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Case Report

IDIOPATHIC FROSTED BRANCH ANGIITIS IN PAEDIATRIC PATIENTS: CASE SERIES

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ABSTRACT

Frosted branch angiitis is typically a bilateral diffuse retinal periphlebitis that can occur in a number of varying condition. It is a rare entity and a diagnosis of exclusion. We report a case series of primary idiopathic frosted branch angiitis in 2 young healthy girls with different ocular manifestations. Both girls presented with symptoms of sudden severe blurring of vision with only perception to light. In Case 1, patient had left reactive cervical lymphadenopathy and in Case 2, patient presented with both eye redness and mild pain. There were no systemic association in both cases. Fundus examination revealed retinal vasculitis with perivascular exudates and disc hyperemia in both patients, however Case 2 showed dense vitritis and retinal hemorrhages as well. Blood investigations, cultures, infection screening and TORCHES were unremarkable in both cases. Ocular coherence tomograpghy (OCT) in both patients showed retinal edema with subretinal fluid in the earlier part of disease, however in Case 2, the disease resolved with foveal atrophy. Both patients were treated with Intravenous Methylprednisolone and Intravenous Acyclovir followed by tapering dose of oral corticosteroids and acyclovir for 6 week duration. Following treatment, the uveitis completely resolved in Case 1, however Case 2 was complicated with posterior subcapsular cataract and foveal atrophy. On subsequent follow up, Case 1 had good visual outcome and Case 2 had poorer vision due to cataract and foveal atrophy. Frosted branch angiitis shows an excellent response to systemic corticosteroid and has a good prognosis with early treatment.

INTRODUCTION

Frosted branch angiitis (FBA) was first described in Japanese literature by Ito in 1976 in a 6-year-old child [1]. It is a rare entity with approximately 100 cases described in literature till 2017. The great majority (75%) of patients are Japanese, indeed it was not until 1988 that any patient outside Japan was reported [2]. The diagnosis is made clinically with typical periphlebitis, veins being involved more commonly than arteries in a pattern of frosted branches of a tree supplemented by fundus fluorescein angiography findings [1]. We report the ocular manifestation, management and visual outcome of 2 patients with frosted branch angiitis seen in our centre.

CASE SERIES

Case 1

An 8-year-old girl with no known medical illness was referred from Hospital Melaka to our clinic with a history of sudden onset of bilateral blurring of vision. There was history of painless neck swelling on the left side associated with fever 2 days prior to the blurring of vision. There was no history of upper respiratory tract infection or diarrhea. On examination, vision was vague perception to light in both eyes. Both pupil were dilated with poor reaction to light. The anterior chamber showed 1+ cells with iris pigments on lens. Funduscopy revealed clear media with hyperemic optic discs. There were dilated and tortuous retinal vessels with perivascular sheathing and dull foveal reflex (Figure 1, 2).

Optical Coherent Tomography of both maculae showed the presence of subretinal fluid. The diagnosis of bilateral frosted branch angiitis was made. Hematological investigations revealed normal hemoglobin of 11.3 g/dL and a normal white cell count of $7.6x10^3$/mL. Erythrocyte sedimentation rate (ESR) was slightly elevated, 51 mm/h. Serology for Toxoplasma, Hepatitis B, C and

