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Idiopathic Unilateral Frosted Branch Angiitis: A Case Report and Review

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Abstract

Aim: The purpose of this case study is to present the first report of primary frosted branch angiitis in the Maltese islands and to review this rare disease and its aetiology. Background: Frosted Branch Angiitis (FBA) is described as a rare, acute panuveitis with severe vasculitis affecting the entire retina. It can be classified as idiopathic (primary) or associated with ocular and systemic disease (secondary) such as toxoplasmosis, cytomegalovirus retinitis or leukaemia. Visual prognosis is variable as it depends on the underlying pathology and worsens with complications such as macular oedema, retinal detachment (RD), or optic atrophy. The optimal treatment is, yet, unclear. Case Presentation: This case report describes the presentation, diagnosis, and management of a 40-year-old male with unilateral frosted branch angiitis (FBA) in Malta. The patient presented with sudden vision loss, retinal vasculitis, and hemorrhages in the left eye. Following extensive investigations to rule out other causes, a diagnosis of primary idiopathic FBA was made. Treatment with oral prednisolone resulted in improvement in retinal inflammation but limited visual recovery. Conclusion: While corticosteroids remain the first-line treatment, additional immunosuppressive therapies or intravitreal injections may be warranted in severe cases.

Keywords

Frosted Branch Angiitis, Idiopathic Vasculitis, Pre-Retinal Haemorrhage

1. Introduction

Frosted branch angiitis (FBA) was first described in 1976 in a 6-year-old Japanese child presenting with diffuse sheathing of all retinal vessels, giving the appearance of frosted branches of a tree [1]. It is a rare, acute panuveitis with severe vasculitis

affecting the entire retina, of which "a total of 57 cases have been reported in the world literature" [1]. It can be classified as idiopathic (primary) or associated with ocular and systemic disease (secondary) such as cytomegalovirus retinitis, toxoplasmosis or leukaemia. FBA is typically bilateral, although unilaterality has been reported [2].

2. Case Description

Our case report describes a 40-year-old Caucasian male, who presented with a one-day history of sudden decreased vision in his left eye. He had no previous ophthalmic, medical or surgical history and denied any systemic or other ocular symptoms recently. On examination, his visual acuity was light perception on the left and 6/6 vision on the right. A mild left afferent pupillary defect was noted. Anterior segment examination showed a white conjunctiva, clear anterior chamber and normal intraocular pressure bilaterally. Dilated fundal examination showed right clear retina and optic disc with no macular changes (**Figure 1(a)**) with left widespread retinal vasculitis, severe papillitis and prominent vascular sheathing, extensive pre-retinal macular haemorrhage and scattered intraretinal, preretinal and subretinal haemorrhages in all quadrants (**Figure 1(b)**). General clinical examination was normal. Fundus fluorescein angiography (FFA) on presentation revealed masking in the macular area due to the haemorrhage, but diffuse staining and leakage of affected vessels with notably delayed filling in both arterial and venous systems in the left eye, with completely normal FFA results in the right eye (**Figure 1(c)**, **Figure 1(d)**). Optical coherence tomography (OCT) was attempted but no uptake was possible.

