



# Behçet's Uveitis

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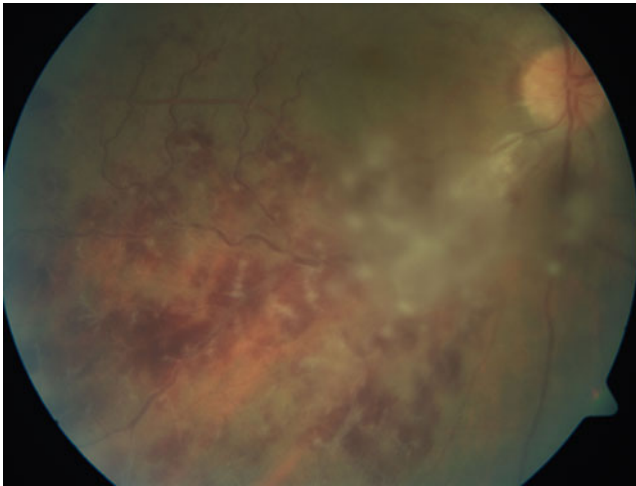
## Introduction

Behçet's uveitis is classically defined as a bilateral non-granulomatous panuveitis and retinal vasculitis. The disease course is marked by recurrent exacerbations followed by spontaneous resolution of acute inflammatory signs. Anterior and/or posterior segment of one or both eyes may be acutely inflamed at a given episode of activation, manifesting as high-grade anterior chamber cells with or without hypopyon formation, vitreous cells and haze, optic disc inflammation, retinal infiltrates, retinal venous sheathing and occlusions, retinal hemorrhages, necrotizing retinitis, retinal edema, and exudative retinal detachment. Fluorescein angiography is the gold standard in monitoring both leaky and occlusive nature of retinal vasculitis. The diagnostic criteria of Behçet's uveitis has been summarized in our previous publication of over 880 patients with the disease.

## Case 1: Occlusive Retinal Periphlebitis

A 43-year-old man presented with an acute visual loss in the right eye. He had a history of recurrent oral ulcers, genital ulcers, erythema nodosum, pseudofolliculitis, and arthritis and had been diagnosed with Behçet's disease 10 years ago. He had been on azathioprine until 7 months prior to the onset of ocular symptom. He had count fingers vision, 2+ anterior chamber, and 2+ vitreous cells in the right eye. Fundus exam revealed occlusive periphlebitis of the inferior temporal retinal vein in the right eye (Fig. 1). Three days after starting the treatment with intravenous pulse methylprednisolone 1 g per day, azathioprine 100 mg/day, and cyclosporine 200 mg/day, there was a linear accumulation of pearl-like precipitates on the surface of the inferior peripheral retina (Fig. 2). Five months later, while the patient was on a tapering dose of oral prednisone combined with azathioprine and cyclosporine, visual acuity was 0.8, there was no sign of active intraocular inflammation, and fluorescein angiography showed capillary rearrangements, late segmental leakage of the inferior temporal vein, and peripheral areas of retinal capillary nonperfusion (Fig. 3a–c).

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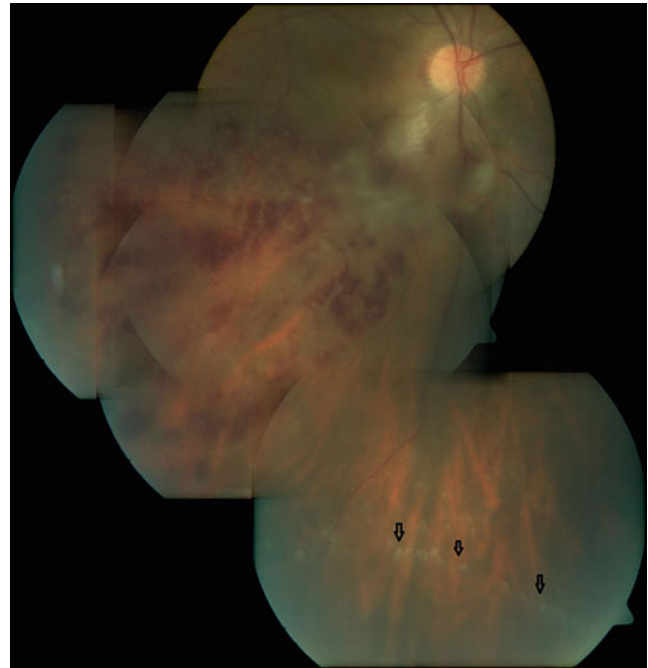
**Fig. 1** Color fundus photograph of the right eye of a patient with Behçet's disease shows hyperemic optic disc, retinal infiltrate and overlying confluent snowballs inferotemporal to the disc, increased tortuosity and sheathing of the inferior temporal retinal vein, marked sheathing of its branches, and retinal hemorrhages along the inflamed vasculature

### Case 2: Recurrent Occlusive Retinal Periphlebitis and Panuveitis

A 33-year-old man with Behçet's disease treated elsewhere with combined oral prednisolone, azathioprine, and cyclosporine presented with acute visual loss in the right eye. His vision was hand movements in the right eye and 0.1 in the left eye. He had hypopyon panuveitis in the right eye with 4+ vitreous haze. In the left eye, there were no cells in the anterior chamber, but there were 1+ vitreous cells. Fundus exam of the left eye revealed pallor of the optic disc, occluded superior and inferior temporal retinal veins, and retinal hemorrhages (Fig. 4a–c). The occluded vessels looked like white cords and the retinal hemorrhages were darker inferiorly, indicating that the inferior temporal vein occlusion preceded occlusion of the superior temporal vein and proving the recurrent nature of occlusive retinal periphlebitis. Fluorescein angiography showed extensive nonperfusion of the posterior pole, superior temporal, temporal, and inferior retina; and diffuse capillary leakage was seen in the superior nasal and nasal peripheral retina (Fig. 5). An EDI-OCT section through the macula in the left eye showed retinal atrophy and disruption of outer retinal layers at the fovea (Fig. 6).

