Case Report

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Frosted branched angiitis due to viral meningo-encephalitis and ocular toxoplasmosis; a rare case report from Nepal

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Introduction: Frosted branched angiitis (FBA) is characteristic florid translucent retinal perivascular sheathing of both arterioles and venules in association with variable uveitis and vasculitis affecting the entire retina. The vascular sheathing is supposed to be an immune-mediated reaction, possibly due to immune complex deposition in vessel walls secondary to various underlying etiologies. The authors aim to report a case of FBA secondary to herpes simplex virus and *Toxoplasma gondii* infection causing the diagnostic dilemma. This is the first case report on FBA from Nepal.

Case report: An 18-year-old young boy hospitalized with the diagnosis of acute viral meningo-encephalitis presented with the complaint of diminution of vision and floaters in both eyes for a week. Herpetic infection was confirmed with the cerebro-spinal fluid analysis and was under antiviral drugs. His presenting visual acuity was 20/80 in both eyes and ocular features were suggestive of FBA. The vitreous sample analysis revealed raised toxoplasma titre so intravitreal clindamycin was administered twice. The ocular features resolved in the subsequent follow ups with intravenous antiviral treatment and intravitreal antitoxoplasma treatment.

Conclusions: FBA is a very rare clinical syndrome secondary to many immunological or pathological causes. So, possible etiologies must be ruled out for timely management and good visual prognosis.

Keywords: frosted branched angiitis, herpex simplex, papillitis, phlebitis, *toxoplasma gondii*, vasculitis

Introduction

Frosted branched angiitis (FBA) is characteristics diffuse sheathing of arteries and veins affecting the entire retina[1]. It is so called because of its unusually thick sheathing surrounding maximum retinal veins suggesting the appearance of frosted tree branches in the winter[2]. It is characteristic florid translucent retinal perivascular sheathing of both arterioles and venules in association with variable uveitis, retinal oedema, and visual loss, normally with good recovery. It is also termed "acute frosted retinal periphlebitis."[3] It can be either a primary or a secondary condition characterized by rapid deterioration of vision and fulminant retinal vasculitis that manifests as diffuse sheathing of retinal vessels, macular oedema, papillitis, vitritis, anterior uveitis, etc[4]. It has been reported secondary to various infective agents, such as cytomegalovirus, herpes simplex, varicella zoster, and human immunodeficiency virus. In many cases, toxoplasma and rubella are also isolated for the causing FBA. It is also due to various autoimmune disorders, and malignancies such as lymphoma, etc[5]. Herein, we present a case of a young boy with the ocular manifestation of FBA, due to both dual infection of Herpes Simplex Virus and *Toxoplasma gondii*.

HIGHLIGHTS

- Frosted branched angiitis (FBA) is characteristics special type of vasculitis with diffuse sheathing of arteries and veins affecting the entire retina.
- An 18-year-old male, admitted with a diagnosis of acute viral meningo-encephalitis presented to for Ophthalmology consultation. On examination, FBA
- The possible diagnosis of bilateral FBA due to the herpetic meningo-encephalitis with concomitant toxoplasmosis was made.
- The intravitreal injection of Ganciclovir (2.0 mg/0.04 ml) was given but the ocular findings did not improve. Then for raised Toxoplasma IgG vitreous titre, he was given an intravitreal injection of Clindamycin (1.0 mg/0.1 ml) and intravitreal dexamethasone (200 mg/0.05 ml). Retinal haemorrhage started to regress, and sheathing decreased. He also underwent two settings of panretinal photocoagulation in both eyes.
- For systemic manifestation, intravenous injection of acyclovir (750 mg TDS) was continued for 21 days then switched to oral acyclovir (800 mg five times per day) and oral steroid (Prednisolone 1 mg/kg/day) was continued in tapering doses.

