Case Series

Diagnostic features of the presumed focal viral retinitis: A case series

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Abstract

Introduction: Other than well-known herpetic retinopathies like acute retinal necrosis, progressive outer retinal necrosis and cytomegalovirus retinitis, there are few reports on atypical forms of viral retinitis caused by herpes virus from around the world.
Cases: Presenting symptom was sudden onset of diminution of vision in all 6 cases. Mean duration of symptoms at presentation was 7.6 days. The mean age was 27.3 years (range 22-40 years). All were immunocompetent (4 females and 2 males), with unremarkable review of system. All had unilateral involvement. Presenting visual acuity ranged from CFCF to 6/60. Granulomatous anterior uveitis was present in 4 cases. All had focal retinitis with irregular margins, either juxtapapillary, macular or over one of the major vascular arcades. The diagnosis of focal viral retinitis was made solely based upon the clinical findings. All recovered after a course of oral acyclovir (one was given additional intravitreal acyclovir as well) and oral prednisolone, with final visual acuity of 6/6P to 6/9 in all except one.
Conclusion: In case of focal retinitis with irregular margin, viral etiology should be borne in mind. Clinical features are typical enough to help in diagnosing without PCR test.

Introduction

Infections of various body tissues with viruses of herpetic family occur all around the world irrespective of age, sex or race. Intraocular manifestations of herpetic infection include iridocyclitis, choroiditis retinitis, optic neuritis. Acute retinal necrosis (ARN), progressive outer retinal necrosis (PORN), cytomegalovirus (CMV) retinopathy are the known clinical conditions very well described in the literature in the past. However, there are few patients having few clinical features consistent with these known conditions, but still differ in many ways. . There are few reports on the atypical forms of viral retinitis outside Nepal (Matsuo et al 1988, Margolis et al 2007, Hazirolan et al 2010, Brydak-Godowska et al 2014). Similar cases are seen in Nepalese population. Based on the clinical diagnosis of focal viral retinitis, when treated with systemic antiviral medications, good clinical outcome was seen in such patients. There has been no report on those cases from Nepal. So, the purpose of this study is to define the diagnostic clinical and demographic features of such focal viral retinitis cases.

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Materials and methods

This is a retrospective case series. The charts of 6 cases referred to the uveitis department of

Tilganga Institute of Ophthalmology between 2010 and 2018, clinically diagnosed as and successfully treated for focal viral retinitis, were reviewed. The clinical diagnosis was not confirmed by PCR on intraocular fluid in any of the cases. The detailed data on each patient's demographic, clinical features, blood investigations, fundus photos, optical coherence tomography (OCT) and fundus fluorescein angiography (FFA), treatment, length of follow-up were collected. Snellen's visual acuities, finding of anterior segment on slit lamp examination and those of posterior segments on slit lamp examination using 90 D lens and indirect ophthalmoscope using 20 D lens, intraocular pressure measured with Goldmann applanation tonometer, and qualitative measurement of corneal sensation using cotton tipped applicator were collected. Anterior chamber reaction and vitreous opacity were graded according to the standardization of uveitis nomenclature (SUN) grading (Jabs et al 2005). Approval from IRC of Tilganga Institute of Ophthalmology was taken.

Criteria for selection of cases: Only those cases with focal retinitis lesion posterior to the equator, with photographic and clinical documentation of response to systemic acyclovir within 4 to 5 days of its initiation (before starting oral prednisolone), were included in this study.

Results

Total six (four female and two male) cases were identified with unilateral involvement. They were in the age range of 22-40 years (mean age 27.3 years).

Patients came 3 to 11 days (mean 7.6 days) after the sudden onset of diminution of vision. Presenting visual acuity ranged from CFCF to 6/60 (CFCF in 2 cases, 6/24 to 6/60 in 4 cases).