### Case 3: Diffuse Retinal Capillary Leakage

A 30-year-old man with Behçet's disease, treated with interferon alpha-2a for 3 years, came for a second opinion on his treatment options. His visual acuity was 0.9 in the

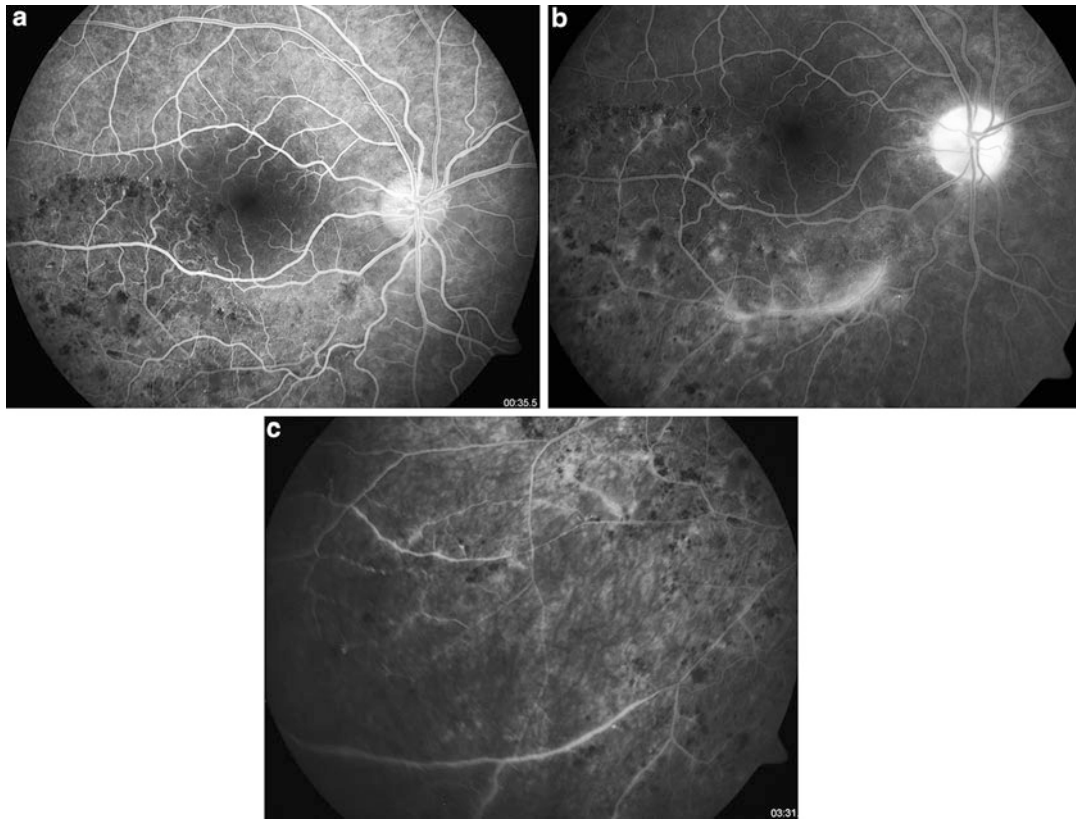


**Fig. 2** A composite color fundus photograph shows resolving retinal infiltrate and vitreous inflammation, vascular sheathing, and retinal hemorrhages in the inferior temporal vein region and pearl-like precipitates in a linear pattern on the surface of the inferior peripheral retina (arrows)

right and 0.5 in the left eye. There was no sign of active inflammation in either eye. Fluorescein angiography showed optic disc staining, vascular wall staining, and diffuse capillary leakage in both eyes (Fig. 7a and b). Anti-TNF therapy was advised because of an incomplete response to interferon alpha and a high risk of recurrent uveitis attack in this patient.

