Eye as the First Clue: Behçet's Disease Unveiled by Retinal Vasculitis and Vein Occlusion

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Abstract

Summary: Behçet's disease is a multisystem vasculitis of unknown etiology that is chronic and recurrent. One of the most severe and vision-threatening implications is ocular inflammation. We present a case of severe ocular Behçet's disease with occlusive retinal vasculitis in a young male. A 20-year-old boy had gradually deteriorating vision in both eyes for three months before experiencing a sudden loss of vision in the left eye for two weeks. Ocular examination showed bilateral anterior uveitis with vitritis and perivasculitis. Branch retinal vein occlusion (BRVO) with macular edema and macular pseudohole was seen in the left eye, which was confirmed by fundus fluorescein angiography and optical coherence tomography. A positive pathergy test, as well as repeated oral and vaginal ulcers, confirmed the diagnosis of Behçet's syndrome with panuveitis and occlusive vasculitis. Adalimumab, azathioprine, and systemic corticosteroids were used to treat the patient; this led to a partial recovery of vision and a noticeable reduction in inflammation. Early detection of Behçet's uveitis and timely beginning of immunomodulatory therapy are essential to prevent irreversible retinal damage and subsequent visual loss.

Keywords: Behçet's Disease, Retinal Vasculitis, Branch Retinal Vein Occlusion, Macular Edema, Adalimumab, Uveitis.

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Introduction

Behçet's disease (BD) is a chronic, relapsing vasculitis affecting many organs with uncertain etiology. The disease involves a triad of recurrent oral aphthous and genital ulcers, skin lesions, and ocular inflammation.[1] It is most prevalent along the ancient Silk Road region, with greater rates in Turkey, the Middle East, and East Asia.[1] The condition primarily affects young adults, mainly boys, and can cause considerable morbidity due to vision loss when ocular involvement develops.[1,2]
Behçet's uveitis is usually bilateral, recurring, and non-granulomatous, with a relapsing-remitting history.[3] Ocular symptoms appear in up to 70-80% of patients and frequently affect the disease outcome.[4] The most frequent ocular manifestations are pan-uveitis with retinal vasculitis, which can cause vascular occlusions along with macular edema, which is cystoid in nature. Anterior uveitis in Behçet's disease is non-granulomatous with mobile hypopyon.[4,5] On fluorescein angiography, BD uveitis exhibits fern-pattern leakage, superficial hemorrhages, and occlusive periphlebitis, in contrast to sarcoid or tuberculosis-associated uveitis.[5,6]
The International Criteria for Behçet's Disease (ICBD) combines ocular signs with systemic features such as recurring oral mucosal and genital ulcers, erythema nodosum, papulopustular skin lesions, and a positive pathergy test, which serve as the basis for the predominantly clinical diagnosis.[1,7] For accurate diagnosis and treatment of non-granulomatous uveitis, other differentials need to be ruled out, such as sarcoidosis, reactive arthritis, systemic lupus erythematosus, inflammatory bowel disease, or herpes infections.[8]

Case Presentation

A 20-year-old man presented at OPD with a gradually progressive, painless blurring of vision in both eyes for three months, followed by an abrupt onset of loss of vision in the left eye. He stated that for the past four years, he had suffered from excruciating, recurrent genital and oral ulcers, each of which healed on its own but left scars. He had intermittent erythematous papulopustular skin lesions but no history of fever, joint pain, backache, cough, weight loss, or prior ocular injury.
On examination, best-corrected visual acuity (BCVA) was 6/12 in the right eye and finger counting at 1 meter in the left eye. The anterior chamber of both eyes showed 2+ cells with mild flare along with bilateral vitritis (2+), with more pronounced haze in the left eye. Fundus examination revealed temporal mild disc pallor, perivasculitis, scattered hemorrhages in all quadrants, ghost vessels inferonasally, and a macular pseudohole in the left eye.
Systemic evaluation revealed a history of recurrent oral and genital ulcers, as well as erythematous papulopustular skin lesions.

