

CASE STUDY

Clinical profile and visual outcomes in post-fever retinitis—a case series

Sonal Paliwal* and Prerna Upadhyaya

Sewa Sadan Eye Hospital, Bhopal, India

***Correspondence:**

Sonal Paliwal,
sonal22paliwal@gmail.com

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Post-fever retinitis mostly represents a para-infectious etiology with a seasonal pattern in endemic areas without a uniformly identifiable cause. It mostly affects young immunocompetent individuals and has a self-limiting course. We present a single-center retrospective case series of five patients presenting with acute retinitis, following a febrile illness with no specific etiology from December 2022 to January 2023. The retinitis lesions had a sudden onset with rapid evolution, preceded by a febrile episode within one month of presentation, in all cases. Serology testing was non-contributory in guiding the therapy. Oral corticosteroid therapy was effective in the resolution of lesions and improving the visual outcomes. Post-fever retinitis is easily diagnosed on the basis of clinical features and a history of flu like illness and responds very effectively to oral corticosteroid therapy.

Keywords: post-fever retinitis, para infectious, visual acuity, oral corticosteroids therapy, immunocompetent

Introduction

Post-fever retinitis is a para-infectious uveitis entity caused by various bacteria and viruses, commonly seen in tropical countries like India (1). It is characterized by focal or multifocal retinal infiltrates, cotton-wool spots, and retinal hemorrhages presenting days or weeks after the initial febrile illness (2). The exact etiology of this condition is not known and the majority of these cases are idiopathic. Often treated by oral corticosteroids there are no set guidelines to manage these cases. It is important to do the serological testing to rule out infectious etiology before initiating the corticosteroid therapy.

Few cases of post-fever retinitis have been published in South India (3, 4). India being a tropical country, these cases specifically present during the cooler months of the year, with an annual recurrence pattern (5). We describe the clinical presentation, clinical course, and outcomes in 5 cases of post-fever retinitis from central India with a common history of fever preceding the retinitis and a relevant review of the literature.

Methodology

This is a retrospective observational case series done at a tertiary referral eye institute in central India. Five cases of acute retinitis with a common history of fever with no specific etiology from December 2022 to January 2023 were included. Patients with known etiology like toxoplasma or CMV retinitis which require specific therapy were excluded.

Ocular examination including best corrected visual activity (BCVA), intraocular pressure (IOP), anterior and posterior segment evaluation, fundus photography, and optical coherence tomography was done.

Detailed history like details of fever, history of travel and treatment received for the same, any ocular intervention, systemic investigations, previous laboratory test or microbiological evidence, and any other relevant information were documented.

Investigations done were a complete hieogram, venereal disease research laboratory tests (VDRL), human immunodeficiency virus (HIV), hepatitis B surface antigen, Mantoux test, and radiograph chest. All the patients tested COVID-19 RT-PCR negative at the time of diagnosis of

retinitis. Detailed laboratory work including malaria parasite, widal test, and Toxoplasma immunoglobulins was done.

All patients received oral steroids for retinitis, after ruling out any infectious etiology. Detailed history about the dose and duration of steroid therapy was noted.

There was no history of travel in all the patients and all were from central India only.

The research adhered to the tenets of the Declaration of Helsinki and informed consent from patients was taken.

Results

Five immunocompetent patients with a mean age of 34.6 years with age ranging between 20 and 50 years were included. All patients presented with acute retinitis, following an episode of fever. Out of 5 patients 3 patients were male and 2 were female. Four patients had unilateral involvement and one had bilateral involvement. The average duration between the febrile episode and the onset of ocular symptoms was approximately 4 weeks. None of the patients showed evidence of anterior segment inflammation or raised IOP and systemic examination was unremarkable. There was no evidence of vitreous in any case and disc examination showed mild hyperemia in few cases. Retinitis lesions in all the cases were localized to the posterior pole with macular involvement in most of the cases. Laboratory workup was inconclusive. All patients received oral steroid therapy 1 mg/kg followed by weekly tapering doses. The ocular examination findings and visual acuity were noted at presentation, one-week and six-week follow-up visits. A good response to oral corticosteroid therapy with a significant decrease in size of the retinitis lesions and a decrease in macular edema was seen. All patients were followed for a period of 6 weeks and a significant improvement in visual acuity was noted only with corticosteroid therapy without adding any antiviral drug. None of the patients showed any evidence of recurrence or any other complications like neovascularization or retinal detachment.