Anterior chamber cellular reaction was present in 4 cases ranging from 1 + to 4 +. Granulomatous keratic precipitates were seen in all 4 cases with anterior uveitis. Corneal sensation was reduced in 3 cases, normal in one case and was not checked in 2 cases. One case had a mid-dilated sluggishly reacting pupil in the affected eye. Intraocular pressure was high in one case and normal in the rest of the 5 cases. Four cases had trace to 1+vitreous opacity. Two did not have vitreous opacity at all.

Deep (dot and blot) retinal hemorrhage was present in only one case. Focal retinitis of 1 to 4 DA was located posterior to the equator in all 6 cases. One was juxtapapillary. One was located along the cilioretinal artery (Figure 3a & 3b). The rest four were located along one of the major vascular arcades. Four were elongated and two were circular in shape. But all 6 had irregular, wavy and ill-defined borders. Focal retinal arteritis was present in four cases and focal retinal phlebitis in one case. In one case, clinical evidence of vasculitis was not present and FFA was not done. Disc edema was present in all 6 cases. Pigmented scars next to the active retinal lesions were present in 3 cases during the first presentation (Figure 4a & 4b, 5a, 5b, 6a and 6b).

The demographic and salient clinical features are given in the table 1.

FFA was done in 4 cases (case 3, 4, 5 and 6). In three cases (case 4, 5 and 6), leakage occurred from the area of retinitis (Figure 7a & 7b). But in one case (case 3), leakage occurred only from the nasal half of the margin of the retinitis despite the fact that the whole lesion healed with scar formation just like any other retinitis (Figure 8a & 8b). Most probably, the retinal infiltration was overlapped by nerve fiber layer infarction from cilioretinal artery occlusion.

SD OCT was done in 4 cases (case 3, 4, 5 and 6). All showed thickened hyper-reflective and disorganized inner retinal layers, intraretinal fluid and subretinal fluid collection. The OCT of case 5 is in figure 9.

All improved with oral acyclovir. The length of acyclovir treatment was 5 weeks to 3 months. The starting dose was 800 mg 5 times a day for a week. Only one (case 3) was given intravitreal

acyclovir along with the oral administration (this patient had central macular lesion). Three cases were given anti-toxoplasma treatment prior to giving antiviral. All cases received a 5 to 8 weeks long course of oral prednisolone from 4th or 5th days of initiation of antiviral treatment. The starting dose was 1 mg/kg/day. Visual acuity improved to 6/6P to 6/9 in all except one, who had presented with central macular lesion. This particular patient improved from CFCF to 6/36.

All cases were immunocompetent suffering from no known systemic diseases. None had a history of fever in the recent past. Only one case had a history of Shingles (in the thoracic dermatome) in the past.

Investigations revealed normal blood counts, negative RPR and TPHA, non-reactive HIV 1+2 in all cases, positive IgG level of HSV 1 in 4 cases (not done in two cases). Antitoxoplasma IgG was positive in four cases, negative in one case, and the report of one case was not found one.

Follow up period was 36 days to 2 years (mean f/u = 7 months)

Table 1: Demographic and salient clinical features of presumed focal viral retinitis patients

Case	Age, year	Sex	Presenting VA	Ocular pain	Corneal sensation	Site of retinitis	Shape/size of retinitis	Associated focal vasculitis	Final VA
1	22	F	6/60	Absent	Not checked	Vascular arcade	Elongated/1DA	Phlebitis	6/9
2	28	F	6/24	Present	Not checked	Juxta papillary	Circular/1.5 DA	No clinical evidence	6/6p
3	27	F	CFCF	Present	Reduced	Cilioretinal artery	Elongated/2.5 DA	Arteritis	6/36
4	22	F	6/36	Absent	Reduced	Vascular arcade	Elongated/2.5 DA	Arteritis	6/6p
5	40	M	CFCF	Absent	Normal	Vascular arcade	Circular /1 DA	Phlebitis	6/6p
6	25	M	6/36p	Absent	Reduced	Vascular arcade	Elongated /4DA	Arteritis	6/6

