Behçet’s disease: diagnostic and prognostic aspects of neurological involvement

Introduction and background

Behçet’s disease (BD), originally described in 1937 by Behçet [7] as a distinct disease with orogenital ulceration and uveitis, is an idiopathic chronic relapsing multisystem vasculitis. Although previously various different criteria [8, 14, 26, 30] have been used for the diagnosis, the International Criteria for Classification of Behçet’s disease are now accepted [17, 18]. Attacks of BD become less frequent and less severe over time. Male patients whose disease began at a young age have the worst prognosis.
Despite being originally described as a dermatological disease, the major causes of morbidity and mortality result from ocular, vascular, or neurological involvement [9, 15, 36]. Acute panuveitis occurs in 42–74% of patients [17, 18]. Optic nerve involvement has also been rarely reported [20, 22]. Arterial and venous large vessel complications are seen in 25–30% of the cases while a possibly higher proportion may have small vessel involvement including postcapillary venules [12, 19, 23, 31, 34]. Venous vascular involvement is more common then arterial lesions in Turkish patients [23].

Neurological involvement most commonly is reported to manifest as brainstem or corticospinal tract syndromes (neuro-Behçet syndrome, NBS), increased intracranial pressure mostly related to venous sinus thrombosis (VST) or aseptic meningitis, isolated behavioral symptoms (psycho-Behçet syndrome, PBS), or isolated headache [1, 2, 11, 13, 33, 36–39, 43]. Rare presentations include intracerebral hemorrhage due to ruptured aneurysms, peripheral neuropathy, isolated optic neuritis, and a parkinsonian syndrome [6, 10, 20, 35]. Magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) in visualizing reversible inflammatory parenchymal lesions, which are generally located within the brainstem, occasionally with extension to the diencephalon, or within the periventricular and subcortical white matters [3–5, 16, 24, 27, 29, 39, 42]. A limited number of series describing neurological involvement in BD have been published [1, 2, 22, 37, 43]. The present study describes demographic, clinical, and diagnostic features of a hospital-based series of patients seen at a single center with BD and neurological involvement, to study the prognostic effects of associated variables and to describe differences among major clinical patterns of presentation.

Material and methods

Patient source and collection

The Behçet’s Disease Research Center at Istanbul University Cerrahpasa Medical School has been in existence since 1978. It is a weekly multidisciplinary outpatient clinic in which rheumatologists, dermatologists, and ophthalmologists participate. Neurological and other consultations are obtained as indicated by patients’ symptoms and signs. While the outpatient clinic for patients with NBS in the Neurology Department was officially established only in 1987, earlier neurological consultations were carried out on individual basis, and patient records date back to 1983. A database was formed in 1994 to study the demographic, clinical, radiological, and prognostic aspects of the patients with BD and neurological involvement. Records of patients who had been seen and followed before 1994 were retrospectively evaluated. Between April 1994 and January 1998 entries were prospectively updated. Retrospective and prospective data were pooled. The final status of patients who had not been seen on follow-up visits within the past 2 years of the study was assessed by telephone interviews. In the case of any new complaint, patients were scheduled for follow-up visits. The inclusion criteria were as follows:

- a) Filling the international diagnostic criteria for BD [17, 18]
- b) Onset of neurological symptoms otherwise not explained by any other known systemic or neurological disease or treatment
- c) Presence of at least one of the following:
  - Objective abnormalities on neurological examination (clinically definite)
  - Abnormal neuroimaging findings suggestive of CNS parenchymal involvement [24] or VST due to BD (radiologically supported–definite)
  - Cerebrospinal fluid findings of aseptic inflammation or increased pressure suggestive of CNS parenchymal involvement or VST due to BD (CSF-supported, definite)
- d) In the case of isolated chronic headache syndromes which do not fulfill the previous criterion; onset or change in character (e.g., increased attack rate or intensity) of the syndrome within 6 months of the onset of BD

Headache is a very common symptom in the general population. Unless other CNS signs or symptoms were present, only cases with a change in character of an existing headache or an onset of headache within 6 months of the BD onset, where imaging and CSF studies are justified, were included in the study.

Data classification and statistical analysis

Independent factors studied were: demographics (gender, age at onset of BD, age at onset of neurological involvement), clinical aspects at disease onset (single, disease course (single episode, relapsing-remitting or chronic-progressive), diagnostic studies (CSF, CT and MRI) and the final diagnoses. The outcome variable considered for survival analysis was time to the final level of disability reached due to neurological involvement.

Patients who fulfilled the inclusion criteria were categorized into three groups according to clinical characteristics at onset: headache with or without papilledema (HA-), localizing CNS symptoms and signs with or without headache (CNS Sx), other symptoms or signs (i.e., isolated optic neuritis, nonlocalizing CNS symptoms such as generalized seizures, or peripheral nervous system involvement) with or without headache (other Sx). Imaging findings were grouped into three categories: normal MRI, VST, and CNS parenchymal lesions (CNS-p). In cases in which MRI was not performed, CT demonstrating a lesion was considered diagnostic, while normal CT finding was not, due to the relatively low sensitivity in detection of parenchymal lesions. Similarly, CSF studies were grouped into three broad categories: normal, increased CSF pressure (> 180 mmHg) alone, inflammatory findings (white blood cell counts > 5 cells/ml or an elevated protein level) with or without increased pressure.

The final diagnoses were classified as: VST, parenchymal NBS, isolated PBS unrelated to corticosteroid use and without any clinical or laboratory support for VST or NBS, isolated cognitive changes, isolated optic neuritis, aseptic meningitis, and peripheral neuropathy. Patients who had a clinically suspected syndrome but in whom imaging and CSF results were inadequate to establish a definite diagnosis were classified as indefinite (Fig. 1).

We rated disability using Kurtzke’s [25] Expended Disability Status Scale (EDSS). This is an ordinal scale from 0 to 10, with 6 representing a moderate disability (patient requires assistance in walking and during other activities of daily life) and 10 representing death. It was originally devised for disability associated with multiple sclerosis. Although the scale has not been validated as a measure of long-term neurological disability in BD, the functional systems involved in the two disorders are similar, and we have extensive previous experience with this scale [21]. Slight modification was necessary because in BD visual disability is most commonly due to uveitis except for rare cases of optic neuritis. Hence visual problems had to be eliminated from the original scale since they do not contribute significantly to neurological burden.

To evaluate the compatibility of the retrospective and prospective data for pooling, demographic and clinical features of the group with