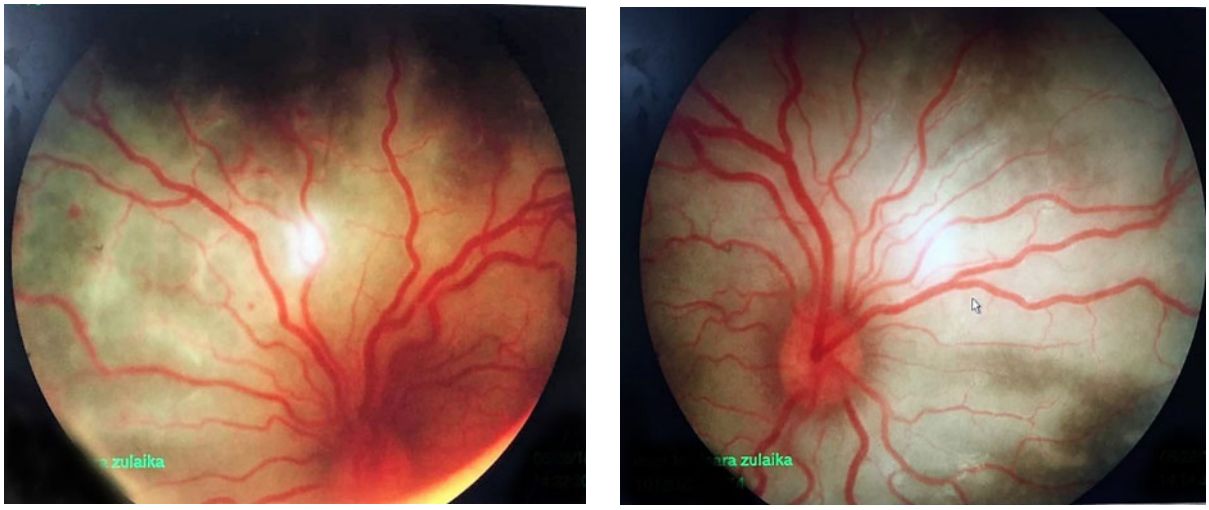

Figure 1. Fundi of both eyes at initial presentation showing hyperemic discs, dilated and tortuous vessels with perivascular sheathing, extensive retinal oedema involving the macula.

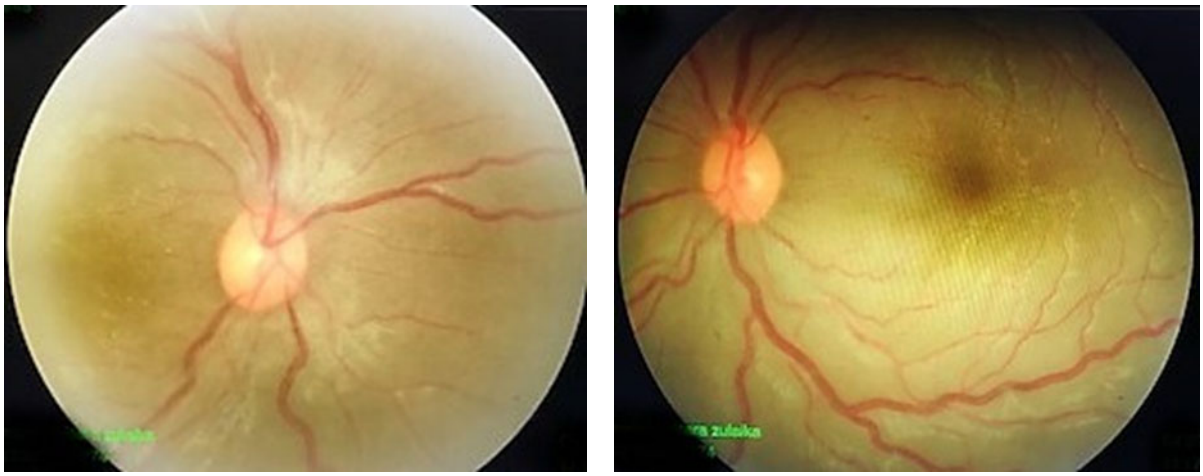

Figure 2: Appearance of both fundi at one week following treatment showing improvement.

