# BEHCET DISEASE

Eye Learn

All about the Eye

Dr. Krati Gupta

Dr. Saurabh Deshmukh

www.eyelearn.in

# BEHCET'S DISEASE

1. Write the ocular manifestations, systemic associations and management of Behçet's disease including recent drugs available for treatment. 3+1+6 D2013
2. A 30 year old male presented with genital lesions and complained of sudden diminution of vision is one eye followed 6 weeks later by similar diminution in the other eye. What are the possible diagnoses? Give broad guidelines in the management of each situation. 2+8 D2015

**Introduction**

- Behçet disease (BD) is a chronic, relapsing, occlusive systemic vasculitis of unknown etiology that is characterized, in part, by a uveitis that can affect both the anterior and the posterior segments of the eye, often simultaneously.

**Epidemiology**

- The typical age of onset is between 25 and 35 years, but BD can also develop as early as age 10–15 years.
- Although there have been some familial cases of BD, most are sporadic.

**Diagnostic criteria**

- The diagnostic system for BD was suggested by researchers in Japan,
- Another diagnostic system was suggested by the International Study Group for Behçet's Disease
- BD is a multisystem disease, it can have its predominant effect on a single system
- Special clinical types of BD occur— namely, neuro-BD, ocular BD, intestinal BD, and vascular BD

**Table 6-4 Diagnostic System for Behçet Disease (Japan)**

**Major criteria**
- Recurrent oral aphthous ulcers
- Skin lesions (erythema nodosum, acneiform pustules, folliculitis)
- Recurrent genital ulcers
- Ocular inflammatory disease

**Minor criteria**
- Arthritis
- Gastrointestinal ulceration
- Epididymitis
- Systemic vasculitis or associated complications
- Neuropsychiatric symptoms

**Types of Behçet disease**
- Complete (4 major criteria)
- Incomplete (3 major criteria or ocular involvement with 1 other major criterion)
- Suspect (2 major criteria with no ocular involvement)
- Possible (1 major criterion)

- The "complete" type of BD is more common in men
- The "incomplete" is equally frequent in men and women

**Table 6-5 Diagnostic System for Behçet Disease (International Study Group for Behçet's Disease)**

Recurrent oral aphthous ulcers (at least 3 or more times per year) plus 2 of the following criteria:
1. Recurrent genital ulcers
2. Ocular inflammation
3. Skin lesions
4. Positive cutaneous pathergy test

**Pathogenesis**

1. The immunopathogenesis of BD remains unknown.
2. Many environmental factors have been suggested as potential causes, but none has been proved.
3. No infectious agent or microorganism has been reproducibly isolated from the lesions of patients with BD.
4. The disorder is clinically and experimentally unlike other autoimmune diseases.
5. Specific HLA associations have been found in certain systemic forms of BD: HLA-B12 with mucocutaneous lesions and HLA-B51 with ocular lesions.
6. These associations are not reproducible in all populations and are of little diagnostic value.

**Histology**

1. The lesions of BD resemble those of delayed-type hypersensitivity reactions early on;
2. Late lesions resemble those of immune-complex–type reactions.

**Non-ocular systemic manifestations**

| | |
|---|---|
| **1. Oral aphthous ulcer** | 1. Are mc finding in BD. These lesions are recurrent mucosal ulcers that produce significant discomfort and pain. They can occur on the lips, gums, palate, tongue, uvula, and posterior pharynx.<br>2. They are discrete, round or oval, white ulcerations with red rims vary in size from 2 to 15 mm.<br>3. They recur every 5–10 days or every month, last 7–10 days, and heal with little scarring unless large. |
| **2. Skin lesions** | 1. Can include painful or recurrent **erythema nodosum** over extensor surfaces such as the tibia also on the face, neck, and buttocks. They disappear with minimal scarring.<br>2. **Acne vulgaris or folliculitis-like skin** lesions may frequently appear on the upper thorax and face.<br>3. 40% of patients with BD exhibit cutaneous **pathergy**, which is characterized by the development of a sterile pustule at the site of a venipuncture or an injection but is not pathognomonic of BD. |
| **3. Genital ulcers** | 1. Appear grossly similar to **oral aphthous ulcers**. In male patients, they can occur on the scrotum or penis.<br>2. In female patients, they can appear on the vulva and the vaginal mucosa.<br>3. These lesions are associated with variable amounts of pain. Genital lesions can be deep and leave scars that may be apparent on examination even if patients have no acute symptoms. |
| **4. Systemic vasculitis** | 1. May also occur in up to 25% of patients with BD, and any size artery or vein in the body may be affected.<br>2. 4 different vascular complications can develop from the systemic vasculitis of BD: arterial occlusion, aneurysm, venous occlusion, and varices. |
| **5. Cardiac involvement** | From BD can include granulomatous **endocarditis, myocarditis, endomyocardial fibrosis, coronary arteritis, and pericarditis**; cardiac effects can occur in up to 17% of patients. |
| **6. GI lesions** | Can include multiple ulcers involving the esophagus, stomach, and intestines. |
| **7. Pulmonary** | Involvement is mainly pulmonary arteritis with aneurysmal dilatation of the pulmonary artery. |
| **8. Arthritis** | 50% of patients with BD develop; in 50% of these, the knee is most affected. |
| **9. Neurologic involvement** | 1. Neurologic involvement is the most serious of all manifestations of BD & occur in 10% of patients.<br>2. CNS involvement affects mainly areas of motor control.<br>3. Vasculitis in the CNS can result in headaches<br>4. **S**trokes, palsies, and a confusional state may develop in 25% of patients.<br>5. Mortality had been reported to be 10% in patients with neuro-BD, but it has lowered due to IMT.<br>6. More men than women appear to develop neuro-BD. |