Case 1

A 30-year-old female presented with complaints of painless diminution of vision in the right eye for 2 weeks. The patient had an episode of fever one month ago for 4 days. The patient was diagnosed as a case of seasonal flu-like illness and treated symptomatically. Systemic examination was within normal limits. At presentation, the right eye's visual acuity was counting fingers and the left eye was 6/6. IOP was right eye 10 mmHg and left eye 12 mmHg respectively. The anterior segment was quiet and pupillary reflexes were normal. Posterior segment examination revealed mild vitreous in the right eye. The

optic disc appeared mild hyperemic in the right eye with multiple small creamish lesions in the supertemporal quadrant with few superficial hemorrhages. The foveal reflex in the right eye was dull with a macular star (**Figure 1A**). The left eye fundus examination was within normal limits. Optical coherence tomography of the right eye showed a distorted foveal contour with the presence of subfoveal serous detachment and intraretinal edema (**Figure 1B**).

A specific etiology could not be established due to non-contributory laboratory workup. The patient was started on 1 mg/kg body weight oral steroids followed by a weakly tapering dose for 6 weeks. Lesions in the right eye started showing resolution at one week followed up with a significant improvement in vision to 6/12 after 6 weeks (**Figure 1C**). Right eye optical coherence tomography also showed a significant decrease in macular edema at 6 weeks (**Figure 1D**).

Case 2

A 20-year-old male patient presented with chief complaints of diminution of vision in the left eye for 20 days. The patient had a history of fever 1 month back. On presentation, right eye vision was 6/6 and left eye vision was 6/18. IOP was right eye 10 mmHg and left eye 14 mmHg. Anterior segment examination was completely unremarkable and pupillary reflexes were within normal limits. On examination, the right fundus examination was within normal limits. Left eye fundus examination showed creamish lesions just below the macula with surrounding exudation. The left eye optic disc showed mild hyperemia and vitreous was completely within normal limits (**Figure 2**).

Optical coherence tomography of the right eye was within normal limits. Left eye OCT showed full thickness hyper-reflectivity and effacement of the affected retina along with subretinal fluid with macular involvement.

Since patient said that he had a mild flu-like illness and responded to over-the-counter medications. With negative laboratory work, patient was started on oral corticosteroids—1 mg/kg body weight in tapering doses. After 1 month of treatment, visual acuity in the left eye returned to 6/6 along with resolution of retinitis and subretinal fluid.

Case 3

A 24-year-old male patient presented with chief complaints of diminution in vision in the Left eye for 20 days with a history of fever two weeks ago. The fever was mild with associated upper respiratory tract symptoms that had fully resolved with treatment at a local hospital with no admission or further investigation required. On presentation, his visual

Clinical summary of all cases of post-fever retinitis.

S NO	Features	Case 1	Case 2	Case 3	Case 4	Case 5
1	Age/Gender	30/F	20/M	24/M	50/F	49/M
2	Laterality	Unilateral	Unilateral	Unilateral	Unilateral	Bilateral
3	BCVA at presentation	RE CF/CF LE 6/6	RE 6/6 LE 6/18	RE 6/6 LE 6/18	RE 6/9 LE 6/6	RE 6/60 LE 6/36
4	Anterior uveitis	NO	NO	NO	NO	NO
5	H/O Fever	YES	YES	YES	YES	YES
6	Interval between onset of fever and ocular symptoms	4 weeks	4 weeks	2 weeks	4 weeks	2 weeks
7	Systemic history	Nil	Nil	Nil	Nil	Nil
8	Laboratory investigations	Inconclusive	Inconclusive	Inconclusive	Inconclusive	Inconclusive
9	Immune status	Immunocompetent	Immunocompetent	Immunocompetent	Immunocompetent	Immunocompetent
10	Treatment	Oral corticosteroid therapy 1 mg/kg dose followed by tapering weekly	Oral corticosteroid therapy 1 mg/kg dose followed by tapering weekly	Oral corticosteroid therapy 1 mg/kg dose followed by tapering weekly	Oral corticosteroid therapy 1 mg/kg dose followed by tapering weekly	Oral corticosteroid therapy 1 mg/kg dose followed by tapering weekly
11	Follow up	6 Weeks	4 weeks	4 weeks	4 weeks	6 weeks