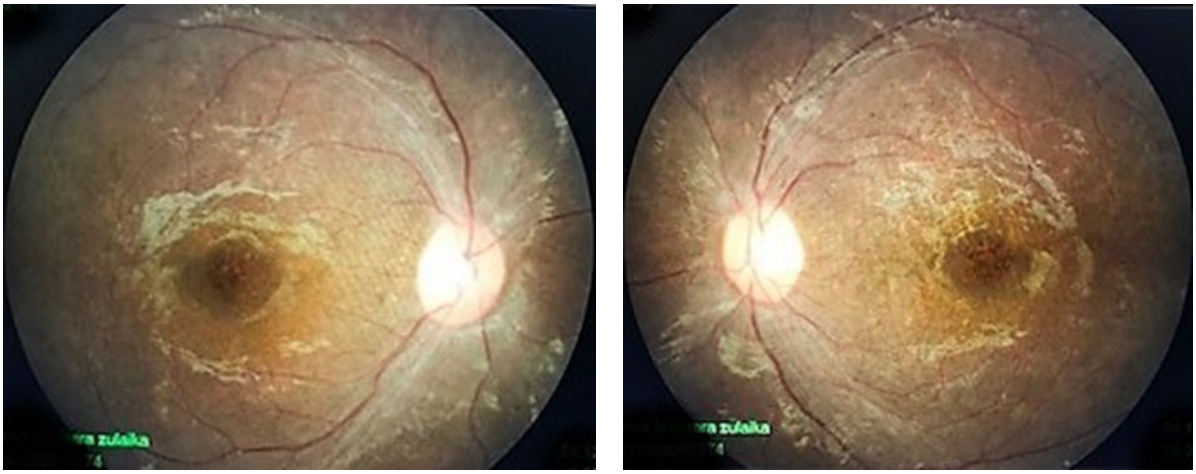

Figure 3: At 6 months post treatment : the vessels were attenuated and there were pigmentary changes at the periphery.

Human immunodeficiency Virus (HIV) were all non reactive, however Mantoux test was 0 mm. Ultrasound of neck revealed left cervical lymphadenopathy, Chest X ray and Contrast enhanced computed tomography (CECT) of orbits were normal. Histopathology examination of biopsy of left neck lymph node revealed reactive lymphadenitis. The patient was started on Gutt Prednisolone acetate 1% hourly and Intravenous (IV) Acyclovir infusion 20 mg/ kg three times a day for 1 week followed by oral Acyclovir at the same dose four times a day for the next 6 weeks. A 3-day course of IV Methylprednisolone was administered at 10mg/kg followed by oral prednisolone at a dose of 1 mg/ kg and slowly tapered over the next 2 months. There were resolution of severe vasculitis over the next 6 weeks. (Figure 3). The best corrected vision (BCVA) was 6/18 and 6/15 in the right and left eye respectively at 6 months.

Case 2

A 7-year-old girl with no known medical illness was referred from Hospital Seremban to our eye clinic with sudden onset of blurring of vision in both eyes of 4 days duration, associated with redness and mild pain. There were no history of fever, upper respiratory tract infection or diarrhea. On ocular examination, vision were perception to light bilaterally. There were intense inflammation in both eyes evidenced by ciliary injection and anterior chamber reaction. There were 4+ cells, 360 degrees of broken posterior synechiae and the presence of posterior subcapsular cataract. Otherwise, there were no keratic precipitates or iris nodules seen. Funduscopy revealed hazy media due vitritis, hyperemic optic discs with macula edema. There were tortuous and sclerosed vessels with arteritis, perivascular sheathing and retinal hemorrhages in all quadrants(Figure 4, 5, 6,7). Macular OCT showed foveal atrophy with loss of inner segment (Figure 8). The

