Intracranial Hemorrhage in Neuro-Behçet’s Syndrome

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Abstract

Objective Most cerebrovascular disturbances in Behçet’s syndrome are occlusive in nature, while hemorrhage is rare. In this paper, we report three cases of neuro-Behçet’s syndrome presenting with intracerebral hemorrhaging, and discuss the possible causes as they relate to cyclosporine treatment.

Patients Three cases of neuro-Behçet’s syndrome presented with intracranial hemorrhage. One patient had been taking cyclosporine, and the other two patients had never taking cyclosporine.

Results Together with previous reports, these cases suggest that there are two types of intracranial hemorrhage in neuro-Behçet’s syndrome. One type occurs in the center of a lesion and during the acute phase of the disease, while the other occurs in the peripheral lesion and during the subacute phase.

Conclusions It appears that the intracranial hemorrhages in neuro-Behçet’s syndrome can be divided into two groups. It is possible that the vascular pathologies caused by Behçet’s syndrome and by cyclosporine conspire to induce CNS hemorrhaging in some cases.

Key words: CT, MRI, cyclosporine, central nervous system

Introduction

Behçet’s syndrome, a multiple-system disease first described in 1937 by the Turkish dermatologist Hulusi Behçet (1), occurs with a high prevalence in Japan, and in Mediterranean and Middle Eastern countries. Clinically, it is characterized by uveitis, oral aphthae, genital ulcers, and skin lesions, although gastrointestinal, articular, pulmonary, and neurological lesions can also develop. Central nervous system (CNS) involvement has been reported in 10% to 49% of cases (2, 3) and was characterized by meningencephalitis, benign intracranial hypertension, headaches, seizures, cerebral vessel thrombosis, and vasculitis (4, 5). Five percent of Behçet’s syndrome patients were found to develop mucocutaneous lesions only after the appearance of CNS lesions (6).

Vascular lesions are common in many of the complications of Behçet’s syndrome. Most of these lesions are thought to contribute to the occlusive process or to aneurysm formation in large vessels (7). Most cerebrovascular disturbances in Behçet’s syndrome are occlusive in nature such as in dural sinus thrombosis (5), while hemorrhage is rare. In this paper, we report three cases of neuro-Behçet’s syndrome presenting with intracerebral hemorrhaging, and discuss the possible causes as they relate to cyclosporine treatment.

Case Reports

Patient 1

A 49-year-old man with recurrent uveitis and oral aphthae was diagnosed with Behçet’s syndrome and had been taking cyclosporine for more than 5 years. He developed a headache and fever, followed three days later by the appearance of a genital ulcer. A week later, he was admitted to our hospital, complaining of difficulty walking. Neurologic examination revealed right ptosis, weakness of the left orbicularis oculi muscle, generalized hyperreflexia with pathologic reflexes, and mild truncal ataxia. Cerebrospinal fluid (CSF) showed 4 cells/mm³ and 45 mg/dl of protein.

A brain computed tomography (CT) scan taken on admission (Fig. 1) showed a high-density area in the mid-pons consistent with a pontine hemorrhage. An MRI revealed small scattered lesions, enhanced by gadolinium, in the bilateral frontal, parietal, and temporal lobes, supporting a diagnosis of neuro-Behçet’s syndrome.

Patient 2

A 30-year-old man who had suffered from recurrent uveitis and genital ulcers for 2 years, was admitted to our hospital with left leg weakness. Initial examination revealed an absence of mucocutaneous lesions and uveitis. Neurological examination of this patient, who had not been taking cyclosporine, showed restricted left eye adduction, mild left hemiparesis with Babinski’s sign, and left limb and truncal ataxia. Examination of the CSF revealed pleocytosis (90 cells/mm³; 63% segmented-nuclear and 37% mononuclear cells) and a protein concentra-
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Figure 1. Brain CT of patient 1 on admission showed a high density area in the mid-pons, suggesting the presence of an acute hemorrhage (Patient 1).

Figure 2. Seven weeks after admission, follow-up MRI detected bilateral low intensities on T2WI in basal ganglionic regions, suggesting post-hemorrhagic hemosiderin deposition (Patient 2).

Figure 3. The follow-up brain MRI of patient 3 demonstrated a low signal intensity on T2WI suggesting the presence of a hemorrhagic lesion at the margin of a large high signal intensity area in the head of the right caudate (Patient 3).

tion of 33 mg/dl.

