Behçet’s syndrome (BS) is a multisystem disease of unknown etiology, characterized by chronic relapsing cardinal symptoms of orogenital ulcers, uveitis, and different skin lesions. Its major pathologic feature is vasculitis. Neuro-Behçet’s syndrome (NBS) is defined as a constellation of neurologic manifestations with characteristic neuropathologic findings, usually confirmed by ancillary investigations, in patients who meet the diagnostic criteria for BS. Neurologic manifestations of the syndrome are more common in male patients and have been reported to occur in anywhere from 5% to 50% of BS patients, depending on their geographical region. NBS primarily affects the central nervous system and includes parenchymal and nonparenchymal involvement. Peripheral neuropathy and myopathy are rare. Immunosuppression is widely used for treatment.

Introduction
Behçet’s syndrome (BS) is a systemic inflammatory condition involving blood vessels of all sizes and characterized by recurrent mucocutaneous lesions associated with frequent ocular involvement. The cause of BS is unknown, and its major pathologic feature is vasculitis [1•]. Neurologic involvement in BS is a less frequent feature, but when it does occur, it produces severe disability and increased mortality.

The syndrome is named after Turkish dermatologist Hulusi Behçet, who, in 1937, reported three cases of oral and genital ulceration and hypopyon uveitis [2]. Although BS is usually accepted as a disease, its wide spectrum of complex manifestations makes it difficult to explain the condition within a single entity [1•,3,4•]. In a masked-prospective study, although acneiform skin lesions were found to be increased in Behçet’s patients with arthritis, there was no similar correlation between eye involvement and arthritis [5], making it highly possible that BS includes more than one disease condition.

BS usually affects people in their early 20s [6]. The disease is more prevalent in Far East, Middle East, and Mediterranean countries, and its global distribution suggests a geographic pattern coincident with the ancient “Silk Road” [7]. Its prevalence is sporadic in indigenous West African or Afro-Caribbean populations [8]. Though some series report BS to be more common among men than women in Middle Eastern countries, well-designed epidemiologic studies show the syndrome equally affects both genders in this region [9]. However, in Japan and Korea, BS is somewhat more common among women [10]. In young men, BS is associated with a poorer prognosis [11]. The association with HLA-B51 shows regional variation [12•].

The hallmark of BS is the recurrence of painful oral ulcers resembling ordinary canker sores [6,7]. In men, genital ulcers are less frequent but more specific than oral ulcers, and they usually cause scars on the scrotum but are absent on the glans penis and urethra. In women, labia are the most common sites of involvement [4•,7]. Cutaneous manifestations of the disease include erythema nodosum-like lesions, pseudofolliculitis, folliculitis, acnelike lesions, superficial thrombophlebitis, cutaneous vasculitis, and papulopustular lesions [4•,6]. Acne in patients with BS has been reported to be closely associated with the nondeforming oligoarthritis that affects 50% of patients [5].

The pathergy reaction, skin hyperactivity induced by intradermal needle prick, is quite specific to BS. However, wound healing after biopsy-induced skin trauma is normal. The rate of the positive pathergy phenomenon test varies from region to region: 60% to 70% in Turkey or Japan, and lower as reported from northern Europe or the United States [7,13].

Eye involvement, a significant cause of morbidity, manifests as chronic, relapsing, bilateral, anterior and posterior uveitis. Anterior uveitis may present with hypopyon, can be seen in 20% of patients, and indicates poor prognosis. Posterior uveitis can be associated with retinal involvement [14].

Cardiovascular involvement includes superficial thrombophlebitis; deep-vein thrombosis; thrombosis of the major vessels, such as obstruction of the vena cava and occlusion of the suprahepatic veins (Budd-Chiari
Neurologic Involvement in BS

According to a review by Borhani Haghighi et al. [18••], the first case of neurologic involvement in BS was reported in 1941. The term neuro-Behçet's syndrome (NBS) was introduced in 1954, and neurologic complications were classified a few years later. NBS is defined as a constellation of neurologic manifestations with characteristic neuropathologic findings, usually confirmed by ancillary investigations, in patients who meet ISG diagnostic criteria.