Investigations

Ocular Investigations

Optical coherence tomography (OCT) confirmed macular edema in the left eye. Fundus Fluorescein Angiography (FFA) showed fern-pattern leakage and areas of capillary non-perfusion consistent with occlusive vasculitis and BRVO.
Dermatographia may be seen in some Behçet's patients as a sign of skin hyperreactivity, but it is nonspecific. The pathergy test remains the relevant diagnostic skin test for Behçet's disease.

Systemic Investigations

Parameter	Findings
ESR	**62 mm/hr.** (elevated)
CBC, LFTs, RFTs	Within normal limits
Serum ACE	13 U/L (normal 9–67 U/L)
Serum Calcium	9.9 mg/dL
Pathergy Test	**Positive** (pustule formation at 48 hours)
HLA-B51	**Positive**
Chest X-ray/HRCT	No hilar lymphadenopathy or pulmonary lesions
ANA, ANCA, Infectious panel (TB, syphilis, HSV)	Negative

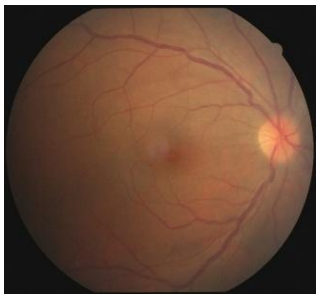

Figure 1: Fundus Photograph showing hazy fundal view in the Right eye and temporal disc pallor with occlusive perivasculitis, and a macular pseudohole in the left eye

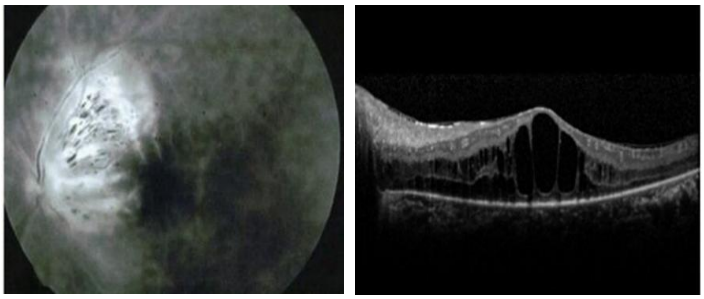

Figure 2: FFA image of the Late phase showing fern pattern vasculitis in the Left eye and OCT of the Left eye showing macular edema

ICBD Classification Criteria Fulfillment

Diagnosis was made clinically using the International Criteria for Behçet's Disease (ICBD).

According to the International Criteria for Behçet's Disease (ICBD), the patient met the diagnostic threshold:

- Recurrent oral ulcers history (2 points)
- Genital ulcers history (2 points)
- Ocular lesions (uveitis + retinal vasculitis) (2 points)
- Positive pathergy test (1 point)

Figure 3: Dermatographia

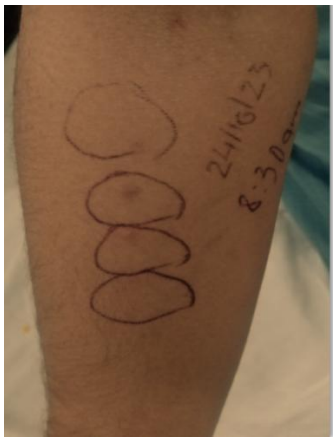

Figure 4: Positive Pathergy test

The total score of **7 points** exceeds the ≥4 requirement, confirming the diagnosis of Behçet's disease.

The uniqueness of this case lies in the unusually early and severe posterior segment involvement, including BRVO and macular pseudohole, as the first major presenting ocular feature.

These results excluded other granulomatous and autoimmune diseases, including sarcoidosis, tuberculosis, systemic lupus erythematosus (SLE), and inflammatory bowel disease (IBD).

Differential Diagnosis

1. Inflammatory Bowel Disease (IBD)

IBD can present with oral ulcers and uveitis; however, this patient had no gastrointestinal symptoms or colonoscopic evidence of IBD. The ocular pattern—occlusive retinal periphlebitis with BRVO and macular edema—is more typical of Behçet's, as IBD rarely causes occlusive posterior vasculitis.

2. Systemic Lupus Erythematosus (SLE)

SLE may cause retinal vasculitis and oral ulcers, but this patient had no systemic features (photosensitivity, rash, serositis, renal disease) and negative ANA. The presence of genital ulcers and a positive pathergy test further favored Behçet's over lupus.