Figure 1a: Fundus photo of case 1 before treatment

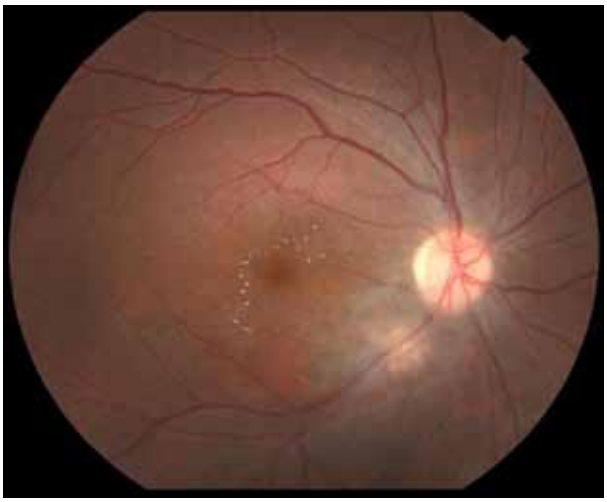

Figure 1b: Fundus photo of case 1 after treatment

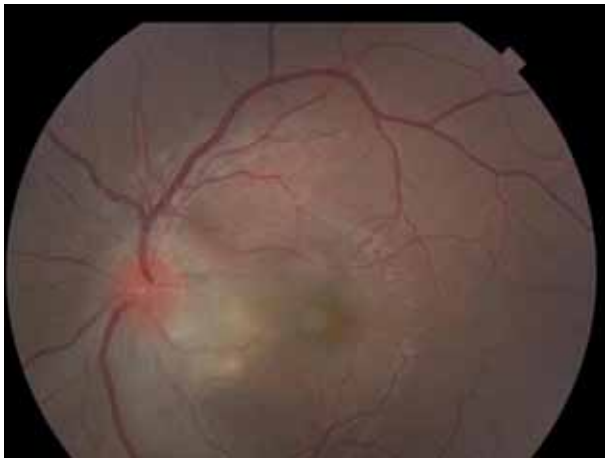

Figure 2a: Fundus photo of case 2 before treatment

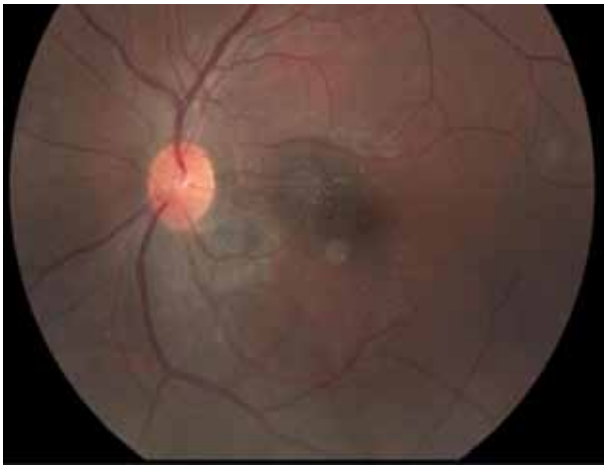

Figure 2b: Fundus photo of case 2 after treatment

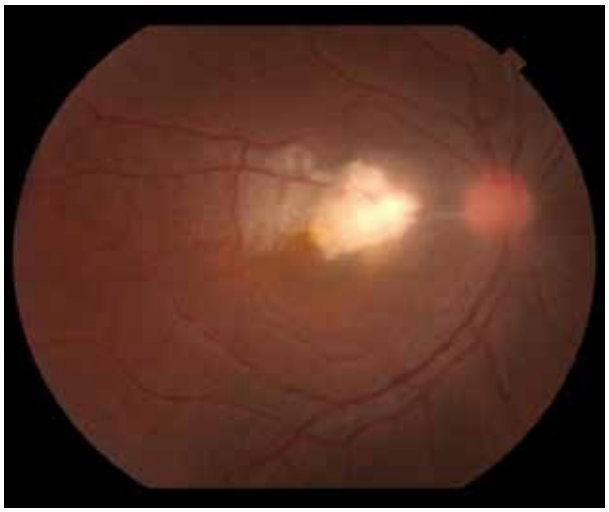