### Case 4: Recurrent Superficial Retinal Infiltrates and Retinal Nerve Fiber Layer Atrophy

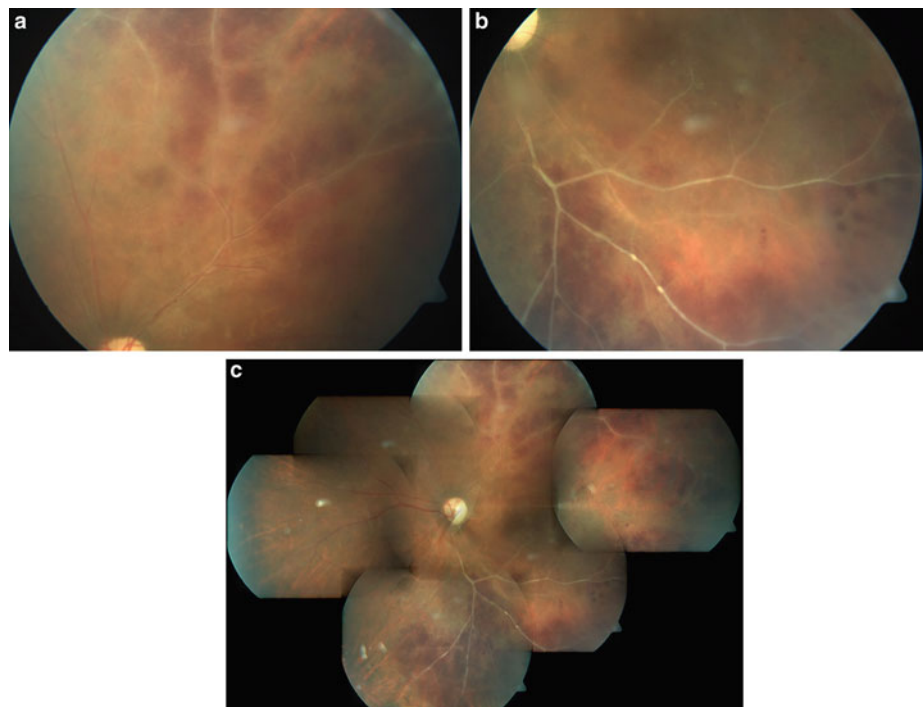
A 42-year-old woman diagnosed with mucocutaneous and neuro-Behçet's disease 17 years ago presented with acute visual blurring in the left eye. Her visual acuity was 0.2, and she had 1+ anterior chamber and 2+ vitreous cells in the left eye. Fundus exam revealed retinal infiltrates and hemorrhages at the posterior pole (Fig. 8). Fluorescein angiography showed early hypofluorescence and late staining of the infiltrates and focal hyperfluorescence of the inflamed venular branches corresponding to the infiltrates, suggesting that superficial retinal infiltrates could be associated with focal periphlebitis (Fig. 9a and b). OCT imaging showed focal hyperreflective thickening of the retina at the site of the infiltrate (Fig. 10) and exudative foveal detachment (Fig. 11). The patient refused systemic therapy because she

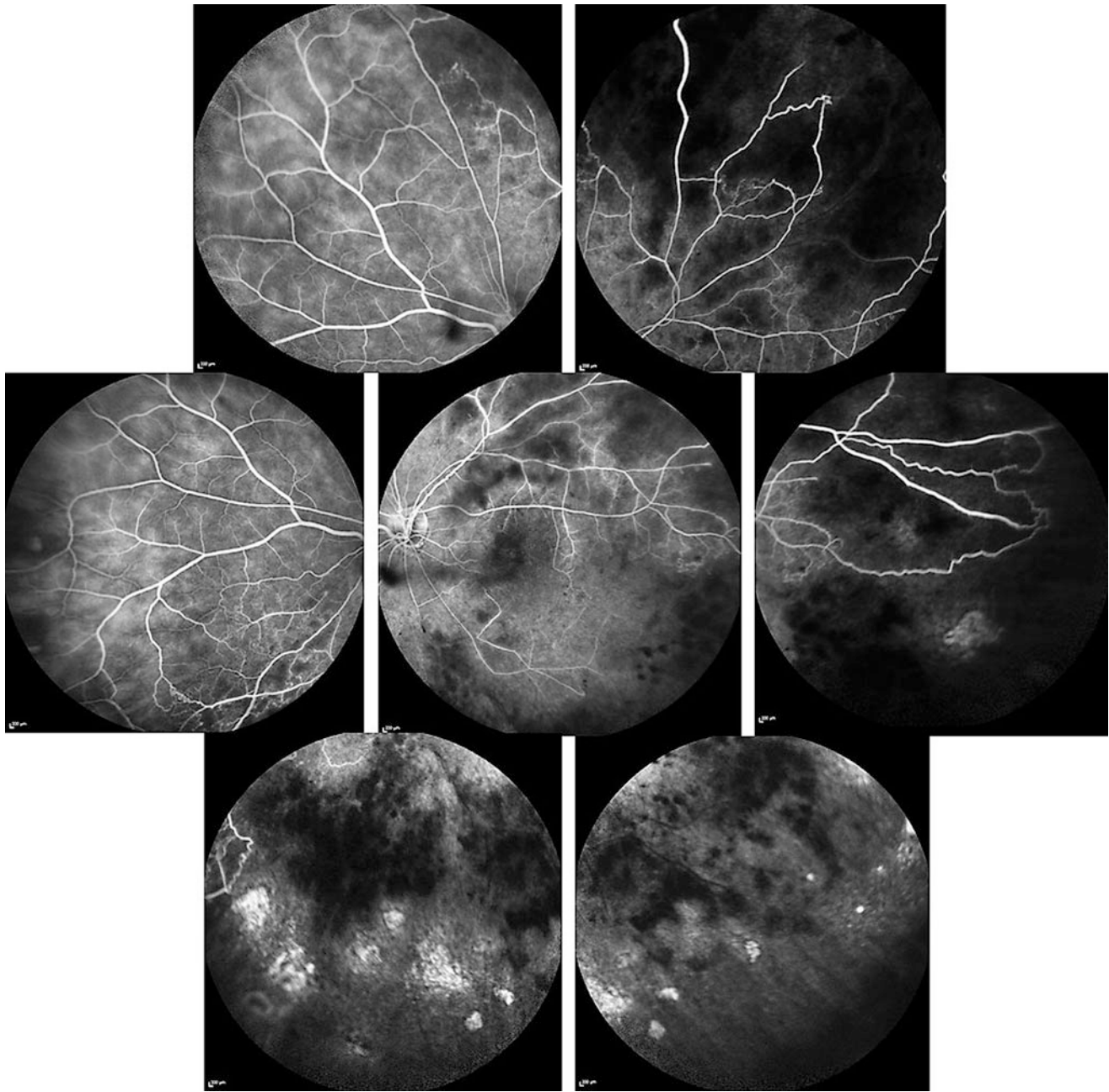


**Fig. 3** Fluorescein angiography of the right eye after 5 months of treatment. Posterior pole at early (a) and late (b) phase shows staining of the optic disc, capillary dilatations and vascular rearrangements, and late