3. Seronegative / Reactive Arthritis
These can present with mucocutaneous lesions and uveitis, but posterior occlusive vasculitis and BRVO are rare. Absence of arthritis, prior infection, and the presence of recurrent oral/genital ulcers with positive pathergy ruled out reactive arthritis.
4. Herpetic Infections (HSV/VZV)
Herpetic retinitis is usually unilateral, necrotizing, and rapidly progressive. The bilateral, occlusive periphlebitis without necrosis, and absence of corneal or serologic evidence excluded viral etiology.
5. Sarcoidosis
Sarcoidosis causes granulomatous uveitis with hilar lymphadenopathy and elevated ACE. This patient had non-granulomatous uveitis, normal imaging, and normal ACE, making sarcoidosis unlikely.
6. Other Systemic Vasculitides (e.g., Granulomatosis with Polyangiitis, Polyarteritis Nodosa)
These typically cause systemic involvement (renal, ENT, or neurologic) with positive serology such as ANCA. The absence of multisystem disease and mucocutaneous ulceration pointed instead toward Behçet's.
7. Relapsing Polychondritis
Characterized by auricular and nasal cartilage inflammation with audio vestibular symptoms, which were not present in this case.
8. Multiple Sclerosis (MS)
MS can present with intermediate uveitis but lacks oral/genital ulcers, pathergy positivity, or occlusive retinal vasculitis. Normal neuroimaging further excluded MS.

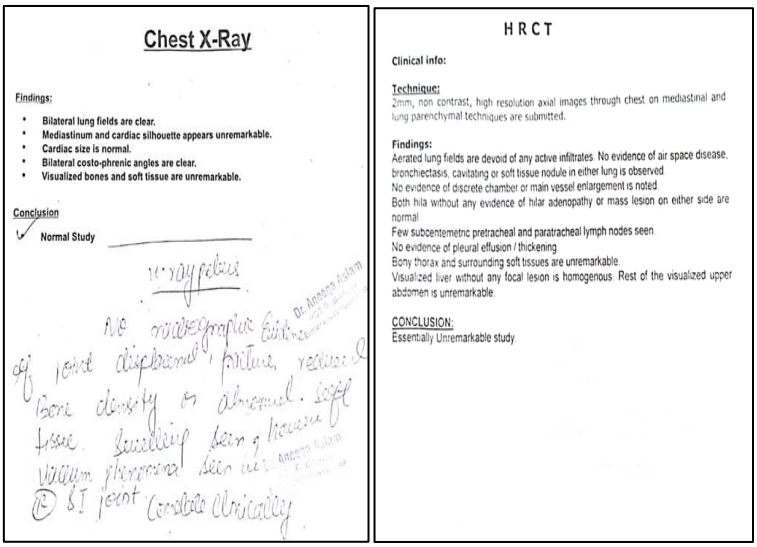

Figure 5: Normal chest X-ray and HRCT

Diagnosis
Based on clinical findings and systemic manifestations, a diagnosis of Behçet's disease with severe ocular involvement (Pan-uveitis with occlusive vasculitis) was made.
Treatment
The patient was started on oral prednisolone 1 mg/kg/day for 3 weeks, followed by gradual tapering. Azathioprine 100 mg twice daily was initiated as a steroid-sparing agent.[4,9] Owing to severe posterior segment inflammation, adalimumab was added (loading dose 80 mg subcutaneously, followed by 40 mg every other week).[1,10] Supportive therapy included omeprazole, folic acid, and calcium with vitamin D3 supplementation.
Outcome And Follow-Up
At one month, ocular inflammation had markedly subsided with clearing of vitreous haze. At three months, OCT demonstrated resolution of macular edema. The final BCVA was 6/6 in the right eye and 6/18 in the left eye. The patient remains under close follow-up on maintenance immunomodulatory therapy with Adalimumab 40 mg administered subcutaneously every two weeks, planned for 18–24 months to maintain remission and prevent ocular relapses.[9,10]