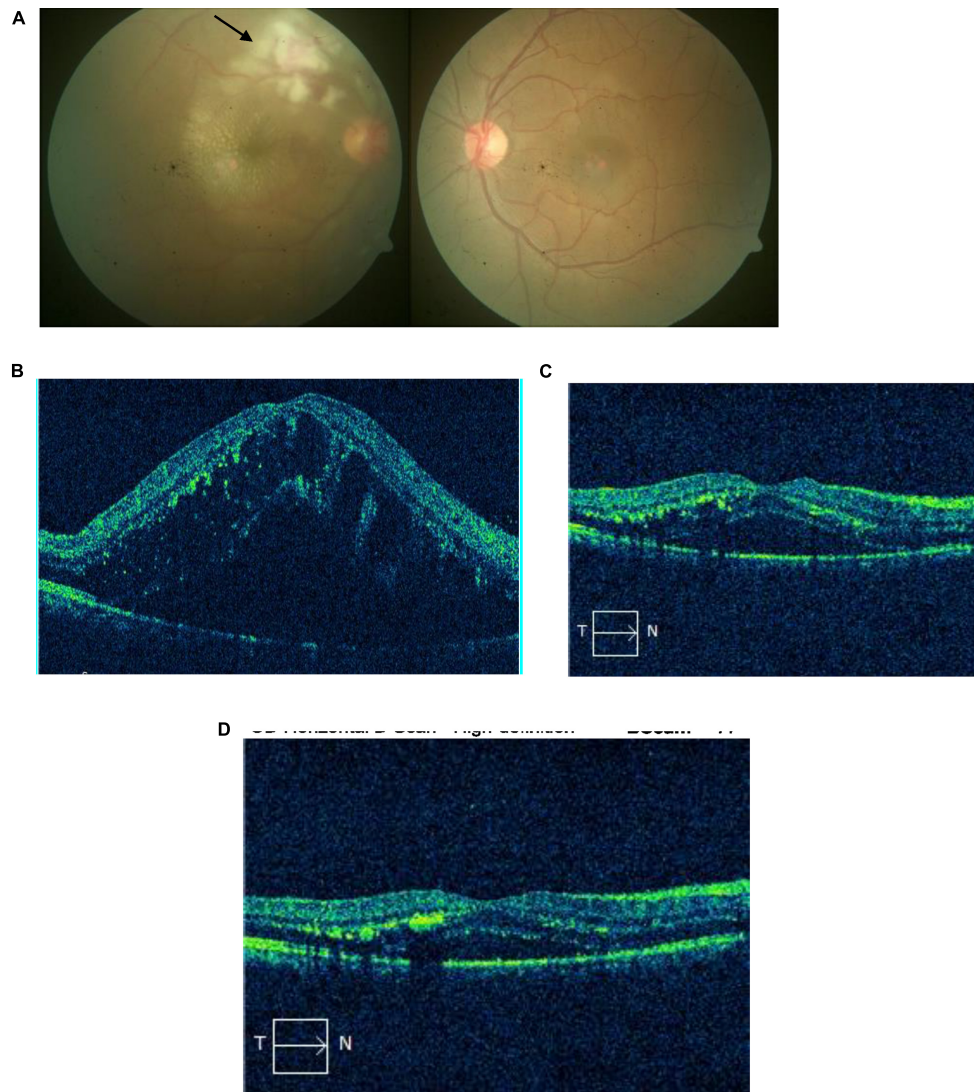


FIGURE 1 | (A) Fundus photograph of the right eye showing retinitis lesion (black arrow) with exudation and left eye fundus is normal. **(B)** OCT of RE Passing through macula showed macular edema. **(C)** OCT of RE showed a decrease in macular edema after 1 week. **(D)** OCT OF RE showed a decrease in macular edema after 6 weeks.

acuity and IOP were 6/6,11 mmHg and 4/60, 10 mmHg in the right eye and left eye respectively. Fundus examination in the right eye was within normal limits. His left eye fundus examination showed a creamy white lesion inferior to the macula associated with macular fluid (**Figure 3A**). The vitreous in the left eye was clear and the optic disc was completely normal. Optical coherence tomography of the left eye showed hyperreflectivity and effacement of inner retinal layers and the presence of subretinal fluid at the macula (**Figure 3B**). The patient was started on oral steroids at the dose of 1 mg/kg body weight in tapering doses. After 1 month visual acuity recovered to 6/18 with significantly resolving retinitis lesions and subretinal fluid (**Figures 3C, D**).

