International Journal of Retina (*IJRETINA*) 2023, Volume 6, Number 2.
P-ISSN. 2614-8684, E-ISSN.2614-8536

IJRETINA
International Journal of Retina

POST FEVER RETINITIS AND SINGLE WONDER DRUG FOR ITS VARIOUS ETIOLOGIES

Vikas Sharma[1], Raji K[2], Sankalp Seth[3], Yogesh Yadav[4], Gaurav Kapoor[5]

[1]*5 Air Force Hospital, Jorhat, Assam, India*
[2]*INHS Asvini, Mumbai, India*
[3]*CH(CC), Lucknow, India*
[4]*Nirmal Ashram Eye Institute, Rishikesh, India*
[5]*Command Hospital, Chandimandir, Chandigarh, India*

Abstract

***Introduction**: Post-fever retinitis is an infectious or para-infectious entity which involve retinal layer of the eye and has variable clinical manifestations. Post-fever retinitis has varied etiologies, namely bacteria or viral.*

***Case Report**: We present a series of four cases of post fever retinitis with common history of flu-like illness followed by blurring of vision, all four patients had different clinical picture, they were investigated thoroughly to ascertain etiological agents and were treated with oral Doxycycline. All cases had an excellent visual recovery by the end of the treatment with complete resolution of clinical signs.*

***Discussion**: It is difficult to pin-point the exact etiology of PFR just on the basis of clinical presentation and hence, proper history, clinical examination, serological investigations and awareness of ongoing epidemics may help to identify the etiological organism.*

***Conclusion**: Post fever retinitis is an easy diagnosis based on antecedent history of flu like illness and typical fundus findings. Oral doxycycline is a safe and wonderful drug for PFR cases.*

Keywords: Post fever retinitis, Flu Like illness, Subretinal fluid, Doxycycline, Steroids
Cite This Article: SHARMA, Vikas et al. POST FEVER RETINITIS AND SINGLE WONDER DRUG FOR ITS VARIOUS ETIOLOGIES. International Journal of Retina, [S.l.], v. 6, n. 2, p. 153, sep. 2023. ISSN 2614-8536. Available at: <https://www.ijretina.com/index.php/ijretina/article/view/219>. Date accessed: 28 sep. 2023. doi: https://doi.org/10.35479/ijretina.2023.vol006.iss002.219.

Correspondence to:
Vikas Sharma
5 Air Force Hospital, Jorhat,
Assam, India
vikas.sharmadr@gmail.com

INTRODUCTION

Post-fever retinitis (PFR) is an infectious or para-infectious entity which involves retinal layer of the eye and has variable clinical manifestations. PFR has varied etiologies, namely bacteria or viral. Sometimes It can also presents as uveitidis which can affect different coats of the eye and hence have variable clinical manifestations. PFR usually involves retina and hence the name retinitis is most appropriate. We came across four cases of PFR with varied clinical manifestations. The common factor in all our patients was a past history of fever.

CASE REPORT

Case 1: A 35-year-old male, resident of Andhra Pradesh, India presented with sudden onset of painless diminution of vision in both eyes, he also gave history of flu-like symptoms two weeks back. He was treated at other centre as Branched Retinal Vein Occlusion and had received Intra-vitreal injection Avastin (Bevacizumab) in left eye. On presentation, his visual acuity was 6/24 and 6/60 in right eye and left eye respectively. Anterior segment was with in normal limits and posterior segment had vitreous cells, multiple fluffy yellowish white edematous retinal lesions along with inferior arcade and few splinter haemorrhages in right eye and same was seen along both superior and inferior temporal arcades in left eye suggestive of retinitis. Both eyes had elevated macula suggestive of fluid with macular star configuration due to hard exudates in left eye (Figure 1). Level and amount of fluid was further quantified by Optical Coherence tomography (OCT).