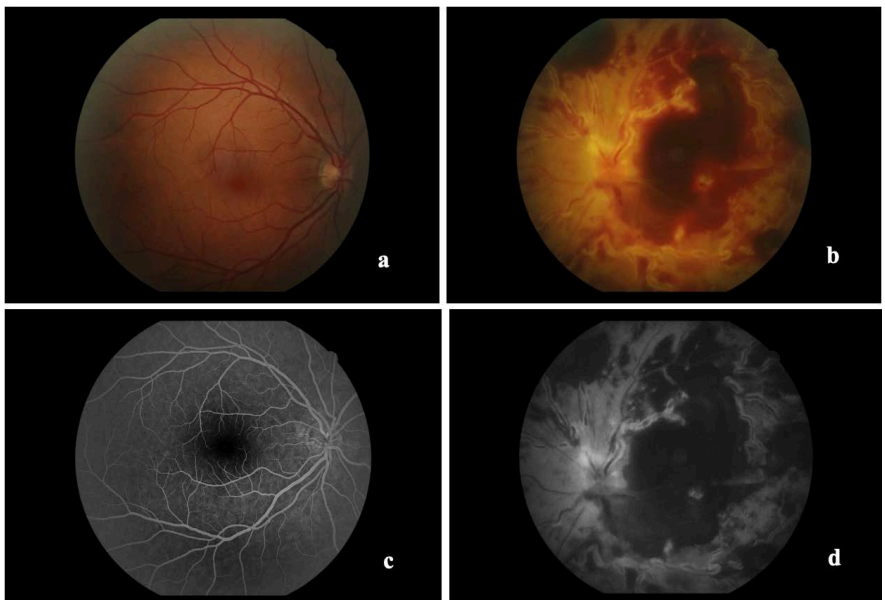

Figure 1. (a) Fundal photo right eye on presentation, no abnormality (b) Fundal photo left eye on presentation, multiple haemorrhages, papilloedema and vasculitis (c) Right eye late stage FFA (d) Left eye late stage FFA corresponding to fundal photo changes.

Blood and radiological investigations were carried out. These included full blood count, renal profile, liver, thyroid function, lipid and glucose testing, inflammatory markers and chest X ray. Auto-antibody screen was negative as well as serology for cytomegalovirus (CMV), Epstein-Barr Virus (EBV), rubella, hepatitis, syphilis, and human immunodeficiency virus (HIV). CT brain was also carried out to exclude any intracranial cause, however results yielded no underlying cause.

A diagnosis of primary frosted branch angiitis was made. In view of the visual acuity, he was started on oral prednisolone at 1 mg/kg/day. Clinical examination after 1 week of treatment showed improvement in the retinal picture with a significant reduction in vasculitis (Figure 2(a)). Further improvement was noted one month after presentation, with resolution of the haemorrhages, mild optic disc pallor and macular exudates. (Figure 2(b)). Vision improved to counting fingers at 1.5 metres. OCT of the left eye displayed inner retinal layer hyperreflectivity, suggesting ischaemia with multiple hyperreflective dots suggestive of exudates. At this stage, systemic treatment was tapered off over 4 weeks. Repeat ophthalmic examination showed complete resolution after 6 months with reduced foveal reflex (Figure 3(a)) and left eye FFA showing no further leakage and normal timed filling of vessels, with mildly increased foveal avascular zone compared to the right eye (Figure 3(b)). Vision remained stable.

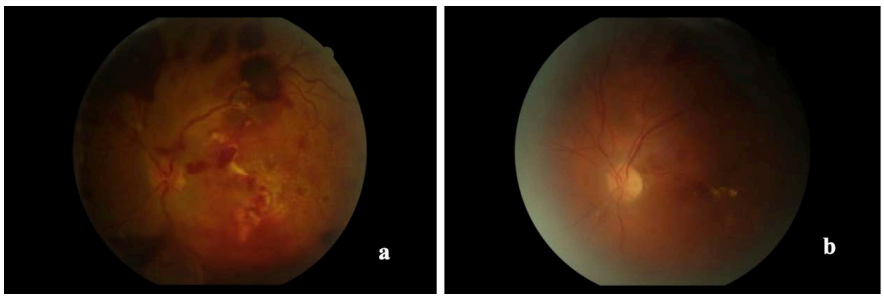

Figure 2. Left eye fundal photo (a) 1 week after presentation, showing reduced inflammation and haemorrhages (b) 4 weeks after presentation showing macular exudates and almost resolved haemorrhages.