A brain CT scan a day after admission showed abnormal enhancement at the bilateral genu of the internal capsule without any signs of hemorrhage. The patient was treated with corticosteroids and his symptoms gradually improved. Seven weeks later, follow-up MRI detected bilateral low intensities on T2WI in basal ganglionic regions, suggesting post-hemorrhagic hemosiderin deposition (Fig. 2).

Patient 3

A 48-year-old man had uveitis consistent with Behçet’s syndrome for which he was treated with colchicine. A month after developing a high fever and genital ulcer, he was admitted to our hospital complaining of drowsiness. The initial MRI on admission showed a large area of high signal intensity in the right basal ganglia. Four days later, the patient complained of severe abdominal pain necessitating emergency surgery, which revealed multiple ulcers in the ileum and colon. The patient made a moderate recovery after steroid treatment. In a follow-up MRI over two weeks later, a low signal intensity on T2WI suggesting the presence of a hemorrhagic lesion was detected at the margin of a large high signal intensity area in the head of the right caudate (Fig. 3).

Discussion

Neuroradiological studies suggested that neuro-Behçet’s
syndrome resulted in the development of inflammatory lesions in the brainstem as well as in a breakdown in the blood-brain barrier (8, 9). Neuropathologically, the syndrome has been described as representing a vasculitis with cellular infiltrates mainly affecting postcapillary venules (10), with reports of intracranial hemorrhages being rare.

The CT and MRI findings in our cases indicated the presence of hemorrhages. One patient had a massive hemorrhage at the mid-pontine level, and the other two suggested small hemorrhages in the basal ganglia and caudate nucleus. The pontine hemorrhage was identified at the onset of neurological symptoms, while the hemorrhages in the other two cases were thought to be in the subacute phase during the course of treatment as indicated by the precipitation of hemosiderin.

There have been 5 previous reports of neuro-Behcet’s syndrome presenting with intracranial hemorrhage, as determined by CT scan and/or MRI (Table 1). Taken together with our data, it appears that neuro-Behcet’s syndrome patients can be divided into two groups: those with hemorrhages in the center of their lesion identified during the acute phase of their illness and those with hemorrhages at the periphery of their lesion identified during their subacute phase.

Our patients’ histories and laboratory findings suggested that it was unlikely that the described hemorrhages developed as a result of hypertension, a vascular anomaly, or a coagulation abnormality. Bleeding of a cryptic angioma was also unlikely since it is characterized by heterogenous intensities with heterogenous enhancement on CT scan and/or MRI. Similarly, venous thrombosis was ruled out since our patients’ sinuses were patent and since these patients did not have any coagulation problems. Particularly in the case of the basal ganglia, the hemorrhages were thought to be caused by the vasculitic changes associated with Behcet’s syndrome, since they appeared at the same site as the inflammatory lesion in the acute phase of the disease.

It is conceivable that the massive pontine hemorrhage described in our first case could have been induced by the vascular changes associated with Behcet’s disease, as previously suggested by pathological studies showing small hemorrhagic changes resulting from disruption of the integrity of small vessels in this syndrome (11). A recent report suggested that cyclosporine might also be implicated in the development of neuro-Behcet’s syndrome (12). Cyclosporine is known to damage endothelial cells and to induce reversible ischemia resulting in “reversible posterior leukoencephalopathy” (13). It is possible that cyclosporine-induced damage of endothelial cells contributed to the development of the hemorrhagic lesion in this patient. However, several studies that reported cerebral hemorrhage in patients taking cyclosporine also reported hypertension in these patients (14), a finding that was not observed in the present patient. The foregoing notwithstanding, the administration of cyclosporine might influence the timing and size of a hemorrhage as well as the course and severity of neurological symptoms. It should be noted that Hasegawa et al reported the case of a cyclosporine-treated patient who presented with an acute, massive hemorrhage in the pons (15). It is possible that the vascular pathologies caused by Behcet’s syndrome and by cyclosporine conspire to induce CNS hemorrhaging in these patients.

Approximately 5% of Behcet’s syndrome patients do not develop mucocutaneous manifestations even after neurologic involvement (16). Thus, it is important to consider neuro-
Behçet’s syndrome as a diagnosis in patients with intracerebral hemorrhages in general, and in patients with an acute pontine hemorrhage in particular.

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References