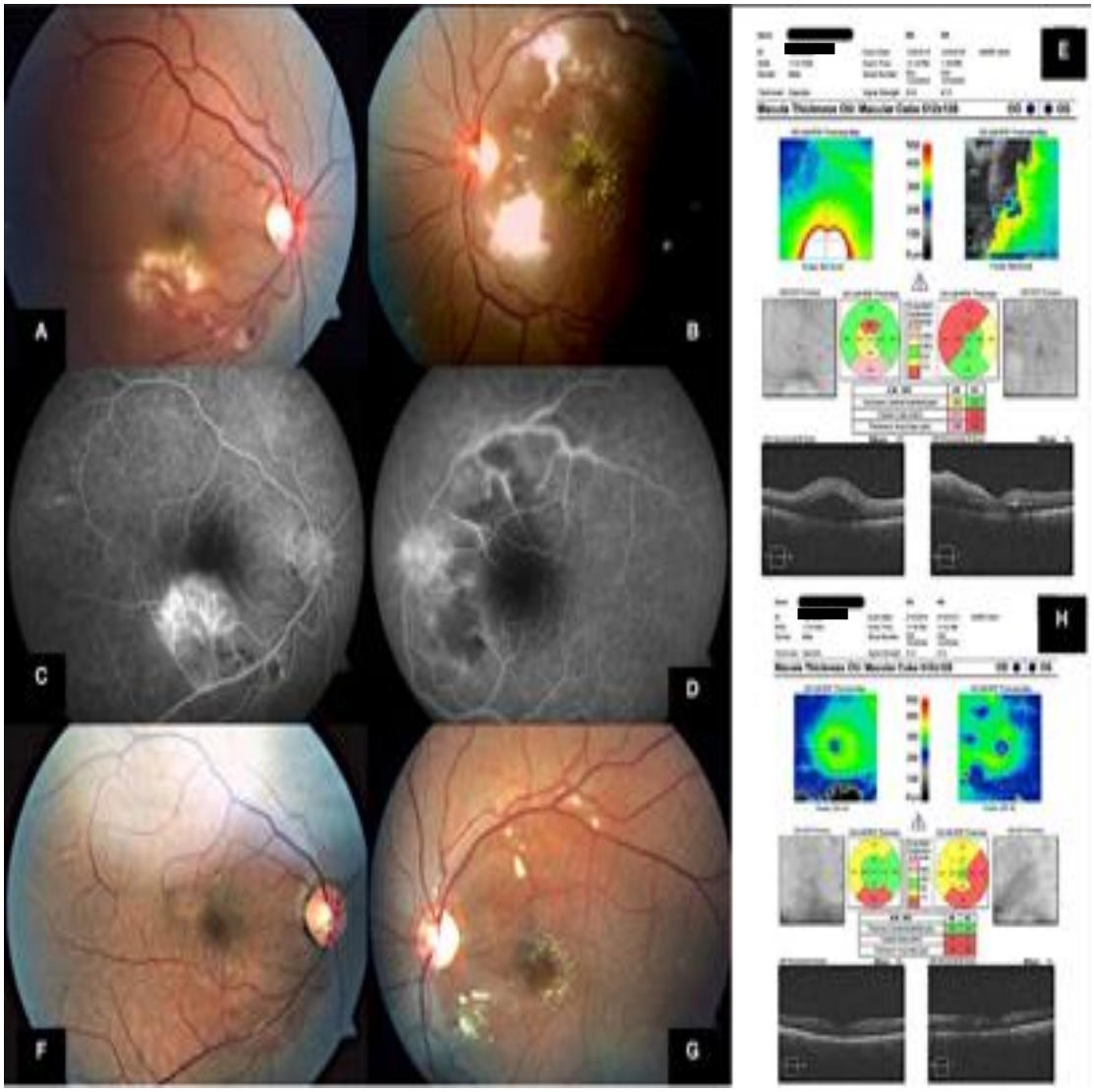

Figure 1 **Fundus photo of right eye and left eye (A & B) of case 1, Fluorescein angiography (FFA) showing leakage in both eyes (C & D), OCT Macula showing subretinal fluid (E), Post treatment fundus photos of Right eye (F) and Left eye (G), Post treatment resolution of SRF on OCT (H)**

Case 2: A 26-year-old male presented with complaints of sudden onset of diminution of vision in right eye of 10 days duration. Patient gave history of fever with rashes one month back before the onset of visual complaints. On examination his visual acuity in the right eye was 3/60 not improving further with pin hole and refraction and 6/6 in the left eye. Retina showed retinitis with localized haemorrhages along the superior vascular arcade. Macula showed thickening and hard exudates suggestive of edema (Figure 2).