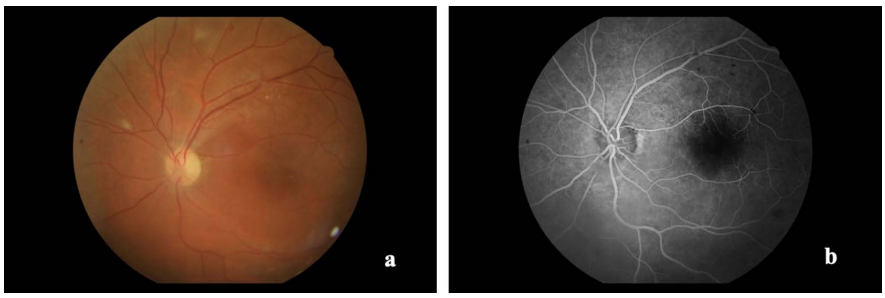

Figure 3. (a) Left eye fundal photo 6 months after presentation (b) Left late stage FFA, 6 months after presentation.

3. Discussion

FBA predominantly affects retinal vasculature, leading to widespread perivascular

inflammation. The pathogenesis is not fully understood, but it is believed to involve an immune-mediated response that is potentially triggered by infections or systemic autoimmune diseases [2]. Secondary cases of FBA have been linked to viral infections such as CMV, EBV, herpes simplex virus (HSV), and HIV, in fact, a presumed viral illness has preceded the onset in 33% of cases [3]. Additionally, systemic conditions like systemic lupus erythematosus (SLE) and Behçet's disease have been implicated in other cases [4]. However, our patient's extensive serological and autoimmune screening returned negative, supporting a diagnosis of primary FBA.

The hallmark features of FBA include severe visual impairment, retinal vasculitis affecting both arterioles and venules, and prominent vascular sheathing [3]. In our case, the patient presented with sudden vision loss in the left eye, with light perception vision, a relative afferent pupillary defect, and extensive retinal involvement. FFA revealed delayed filling in both arterial and venous systems, indicating significant retinal ischemia. OCT demonstrated hyperreflectivity of the inner retinal layers, also suggestive of ischemia, further contributing to the poor prognosis.

FBA must be differentiated from other causes of retinal vasculitis, such as Eales disease, sarcoidosis, and infectious uveitis. Kleiner *et al.* [5] classified FBA into three subgroups, broadly categorizing it into idiopathic and non-idiopathic types. Idiopathic cases have no identifiable underlying cause but typically respond well to corticosteroids, suggesting an immune-mediated mechanism. Non-idiopathic cases are associated with viral infections such as EBV, rubella, CMV, and HIV, where viral antigens may form immune complexes that deposit in retinal vessels, triggering inflammation. Additionally, some viruses, particularly CMV, can directly damage endothelial cells, contributing to vasculitis [5]. In our case, the absence of systemic symptoms and negative serology excluded these secondary causes, reinforcing a diagnosis of primary FBA. A thorough systemic examination was crucial in ruling out alternative etiologies and ensuring appropriate management.

There is no standardized treatment for FBA, but corticosteroids remain the mainstay of therapy in immunocompetent patients, due to the presumed immune-mediated pathophysiology, as depicted in a recent case series [2]. Most of these cases respond well to high-dose systemic corticosteroids, leading to resolution of vasculitis and gradual improvement in vision [5].

In cases which do not resolve with the above management, immunosupression and biologicals have been suggested to prevent recurrence [2]. Visual impairment in FBA is often due to macular oedema, and interventions such as anti-vascular endothelial growth factor (anti-VEGF) therapy and laser treatment have been employed to manage this complication [6]. In a recent report describing a case of FBA in a 14 year old female with systemic idiopathic juvenile arthritis [6], despite negative polymerase chain reaction (PCR) testing for viral pathogens, antiviral therapy was initiated preemptively to mitigate retinal vascular inflammation and

preserve vision. However, no significant improvement was observed with antiviral treatment alone, necessitating a shift in immunosuppressive strategy and TNF-α inhibitor was added. There have also been instances where increasing corticosteroid doses or switching to biologic therapies, such as tumor necrosis factor-alpha (TNF-α) inhibitors, has led to clinical improvement. Additionally, alterations in immunomodulatory therapy, such as transitioning from interleukin-1β (IL-1β) inhibitors to interleukin-6 (IL-6) inhibitors, have been explored, as in this case, and even though the pathogenesis remains unclear, the case described improvement on infliximab infusion [6].

