Behçet’s syndrome

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Introduction

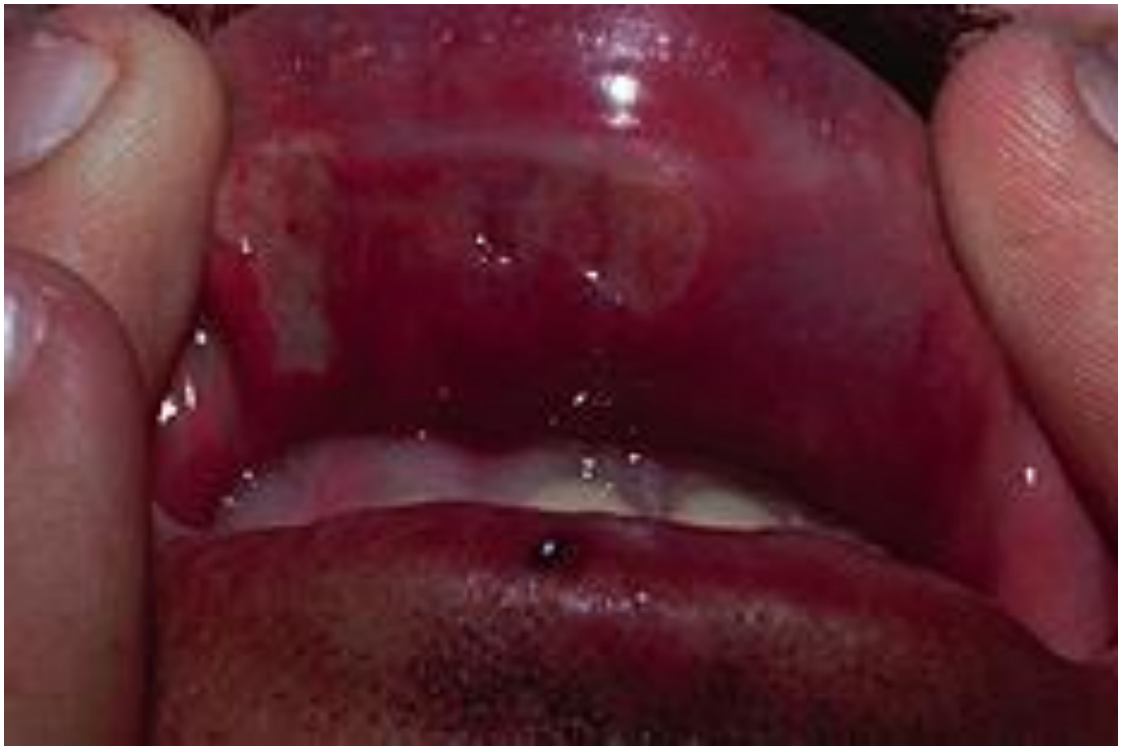
- Behçet's syndrome is characterized by recurrent oral aphthae and any of several systemic manifestations including genital aphthae, ocular disease, skin lesions, gastrointestinal involvement, neurologic disease, vascular disease, or arthritis.
- Most clinical manifestations of Behçet's syndrome are believed to be due to vasculitis
- Among the systemic vasculitides, Behçet's syndrome is remarkable for its ability to involve blood vessels of all sizes (small, medium, and large) on both the arterial and venous sides of the circulation

Epidemiology

- Young adults 20 to 40 years of age
- The disease appears to be more severe in young, male, and Middle- or Far-Eastern patients
- Most cases of Behçet's are sporadic, although families clustering has been reported
- More common (and often more severe) along the ancient silk road, which extends from eastern Asia to the Mediterranean

Clinical finding- Oral ulceration

- **Oral ulcerations** — Most, but not all, patients initially manifest recurrent oral aphthous ulcerations.
- The ulcers are painful and, in severe cases, may limit eating. They are rounded and range in size from a few millimeters to 2 cm
- Major ulcers may scar
- Outer portions of the lips are not involved
- Healing of oral ulcers is typically spontaneous within one to three weeks