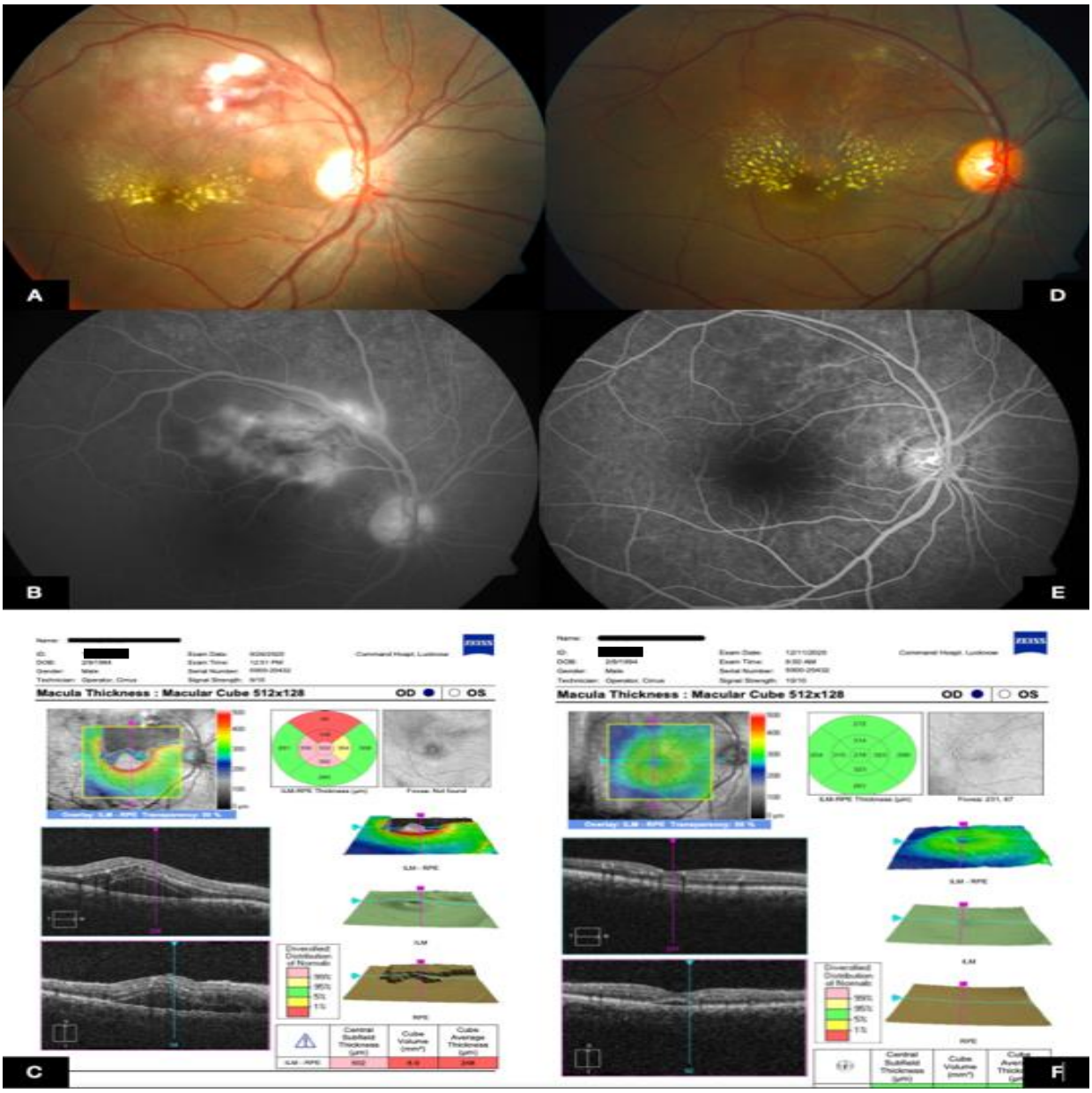

Figure 2 **Fundus photos of case 2 right eye showed yellowish retinal lesions with NFL hemorrhages and macular edema (A) FFA revealed corresponding area of vascular leak in right eye (B) OCT showed multiple small pockets of intra retinal fluid and large subretinal fluid (C). Post treatment fundus photo right eye (D) showed clinical resolution of retinitis, resolution of vascular leak on FFA (E) and minimal SRF in right eye on OCT (F).**

.

Case 3: A 32-year-old, male presented with painless progressive diminution of vision both eyes over 2 weeks. Patient was more symptomatic in right eye than the left eye. He gave history of fever 04 weeks back. His best corrected visual acuity was 3/60 in the right eye and 6/24 in the left eye. Positive anterior segment finding was trace cells in anterior chamber in both eyes. Fundus examination revealed vitritis with retinitis in both eyes (Figure 3).