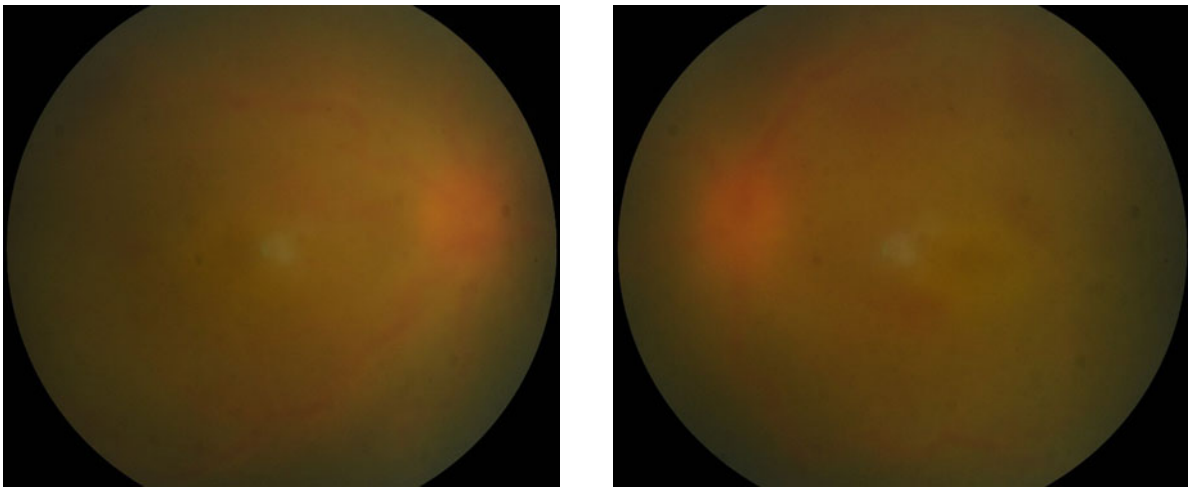

Figure 4 : Fundus photograph showing hazy view of both fundi at presentation.

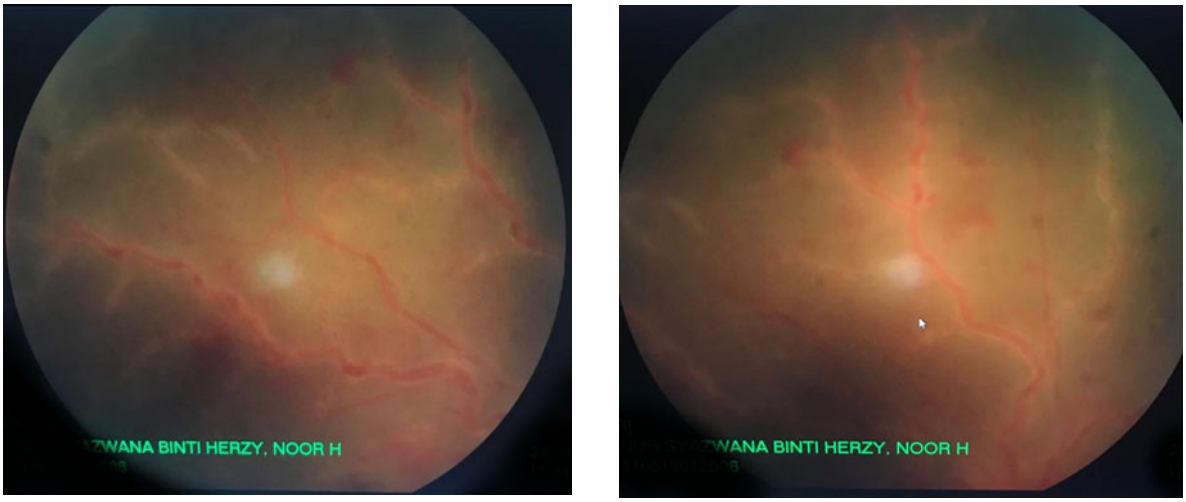

Figure 5. Fundus photograph of superior quadrants of both eyes showing hazy media due to vitritis, hyperemic disc, tortuous and sclerosed vessels with perivascular sheathing and retinal hemorrhages.

diagnosis of bilateral frosted branch angiitis was made. Hematology investigations revealed normal hemoglobin 14.1 gm/dL and a normal white cell of $8.4x10^3$/mL, full blood picture was normal, erythrocyte sedimentation rate (ESR) was 45 mm/h. The serology for TORCHES, Hepatitis B, C and HIV was non reactive. Mantoux test was 0 mm . Blood and urine cultures were negative. We administered intravenous Acyclovir infusion 500mg/m^2 three times a day for 1 week followed by oral acyclovir at the same dose four times a day for the next 6 weeks. IV Methylprednisolone was given at 10mg/kg three times per day for 3 days followed by oral prednisolone at a dose of 1 mg/ kg which was slowly tapered over 2 months. Patient also received topical Prednisolone acetate 1% hourly and prophylactic topical Ciprofloxacin 2- hourly, and topical Tropicamide. There were resolution of the severe vasculitis (Figure 7) over the next 6 weeks however patient developed posterior subcapsular cataract and foveal atrophy . Best corrected visual acuity were 6/60 in both eyes.