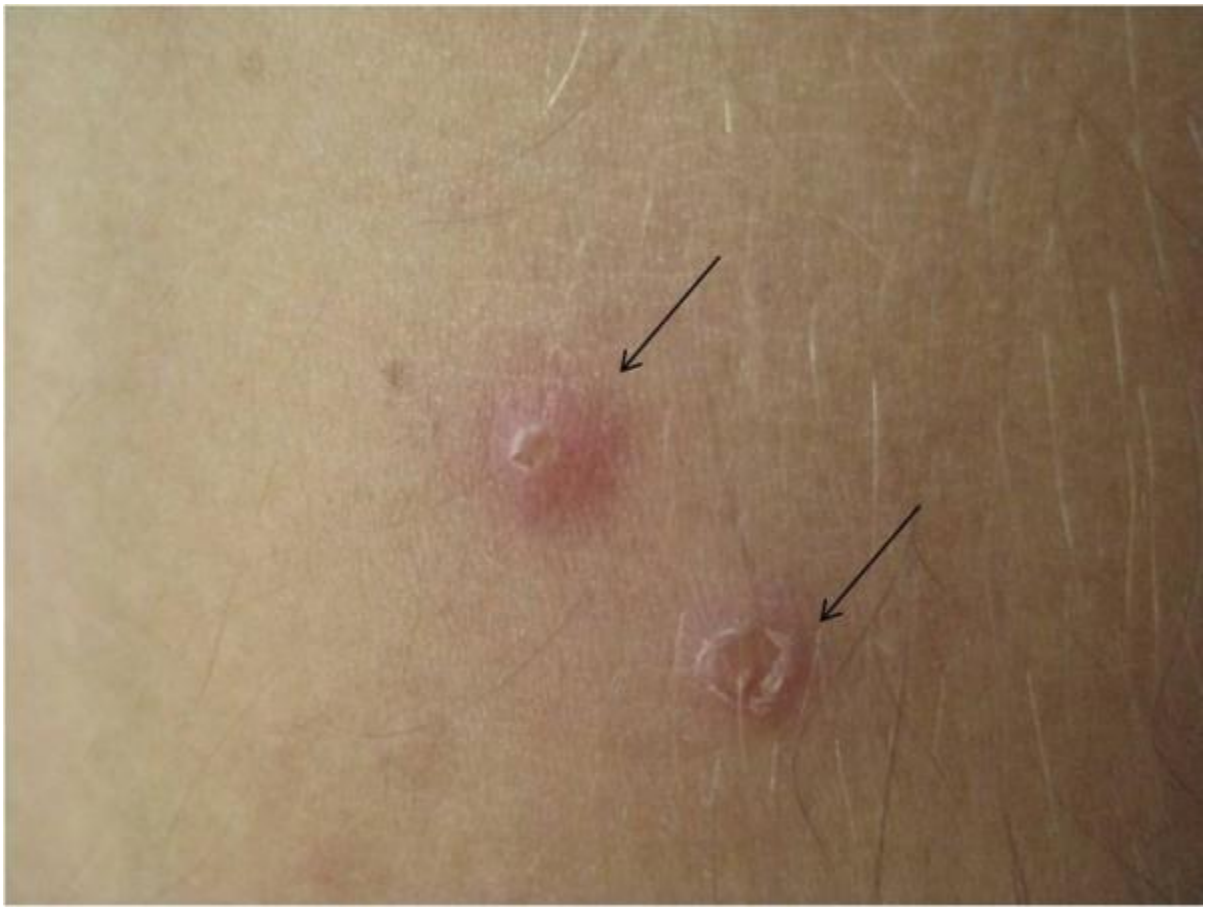


Urogenital ulcers

- Genital ulceration, the most specific lesion for Behçet's syndrome, occurs in 75 percent or more of patients with Behçet's syndrome.
- The ulcers are similar in appearance to the oral ulcers
- Painful
- Genital ulcers are most commonly found on the scrotum in men and the vulva in women
- Recurrence is typically less frequent than with oral ulcerations. Scar formation is frequent for genital lesions.
- Epididymitis, salpingitis, varicocele may also occur