Discussion

Behçet's disease is a systemic vasculitis that affects arteries and veins of all calibers, with ocular involvement being the most serious and vision-threatening component.[1,2] Ocular Behçet's typically presents as bilateral, recurrent, non-granulomatous uveitis, most often involving the posterior segment.[3,4] Retinal vasculitis, particularly occlusive periphlebitis, is the hallmark feature, observed in up to 85% of cases.[6] Recurrent inflammatory episodes can cause retinal ischemia, macular edema, and optic atrophy, and the disease has a relapsing-remitting course.[1]
Our patient demonstrated the characteristic ocular features of vitritis, occlusive retinal vasculitis with perivenular sheathing, along with recurrent oral and genital ulcers and a positive pathergy test. The presence of branch retinal vein occlusion (BRVO) and a macular pseudohole indicated severe vascular inflammation and ischemic damage. A diagnostic gap exists because early ocular Behçet's disease can mimic several inflammatory and infectious uveitic conditions. Retinal periphlebitis and BRVO may be misattributed to other vasculitides, delaying immunomodulatory treatment. This case reinforces the need to recognize ocular clues that point toward Behçet's before systemic manifestations become prominent.[3-6]

Differential diagnoses include infectious and non-infectious uveitic entities such as sarcoidosis, SLE, systemic lupus erythematosus, multiple sclerosis, and inflammatory bowel disease.[8] However, these were excluded based on clinical presentation and relevant investigations. Behçet's disease remains a clinical diagnosis supported by systemic manifestations and exclusion of mimicking conditions. [1,7]

Management of Behçet's uveitis depends on disease severity. Acute attacks require prompt high-dose corticosteroids, either oral or intravenous methylprednisolone (1 g/day for 3 days in severe inflammation), to control acute inflammation.[9,10] To prevent relapses and minimize corticosteroid dependency, long-term immunosuppressive agents such as azathioprine, cyclosporine, and methotrexate are recommended.[2,10] Biologic medicines, especially anti-tumor necrosis factor (TNF) treatments like infliximab and adalimumab, have shown notable effectiveness in managing severe or resistant posterior segment illness. These agents have demonstrated efficacy in reducing inflammation, clearing up macular edema, and lowering the likelihood of relapses.[4,9]

Up to 25% of patients with ocular Behçet's may suffer from serious sight loss despite vigorous therapy, particularly young boys with early-onset posterior illness.[3,5,6] Immunomodulatory treatment must be started as soon as possible to avoid irreparable vascular blockage and optic nerve injury. Long-term disease activity tracking and treatment response, along with side effects associated with therapy, are crucial. When prompt and appropriate therapy is started, about 60% of patients experience remission after the first several years.

Unlike typical Behçet's disease, which usually begins with recurrent oral/genital ulcers followed by anterior uveitis, this case is noteworthy because Behçet's disease rarely presents initially with severe occlusive vasculitis and branch retinal vein occlusion (BRVO) in a young adult. The presence of a macular pseudohole further reflects significant ischemic damage at first presentation, a combination infrequently reported in the literature.[3,10] Early detection of this aggressive ocular phenotype is clinically important because it necessitates rapid escalation to biologic therapy. Reporting this case is significant because it illustrates the importance of considering Behçet's disease in young patients presenting with sudden retinal vein occlusion and occlusive vasculitis. Early recognition allows timely initiation of immunosuppressive and biologic therapy, which is critical for preventing irreversible visual loss.

Young individuals who present with recurrent oral/genital ulcers and ocular inflammation should be suspected of having Behçet's illness. Occlusive retinal vasculitis, macular edema, and recurrent uveitis are the hallmarks of Ocular Behçet's, a unique and potentially blinding condition. To salvage vision, systemic corticosteroids and immunomodulatory medication must be started as soon as possible. In cases where these treatments are ineffective, biologics may be used. To track disease activity and side effects from treatment, routine ocular and systemic follow-up is required.

Conclusion

Behçet's uveitis primarily affects the posterior segment of the eye and is bilateral, recurrent, and non-granulomatous. Retinal vasculitis and vein occlusion are two common disorders that can result in severe vision loss. Biologic treatment and early immunosuppression are essential for maintaining vision. Before establishing BD, always rule out mimics, including lupus, sarcoidosis, and tuberculosis. The best results are guaranteed by multidisciplinary management, which includes dermatology, rheumatology, and ophthalmology. Regular OCT and FFA monitoring helps identify recurrences early.

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