DISCUSSION

Frosted Branch Angiitis (FBA) predominantly affects the young and fit individuals. There appears to be a bimodal age distribution, with one peak in childhood and a second in the third decade of life. There has been a preponderance of females (61%) to males (39%) [2]. In our case series, both our cases were seen in healthy young female patients.

The most common presenting symptoms of FBA are subacute visual loss, floaters and flashes of light. The visual acuity may be reduced to perception of light. Associated systemic symptoms

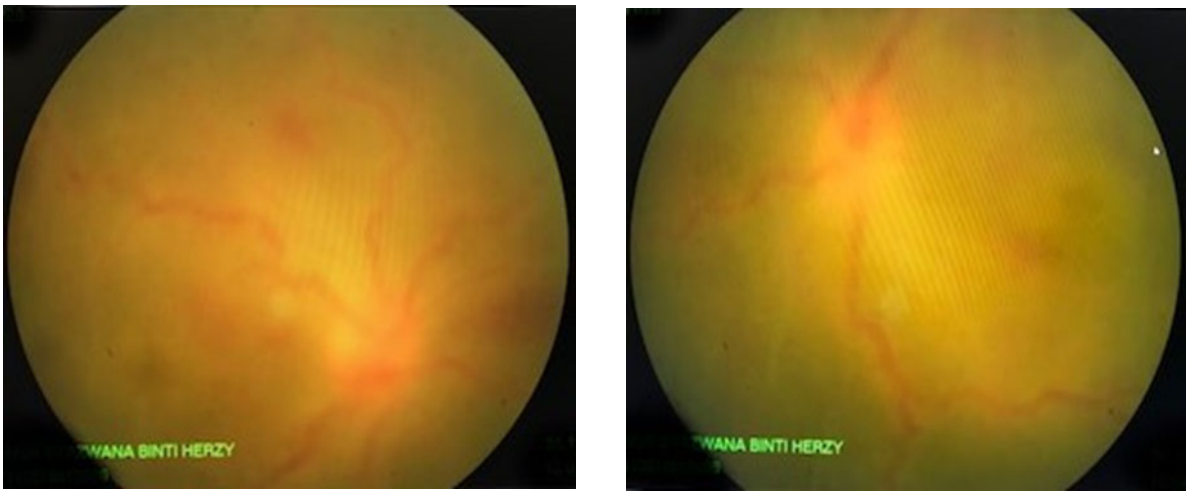

Figure 6: Fundus photograph on Day 3 of treatment.