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Case presentation

An eighteen-year-old male, admitted with a diagnosis of acute viral meningo-encephalitis, presented to the ophthalmology department complaining of floaters and a diminution of vision in both eyes for a few days. His symptoms are not associated with redness, pain, and discharge. He was receiving injectable acyclovir [750 mg TDS] and oral steroids [60 mg OD in tapering dose]. The acute meningo-encephalitis was confirmed clinically in presence of headache (generalized, insidious onset and non-radiating type), fever, vomiting (15–16 episodes for one days then 3–4 episodes/day), and fever, and radiologically with contrast-enhanced MRI of the brain. Cerebro-spinal fluid analysis had lymphocytic pleocytosis with raised glucose and protein levels but normal adenosine deaminase activity. Serum TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex and HIV) IgM was negative but IgG was positive for Herpes Simplex and *Toxoplasma gondii*. His ocular symptoms had developed 10 days after systemic manifestations.

On ocular examination, the best corrected visual acuity in both eyes was 20/80 for distance and N/6 for near. The anterior segment examination was unremarkable. However, grade 2 + vitreous cells were present in both eyes with 2 + and 1 + vitreous haze in right and left eye, respectively. A Dilated fundus examination revealed widespread florid, mostly translucent, whitish perivascular exudates resembling the sight of a frost on a tree branch. Phlebitis with mild arteritis noted in the mid-peripheral and peripheral retina along with diffuse retinal haemorrhage and oedema. The posterior pole and the optic disc appeared bilaterally normal as shown in Figure 1.

The intraocular pressure was 12 mmHg in both eyes. Fundus fluorescein angiography (FFA) showed symmetrical leakage in the mid periphery in the late phase with capillary drop-out areas in greater than 180° of the peripheral retina but new vessels were not noted as shown in Figure 2. Optical coherence tomography of both eyes revealed retinal inflammation sparing macula with normal macular thickness and texture as shown in Figure 3. The vitreous tap was sent for nested polymerase chain reaction for the Herpes virus family and was negative. But the vitreous IgG titre for *Toxoplasma gondii* was raised to 1:16 times in Right Eye and 1:8 times in Left Eye (hemagglutination assay).

The possible diagnosis of bilateral FBA due to the herpetic meningo-encephalitis with concomitant toxoplasmosis was made. The intravitreal injection of Ganciclovir (2.0 mg/0.04 ml) was given to each eye at a week apart. But the ocular findings did not improve. Then in view of raised Toxoplasma IgG vitreous titre, he was given an intravitreal injection of clindamycin (1.0 mg/0.1 ml) and intravitreal dexamethasone (200 mg-/0.05 ml) in each eye at a week apart. Surprisingly, the retinal haemorrhage started to regress, and sheathing decreased by 2 weeks. He also underwent two settings of panretinal photocoagulation to decrease the capillary drop-out area in both eyes. For systemic manifestation, intravenous injection of acyclovir (750 mg TDS) was continued for 21 days then switched to oral acyclovir (800 mg five times per day) and oral steroid (Prednisolone 1 mg/kg/day) was continued in tapering doses.

After 2 months, his best corrected visual acuity improved to 20/20 for distance and N/6 for near in both eyes. Subsequent FFA after 3 months, showed normal vascular flow without any leakage or any areas of retinal ischaemia. Retinal haemorrhages and oedema also resolved as shown in Figure 4. The vitreous haze and cellular activity in both eyes cleared, perivascular exudates resolved, and vessels appeared normal. The patient has been on regular follow up regularly for 2 years with no ocular or systemic complications to date. Thus, a care rare of FBA with dual infections case was managed successfully.