Figure 3a: Fundus photo of case 3 before treatment

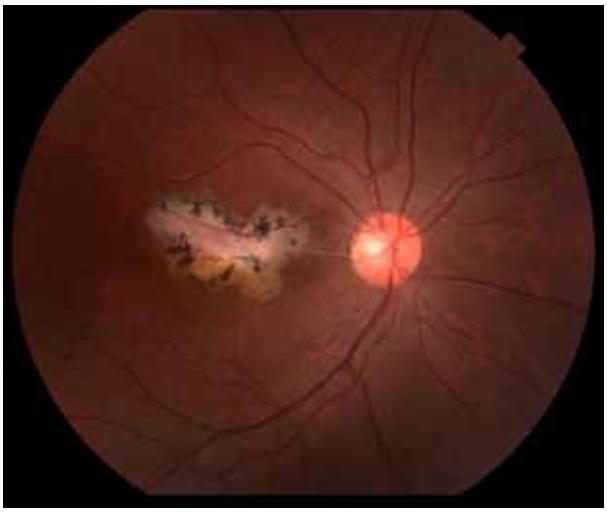

Figure 3b: Fundus photo of case 3 after treatment

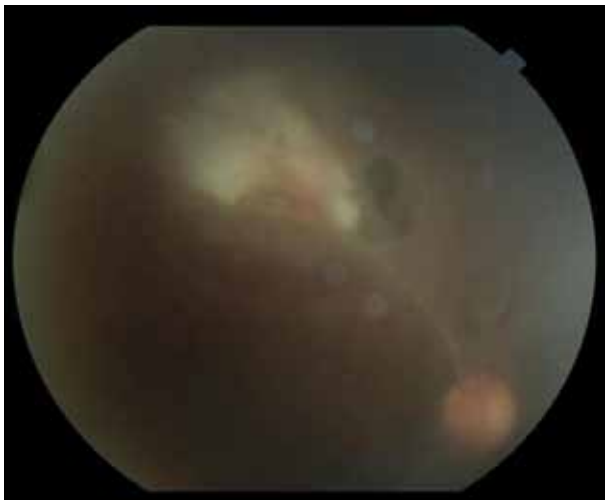

Figure 4a: Fundus photo of case 4 before treatment

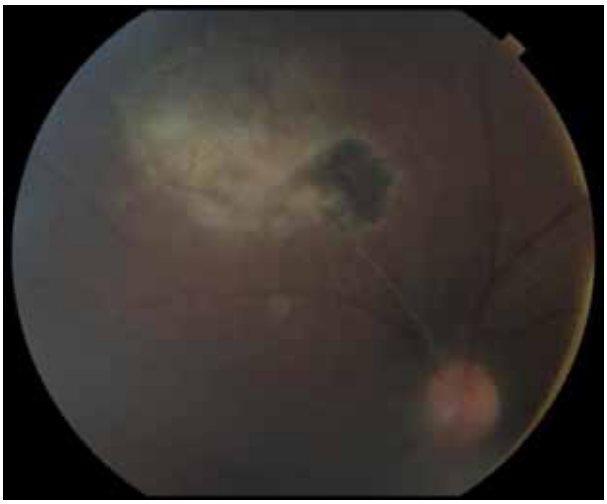

Figure 4b: Fundus photo of case 4 after treatment

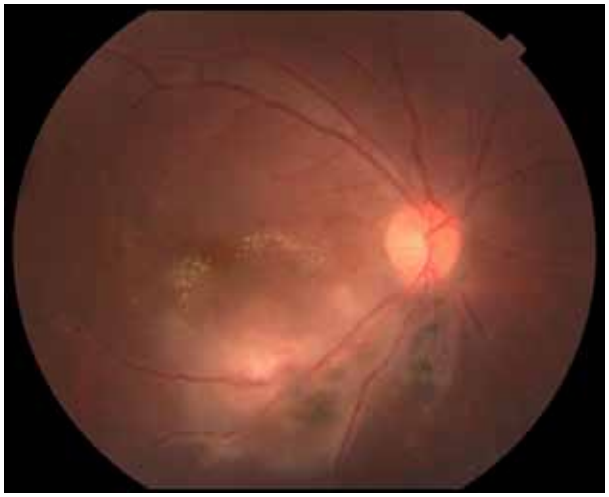