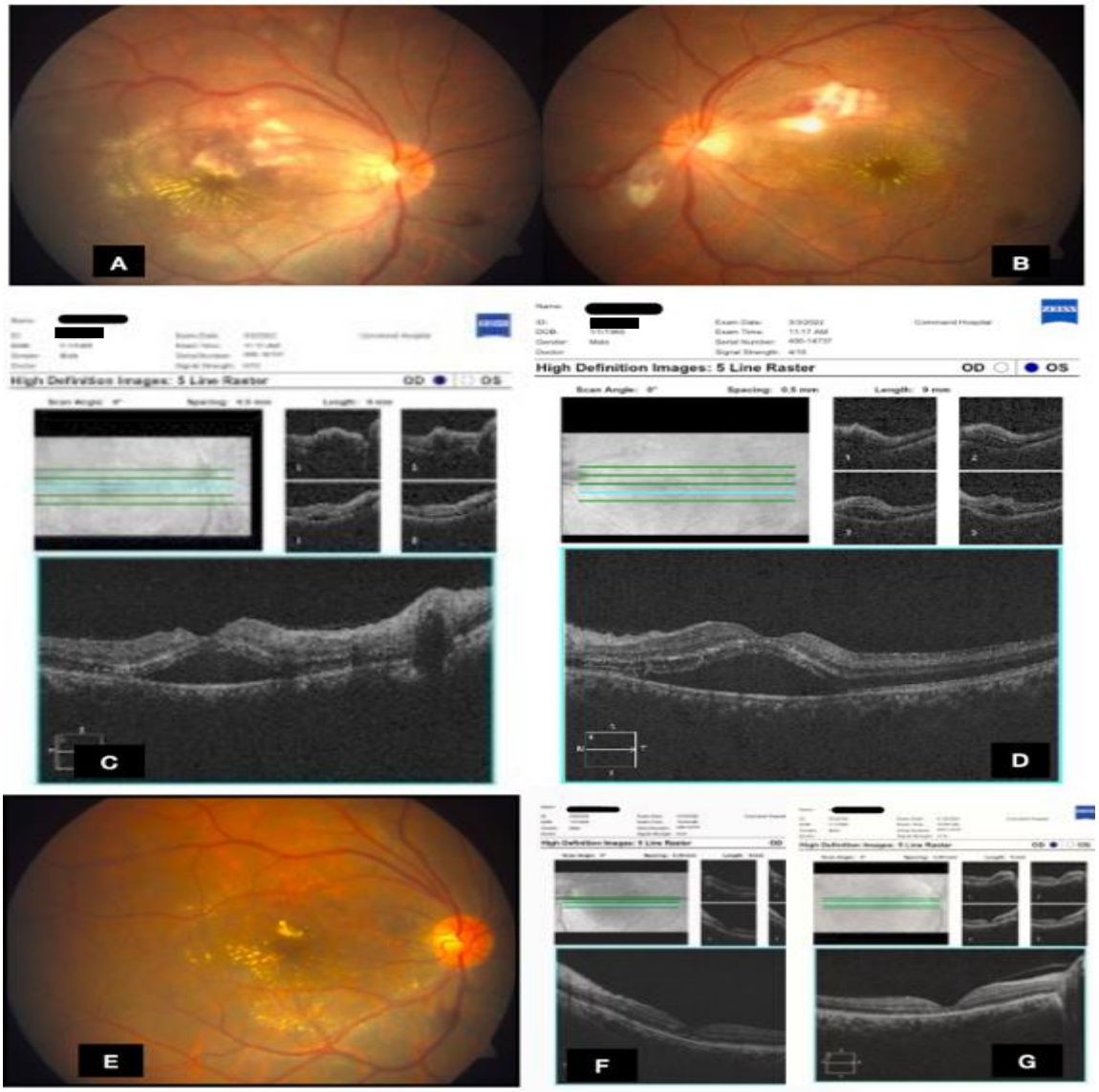

Figure 3 **Fundus photo of right and left eye of case 3 revealed retinitis both eyes (A & B) with large SRF on OCT both eyes (C & D), Post treatment fundus photo of right eye (E) with OCT image showing complete resolution of SRF both eyes (F & G)**

Case 4: A 25-year-old working female with no known co-morbidities developed sudden onset painless diminution of vision and photopsia in right eye. She also gave history of fever 01 week before the onset of ocular complaints. Her BCVA in right eye was finger counting at 1m with accurate projection of rays, left eye was 6/6. Anterior Segment examination was within normal limits both eyes. Fundus examination right eye revealed optic nerve head swelling with area of retinitis inferotemporal to disc, along with foveal neurosensory detachment in the right eye. Left eye fundus was normal (Figure 4).