**Ocular manifestations**

- Ocular manifestations affect up to 70% of patients with BD.
- Symptoms- redness, pain, photophobia, and blurred vision
- They carry serious implications as they are recurrent and relapsing, resulting in permanent, often irreversible, ocular damage.
- Severe vision loss can occur in up to 25% of patients with BD.
- Ocular disease appears to be more severe in men, and more men are affected; up to 80% of cases are bilateral.
- Ocular involvement as an initial presenting problem is relatively uncommon, occurring in about 10% of patients.
- **The intraocular inflammation is characterized by a nongranulomatous, necrotizing, obliterative vasculitis that can affect any or all portions of the uveal tract.**

**Anterior segment**

1. **Anterior uveitis** may be the only ocular manifestation of BD; it presents with a transient **hypopyon** in up to 25% of cases.
2. It can shift with the patient's head position or disperse with head shaking, and it may not be visible unless viewed by gonioscopy.
3. Anterior uveitis may be very severe, it can spontaneously resolve even without treatment; the nature of ocular BD is one of explosive onset over the course of just a few hours.
4. With relapses, **posterior synechiae, iris bombé, and angle-closure glaucoma** may all develop.
5. Other less-common anterior segment findings of BD include **cataract, episcleritis, scleritis, conjunctival ulcers, and corneal immune ring opacities.**

**Posterior segment**

1. The posterior segment manifestations of ocular BD are often profoundly sight threatening.
2. Retinal finding is that of an **obliterative, necrotizing retinal vasculitis that affects both the arteries and the veins**.
3. This form is the most common type of uveitis found in children and adults with BD.
4. Posterior manifestations can include **BRVO, isolated branch artery occlusions**, **combined BRVO and branch retinal artery occlusions**, and **vascular sheathing** with variable amounts of **vitritis**, plus associated **CME**.
5. Retinal ischemia can lead to the development of **retinal neovascularization** and **NVG, NVI**
6. After repeated episodes of retinal vasculitis and vascular occlusions, **retinal vessels may become white and sclerotic**.
7. Active areas of retinal vasculitis may be accompanied by multifocal areas of chalky white retinitis.
8. The ischemic nature of the vasculitis and accompanying retinitis may produce a funduscopic appearance that may be confused with acute retinal necrosis syndrome or other necrotizing herpetic entities

**Neuro-ophthalmic involvement**

1. The optic nerve is affected in 25% of patients with BD.
2. Optic papillitis can occur, but progressive optic atrophy may occur as a result of the vasculitis affecting the arterioles that supply blood to the optic nerve.
3. Neuro-ophthalmic involvement can include cranial nerve palsies, central scotomata caused by papillitis, visual field defects, and papilledema resulting from thrombosis of the superior sagittal sinus or other venous sinuses.

**Diagnosis**

1. Diagnosis of BD is based on clinical findings and the diagnostic criteria
2. **Laboratory tests**—for example, HLA typing, cutaneous pathergy testing, and testing for nonspecific serologic markers of inflammation such as ESR and levels of C-reactive protein—are of little value in confirming the diagnosis.
3. **Fluorescein angiography**
   - Demonstrates marked dilatation and occlusion of retinal capillaries with perivascular staining, evidence of retinal ischemia, leakage of fluorescein into the macula with the development of CME, and retinal neovascularization that may leak.
   - Subtle vascular leakage may be present on FA before there is clinical evidence of disease activity, and adjusting therapy in response to this leakage may prevent the development of inflammatory damage.
4. **OCT imaging** can show structural alterations caused by the vasculitis in the form of macular edema and disruption of the retinal architecture.
5. **Radiologic imaging**, including chest x-ray, chest CT, and brain MRI with contrast enhancement, may be helpful, as indicated by clinical presentation.

