

CASE REPORT

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A pediatric patient with neuro-Behçet's disease

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Abstract Behçet's disease is rare in childhood. We describe a 10-year-old boy with neuro-Behçet's disease (NB) who presented with fever, headache, vertigo, and hearing loss. An examination of the cerebrospinal fluid (CSF) revealed pleocytosis as well as elevated protein and interleukin (IL)-6 levels. Brain magnetic resonance imaging (MRI) showed hyperintensity of the right thalamus and midbrain on T2-WI, and gadolinium (Gd) enhancement of left acoustic nerve origin. HLA-B51 was positive. Prednisolone combined with methotrexate resulted in a complete remission. Brain MRI and the CSF IL-6 level were useful for the diagnosis and monitoring of this pediatric patient with NB.

Key words Cerebrospinal fluid (CSF) · Child · Interleukin (IL)-6 · Magnetic resonance imaging (MRI) · Neuro-Behçet's disease (NB)

Introduction

Behçet's disease (BD) is characterized by recurrent aphthous oral and genital ulcerations, as well as uveitis, and it is recognized as being multisystemic. The disease may include skin, mucosa, joints, gastrointestinal tract, blood vessels, central nervous system (CNS), and other sites.^{1,2} Although the etiology and pathogenesis are under investigation, stud-

ies have shown that HLA-B51 influences genetic susceptibility, since the positive ratio of HLA-B51 in BD is about 60%.^{3,4} Originally described by Knapp in 1941, neuro-Behçet's disease (NB) occurs in 5.3%–38% of patients in whom it is an adverse factor for prognosis.^{5–7} The condition can be separated into two groups according to the site of involvement, primary parenchymal CNS involvement, and nonparenchymal involvement.⁷ The clinical course of NB can manifest as an acute attack, progressive disease, or silent involvement.⁸

The disease is frequent in eastern Mediterranean countries along the Silk Road, and in East Asia, especially Japan. The prevalence of BD among the adult population in Japan is considered to be about 30-fold higher than that of the United States and Europe.⁹ However, BD is a rare disease of childhood and fewer than 100 patients have been described in the literature.^{1,10} Here we present the case of a child with BD, in whom the signs and symptoms included CNS parenchymal involvement following acute meningitis. We describe the magnetic resonance imaging (MRI) findings and cerebrospinal fluid (CSF) interleukin (IL)-6 monitoring, and their contribution to a correct diagnosis.

Case report

A 10-year-old boy was admitted to our department in June 2004 with fever, headache, and vomiting. He had a history of recurrent aphthous oral ulcerations, erythema nodosum, and uveitis after tonsillectomy at 9 years old. He was diagnosed with BD in October 2003 and had been treated with prednisolone (PSL). Four months after starting PSL, he was administered with oral cyclosporine A (CyA) in combination with PSL.

His temperature was 38.8°C, and he was conscious and alert. A neurological examination revealed neck stiffness, but the cranial nerves were intact. The white blood cell count was 13800/ml and C-reactive protein was 1.58 mg/dl. The trough blood cyclosporine A level was 103.3 ng/ml and HLA-B51 was positive. A CSF examination uncovered