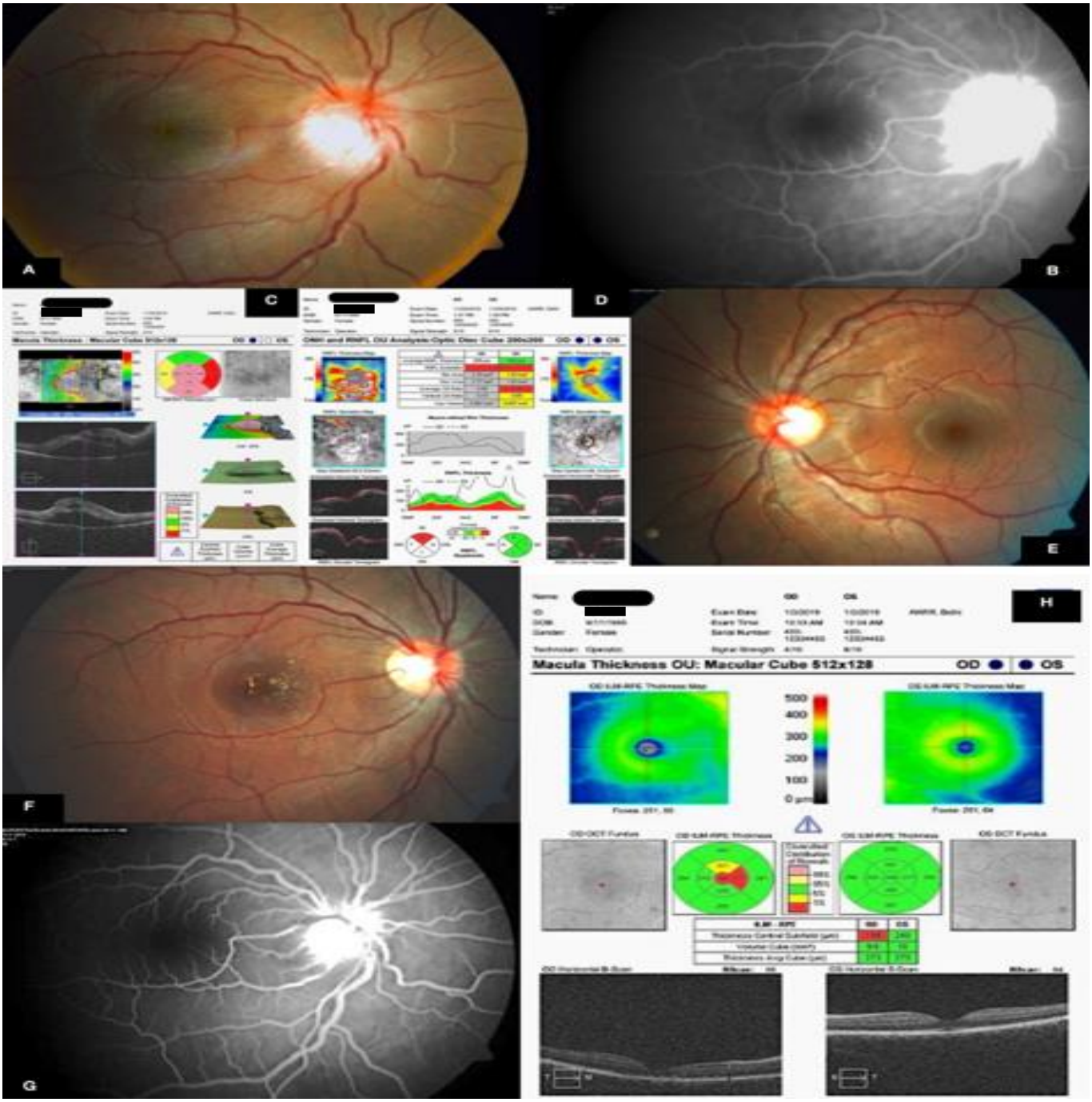

Figure 4 **Fundus picture of case 4 revealed disc edema with sensory detachment in macular region (A) FFA revealed disc leak with pooling of dye in sub retinal space (B) OCT macula (C) and RNFL (D) showed SRF and Disc edema right eye. Normal fundus photo of left eye (E). Post treatment fundus photo right eye showing normal disc and few hard exudates close to fovea (F) however FFA still showed disc leak (G) OCT macula revealed complete resolution of SRF (H).**

All cases underwent a thorough ocular (Visual acuity assessment , fundus examination, imaging and OCT was done during each visit) as well as systemic investigations for etiological diagnosis, documentation and progression. Investigations were mainly focused to rule out common causative agents (bacterial and viruses) causing fever and retinal manifestations. Standard Systemic investigations performed for post fever retinitis for the above cases are as shown in Table 1. Etiological diagnosis could only be possible for our two cases (case 1 and case 2). Both the cases had weil felix test positive.

There is no standardized treatment protocol for PFR, various treatment options available includes empirical treatment targeting the probable causative organism and the inflammatory process. Common treatment options consisting of antibiotics, steroids and intravitreal anti-vascular endothelial growth factor (antiVEGF) agents and combination therapy. [1-3]