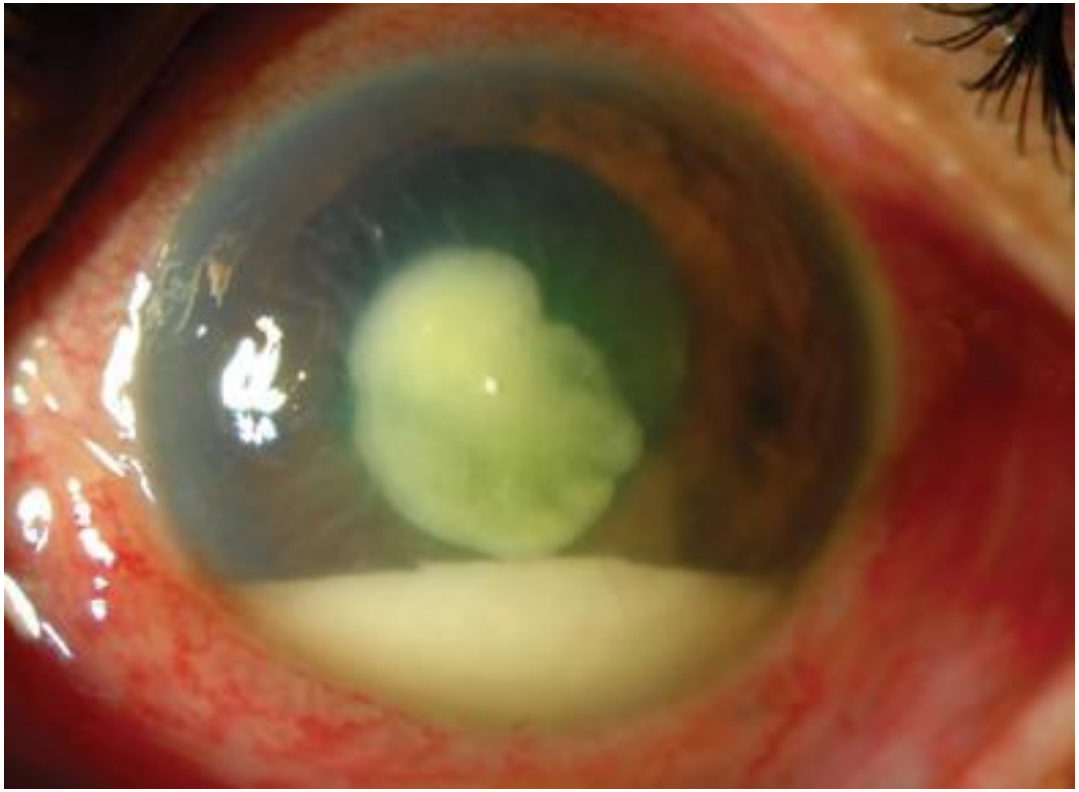
Cutaneous lesions

- **Cutaneous lesions** — 75% of patients:
  - acneiform lesions, papulo-vesiculo-pustular eruptions, pseudofolliculitis, nodules, erythema nodosum (septal panniculitis), superficial thrombophlebitis, pyoderma gangrenosum-type lesions, erythema multiforme-like lesions, and palpable purpura
  - Pathergy
  - Nailfold capillary abnormalities (enlarged capillaries)



Ocular disease

- 50% of patients with Behçet's syndrome
- Progresses to blindness if not treated
- Male patients are more likely to get eye disease, with about 75 to 80 percent developing involvement, and also have worse visual outcomes, even with treatment
- Uveitis is often the dominant feature - bilateral and episodic, often involves the entire uveal tract (pan uveitis), and may not resolve completely between episodes
- Hypopyon is a severe anterior uveitis with purulent material in the anterior chamber.
- Posterior uveitis, retinal vasculitis, vascular occlusion, and optic neuritis require systemic immunosuppressive treatment and may irreversibly impair vision and progress to blindness if untreated