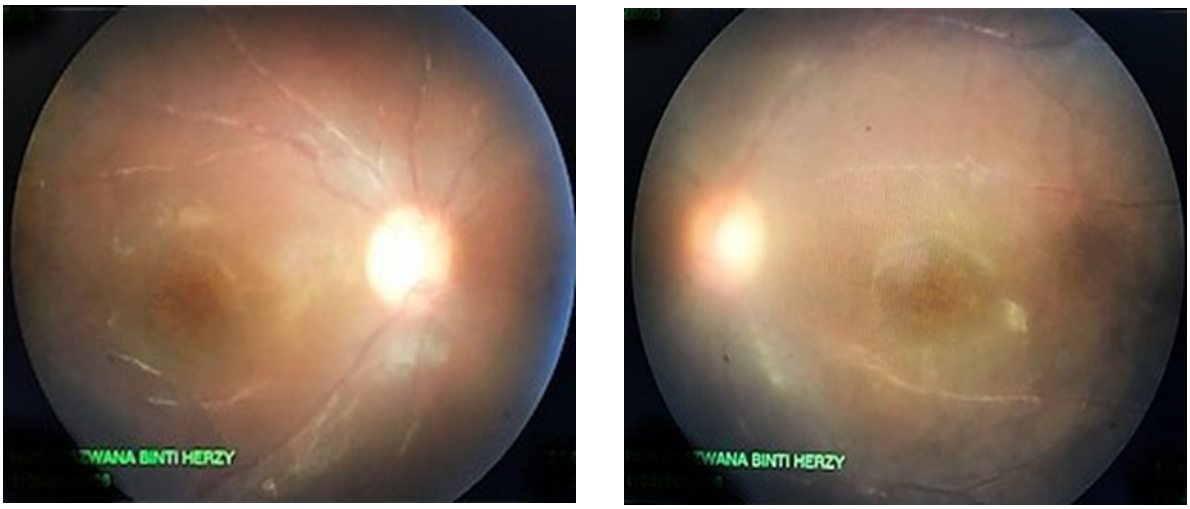

Figure 7: Fundus photograph after 6 weeks of treatment showing minimal vitritis, attenuated vessels with resolution of perivascular sheathing and macula scar.

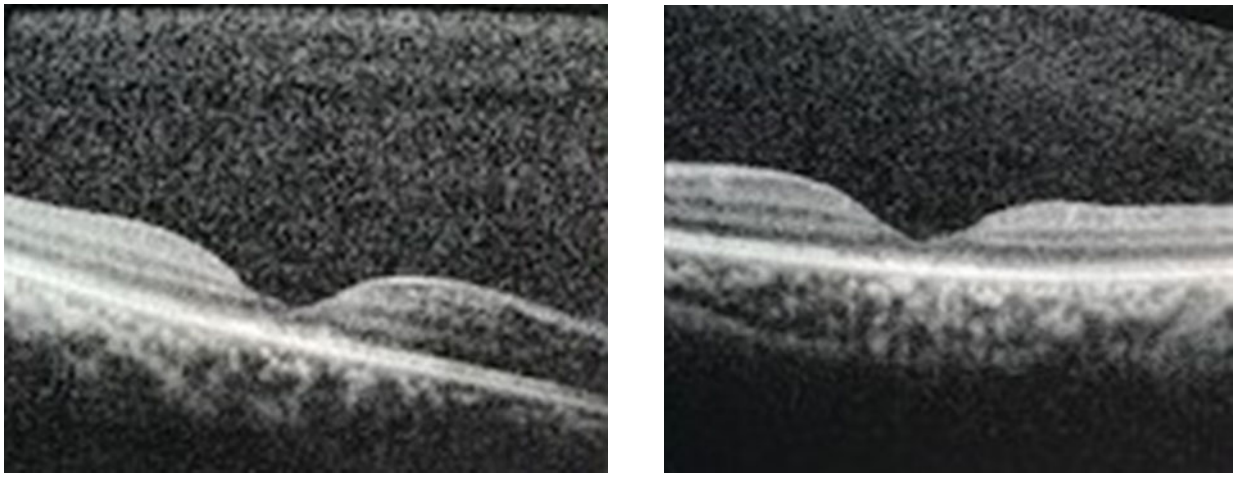

Figure 8: OCT of the right and left macula showing foveal atrophy with loss of inner segment.

are non-specific, such as flu-like syndrome including upper respiratory infection, sore throat, fever and malaise, back pain and headache. Most patients (75%) have bilateral disease [2,3] . Both our patients presented with sudden onset of blurring of vision in both eyes with perception to light.

Frosted branch angiitis can be an idiopathic disorder or can be associated with ocular and systemic diseases. Cytomegalovirus (CMV) retinitis, Acquired immune deficiency syndrome (AIDS) retinitis and Toxoplasma chorioretinitis are the most frequent ocular associations, while systemic lupus erythematosus, Crohn's disease, large cell lymphoma and acute lymphoblastic leukemia have been described as systemic disorders associated with frosted branch angiitis [3]. In both our cases, there were no systemic causes identified, though the ESR in both cases were moderately elevated, while zero reading for Mantoux were most likely due to the corticosteroid administered.