However, none proved to be the gold standard treatment for PFR. We treated all our patient with Oral doxycycline 100mg BD for 04 weeks to 06 weeks depending on the treatment response. All the cases not only showed faster resolution of symptoms and macular edema, but also had complete/near normal visual acuity post treatment. The same is summarised in Table 2.

Table 1: **Standard systemic investigations for PFR**

	Investigations	Etiology	Remarks
	Complete blood count		within-normal-limits in all our cases
	C-reactive protein (CRP)	Marker of inflammation	Raised in case 4
In viral serology	ELISA	Human immunodeficiency virus (HIV)	Negative in all
	Serum immunoglobulin IgG and IgM	Dengue, Chikungunya and Lyme disease	Negative in all
	RT-PCR	SARS-COV-2	Negative in all
For Bacterial etiology	Venereal Disease Research Laboratory test(VDRL)	Syphilis	Negative in all
	Widal Test	Typhoid	Negative
	Weil Felix (OX 2, OX K, OX19) agglutination Test	Rickettsia	Positive for case 1 (OX2 1:320) and case 2 (OX19 1: 160)
Anterior Chamber (AC) Tap		Rickettsia, Bartonella, Chikungunya and West Nile Fever Virus	Negative in all cases
Serum sample	Polymerase chain reaction (PCR)	- Do -	Positive in case 1 for Rickettsia Tsutsugamushi