Case 4

A 50-year-old female presented with a slight blurring of vision in her right eye for 2 weeks. The patient had a history of fever 1 month back. Her presenting visual acuity and IOP were 6/9,12 mmHg and 6/6,15 mmHg in her right eye and left eye respectively. Fundus examination in the right eye showed creamy white-yellow lesions in the supertemporal quadrant with mild vitreous and normal optic disc. Kyrieleis arterioles were also seen in supertemporal vessels as a sign of inflammation (**Figure 4A**). The left eye fundus examination was unremarkable. Right optical coherence tomography was within normal limits (**Figure 4B**). A complete uveitis profile was done and disease entities like Toxoplasmosis, Bechet's, TB, and Syphilis were ruled out. Aqueous samples were negative for CMV, HSV, and HZV. The patient was started on oral steroids at 1 mg/kg body weight in tapering doses. After one month of therapy, patient was comfortable with vision and the lesion was decreasing in size and vitreous was resolving.

Case 5

A 49-year-old male patient presented with chief complaints of a decrease in vision in both eyes for 4 days. He gave a history of fever 2 weeks back. On presentation, his visual acuity and IOP were 6/60, 14 mmHg and 6/36, 12 mmHg in the right eye and left eye respectively. Fundus examination of both eyes showed a clear vitreous and normal optic disc. Both eyes fundus examination showed a creamy white lesion inferior to the macula with a macular star. Optical coherence tomography of both eyes showed subretinal fluid at the macula. After ruling out infectious etiology patient was started on oral steroids 1 mg/kg in tapering doses. The patient responded well with a decrease in subretinal fluid over time and visual acuity improving to 6/18 in both eyes after 1 week and to 6/9 after 6 weeks (**Figures 5A–D**).



FIGURE 2 | Left eye fundus photograph showing retinitis lesions with exudation.

Discussion

This case series shows clinical presentations and outcomes of acute retinitis, the etiology of which remains somewhat unclear. It could be grouped as an immune-mediated subset of acute retinitis secondary to para-infectious etiology most probably of viral origin which has been hypothesized previously as well (6).

Post-fever retinitis is common in young and middle-aged patients as described in other studies (7). The average age of study participants in our study was 34.6 years with age ranging from 20 years to 50 years. Thus post-fever retinitis is more common in young adults probably because of the stronger immune system in the younger population as compared to the elderly.

In our case series, all patients had a history of fever in common and were treated symptomatically in all cases at the local hospital without extensive diagnostic evaluation. All patients belonged to central India and none of them had a history of travel. None of the patients gave a history of fever associated with rash or joint pains and all tested negative for HIV, VDRL, or TPHA. All the patients tested negative for COVID-19-RTPCR.

The lesions were unilateral in four cases and bilateral in 1 case. The lesions were mostly unifocal, with a predilection for the posterior pole causing serous macular detachment as an exudative response. IOP was normal at the presentation and all visits. The time duration from the onset of fever to ocular symptoms was two to four weeks. Fever usually subsided till the patient presented to an ophthalmologist. These features are similar to cases previously reported by other authors. Except in one case, we could see Kyrie leis arteritis a finding which was never seen in previously reported cases.

Differential diagnosis for this condition includes other causes of retinitis which may be viral, bacterial, or other specific agents which have been ruled out by doing a detailed laboratory evaluation.