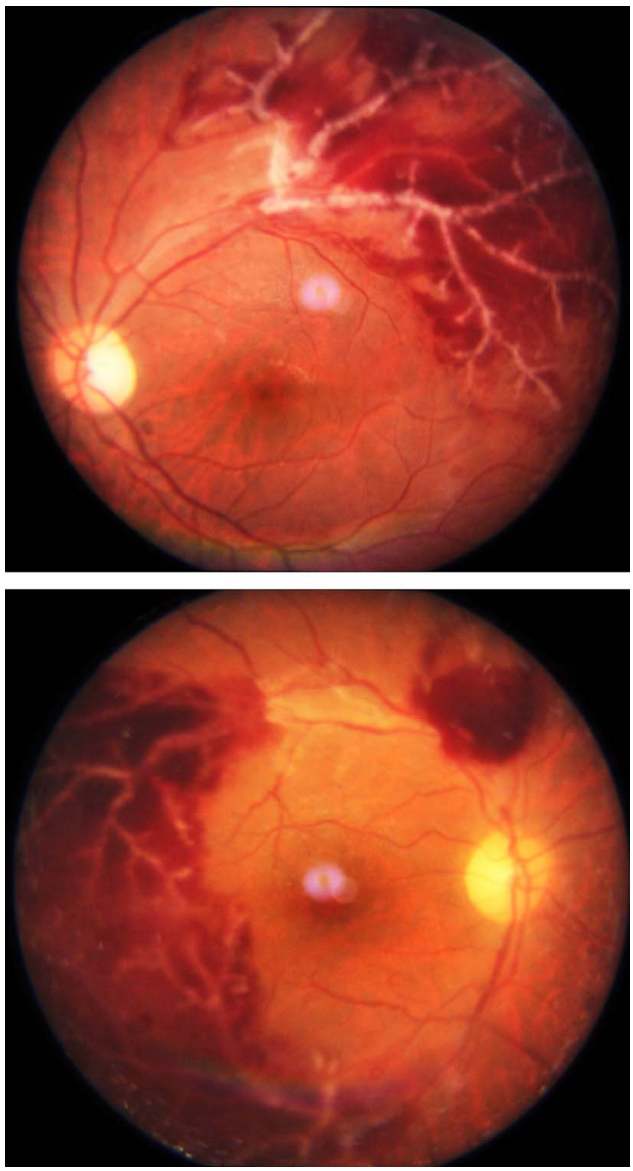

Figure 1. Whitish perivascular exudates resembling the sight of a frost along with intraretinal haemorrhages.

Discussion

FBA is a special form of vasculitis, affecting the entire retina. The funduscopic findings of FBA include bilateral widespread retinal vasculitis with severe sheathing of the retinal vessels, resembling frosted branches of a tree, especially at the periphery, and mild to moderate iritis or vitritis[6]. Our case had translucent, whitish perivascular exudates sheathing resembling frosted branch on the tree and Phlebitis with mild arteritis also present. Vascular sheathing is due to an immune-mediated reaction, possibly due to

Figure 2. Showing symmetrical leakage in the mid periphery in the late phase with capillary drop-out areas in greater than 180° of the peripheral retinae.

immune complex deposition in vessel walls[7]. It has seen to be a bimodal age distribution with one peak in childhood and another in second or third decade of life with a predominance of females to males[7]. Most patients (75%) have bilateral disease[8]. Our patient is also in second decade of life and has bilateral FBA manifestations.

FBA is not itself a disease but is a clinical sign seen in many pathological conditions. So, Kleiner *et al*.[9] classified FBA into three subgroups. The first group is characterized by the "frosted branch appearance" only, but they do not have true FBA. The white vessel sheathing is due caused due to infiltration with malignant cells (acute lymphoblastic leukaemia and large cell lymphoma). The second group is associated with viral infection (herpes simplex virus, cytomegalovirus toxoplasmosis, syphilis, human immunodeficiency virus) or autoimmune disease (systemic lupus erythematosus, Crohn's disease, Behcet disease, sarcoidosis, and multiple sclerosis). FBA is a clinical sign possibly of immune complex deposition giving the frosted branch response to underlying disease. This is termed as "secondary frosted branch angiitis". The third group is of healthy young patients described initially. The vasculitis in such patients represents an immune response to any underlying stimulus of viral infection or other and termed as "acute idiopathic frosted branch angiitis", in which acute infections is responsible for triggering the vasculitis. FA is near normal in the early phase, but later on various sight threatening consequences might seen.