Table 2: **Treatment duration and final visual outcome**

Case	Duration of treatment	Indications to stop treatment	Final Visual acuity
Case 1	6 weeks	Improvement in clinical picture and resolution of SRF on OCT	OD - 6/6, OS – 6/12
Case 2	4 weeks		OD - 6/9
Case 3	6 weeks		OD – 6/9, OS – 6/6(P)
Case 4	4 weeks		OD – 6/6

DISCUSSION

Post-fever retinitis (PFR) also known as epidemic retinitis is an emerging ocular condition. Early diagnosis of PFR is possible due to its typical clinical picture which is characterized by multifocal cotton wool spot like lesions, predominantly along the vascular arcade and posterior pole of retina which is generally manifesting around 4 weeks (2-8 weeks) following the fever episode.[1–4]

The pathophysiology of PFR is considered para infectious by some authors and immune-mediated by others due to reasons like bilaterally symmetrical presentation and clinical response to steroids.[1–3] The delay in the onset of PFR from the initial systemic symptoms has been attributed to the corresponding phase for antibody production, immune complex and autoimmune antibody formation. [4]

Common clinical finding in PFR includes diffuse multifocal , pale white retinal lesions , localized around the posterior pole or along the vascular arcades which are associated with hard exudates and flame shaped retinal hemorrhages. Another common clinical finding is stellate maculopathy or macular star, first described by Leber. It is a prominent finding in conditions affecting the optic disk, like neuro-retinitis and malignant hypertension and is due to the leaky optic disk vasculature.[5] The accumulation of lipid-rich exudates in the outer plexiform layer gives it a characteristic stellate pattern due to the arrangement of nerve fibers and the fluid seeps in the subretinal space leading to neuro-sensory detachment .[6,7] Hence, the etiopathogenesis may be similar to neuroretinitis. These clinical features were present in all our cases including disc edema in case 4.

The treatment options available for PFR are plenty. Some reports suggest only observation for PFR which has given promising results probably due to the self-limiting course of the disease. Few authors suggest treating bacterial retinitis with antibiotic and steroid combination and viral retinitis with steroids. However, none prove to be accurate. Few studies have showed the detrimental effects of steroids which acts as double edge sword causing worsening of retinitis.[8]

Studies on PFR have shown benefit of antibiotics like doxycycline in some of these cases.[9,10,11] This may be plausible as some of the common cases of PFR occur following infections such as rickettsia, typhoid and Lyme's disease which respond well to oral doxycycline.[12] There are reports of doxycycline also being effective in vitro against viruses like dengue and chikungunya.[13,14] Thus, it might have a role in virus associated retinitis as well. There are few reports where worsening of retinitis was noted in patients treated only with steroid which dramatically reversed after starting systemic doxycycline therapy.[15,16] The findings of our study is similar to a very recent study on epidemic retinitis in which eight cases positive for weil felix test received only antibiotics (doxycycline or ciprofloxacin) without steroids and showed complete resolution of macular oedema and retinitis in 1-2 months' time.[11] Doxycycline, play a role in the regulation of inflammation, immunomodulation, cell proliferation, and angiogenesis. Doxycycline has wide spectrum of ocular use and being prescribed for various ocular pathologies viz meibomian gland related ocular surface disorders, ARMD, and various retinal pathologies including PFR.

Few studies suggest role of Anti VEGF however their role is controversial. In our study case 1 received intravitreal anti-VEGF injection due to wrong diagnosis because sometimes these cases can be misinterpreted as branch retinal vein occlusion.

If clinical features are suggestive of PFR, patients may be started on oral doxycycline 100 mg twice

daily till lab reports and definitive diagnosis are not available. Later on, steroids can be added to the treatment regimen. However, all our patients responded well to only oral doxycycline and did not require additional steroids. Oral doxycycline has emerged as a wonder drug in all four cases because all had faster and complete/ near normal visual recovery post treatment. Substandard vision post treatment can be attributed to macular edema , hard exudates in foveal region and macular ischaemia. Since no standard care of management is available for PFR a Randomized placebo-controlled trial will be beneficial to device a management plan.