The cause of FBA is unknown. The typical onset of FBA after a prodromal illness has led to the suggestion of a hypersensitivity reaction to various infective agents, which may initiate FBA via a common pathway, possibly of immune-complex deposition [3].

Based on the underlying pathology, Kleiner suggested classifying patients into three different subgroups. The first group comprises patients affected by lymphoma and leukemia that can present with a frosted branch-like appearance in the fundus. The second group includes patients with associated autoimmune or infectious diseases which presented with FBA as a clinical sign of the underlying disease. Cytomegalovirus has been found to be the most common underlying infectious pathology followed by toxoplasmosis. These cases may show focal retinitis in addition to the vasculitis. Among autoimmune diseases, Behcet's disease is most frequently associated with FBA. The third group comprises patients with no identifiable cause and is classified as having primary idiopathic FBA. Patients with primary idiopathic FBA tend to be of younger age group, with bilateral involvement [2,3] .

Typically FBA has a striking fundus appearance of bilateral diffuse retinal vasculitis with a 'frosted' quality due to the perivascular exudate. Mild to moderate iritis with vitritis is common, as is retinal oedema. Intraretinal haemorrhages and punctate hard exudates are only occasionally seen. Papillitis, if present, is usually mild. Both our cases showed diffuse retinal vasculitis with perivascular exudates and disc hyperemia. However in case 2,the patient also had intense vitritis and retinal hemorrhage. In Case 1, OCT showed macula and retinal edema with subretinal fluid, however in Case 2, patient had foveal atrophy. Fluorescein angiography in case 2 was near normal in the early phase, but there was late leakage from the larger affected retinal vessels. In the recovery phase, microaneurysms have been described. The vasculitis is usually nonocclusive. Visual field analysis reveals constriction or relative central field defects that improve after clinical resolution. The latter are thought to be due to macular oedema [1,4,5,6].

Electrophysiology has shown a reduction in the amplitudes of the electroretinogram (ERG), electrooculogram (EOG) and visually evoked response (VER). This would be consistent with a widespread dysfunction of the retina, pigment epithelium and optic nerve. The EOG and VER may return to normal, but the ERG changes have generally persisted beyond convalescence, suggesting permanent retinal damage [1,6].

Complications include retinal vein or artery occlusion, macular epiretinal membrane formation, macula scarring, diffuse retinal fibrosis, retinal tear

formation, vitreous haemorrhage, optic disc atrophy and peripheral atrophic retinal lesions [1,5]. In our patients, Case 1 showed peripheral atrophic retinal changes and in Case 2 there was macula atrophy. Nevertheless, despite the severe retinal appearance, the prognosis is usually good, with rapid recovering of visual acuity after prompt systemic corticosteroid treatment. Visual field and electrophysiological tests return completely normal after one or two months from the disease onset [3,6].

There is no definite treatment protocol for this disease. In most of the previous studies no medication apart from corticosteroids were given, whereas some had opted a combination of corticosteroids and acyclovir. We observed good response with combination of acyclovir and corticosteroids in our cases. Following 6 weeks of therapy, the anterior uveitis, vitritis, and vasculitis completely regressed, leaving minimal morphological sequelae. The disease is frequently limited to an isolated acute episode, although rare cases of recurrence have been described [3].

CONCLUSION

Frosted branch angiitis is typically a bilateral diffuse retinal periphlebitis that may occur in a number of varying conditions. It is a diagnosis of exclusion with characteristic clinical presentation and typically affects children and younger adults. Before making a diagnosis of primary idiopathic frosted branch angiitis, infiltrative disorders such as leukemia and lymphoma, infective causes such as cytomegalovirus retinitis, and diseases such as Behcet's and sarcoidosis, which may cause widespread vasculitis, should be ruled out. It is responsive to corticosteroid therapy and prognosis is good with timely intervention.

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