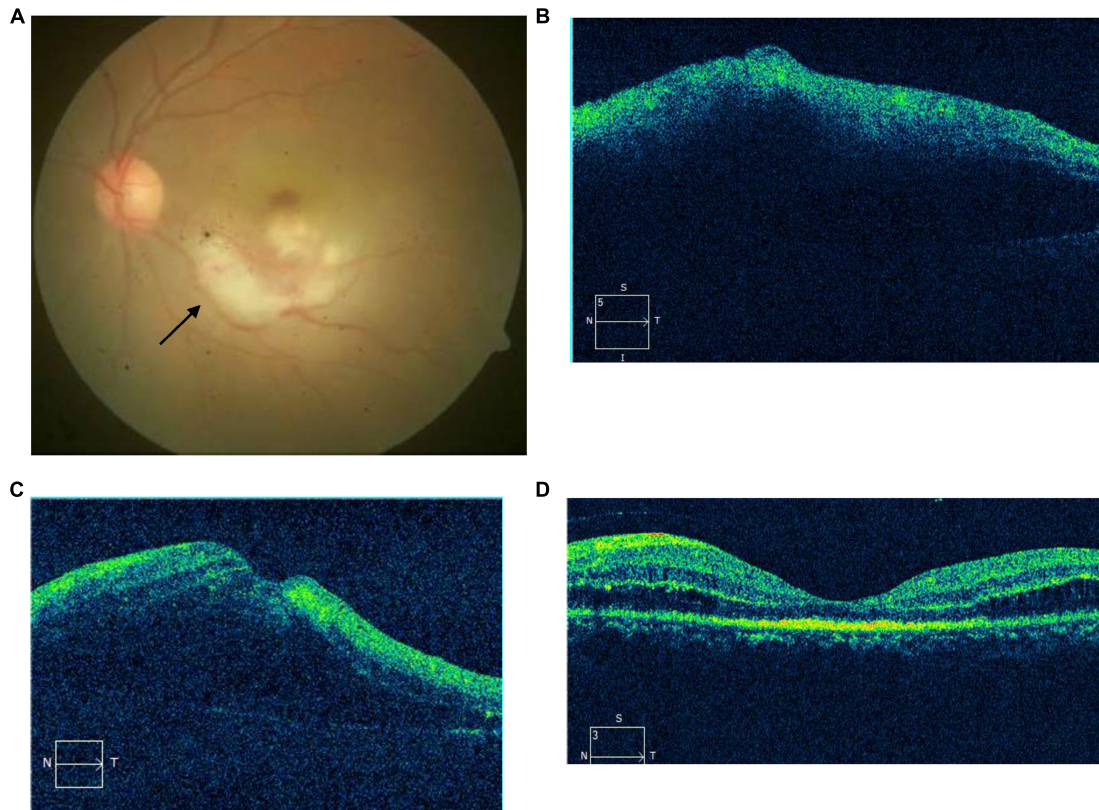


FIGURE 3 | (A) Fundus photo of the left eye showing retinitis lesions with macular involvement. **(B)** OCT of the left eye showed hyperreflectivity of inner layers. **(C)** OCT of the left eye showed a decrease in subretinal fluid at the 1-week follow-up. **(D)** OCT of the left eye showed resolving subretinal fluid at 4 weeks.

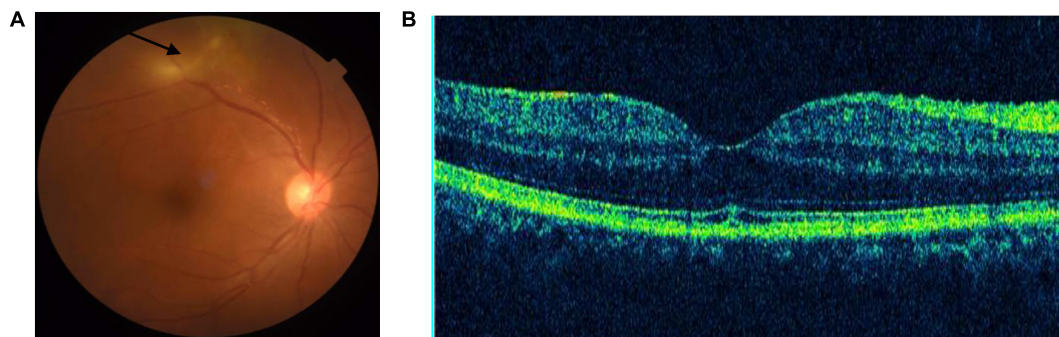


FIGURE 4 | (A) Fundus photo of the right eye showing retinitis lesion in superotemporal quadrant. **(B)** Right eye OCT showed normal foveal contour.

Many such case series have been reported in literature prior from south India. But from Central India, very few case series of this have been published earlier by Karkhur et al. (6) and Shenoy et al. (8).

All these cases presented with similar clinical presentation, the immunocompetent status of all the patients and clinical resolution after starting corticosteroids point toward an immunological cause as against an infectious cause as described in earlier case series also (6). Since there was no systemic involvement, all cases were considered as retinitis—probably immune-mediated following a viral flu-like episode.

In a similar study by Kawali et al. (3), there was no significant difference in outcome after treatment with or without steroids as well as in patients whose therapy was guided by serological diagnosis.

In a similar study first published by Vishwanath et al. (1), all 14 cases had a similar clinical presentation with retinitis involving the posterior pole and a favorable response to steroids, suggesting a possible immunological basis for this condition. But among the 14 cases, only 4 cases had identifiable etiology and all cases presented with anterior segment inflammation.