segmental leakage of the inferior temporal vein as well as scattered leakage of the capillaries. Inferior temporal frame (c) shows diffuse staining of inferior temporal vein branches and retinal capillary nonperfusion

**Fig. 4** Color fundus photographs of the left eye of a patient with Behçet's disease shows diffuse sheathing of the retinal vessels superiorly (a), empty vessels that look like white cords inferiorly (b), and a composite photograph shows optic disc pallor and distribution of retinal hemorrhages in the superior and inferior temporal retina (c)





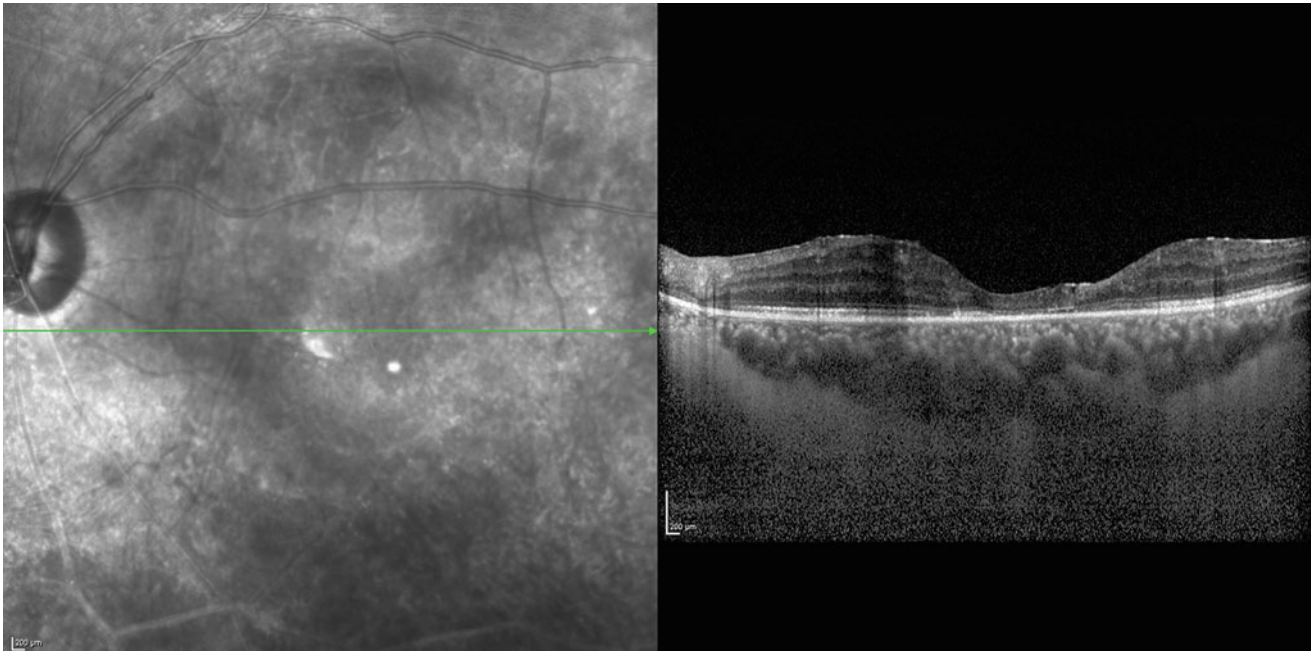
**Fig. 5** Fluorescein angiography of the left eye shows extensive non-perfusion of the posterior pole and superior temporal, temporal, and inferior retina. Note the dark hypofluorescence of the superior temporal

retina due to hemorrhages and nonperfusion, patchy areas of hyperfluorescence inferiorly, associated with retinal pigment epithelial atrophy, and diffuse capillary leakage in the nasal peripheral retina

was breastfeeding and a subtenon triamcinolone injection was administered. One month later, her visual acuity increased to 0.6 with resolution of macular detachment. A slit-like retinal nerve fiber layer atrophy appeared extending from superior temporal margin of the optic disc and the OCT section through the previously infiltrated retina showed thinning and hyperreflectivity of inner retina (Fig. 12). At 8th month of follow-up the patient presented with new retinal infiltrates in the same eye (Fig. 13).