Our patient was a healthy immunocompetent person with no past history of any autoimmune disease nor viral infections. But developed meningoencephalopathy secondary to herpetic and toxoplasmic infection as depicted cerebro-spinal fluid, serum and vitreous analysis. So, FBA was considered as consequences of these aetiology in our patients. FBA in our patient falls under group third as all consequences are the immune response of underlying ocular toxoplasmosis and systemic acute viral meningo-encephalitis. In contrast, diffuse intraretinal haemorrhages were also seen along with frosted branched like vessels of retina and symmetrical leakage in the mid periphery in the late phase with capillary drop-out areas the peripheral retina seen during FFA. Although the patients had given intravitreal

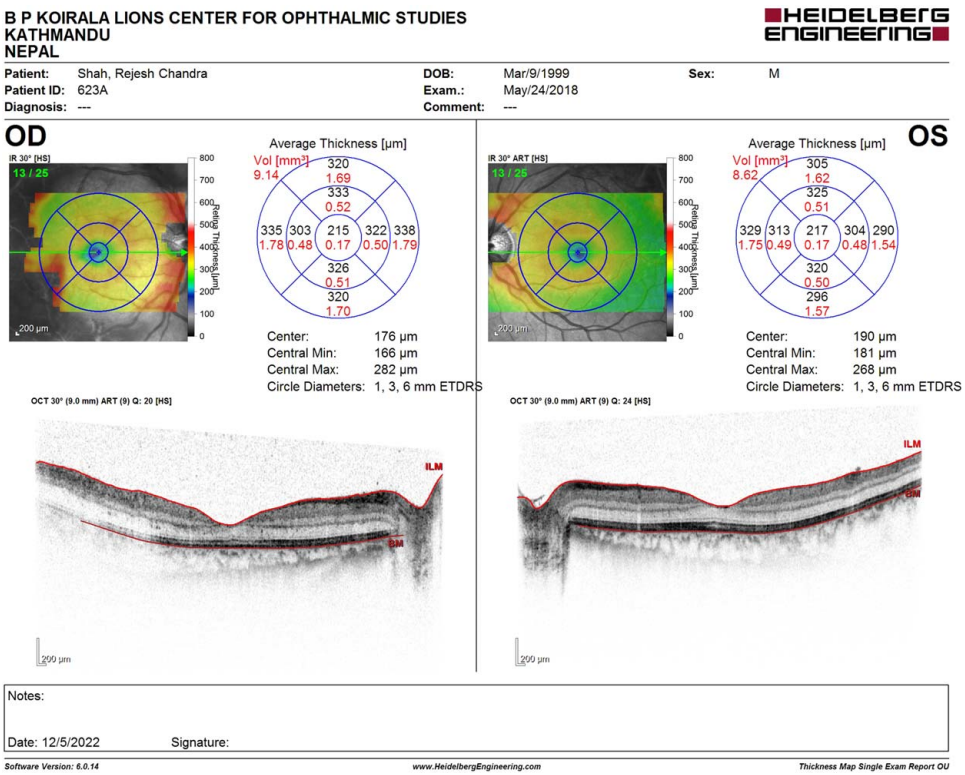

Figure 3. OCT showing retinal inflammation sparing macula. OCT, optical coherence tomography.