Figure 5a: Fundus photo of case 5 before treatment

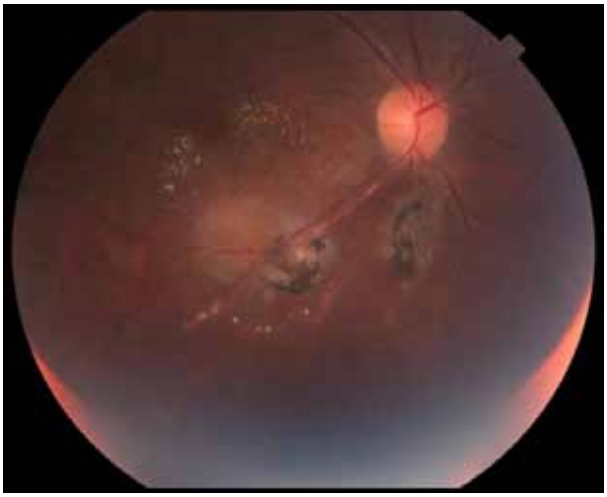

Figure 5b: Fundus photo of case 5 after treatment

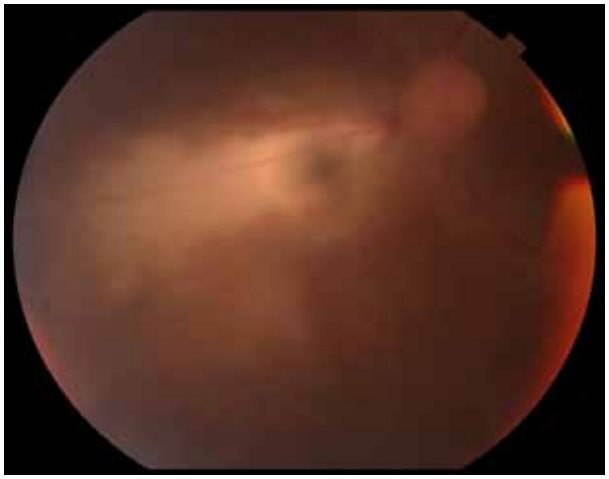

Figure 6a: Fundus photo of case 6 before treatment

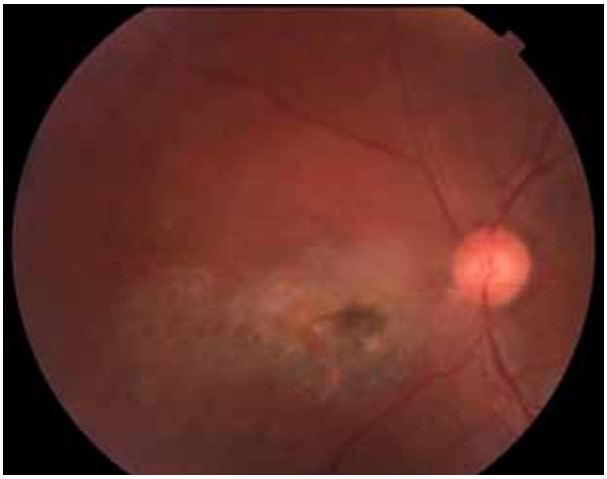

Figure 6b: Fundus photo of case 6 after treatment

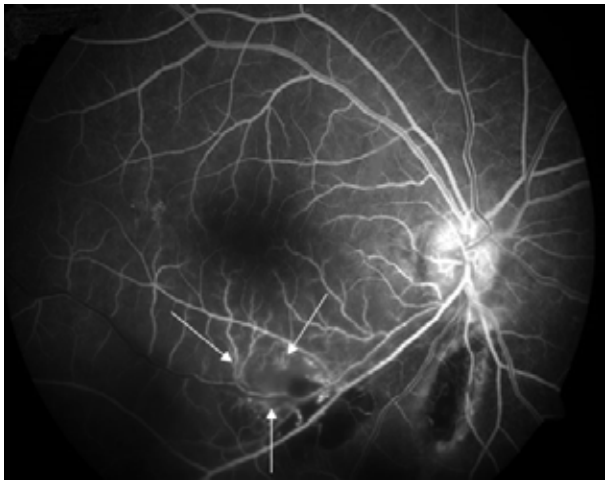