The frequency of neurologic manifestations differs in the literature, from 5% to 50% [4•,6,19•,20,21••]. The wide variation can be explained by geographic and ethnic factors, varied definitions of the disease, and different inclusion and exclusion criteria in studies. Autopsy series have reported that 20% of patients with BS revealed pathologic signs of neurologic involvement [22]. NBS primarily affects male patients in whom the illness began at an early age [8•]. In general, systemic symptoms antedate neurologic manifestations. Although an isolated neurologic manifestation or a primary neurologic course is rare, in two Turkish studies of NBS, neurologic findings antedated the other more common manifestations of illness in 3% of patients [19••,21••]. The frequency of neurologic complications in pediatric patients with BS has been reported to be 20% [23].

In a large, well-designed study from Turkey, the demographic features of 164 NBS cases (146 with definite diagnoses and 18 with indefinite diagnoses) included male/female ratio 3.82, age at onset of BS 26.7 years, and age at onset of neurologic involvement 32 years. The most common presenting symptom was headache (61.6%), followed by motor symptoms (53.7%), cerebellar symptoms other than dysarthria (29.9%), brainstem symptoms other than dysarthria (29.3%), dysarthria (22.6%), behavioral symptoms (12.2%), sensory symptoms (11%), alteration of consciousness (7.3%), and cognitive symptoms (2.4%). After cerebral spinal fluid (CSF) and imaging diagnosis, neurologic involvement was categorized into a final diagnosis of venous sinus thrombosis (12.2%), NBS (75.6%), optic neuritis (0.6%), psycho-Behçet's syndrome (0.6%), and indefinite diagnosis (11%). None of the patients had both parenchymal disease and venous sinus thrombosis [24••].

Central Nervous System Manifestations

Parenchymal involvement

Parenchymal manifestations occur in 80% of patients with pyramidal, cerebellar, and sensory signs and symptoms; sphincter disturbances; and behavioral changes. This form has a more serious prognosis and is usually associated with brainstem involvement. Akman-Demir et al. [21••] reported that parenchymal neurologic onset began with an attack, which usually lasted a few days and had a rather subacute course in 102 of 162 (63%) cases. In 60 (37%) cases, the evolution of signs and symptoms was slow.

The most common findings of parenchymal involvement are pyramidal signs, which are usually bilateral. Other less common manifestations include hemiplegia/paresis; behavioral changes; sphincter disturbance and/or impotence; movement disorders, such as hemichorea, hemiballismus, and hemidystonia; hypersomnia and/or hyperphagia; and cranial nerve palsies [18••,20,21••,25,26]. Aseptic meningitis is commonly associated with different parenchymal central nervous system (CNS) manifestations of BS, but pure meningoencephalitis as a presentation of NBS is rare [27]. Paroxysmal attacks, seizures, psychiatric manifestations (eg, acute psychotic reaction, cerebellar syndrome), vestibular abnormalities similar to Meniere's disease, optic neuropathy/neuritis, hemianopia, paroxysmal dysarthria or aphasia, and tumoralike manifestations have also been reported [18••,20,21••,24••,25].

Nonparenchymal involvement

The predominant syndrome of nonparenchymal involvement is intracranial hypertension, which can occur with or without altered consciousness and can manifest as headache, papilledema, focal neurologic deficits, seizures, and sixth-nerve palsy [21••,28]. Despite being the most common symptom of this syndrome, headache in patients with BS is primarily nonspecific. A recent study concluded that the majority of the headaches of patients with BS did not indicate any neurologic involvement. Rather, they were usually due to a migraine or tension-type headache [28].

The main cause of intracranial hypertension is dural sinus thrombosis, which is most commonly seen in the superior sagittal sinus, followed by the transverse sinuses, deep cerebral veins, and cavernous sinuses. However, in some cases the etiology cannot be determined with investigations. Superior vena cava occlusion, aseptic meningitis with papilledema, external carotid artery aneurysm, and vertebral artery dissection have also been reported among causes [18••,21••,24••,29,30].