CASE REPORT

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Neuro-Behçet's disease with chorea after remission of intestinal Behçet's disease

Received: 27 October 2003 / Accepted: 23 January 2004 / Published online: 17 April 2004 © Clinical Rheumatology 2004

Abstract Neuro-Behçet's disease shows various neuropsychiatric symptoms, but chorea has rarely been reported. We report a case of neuro-Behçet's disease in a 67-year-old woman with depression and chorea that occurred 22 years after the onset of intestinal Behçet's disease. Brain magnetic resonance imaging (MRI) using a fluid-attenuated inversion-recovery (FLAIR) sequence demonstrated lesions more clearly than did T₂-weighted MRI. Some of the lesions appeared as small ring-like foci, i.e. low-intensity spots rimmed with remarkable hyperintense signals, in the periventricular white matter and basal ganglia. A review of the literature revealed that the onset of chorea in cases of Behçet's disease varied from the time of onset of Behçet's disease to 31 years after onset of the disease. Psychiatric manifestations have often been associated with neuro-Behçet's disease. In the present patient, treatment with prednisolone resolved the chorea, suggesting that the chorea was caused by an autoimmune mechanism. It seems likely that the long-term development of vasculitis in patients with Behçet's disease results in the formation of these particular brain lesions on FLAIR MR images. Chorea should be taken into consideration as one of the manifestations of Behçet's disease, even many years after remission of the disease.

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Department of Medicine and Bioregulatory Sciences, University of Tokushima, Graduate School of Medicine, Tokushima, Japan **Keywords** Chorea · Depression · FLAIR MRI · Neuro-Behçet's disease · Vasculitis

Abbreviations ANCA: Antineutrophil cytoplasmic antibodies · FLAIR: Fluid-attenuated inversion-recovery · MRI: Magnetic resonance imaging

Introduction

Behçet's disease is a systemic inflammatory disorder characterized by recurrent oral and genital ulcers, uveitis and skin lesions, and is sometimes associated with neurological, intestinal or vascular involvement [1]. Chronic, progressive deficit of the central nervous system (CNS) is known as neuro-Behçet's disease [1, 2]. Psychiatric symptoms, including psychoneurosis/ depression, memory disturbance, attention deficit and behavioral change, as well as neurological manifestations, including central motor paralysis and brain stem signs, are often observed [1, 2], but chorea has rarely been reported [3, 4, 5, 6, 7, 8]. Furthermore, only a few patients with Behçet's disease have been reported as having both neurological and intestinal involvement [9, 10]. Brain magnetic resonance imaging (MRI) is useful for the diagnosis of neuro-Behçet's disease, which shows lesions usually in the brain stem, basal ganglia and/or white matter [11, 12]. However, it is often difficult to distinguish a small brain lesion from lacunar infarction. We report unique findings of brain MRI using a fluid-attenuated inversion-recovery (FLAIR) sequence in a case of neuro-Behçet's disease that presented with depression and chorea after remission of intestinal Behçet's disease. The lesions may be differentiated from those in lacunar infarctions.

Case report

The patient was a 67-year-old woman with a history of recurrent stomatitis, genital ulcer and ileocecal Fig. 1 Axial brain MRI revealed multiple foci in the white matter and basal ganglia, appearing hyperintense on T_2 -weighted image (**a**, **b**). MRI using the FLAIR sequence (**c**, **d**) demonstrated lesions more clearly, and some of the lesions appeared as lowintensity spots rimmed with high-intensity signals in the periventricular white matter (*arrowhead*) and putamen (*arrow*)



resection necessitated by intestinal Behcet's disease that had occurred 22 years ago. She had no family history of Huntington's disease and involuntary movement. Chorea suddenly occurred in her lower extremities, and she visited the emergency room of our hospital in October 1999. Her oral and genital ulcers had improved over the previous 15 years. She had been treated for headache and depression at a mental hospital. She had not recently received dopamine antagonists. On admission, she had stopped taking her medication several days earlier. She exhibited a prominent behavior disorder, including attention deficit, delusion of persecution, hallucination and depression, resulting in social withdrawal. Mini-Mental State Examination score was 23. Ophthalmologic examination revealed no evidence of uveitis. Cranial nerve function and muscle power were spared. Deep tendon reflexes showed bilateral hyperreflexia with a positive jaw jerk and Chaddock sign. Results of routine laboratory examinations were normal except for elevations of serum IgG level (2701 mg/dl; normal, 870–1700) and antinuculear antibody titer (640; normal, <20). Immune complex, C3 and C4 levels were normal. Antineutrophil cytoplasmic antibodies (ANCA) and antiphospholipid antibodies were negative. Her HLA type was B51. There were no findings of fever, hypertension, coagulopathy, hyperlipidemia or other potential causes of cerebrovascular accident. Serum homocysteine concentration was normal. Results of laboratory examinations did not satisfy the criteria for other collagen diseases. Examination of the cerebrospinal fluid (CSF) showed that the cell count was 2 cells/mm³, protein level was 55 mg/dl (normal, < 45) and IgG-albumin index was 0.776 (normal, < 0.7). EEG showed diffuse slowing. Conventional brain MRI revealed multiple foci in the basal ganglia and white matter, appearing hypointense on T₁-weighted images and hyperintense on T₂-weighted images (Fig. 1a, b). MRI using the FLAIR sequence revealed lesions more clearly, and some of them appeared as low-intensity spots rimmed with highintensity signals (Fig. 1c, d). MR angiography was unremarkable. Her choreic movement improved after treatment with diazepam, but subsequently recurred. Anticonvulsants did not resolve the repeated chorea, but 60 mg/day prednisolone induced relief. Despite the administration of antidepressant, anxiolytic and sedative drugs, including maprotiline, zopiclone, diazepam and etizolam (none of which are dopamine antagonists), her headache persisted and her psychotic features initially showed a slight improvement, but later became more serious. She sometimes asked us to terminate her life, and in May 2001 she attempted suicide. She refused repeated lumbar puncture and brain MRI studies.