Figure 7a: FFA of case 5 at 23 seconds (Leakage has started from retinitis)

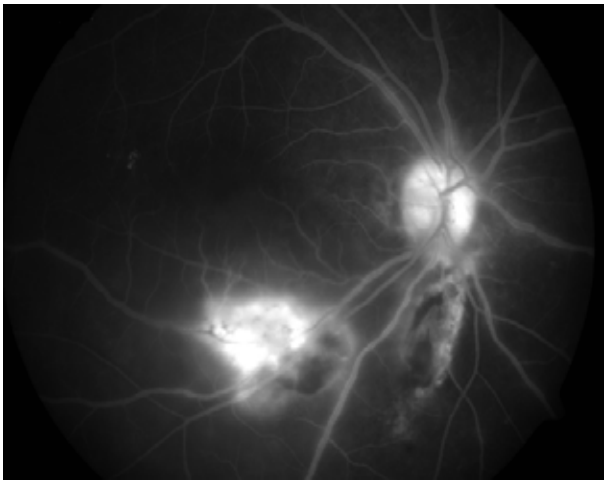

Figure 7b: FFA of case 5 at 5 minutes 29 seconds (The whole area of retinitis shows leakage)

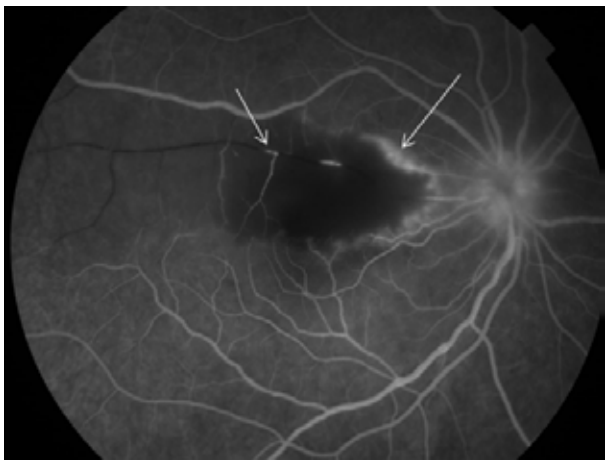

Figure 8a: FFA of case 3 at 31 seconds (Nasal margin of retinitis started leaking. Cilioretinal artery has not filled yet)