Our patient received oral prednisolone at 1 mg/kg/day, resulting in a marked reduction in vasculitis within one week. Despite this improvement, visual acuity recovery was limited, likely due to the extensive ischemia observed on imaging. A similar case in a 5-year-old boy was treated using the same regime as our case, after being diagnosed with primary idiopathic FBA after testing negative for all PCR viral pathogens and negative for malignant disorders [7]. After the second week of treatment with prednisolone, the patient was noted to have a resolution of vascular sheathing and exudates, with an improvement in visual acquity and complete resolution of subretinal fluid on OCT. This positive result further accentuates the use of steroids in the management of FBA. Nevertheless, this is not always the case, as reported in 2013 [8], where the parents of a 14-year-old healthy boy refused corticosteroid treatment for a diagnosed idiopathic FBA in view of previous mood changes when using such treatments, and a single dose of 40mg adalimumab was given subcutaneously instead. Three weeks post injection, improvement was noted in visual acquity, vascular sheathing and macular oedema. This improvement was also noted on OCT and FFA. Improvement was continuous until 6 months post treatment.

The prognosis of FBA varies widely depending on the degree of vascular occlusion and ischemia. Many cases as described above achieve significant visual recovery following corticosteroid treatment, especially when diagnosed and managed early. However, in our patient, the presence of extensive macular hemorrhage and inner retinal ischemia limited visual improvement to counting fingers at 1.5 meters. Ischemia is a well-recognized poor prognostic factor in retinal vasculitis, often leading to macula ischaemia, macular oedema, vitreous haemorrhage and permanent visual impairment [9].

In fact, a recent case of retinal ischaemia secondary to FBA with Purtscher-like retinopathy was treated with steroids, however hyperbaric therapy (HBOT) was also utilised to address the severe macular ischaemia [10]. In view of the several other treatments that this patient was prescribed, including prednisolone, valaciclovir, acetylsalicylic acid, methotrexate and cyclosporin, the effectiveness of HBOT could not be accurately assessed. Moreover, retinal photocoagulation was also performed after the initiation of hyperbaric therapy to prevent neovascular complications such as retinal detachment and vitreous haemorrhage. However, the results in this patient were positive, thus showing that hyperbaric therapy

may prove to be useful for the treatment of retinal ischaemia secondary to FBA. The reasoning behind this is that hyperbaric oxygen therapy is thought to enhance oxygen diffusion from the choroidal circulation to ischaemic retinal tissue, thus potentially reducing neuronal injury and restoring cellular metabolism. In this case, hyperbaric oxygen therapy was prescribed at 2.0 atmosphere absolute for 75 minutes per session, 1 session per day, 5 times per week. A total of 39 sessions were given. HBOT has been utilised for many ophthalmic cases, such as treating central retinal artery occlusion and diabetic macular oedema with promising results [10]. Whilst the exact mechanism of action in FBA remains unclear, the increased oxygen concentration may help restore normal vascular function and support tissue repair in the ischaemic areas. Despite the use of multiple treatments in this case, the positive outcomes observed after HBOT suggest that it could be a valuable adjunct therapy in the management of retinal ischemia associated with FBA, particularly in cases where conventional treatments alone may not be sufficient. More research and controlled trials are needed to definitively establish the role of HBOT in such conditions and determine the optimal treatment protocols for its use.

4. Conclusion

Our case highlights the importance of recognizing FBA as a sight-threatening retinal vasculitis requiring prompt intervention. While corticosteroids remain the first-line treatment, additional immunosuppressive therapies or intravitreal injections may be warranted in severe cases. The prognosis largely depends on the extent of retinal ischemia, and patients with significant vascular occlusion may have poor visual recovery despite adequate treatment. Further studies are needed to establish optimal management strategies for this rare condition.

Consent

Informed consent was obtained from the patient to report this case.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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