#### **Case 5: Panuveitis with Retinal Infiltrates, Retinal Edema, Exudative Retinal Detachment, and Subretinal Hypopyon**

A 24-year-old woman with Behçet's disease presented with a sudden visual loss in the right eye. Her vision was count fingers at 1 m in the right and at 4 m in the left eye. She had 4+ cells in the anterior chamber and vitreous in the right eye,



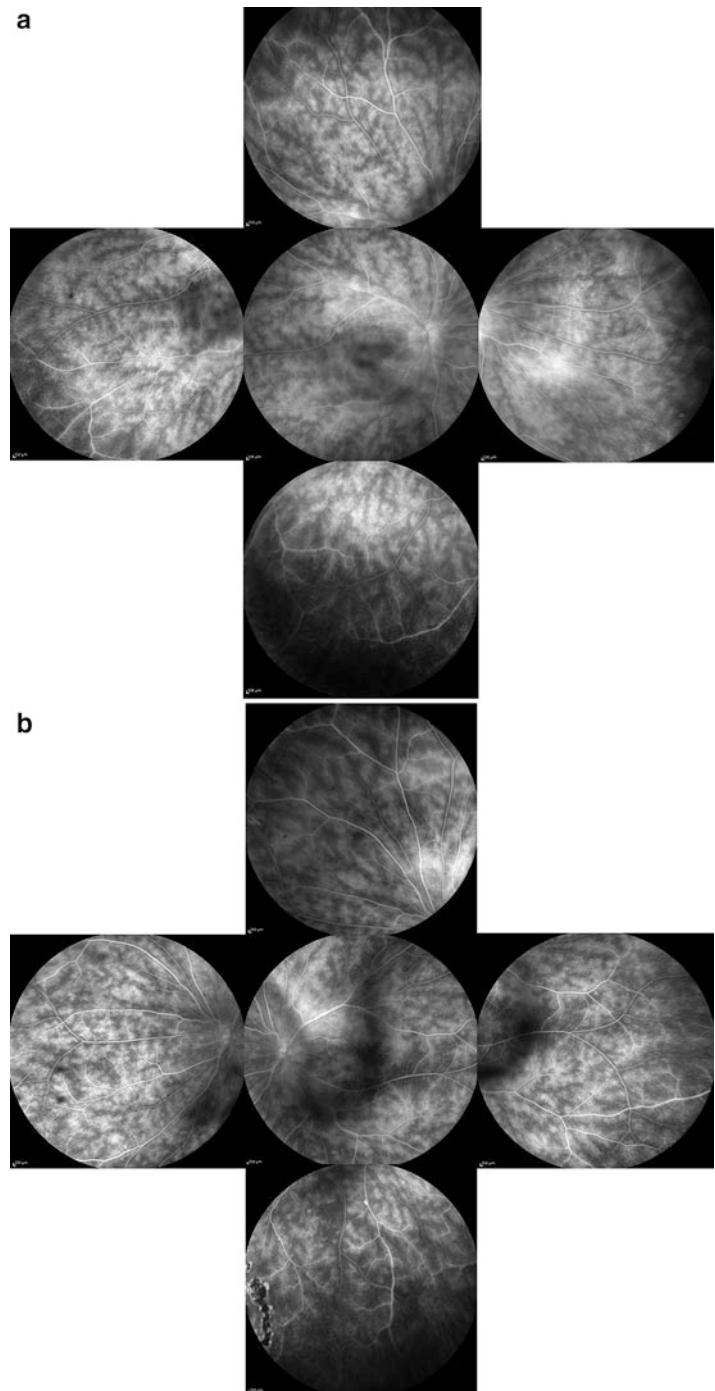
**Fig. 6** EDI-OCT section of the left eye shows retinal atrophy and disruption of outer retinal layer at the fovea

and 1+ cells in the anterior chamber and 2+ cells in the vitreous in the left eye. Fundus exam showed vitreous haze, inflamed optic disc, retinal infiltrates, edema, and hemorrhages in the right eye (Fig. 14a and b). An area of retinal edema and shallow exudative retinal detachment was seen in the inferior nasal retina. A layered collection of exudative material, “subretinal hypopyon,” was seen at the inferior border of the edematous retina (arrow) (Fig. 14c). In the left eye there was macular edema. After high-dose corticosteroid treatment combined with azathioprine and cyclosporine, inflammatory findings resolved in both eyes (Fig. 14d–f).