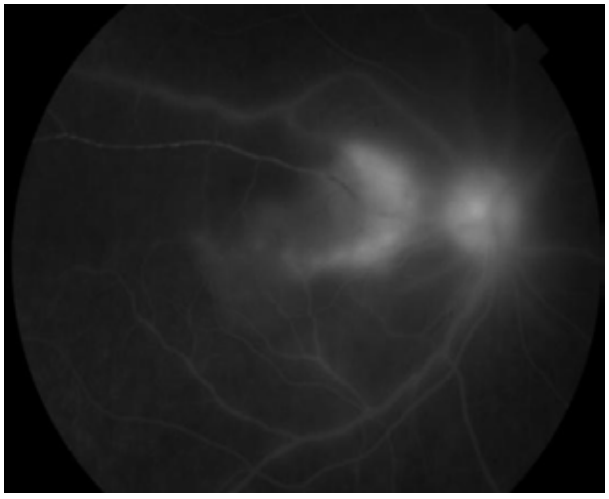

Figure 8b: FFA of case 3 at 11 minutes 42 seconds (No leakage yet seen from the area of retinitis other than nasal part)

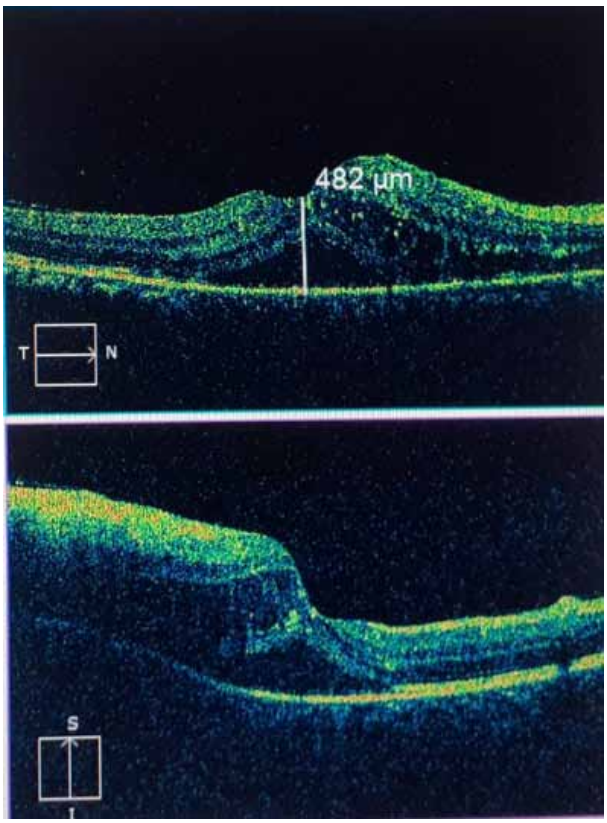

Figure 9: OCT of retinal lesion of case 5 at presentation

Discussion

The most common cause of posterior uveitis in immunocompetent individuals in many parts of the world including Nepal is toxoplasmosis.[6] The diagnosis is made clinically on the basis of the presence of a focal necrotizing retinochoroiditis lesion. Detection of the presence of anti toxoplasma antibody in a patient's serum confirms exposure to the parasite (Intraocular Inflammation and Uveitis, AAO 2017-18). The margin of the toxoplasma retinochoroiditis lesion is smooth and regular. Vitritis might be mild to severe. The lesions are more frequently seen in the posterior pole and in the mid periphery of retina and occur in young adults.

Our cases were somehow consistent with toxoplasma retinitis because of focal lesion, roundish shape at least in 2 cases, presence of pigmented scar in 3 cases, posterior pole lesion, age of patients and also because of the detection of anti toxoplasma antibody in patients' serum in 4 cases. However, our cases were different from Toxoplasma retinitis in terms of elongated shape of lesions in four, wavy irregular margin of the retinitis lesions in all, and the presence of significant edema and hard exudates surrounding the retinitis. Three of the cases initially treated with anti toxoplasma medication failed to show signs of

healing of retinitis. As we all know, detection of anti toxoplasma antibody in serum does not always indicate the presence of toxoplasma retinitis.