CONCLUSION

Post fever retinitis is an emerging ocular insult. An antecedent history of flu-like illness and characteristic retinal findings makes it an easy differential diagnosis. Oral doxycycline therapy has its antibacterial and antiviral actions owing to anti-inflammatory and immunomodulator properties and hence can easily be started in patients of PFR even before the definitive lab diagnosis of organism. Treatment can be modified and oral steroids can be added if there is no response to antibiotic therapy and on definitive diagnosis. Proper history taking and timely intervention can halt the disease progression and save the vision.

REFERENCES

1. Kawali A, Mahendradas P, Mohan A*, et al*. Epidemic retinitis. *Ocular Immunol Inflam* 2019; 27: 571–577.
2. Vishwanath S, Badami K, Sriprakash KS*, et al*. Post-fever retinitis: a single center experience from south India. *Int Ophthalmol* 2014; 34: 851–857.
3. Mahendradas P, Kawali A, Luthra S*, et al*. Post-fever retinitis–newer concepts. *Indian J Ophthalmol* 2020; 68: 1775–1786.
4. Sundar M D, Chawla R, Balaji A, Garg I, Kalathil R, Hasan N, Vikas SJ, Kumar A. Clinical features, optical coherence tomography findings and treatment outcomes of post-fever retinitis. Ther Adv Ophthalmol. 2020 Dec 18;12:2515841420979111. doi: 10.1177/2515841420979111. PMID: 33415316; PMCID: PMC7750750.
5. Dreyer RF, Hopen G, Gass JD*, et al*. Leber's idiopathic stellate neuroretinitis. *Arch Ophthalmol* 1984; 102: 1140–1145.
6. Purvin V, Sundaram S and Kawasaki A. Neuroretinitis: review of the literature and new observations. *J Neuroophthalmol* 2011; 31: 58–68.
7. Abdelhakim A and Rasool N. Neuroretinitis: a review. *Curr Opinion Ophthalmol* 2018; 29: 514–519.
8. Karkhur S, Soni D. Clinical spectrum, disease course and management outcome of post-fever retinitis cases: experience from a tertiary eye institute in central India. Int Ophthalmol. 2022 Sep;42(9):2697-2709. doi: 10.1007/s10792-022-02258-w. Epub 2022 Apr 7. PMID: 35391586; PMCID: PMC8989109.
9. Chawla R, Pundlik GA, Chaudhry R*, et al*. Rickettsial retinitis: direct bacterial infection or an immune-mediated response? *Indian J Ophthalmol* 2017; 65: 1038–1041.
10. Kawali A, Mahendradas P, Srinivasan P*, et al*. Rickettsial retinitis—an Indian perspective. *J Ophthalmic Inflamm Infect* 2015; 5: 37.
11. Kawali A, Srinivasan S, Mohan A*, et al*. Epidemic retinitis with macular edema–treatment outcome with and without steroids. *Ocular Immunol Inflam*. Epub ahead of print 21 January 2020. DOI: 10.1080/09273948.2019.1704792.
12. Smilack JD. The tetracyclines. *Mayo Clin Proc* 1999; 74: 727–729.

13. Rothan HA, Mohamed Z, Paydar M*, et al*. Inhibitory effect of doxycycline against dengue virus replication in vitro. *Arch Virol* 2014; 159: 711–718.
14. Rothan HA, Bahrani H, Mohamed Z*, et al*. A combination of doxycycline and ribavirin alleviated chikungunya infection. *PLoS ONE* 2015; 10: e0126360.
15. ChawlaR,PundlikGA,ChaudhryR,ThakurC.Rick ettsialretinitis: Direct bacterial infection or an immune-mediated response? Indian J Ophthalmol 2017;65:1038-41.
16. AyachitA,AyachitG,JoshiS,SameeraVV.Comme ntary:Rickettsial retinitis - Direct bacterial infection or an immune-mediated response? Indian J Ophthalmol 2017;65:1041-3.