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Case Report / Olgu Sunumu

Isolated neuro-Behçet's disease in a child, from headache to diagnosis: A case report

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Abstract

Behçet's disease (BD) is an immuno-inflammatory multi-systemic disease characterized by ophthalmological and skin involvement, also oral and genital ulcers. Its etiology and pathogenesis are not clearly known. Neuro-Behçet's disease can occur as an isolated form or a rare complication of BD. Besides, diagnosis of neuro-Behçet's disease is difficult. Since Neuro-Behçet can result in morbidity and mortality, early diagnosis and treatment are important. The most important genetic factor in the pathogenesis of BD is Human Leucocyte Antigen (HLA-B 51) allele positivity. A 9-year-old girl was brought to our outpatient clinic for 6 months with a migraine-like headache. The headache of the patient has a partial response to analgesics and rarely awakes from sleep at night accompanied by vomiting. The patient was diagnosed with an isolated neuro-Behçet's disease by HLA-B 51 allele positivity and brain magnetic resonance imaging (MRI) findings. In the current study, the roles of HLA-B 51 allele positivity and brain MRI findings were discussed in the diagnosis of neuro-Behçet's disease.

Keywords: HLA-B51 positivity; Isolated neuro-Behçet's disease; Migrain like headache; MRI.

Baş ağrısından tanıya, bir çocukta izole nöro-Behçet hastalığı: Olgu sunumu

Öz

Behçet hastalığı (BH), oral ve genital ülserlerin yanı sıra oftalmolojik ve cilt tutulumuyla seyreden immüno-inflamatuar multisistemik bir hastalıktır. Etyolojisi ve patogenezi net olarak bilinmemektedir. Nöro-Behçet hastalığı izole veya Behçet hastalığının nadir bir komplikasyonu olarak ortaya çıkabilir. Ayrıca, nöro-Behçet hastalığının tanısı zordur. Nöro-Behçet morbidite ve mortaliteyle sonuçlanabileceği için erken tanı önemlidir. BH'nin patogenezindeki genetik faktörlerin en önemlisi HLA-B 51 allel pozitifliğidir. Dokuz yaşında kız hasta 6 aydır devam eden migrenöz tipte baş ağrısı şikayetiyle getirildi. Hastanın baş ağrısı, analjeziklere kısmi yanıt veren ve nadiren de kusmanın eşlik ettiği gece uykudan uyandıran tarzdaydı. Hastaya HLA-B 51 allel pozitifliği ve beyin manyetik rezonans görüntüleme (MRG) bulguları ile izole nöro-Behçet hastalığı tanısı konuldu. Bu çalışmada nöro-Behçet hastalığı tanısında HLA-B 51 allel pozitifliği ve beyin MRG bulgularının rolü tartışıldı.

Anahtar kelimeler: HLA-B51 pozitifliği; İzole nöro-Behçet hastalığı; Migrenöz başağrısı; MRG.

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INTRODUCTION

Behçet's disease is a multisystemic immuno-inflammatory disease of unknown etiology that is characterized by oral/genital aphthous ulcer and uveitis. Apart from these, joint, pulmonary, gastrointestinal, urogenital, cardiac, vascular, and neurological involvements can also be observed. Pathergy test is helpful in diagnosis. It was first introduced by the Turkish dermatologist Hulusi Behçet in 1937[1]. It is more commonly seen in the Far East, the Middle East, the Mediterranean countries, and along the ancient silk road. There is a strong relationship between HLA-B 51 positivity and disease in high prevalence regions such as the Middle and the Far East[2]. Knapp was the first to discover neurological involvement in BD in 1941[3]. Although the diagnostic criteria of BD are well defined, neuro-Behçet's disease (NBD) does not have clear diagnostic criteria[4]. It may be difficult to diagnose isolated NBD in patients presenting with an isolated neurological attack or who have not met the necessary diagnostic criteria of BD yet. In NBD, the diagnosis is made with the findings of the MRI and cerebrospinal fluid (CSF) in addition to the clinical findings. While neurological involvement of BD is generally seen in the central nervous system (CNS), rarely peripheral nervous system involvement can also be seen[5]. Isolated NBD is extremely rare in children. But when it occurred may generally evolve into classic BD after a while. MRI findings and HLA-B 51 allele positivity are important in the diagnosis of NBD. Early diagnosis may prevent complications.

In this paper, a 9-year-old girl, who has been diagnosed with isolated NBD is presented to emphasize the role of MRI and HLA-B 51 allele positivity in childhood.

CASE REPORT

A nine-year-old girl patient applied to our Pediatric Neurology outpatient clinic with the complaint of headache which is increasing with light and sound, lasting dated from about 6 months, sometimes responding to the analgesic intake, rarely awakening from the sleep at night, and it is accompanied by occasional vomiting. In her family history, there was no parental consanguinity, birth difficulty. Her father has a history of recurrent headaches. The systemic and neurological examination of the patient was normal. In laboratory tests; complete blood count, electrolytes, liver, and kidney function tests, ferritin, folate, vitamin B12, vitamin D, and thyroid function tests were normal. C-reactive protein, sedimentation, anti-nuclear antibody (ANA), anti-double-stranded DNA (dsDNA), C3, C4, and ENA panel were normal. Protein excretion was normal in 24-hour urine. Uveitis was not observed in the eye examination. Pathergy test was negative. CSF protein and CSF glucose (simultaneous blood glucose), oligoclonal band, blood/CSF IgG index, CSF, and serum measles antibodies results were normal. A few numbers of lymphocytes were seen in CSF. Brain MRI showed hyperintense signal changes in T2A and fluid-attenuated inversion recovery (FLAIR) sections starting from the globus pallidus on the left and extending to the mesencephalon (Figures 1 and 2). MR spectroscopy, electroencephalography (EEG), abdominal ultrasonography, and bone marrow aspiration were normal. After evaluation of the patient's brain MRI, the HLA-B 51/52 allele was sent and found positive. Treatment for NBD was planned, but the family did not accept the treatment. Because of the patient's headache migrainous character, fluoxetine was started. But the headache persisted for three months. Therefore, we thought that the headache may be