Other D/D would have been Syphilitic retinitis. However, both VDRL and TPHA were negative in all cases. And there were no systemic features suggestive of Syphilis in any case. Next D/D of retinitis in immunocompetent individuals is acute retinal necrosis (ARN). The retinal vascular involvement is also quite common in ARN. But ARN is characterized by one or more foci of retinal necrosis with discrete borders in the peripheral retina, spreading circumferentially, with rapid progression in the absence of antiviral therapy (Intraocular Inflammation and Uveitis, AAO 2017-18). Next differential diagnosis (D/D) could be the classic or fulminant Cytomegalovirus (CMV) retinopathy. Because, in this type, necrotizing retinitis typically appears in the posterior pole, from disc to vascular arcades and are associated with blood vessels, just like in four of the cases in this series. However, the lesions in this classic type of CMV retinopathy tend to be more than in one vascular arcade, retinal hemorrhage is more common, and it occurs strictly in immunocompromised individuals (Intraocular Inflammation and uveitis, AAO 2017-18).. Another D/D could be Progressive outer retinal necrosis (PORN). Because it presents with retinal necrosis which starts in the posterior pole. However, the patches of retinal necrosis are multiple in PORN and it occurs only in immunocompromised individuals (Intraocular Inflammation and Uveitis, AAO 2017-18).

Another D/D could be post fever retinitis, like post typhoid, post typhus, post dengue retinitis, which also occur in the same age group as of the cases in this series. The usual manifestations of Post fever retinitis include focal or multifocal patches of retinitis which could be unilateral or bilateral and may be associated with RAPD, anterior uveitis (usually non-granulomatous), macular edema, and serous detachment at the macula (Vishwanath et a 2014, Kawali et al 2015). But the strongest point not in favour of this entity is the fact that none of the cases in this series had a history of fever in the recent past.

So, with these exclusions, our cases fitted into the diagnosis of atypical viral retinopathies. Since there are reports of atypical forms of viral retinitis, we presumed our cases as a type of viral retinitis. On doing literature review, I found following few articles on atypical viral retinitis:

Margolis et al (2007) described herpetic retinitis that predominantly affects the posterior pole may have a worse visual prognosis and high rate of retinal detachment- named as multifocal posterior necrotizing retinitis. The affected individuals were from the USA.

Matsuo et al (1988) described six Japanese patients of peripheral retinal lesions typical of ARN syndrome, extending to the posterior pole but not becoming confluent. These cases were not complicated by retinal detachment (mild form of ARN).

Brydak-Godowska et al (2014) described 10 Caucasian patients, who were diagnosed with ARN based on the clinical presentation. Since peripheral retinitis healed completely with oral acyclovir or valacyclovir treatment in all 10 cases, it was given the term- self - limiting ARN. None had any complications.

Hazirola et al (2010) described 8 Turkish patients of focal posterior pole viral retinitis with better prognosis than other forms of necrotizing retinopathy.

Our cases were very similar to those described by Hazirola et al (2010) in the following aspects- size and location of the lesion, less aggressive progression, excellent response to systemic antiviral, age of the patients,

lack of complications. But, there were some differences as well- female predominance (equal distribution in both the sexes in that study), presence of old pigmented scars and decreased corneal sensation in 50% cases, presence of ocular pain in one third of patients and mid-dilated sluggish pupil in one case. Oral Acyclovir treatment was enough. IOP was raised only in one of our cases, whereas in that study, it was high in 50 % cases. Their cases were PCR proven.

Reason why they were presumed to be viral retinitis cases:

1. Treatment failure with anti-toxoplasma medication in three cases
2. Presence of wavy irregular margins of the lesions
3. Decreased corneal sensation in 50 % cases
4. Appearance of signs of healing of focal retinitis with systemic antiviral therapy even before starting systemic steroid.

Conclusion

Diagnostic criteria for all kinds of known herpetic retinopathies are basically clinical findings rather than the modern PCR test result. So, in developing countries like Nepal where PCR test is not easily available, we should rely more on clinical features for the diagnosis of this new entity as well.

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