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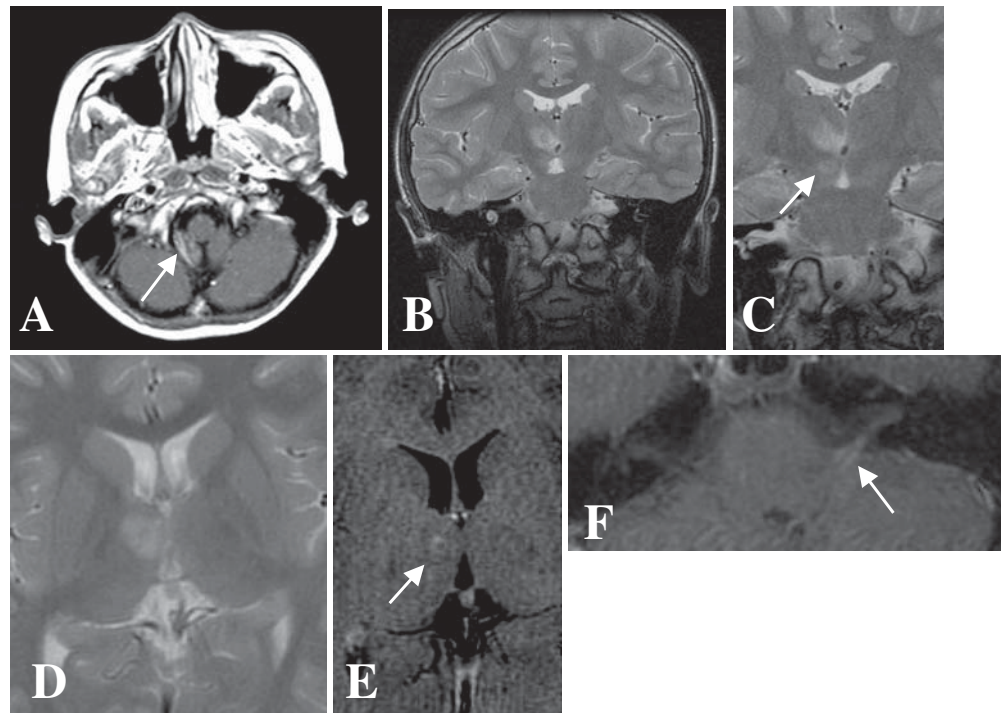
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Fig. 1A–F. Brain magnetic resonance imaging study of the patient. **A** first admission. **B–F** during second admission. **A** Gd enhancement of lesion along folia cerebelli. **B** Hyperintensity of right lateral thalamus on T2-W coronal image. **C** Hyperintensity of right medial mesencephalon on T2-W coronal image. **D,E** Central deficit of hyperintensity on T2-W image (**D**) matches Gd-enhanced spot on same slice of Gd-enhanced T1-W axial image (**E**). **F** Gd enhancement of left acoustic nerve origin



pleocytosis (1467/ μ l) with a predominance of polynuclear cells (848/ μ l), and an elevated protein level of 135 mg/dl. Brain MRI showed hyperintensity of the right cerebellar tonsil on T2-WI (not shown) and gadolinium (Gd) enhancement along the folia cerebelli (Fig. 1A), which seemed to be local inflammation due to meningitis. Although the CSF culture was sterile, the patient recovered immediately within a few days of antibiotic administration. Another CSF evaluation showed that the cell count (88/ μ l) and protein level (50 mg/dl) were decreased. He was discharged from the hospital 10 days after admission.

However, he was admitted to our hospital again 10 days later for vertigo and hearing impairment in the left ear with fever and headache. A neurological examination revealed neck stiffness, horizontal nystagmus to the right, and deafness due to left acoustic nerve palsy. Motor, sensory, and consciousness disturbances were absent. The CSF test again showed pleocytosis (648/ μ l) with a predominance of polynuclear cells (370/ μ l), and an elevated protein level of 73 mg/dl. Brain MRI showed hyperintensity at the right lateral thalamus and medial mesencephalon on T2-WI, and Gd enhancement of the left acoustic nerve origin without exudative otitis media (Fig. 1B–F). Hyperintensity of the right cerebellar tonsil on T2-WI, which was also observed at the first admission, had regressed. We diagnosed NB based on laboratory and MRI findings and the clinical course. The CyA was discontinued and pulse methylprednisolone was administered (500 mg methylprednisolone/day for 3 days; 250 mg/day for 3 days; 125 mg/day for 3 days), followed by daily oral PSL at 1 mg/kg per day. His symptoms disappeared within 1 month. Since the CSF IL-6 level remained elevated (0.947 U/ml) and MRI findings were not completely improved after 1 month of PSL therapy, methotrex-