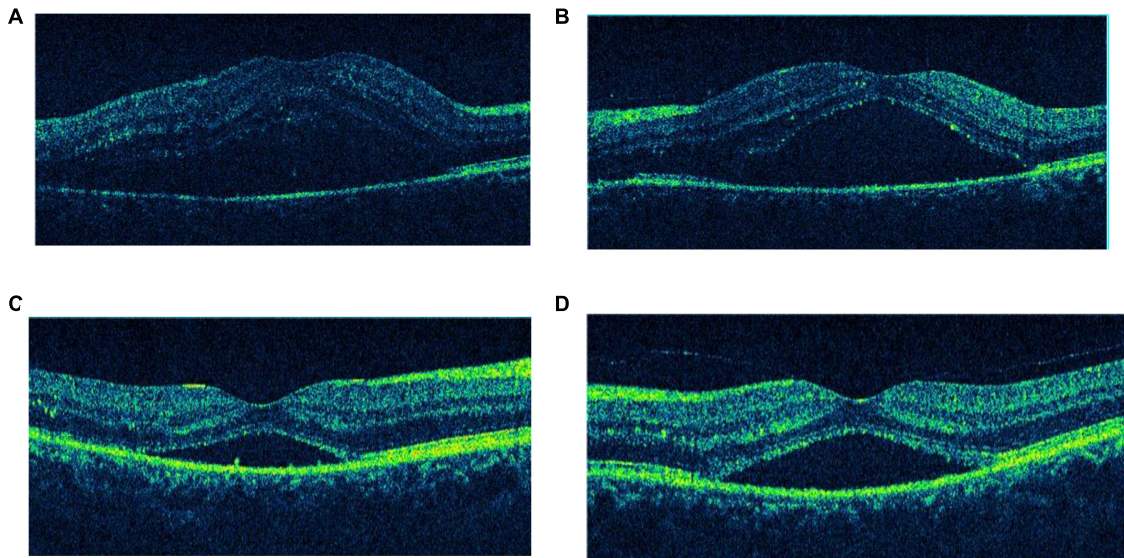


FIGURE 5 | (A) Right eye showing macular edema at presentation. **(B)** The left eye oct showing macular edema at presentation. **(C)** The right eye OCT showing resolution of fluid after 6 weeks. **(D)** Left eye OCT showing resolution of fluid after 6 weeks.

Our case series was similar to one published by Karkhur et al. (6), as no identifiable cause of fever was found and also there was no involvement of the anterior segment in our cases. This may be because of the same geographical location in both case series. Viral infections occur in close association with the environmental factors and the vectors responsible for the transmission of the virus breed in a favorable environment (9).

In this type of case, a proper systemic examination and detailed laboratory workup are important to rule out systemic infections like tuberculosis, and to start corticosteroid therapy to control the inflammation. But depending totally on serological and molecular diagnosis, to guide the approach may cause delays in starting the steroid therapy. Detailed serology undertaken to guide specific therapy does not appear to alter the visual outcome which has been very well proved by our cases as well as the previously published studies (10).

However, detailed laboratory evaluation to know the cause of fever is more practical in the acute phase of fever. But in our case series patient usually presented after subsidence of fever. We ordered investigations like CBC, LFT, RFT, HIV, VDRL, Mantoux test, and Chest x-ray which was a more practical approach in a country like India with limited resources and financial constraints. Advising a detailed battery of investigations which is an out-of-pocket expense for many of our populations may cause a delay in starting the oral steroid therapy and affect the visual outcomes. Detailed invasive investigation can be undertaken if the retinitis is still progressing despite adequate therapy.

Although this condition is considered to be self-limiting but the recovery and the course of the disease could be modified by timely starting of oral corticosteroid therapy which otherwise could have led to suboptimal

visual gains. No recurrence of retinitis lesions or neovascular complications were noted during the short follow-up in our study.

Limitations

However, the small number of cases and the retrospective nature of the study and the small duration of follow-up are the limitations of our study. Also, fundus fluorescence angiography was not done in all patients. More cases are needed to analyze such cases and understand their pathophysiology.

Conclusion

Post-fever retinitis is a distinct subset of retinitis that presents following a febrile illness—possibly a viral flu-like illness. It is mostly an immune-mediated response. It is usually a self-limiting disease with good visual outcomes after adequate steroid therapy.

Author contributions

SP managed the clinical cases. SP and PU performed the literature review and drafted the manuscript.

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None.

Consent

Ethics approval has been taken by the institutional ethical committee and informed consent from patients was taken.

Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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