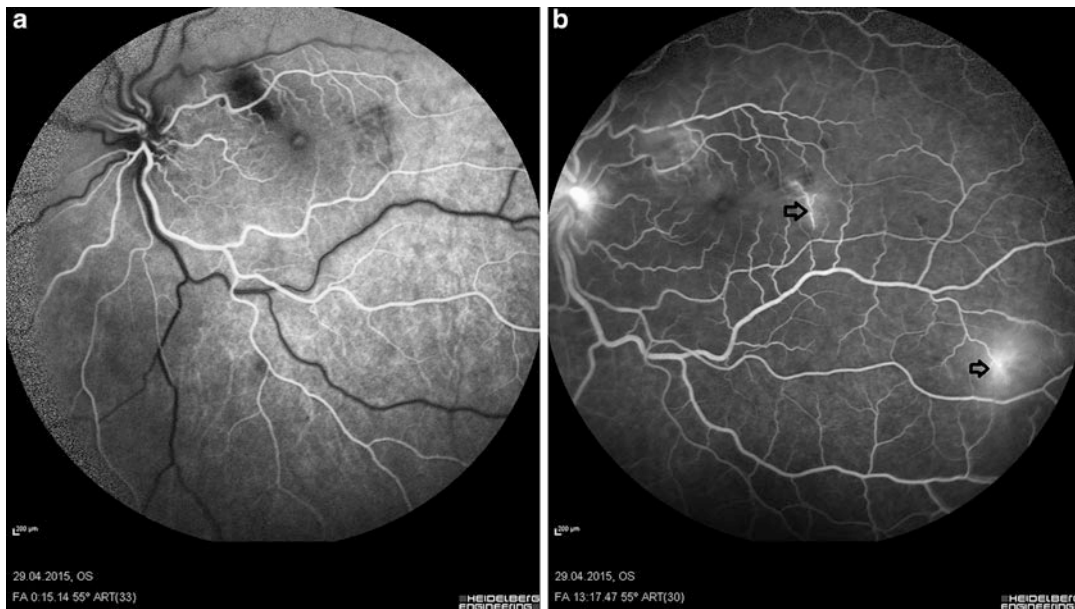
### Key Points

- Ocular involvement in Behçet's disease is characterized by an acute onset of inflammatory episodes and recurrent nature of inflammatory signs. The severity and frequency of posterior segment inflammation determine the visual prognosis.
- Occlusive retinal periphlebitis is considered a hallmark of Behçet's disease. Branch retinal vein occlusions develop in around 10% of patients with ocular involvement. Occluded vessels typically have a frosted branch appearance at onset. The presence of retinal infiltrates, vitreous haze, and subsequent appearance of pearl-like precipitates inferiorly in the same or the other eye helps to differentiate such occlusive episodes from other causes of occlusive retinal vasculopathy. After several weeks to months occluded vessels may show gliotic sheathing or may appear like white cords. Extensive retinal ischemia and atrophy may develop, presumably due to occlusion of arterioles as well. The risk of retinal neovascularization is less than 5%.
- During clinically quiescent periods, there may be persistent diffuse capillary leakage on fluorescein angiography. Treatment needs to be augmented in such cases because of the high risks of a recurrent uveitis attack, cystoid macular edema, and inflammatory disc neovascularization.
- Superficial retinal infiltrates are the most commonly seen inflammatory lesions in the fundus at onset of acute inflammatory episodes. They may be in any number or location. These lesions appear to be foci of severe periphlebitis. When located at the posterior pole, retinal nerve fiber layer defects appear following resolution of retinal infiltrates without any visible scar formation.
- Severe panuveitis attacks in Behçet's disease may need to be differentiated from infectious uveitis, especially endogenous endophthalmitis and viral necrotizing retinopathies.
- Corticosteroids are generally used for the treatment of acute inflammatory episodes. Immunomodulatory agents need to be started from the onset in order to prevent recurrences. Treatment with biologic agents should not be delayed in patients refractory to conventional immunomodulatory therapy, because a single severe attack can cause permanent loss of useful vision.

**Fig. 7** Fluorescein angiography of a patient with Behçet's disease treated with interferon alpha-2a shows optic disc staining and fern-like diffuse retinal capillary leakage in both right (**a**) and left eye (**b**). Note staining of the vessel wall in superior temporal arcade in the right eye, capillary nonperfusion and RPE mottling of the inferior peripheral retina in both eyes, and part of the laser scars surrounding a retinal tear in the inferior nasal retina in the left eye

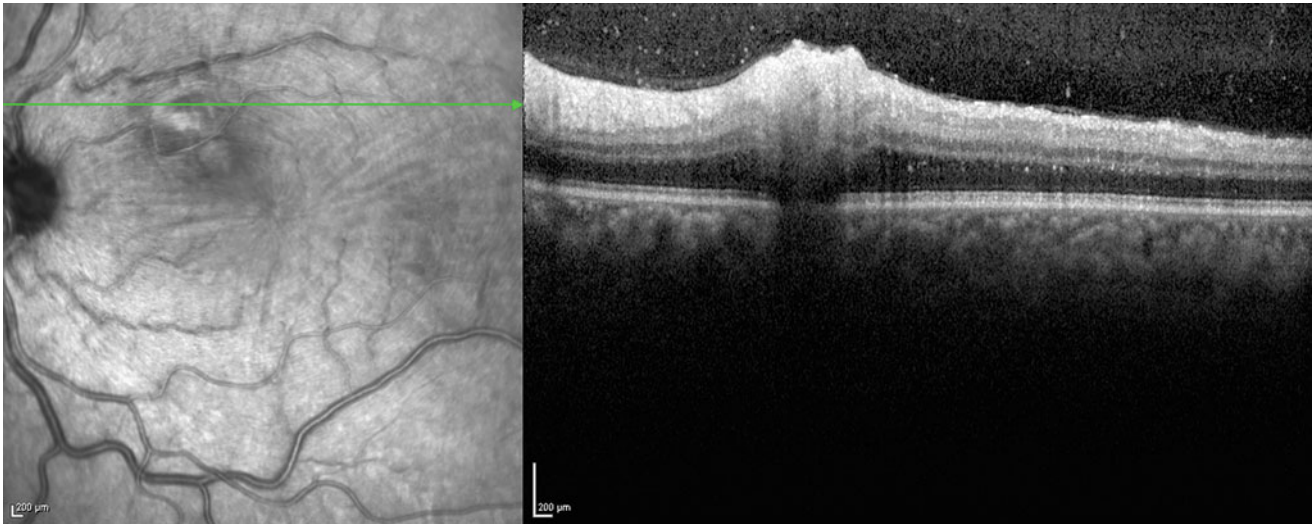


**Fig. 8** A composite color fundus photograph of the left eye of a patient with Behçet's disease shows hyperemic optic disc, retinal infiltrates, and hemorrhages