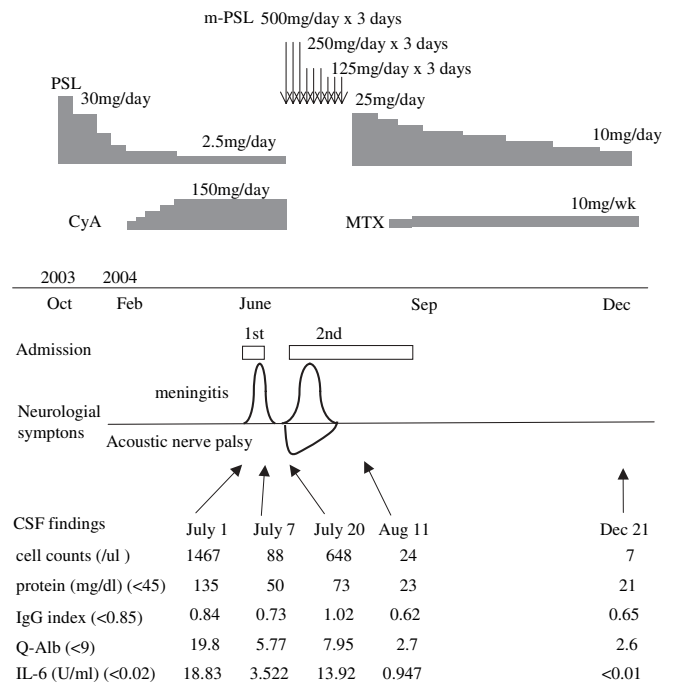


Fig. 2. Clinical course of the patient. Symptoms, therapy, and cerebrospinal fluid (CSF) findings are shown. *m-PSL*, methylprednisolone; *PSL*, prednisolone; *MTX*, methotrexate; *CyA*, cyclosporine A; *IgG*, immunoglobulin G; *Q-Alb*, quotients of albumin; *IL-6*, interleukin-6

ate (MTX) 5 mg/week was started in August and increased to 10 mg/week. The PSL was gradually decreased to 10 mg/day, and MRI findings and the CSF IL-6 level returned to normal after 5 months of therapy, in December (Fig. 2).

Discussion

Behçet's disease is uncommon in childhood. Fujikawa and Suemitsu described the clinical characteristics of BD in childhood based on a retrospective series of patients derived from a questionnaire given to Japanese pediatricians.¹ They reported that entero-BD was more frequent in children than in adults, while ocular complication and NB were less frequent. The frequency of HLA-B51 was lower (14.4%) in children than in adults. Three boys and one girl among 31 Japanese children with BD have developed NB. The age of onset was variable (from 10 months to 13 years), and they had various types of NB, such as transverse myelitis, meningitis, encephalitis, and convulsions. An international collaborative study has also reported that 15% of children with BD had neurological symptoms.¹⁰ Here we described the clinical course of a Japanese boy with NB including CSF and MRI findings.

Both acute and chronic progressive types of BD are recognized. Acute NB is characterized by acute meningoencephalitis with focal lesions in high-intensity areas in T2-weighted images or in FLAIR images on MRI scans, which reflect edema and inflammation.¹¹ Areas in these lesions enhanced by Gd are considered to reflect disease activity. Kocer et al. reported that the most commonly affected regions were the mesodiencephalic junction (46%), the pontobulbar region (40%), and the hypothalamic-thalamic region (23%).¹² The MRI image of our patient was compatible with the characteristics of adult NB in that the thalamus and midbrain were affected. On the other hand, hearing loss is the least common symptom of adult NB.⁷ Because pediatric NB is rare, MRI studies of children are limited in case reports.¹³ The characteristics of pediatric NB should be understood in more detail by publishing more descriptions of such patients.

Acute NB is thought to be induced in 20%–30% of BD patients receiving CyA, and it responds to the cessation of CyA with or without steroid therapy.¹⁴ We considered that CyA, which was administered to treat uveitis, induced acute NB in our patient. Diagnosing NB in our patient was not a simple matter because his symptoms and laboratory and MRI findings mimicked those of acute infectious meningitis and he seemed to improve after antibiotic administration. In fact, NB was diagnosed after the second admission. Our retrospective assessment is that the meningitis at the first admission was part of the NB that was induced by CyA and self-limiting.

Chronic progressive NB is characterized by slowly evolving and progressively worsening neurological symptoms after each attack. Most adult patients with chronic NB are HLA-B51 positive (approximately 90%).^{15,16} The activity of CSF IL-6 is persistently elevated in chronic progressive NB.¹⁷ Because our patient was HLA-B51 positive and CSF IL-6 was substantially elevated after 1 month of PSL therapy, we considered that the NB might be steroid resistant and become chronic and progressive unless recurrent attacks could be prevented. After starting low-dose weekly MTX therapy, the PSL dosage was tapered and both the

CSF IL-6 level and the MRI findings normalized. Although MTX might be effective against chronic progressive NB in children, further detailed studies are necessary.

We described the clinical course of a 10-year-old patient with NB. Brain MRI and CSF evaluations were indispensable for establishing a diagnosis and follow-up. Although NB is rare among children, it should be considered when brain MRI reveals parenchymal inflammatory lesions that include the midbrain and thalamus.

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