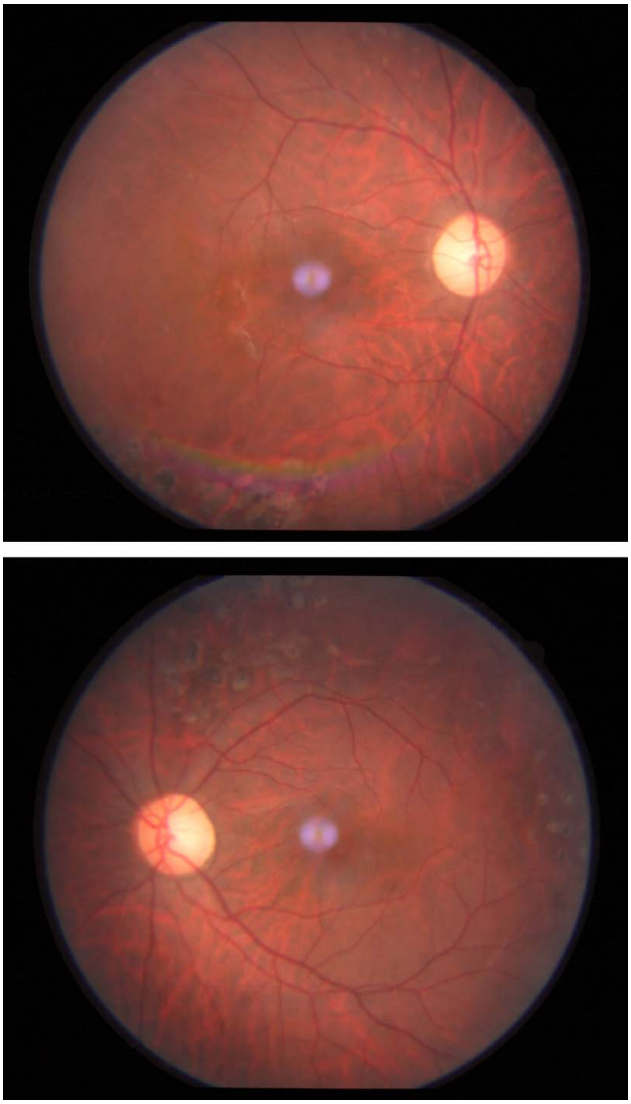

Figure 4. Fundus picture showing resolution of the retinal vessels inflammation in the frosted branched angiitis patient in subsequent follow up.

ganciclovir injection, later he was topped on with intravitreal antitoxoplasma injection For control of dual pathogens[2]. The final outcome yielded weel with good control of intracranial and ocular problems.

Conclusions

FBA is very rare clinical syndrome secondary to many immunological or pathological causes and has not yet been reported from Nepal earlier. Potential infectious etiologies must be ruled out before initiating corticosteroid therapy because this clinical sign may be associated with active viral disease or other many entities capable of progressing to widespread retinitis. A dual infection is less likely but can occur, adding difficulties in the management of such a rare entity.

Ethical approval

None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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No funding was received for the study.

Author contribution

C.P.S. and S.M.S. reviewed the literatures and wrote the original manuscript. R.K.S. is supervisor and reviewed the manuscript and is also responsible for the medical management of the case.

Conflicts of interest disclosure

The authors declare that there are no conflicts of interest regarding the publication of this article

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Data availability statement

All data are attached with manuscript.

References

[1] Díaz-Valle D, Díaz-Rodríguez E, Díaz-Valle T, *et al*. Frosted branch angiitis and late peripheral retinochoroidal scar in a patient with acquired toxoplasmosis. Eur J Ophthalmol 2003;13:726–8.

[2] Kumar A, Yangzes S, Singh R. Frosted branch angiitis in one eye and impending CRVO in the other: a diagnostic dilemma. BMJ Case Rep 2015;2015:bcr2014209073.

[3] Barkmeier AJ, Feman SS. Frosted branch angiitis secondary to herpes simplex virus infection progressing to acute retinal necrosis. Retin Cases Brief Rep 2009;3:36–7.

[4] Ferreira BF, de A, Rodriguez EEC, *et al*. Frosted branch angiitis and cerebral venous sinus thrombosis as an initial onset of neuro-Behçet's disease: a case report and review of the literature. J Med Case Rep 2017;11:104.

[5] Ratra D, Jafferji S, Biswas J. Postsurgical bacterial endophthalmitis presenting as frosted branch angiitis: a case report. Retin Cases Brief Rep 2010;4:20–2.

[6] Tang S, Zhao N, Wang LY, *et al*. Frosted branch angiitis due to cytomegalovirus-associated unmasking immune reconstitution inflammatory

syndrome: a case report and literature review. BMC Infect Dis 2021;21:613.
[7] Walker S, Iguchi A, Jones NP. Frosted branch angiitis: a review. Eye Lond Engl 2004;18:527–33.
[8] Alapati A, Cameron N, Gratton S, *et al*. Frosted branch angiitis presenting after a SARS-CoV-2 infection. J Ophthalmic Inflamm Infect 2022;12:1–5.
[9] Kleiner RC. Frosted branch angiitis: clinical syndrome or clinical sign? Retina Phila Pa 1997;17:370–1.