Neurologic involvement

- Neurologic disease occurs in less than 10 percent of patients
- Men > women
- Neurologic disease is classified as parenchymal or non-parenchymal:
  - **Parenchymal disease** - encephalopathy, hemiparesis, hemisensory loss, seizures, dysphagia, psychosis and cognitive dysfunction
  - Non-parenchymal - vascular thrombosis, meningitis, pseudotumor cerbri
- Progressive personality changes, psychiatric disorders, and dementia may develop
- Peripheral neuropathy is not common

Arterial involvement

- Vascular involvement is one of the major causes of morbidity and mortality in Behçet's syndrome
- In particular, pulmonary artery aneurysm carries a high mortality of approximately 25%
- Pulmonary artery aneurysms involving the large proximal branches of the pulmonary arteries are the most common pulmonary vascular lesion in Behçet's and are uncommonly seen in diseases other than Behçet's
- Hemoptysis is the most common presenting symptom; cough, dyspnea, fever, and pleuritic pain are other presenting symptoms

Venous disease

- Venous disease resulting in venous thrombosis is more common than arterial involvement
- Often an early feature of Behçet's
- DVT, superficial vein thrombosis, SVC, IVC occlusion, Budd-Chiari syndrome, dural sinus thrombosis
- Recurrent thrombosis of the lower extremities may lead to a post-thrombophlebitic syndrome

Vascular disease in 728 patients with Behçet's syndrome

	Number of patients
Venous disease	
Deep venous thrombosis	221
Subcutaneous thrombophlebitis	205
SVC occlusion	122
IVC occlusion	93
Cerebral sinus thrombosis	30
Budd-Chiari syndrome	17
Other venous occlusion*	24
Arterial disease	
Pulmonary artery occlusion or aneurysm	36
Aortic aneurysm	17
Extremity arterial occlusion or aneurysm	45
Other arterial occlusion or aneurysm¶	42
Right ventricular thrombus	2

SVC: superior vena cava; IVC: inferior vena cava.
* Other veins included subclavian, iliac, portal, renal, innominate, brachiocephalic.
¶ Other arteries included iliac, subclavian, renal, carotid, cerebral, coronary, innominate, mesenteric, aorta, basilar, splenic.

Review of 728 cases from Koc, Y, Gullu, I, Akpek, G, et al. J Rheumatol 1992; 19:402.

Arthritis

- Nonerosive, asymmetric, usually nondeforming arthritis occurs in about one-half of patients, particularly during exacerbations
- The arthritis most commonly affects the medium and large joints - including the knee, ankle, and wrist

Diagnostic criteria for Behçet's syndrome

Criterion	Required features
Recurrent oral ulceration	Aphthous (idiopathic) ulceration, observed by physician or patient, with at least three episodes in any 12-month period
Plus any two of the following:	
Recurrent genital ulceration	Aphthous ulceration or scarring, observed by physician or patient
Eye lesions	Anterior or posterior uveitis cells in vitreous in slit-lamp examination; or retinal vasculitis documented by ophthalmologist
Skin lesions	Erythema nodosum-like lesions observed by physician or patient; papulopustular skin lesions or pseudofolliculitis with characteristic acnelform nodules observed by physician
Pathergy test	Interpreted at 24 to 48 hours by physician

Treatment

- **Minor disease manifestations** — Minor disease manifestations are those that interfere substantially with patients' quality of life but do not threaten vital organ function:
  - For arthritis, oral aphthae, genital ulcers – colchicine
  - glucocorticoids or other immunosuppressive agents early in the course of erythema nodosum and pyoderma gangrenosum

Treatment

- **Major disease manifestations** — Ocular and neurological manifestations, complications of large-vessel arteritis and venous thrombotic disease
- Anterior uveitis must be treated with topical corticosteroids with a mydriatic agent to prevent synechiae formation between the iris and lens
- Posterior uveitis poses a major threat to vision - high-dose glucocorticoids and a second immunosuppressive agent:
  - Azathioprine, TNF-alpha inhibitors, cyclosporine, cyclophosphamide, and methotrexate
- Neurological manifestations, encephalitis, medium-vessel vasculitis, and focal parenchymal lesions of significant size should be treated in the same manner as posterior uveitis
- Behçet's syndrome typically has a waxing and waning course