**Differential diagnosis**

1. HLA-B27–associated anterior uveitis, reactive arthritis syndrome,
2. Sarcoidosis,
3. Systemic vasculitides including systemic lupus erythematosus, PAN, and GPA.
4. Necrotizing herpetic retinitis can also mimic occlusive BD retinal vasculitis.

**Treatment**

- The goal of treatment is not only to treat the explosive onset of acute disease with systemic corticosteroids but also to control chronic inflammation and prevent or decrease the number of relapses of ocular inflammation with IMT.

**A. Corticosteroids**

1. These drugs may be used to treat explosive-onset anterior segment and posterior segment inflammation, although most patients eventually become resistant to corticosteroid therapy.
2. Nevertheless, systemic corticosteroids (eg, 1.5 mg/kg/day of prednisone with a gradual taper) are extremely useful in controlling acute inflammation.
3. Periocular and intravitreal steroids may also be useful in selected patients.

**B. Immunomodulatory medications**

- Patients who present with sight-threatening posterior segment ocular BD require prompt initiation of systemic corticosteroids together with IMT, which may include azathioprine, infliximab, cyclosporine, tacrolimus, mycophenolate mofetil, chlorambucil, or cyclophosphamide.
- A European League Against Rheumatism panel has recommended using azathioprine (with corticosteroids) as first-line IMT for ocular BD and cyclosporine or infliximab as second-line treatment.
- A recent American expert panel recommended anti-TNF therapy with infliximab (good quality evidence) or adalimumab (moderate-quality evidence) as first- or second-line corticosteroid sparing therapy.
- Infliximab was recommended as first- or second-line treatment for acute exacerbations of preexisting Behçet disease.

| | |
|---|---|
| **1. Colchicine** | It is used for treatment of mucocutaneous disease; it is ineffective for treating ocular BD. |
| **2. Azathioprine** | In prospective clinical trials, it has been found to be useful in preserving visual acuity in patients with established ocular BD. It can also be effective in controlling oral and genital ulcers and arthritis. |
| **3. Infliximab** | 1. Open-label clinical trials have confirmed the efficacy of infliximab in controlling inflammation, and many uveitis specialists consider infliximab the treatment of choice for Behçet retinal vasculitis.<br>2. Infliximab can result in rapid remission of disease activity and provide long-term disease control.<br>3. Infliximab at doses of 10 mg/kg or more, carries a greater risk of long-term therapeutic complications such as disseminated TB or possibly malignancy. |
| **4. Cyclosporine** | 1. It has been used with limited success in the management of ocular BD, but it is not as effective as other cytotoxic drugs and may carry risks of nephrotoxicity.<br>2. There may also be an increased risk of neuro-BD in patients treated with cyclosporine. |
| **5. Tacrolimus** | It is less toxic & may be used as a substitute for cyclosporine; it has been used successfully in Japan for BD. |
| **6. Mycophenolate mofetil** | It has also been successful in treating ocular BD in small case series. |
| **7. Interferon Alfa-2a** | Recent reports in the European literature emphasize that is efficacious and well tolerated; it is highly effective in Behçet uveitis |
| **8. Alkylating agents** | 1. **Chlorambucil** has been found to be effective in the treatment of BD, even at relatively low doses.<br>2. **Cyclophosphamide** is an alternative to chlorambucil and can be used orally or as pulsed intravenous therapy. Both chlorambucil and cyclophosphamide have been shown to be more effective than cyclosporine in the management of posterior segment ocular BD but carry a greater risk of systemic complications.<br>3. Effective therapeutic reduction of white blood cell counts and proper hematologic monitoring are essential and can be quite complex with these alkylating agents.<br>4. The availability of biologic drugs has led some experts to reserve the use of alkylating agents for patients with refractory disease. |



**Prognosis**

- Prognosis for vision is guarded in patients with BD.
- Nearly 25% of patients worldwide with chronic ocular BD have visual acuity less than 20/200, most commonly caused by macular edema, occlusive retinal vasculitis, optic atrophy, and glaucoma.
- Adult men tend to have poorer vision outcomes.
- The presence of posterior synechiae, persistent inflammation, elevated IOP, and hypotony are all statistically significant predictive factors for vision loss.
- **Complications** such as macular edema, complex cataract, secondary and neovascular glaucoma, retinal and optic disc neovascularization, retinal detachment, and vitreous hemorrhage may require complex medical and surgical intervention