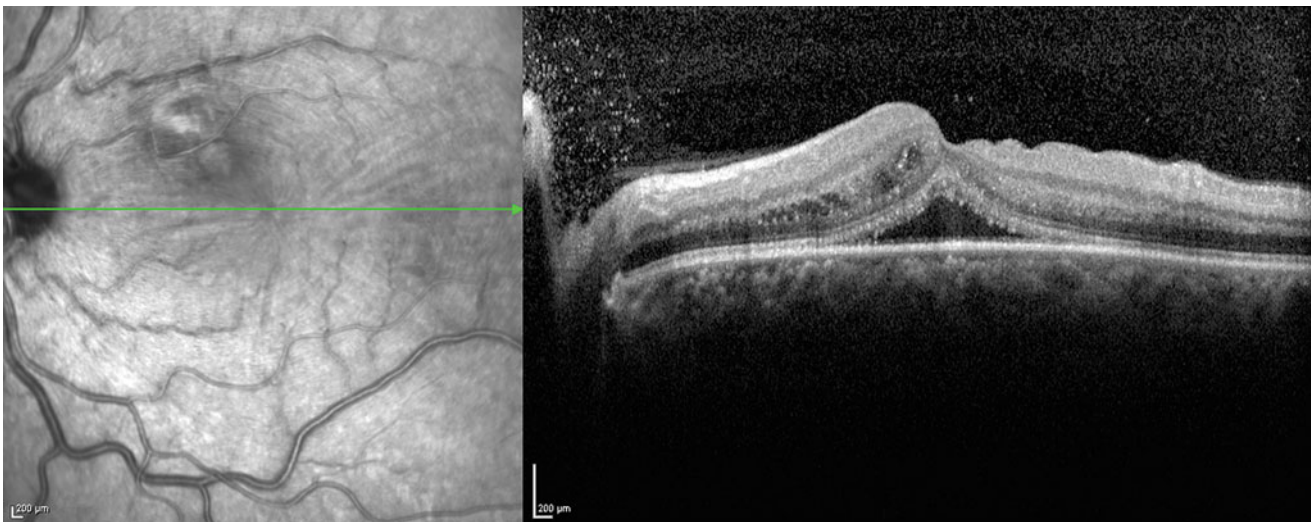


**Fig. 9** Fluorescein angiography at the early phase (a) shows hypofluorescence of the retinal infiltrates superior and inferior to the superior temporal retinal arteriole; at the late phase (b), the infiltrated retina

becomes mildly hyperfluorescent and hyperfluorescence and leakage of the venular branches are seen (arrows)

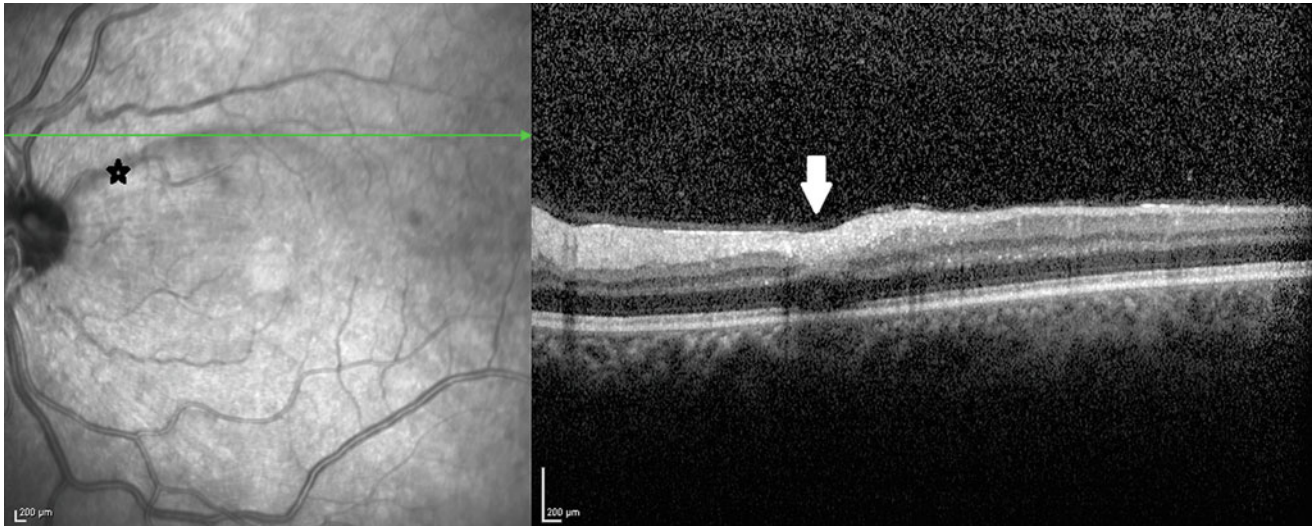


**Fig. 10** OCT section through the retinal infiltrate shows smudging of inner retinal layers and focal hyperreflective thickening that causes shadowing inferiorly