Discussion

Chorea is usually caused by ischemic brain lesions, toxins, neuroleptic drugs, dopamine antagonists and heritable metabolic disorders such as Huntington's disease [13]. In our patient, drug-induced chorea was less likely because none of the previous psychiatric treatments included dopamine antagonists, and she had stopped taking her medication several days before the onset of the chorea. Huntington's disease is also unlikely because there was no family history of involuntary movements or compatible MRI findings. Brain MRI revealed multiple foci in the white matter and basal ganglia. Because chorea has been associated mainly with lesions in the caudate nucleus or putamen [13], the brain lesions in the putamen may have been responsible for her chorea. In a review of 200 patients with neuro-Behçet's disease [2], attacks of neurologic deficits with headache and gradual behavioral changes were a characteristic clinical picture of neuro-Behçet's disease, and 6% of patients had movement disorders such as hemichorea, hemiballismus and hemidystonia. To the best of our knowledge, only 6 cases of neuro-Behçet's disease with chorea have been reported (age range of the patients, 39–55 years; 3 males and 3 females) [5, 6, 7, 8]. Oral and/or genital ulcers were noted in 4 patients [3, 5, 7, 8], but no uveitis was evident in any of the patients at the time of presentation of chorea. The disease duration between onset of Behçet's disease and occurrence of chorea was varied. Three patients presented with chorea at the onset of Behçet's disease [5, 7, 8], and three developed chorea 7 months [6], 6 years [3], and 31 years [4] after onset of the disease. Psychiatric manifestations, including memory disturbance [5, 8], dementia [6], inattention [7, 8] and psychomotor agitation [7], have been noted. Brain MRI was performed in 4 patients, and all of the detected lesions included the caudate nucleus [5, 6, 7, 8]; however, the FLAIR sequence was not used. Neuropsychiatric symptoms were improved by treatment with prednisolone in 3 patients [3, 5, 7], but 2 required the additional administration of colchicine [6] or haloperidol [8]. The present patient had developed headache, depression, delusion and hallucination followed by chorea with no recurrent ulcers on admission, 22 years after remission of intestinal Behçet's disease. The long-lasting clinical course was similar to that of a patient reported by Bussone et al. [4], who developed choreic dyskinesia, anxiety, suspicion and restlessness after improvement of ulcers, and who had been diagnosed as having Behçet's disease 31 years earlier. Neuropsychiatric involvement may progress insidiously and become prominent several years after the onset of Behçet's disease. In the present patient, treatment with prednisolone resolved the chorea, suggesting that the cause was an inflammatory mechanism associated with

Behçet's disease. Therefore, it seems likely that the longterm development of vasculitis results in a unique appearance on brain MRI scans using the FLAIR sequence. The FLAIR sequence allows heavily T2-weighted images to be obtained with no or considerably reduced CSF signals obscuring adjacent brain regions. In a previous study on neuro-Behçet's disease, MRI using the FLAIR sequence revealed significantly more lesions than did MRI using the conventional dual-echo spin-echo (SE) sequence [11]. In the present patient, MRI using the FLAIR sequence also demonstrated brain lesions more clearly than did T₂-weighted MRI. Moreover, some of the lesions appeared as small ringlike foci, i.e. low-intensity spots rimmed with remarkable hyperintense signals, in the periventricular white matter and basal ganglia. It is difficult to distinguish a neuro-Behçet's lesion from lacunar infarction on conventional T_1 - or T_2 -weighted MR images if the lesion is small. On the FLAIR images, lacunar infarction initially appears as a hyperintense spot, and chronic lacunar infarction appears as a hypointense spot occasionally with a hyperintense rim [14]. The latter finding seems to depend on the consequent encephalomalacia in chronic lacunar infarction. Therefore, a hypointense lesion has an equivocal margin with a slightly hyperintense rim, whereas the present case showed small ring-like foci, i.e. low-intensity spots rimmed with remarkable hyperintense signals. The primary pathologic change in Behçet's disease is based on vasculitis, and the neuropathologic features in the brain of a patient with neuro-Behçet's disease are necrotic foci with accumulated microglial phagocytes and focal cuffing of blood vessels by lymphocytes [1]. It has been suggested that cerebral vasculitis should be considered in neuro-Behçet's disease, although low-grade chronic meningoencephalitis is the principal neuropathological process [15]. On FLAIR MR images in the present case, the remarkable hyperintense rim could represent vasculitis and the hypointense spot may represent central necrosis. A similar appearance on brain FLAIR MR images has been in a case of primary vasculitis of the CNS [16].

In conclusion, chorea should be taken into consideration as one of the manifestations of Behçet's disease, even many years after remission of the disease. Brain MRI using the FLAIR sequence has a potential advantage to demonstrate cerebrovascular involvement caused by chronic vasculitis in neuro-Behçet's disease.

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