Two thirds of patients had a visual improvement

and 7 out of 9 patients achieved drug-free remission. However, one patient developed bladder epithelial carcinoma, which may have been related to the use of cyclophosphamide. Alkylating agents should be used with caution in view of the potential life-threatening complications reported.

As the patients may be different in stage and activity of the disease and there is no standardized method of measurement of disease activity and clinical criteria for recurrences treatment is individualized. It is possible that immunosuppressive therapy as monotherapy may be efficacious in a subset of patients who present early in the course of this disease.

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