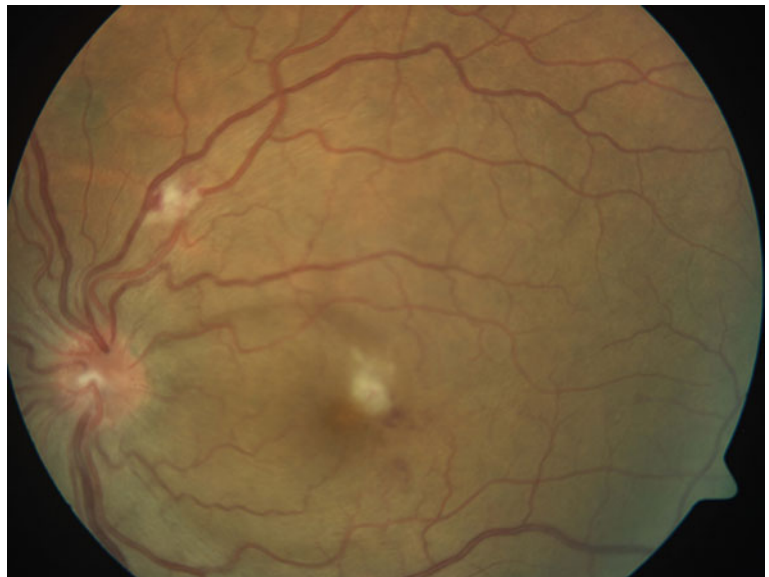
**Fig. 11** OCT section through the macula shows macular thickening, intraretinal hyperreflective dots, and hyporeflective spaces as well as exudative detachment of the fovea. Note the collection of hyperreflective dots (vitreous cells) over the optic disc margin

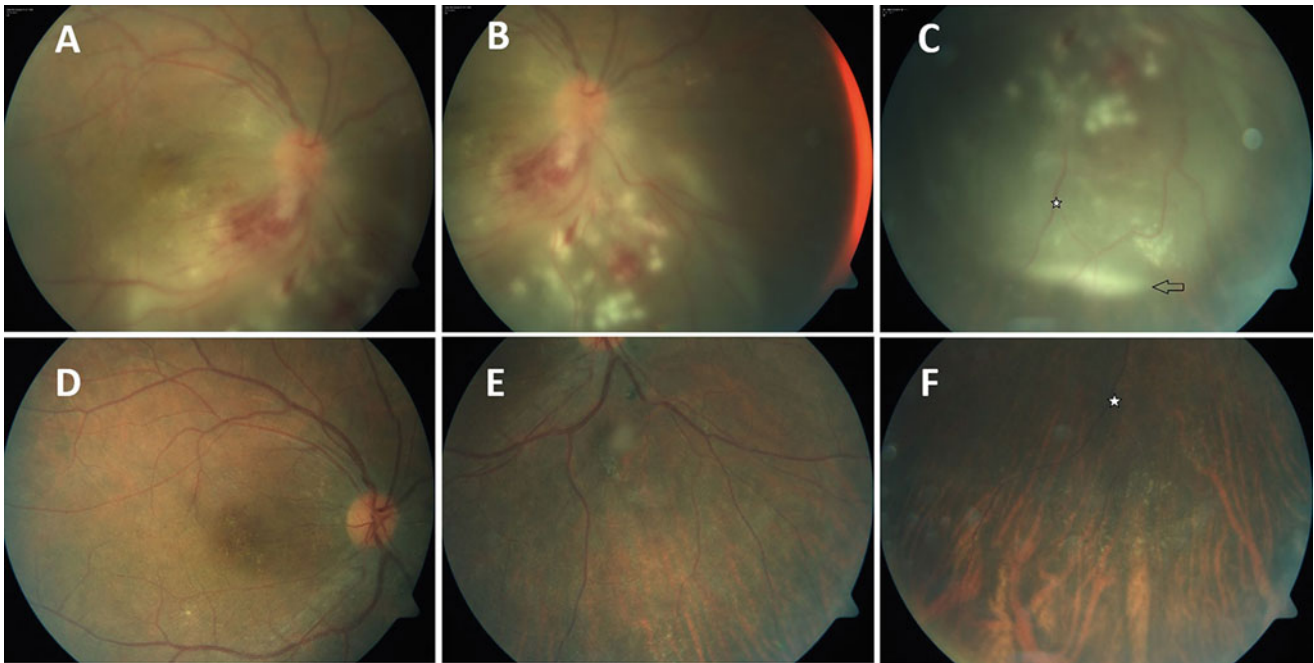




**Fig. 12** OCT section through the previously infiltrated retina shows inner retinal thinning that appears like an indentation (*arrow*). Note the slit-like retinal nerve fiber layer defect (*star*) extending from the superior temporal margin of the optic disc in the SLO image

**Fig. 13** Color fundus photograph shows optic disc hyperemia and new retinal infiltrates and retinal hemorrhages at the macula and between the superior temporal retinal arteriole and vein. The sequel of the previous episode, slit-like retinal nerve fiber layer defect, is evident in this photograph as well





**Fig. 14** Color fundus photographs of the right eye of a patient with Behçet's disease show inflamed optic disc, retinal hemorrhages, infiltrates, and edema (**a** and **b**) and an area of shallow retinal detachment with a layered collection of exudative material, "subretinal hypopyon" (arrow), at the inferior border in the inferior nasal retina (**c**). Two months later there is

resolution of retinal edema, infiltrates, hemorrhages, and subretinal hypopyon without any scar formation (**d**, **e**, **f**). The optic disc is hyperemic, and there are some pigmentary changes and faint white precipitates in the retina that had been previously infiltrated. Note also attenuation of retinal vessels (**f**). The *stars* mark corresponding spots in **c** and **f**

## Suggested Reading

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