a sign of isolated NBD. After a year, the brain MRI was repeated. The lesions showed no differences. Because of a history of headaches in the father, the HLA-B 51/52 allele was sent from the father and it was found positive.

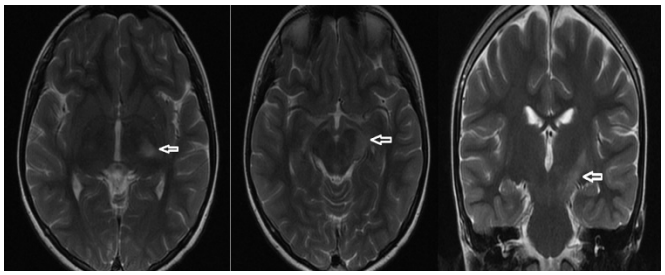

Figure 1: In the axial images **(a, b)** and coronal image **(c)**, the T2A hyperintense signal change in the focal patch style extending from the posterior leg to the cerebral peduncle in the left mesodiencephalic junction was noticed.

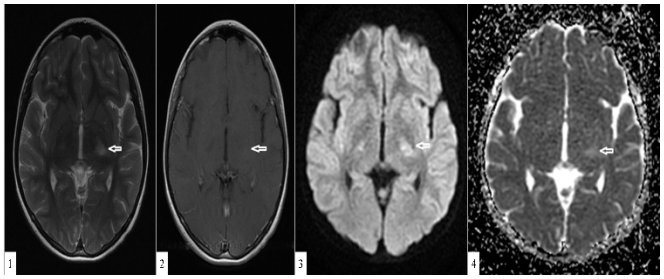

Figure 2: The focal patch-style T2A hyperintense area is selected in the lateral part of the left thalamus **(a)**. In post-contrast images, it is observed that this area does not flick contrast **(b).** Diffusion **(c)** and ADC **(d)** images did not detect diffusion restriction in this area.

DISCUSSION

Isolated NBD is rarely reported in childhood, the part of involvement and the frequency are not clear [6]. In the study in which Uludüz and his colleagues evaluated patients diagnosed with neuro-Behçet, 26 of 728 patients were children (3.6%). The neurological symptom onset age of these children was 13.5±2.4[7]. The most prevalent neurological symptom in BD is headache, which was observed in around 70% of patients[3,7]. Most of them have primary headaches (migraine and tension headache), whereas migraine is the most common primary headache[8]. Our case was a 9-year-old girl, similar to the neuro-Behçet cases. She applied to our clinic with a complaint of a migraine-like headache without systemic findings.

Because of the persistence of migraine-like headaches for 6 months despite fluoxetine, rarely nocturnal headaches accompanied by vomiting, MRI was used for the differential diagnosis. Our patient's MRI findings were compatible with neuro-Behçet's involvement. The characteristic MRI findings of NBD are lesions extending from the upper brain stem to the thalamus and basal ganglia, iso-hypointense in T1A, hyperintense in T2A, and may have a mild mass effect and contrast enhancement[9]. In our case, the area of hyperintense signal change was detected in the T2A and FLAIR series, starting from the globuspallidus on the left and extending towards the mesencephalon on the MRI. However, contrast enhancement and diffusion restriction were not observed. The involvement of our case was parenchymal, and its neuroradiological findings were consistent with the literature and helped to make an early diagnosis. While vascular involvement is observed more frequently in childhood NBD, parenchymal involvement is more common in countries such as Israel, France, and Saudi Arabia [10]. In the study of Uludüz et al.[7], 23 of 26 children had vascular and 3 had parenchymal involvement. Our case had parenchymal involvement.

There is no specific CSF finding in NBD. However, inflammatory changes in the acute period can be detected in patients with parenchymal involvement. There was mild pleocytosis in CSF in our case due to parenchymal involvement, and it was compatible with the literature[11].

The presence of HLA-B 51 is considered the strongest evidence of the role of genetic factors in pathogenesis[12]. HLA-B 51 positivity observe in patients with neurological involvement more frequently and affects the severity of BD[13]. This indicates that HLA-B 51 positivity is a bad

prognostic sign. The genetic result of our patient was positive for the HLA-B 51/52 allele. Also, the positive result of the father's HLA-B 51/52 allele indicates that genetic factors play a role. Due to the parenchymal involvement and the positive HLA-B 51/52 allele showing a risk of poor prognosis, early treatment was planned for our patient. However, in our patient, treatment was not given since the family did not accept treatment. We did not have a prediction about the prognosis. Although the patient did not accept the treatment, no additional neurological findings, and MRI changes were observed in the patient's follow-up.

As a result, one of the most serious reasons for long-term morbidity and death in BD is neurological involvement[3]. NBD usually occurs as a complication of systemic disease, but it can rarely occur as an isolated form also. To the best of our knowledge, our case is the first case to be diagnosed with isolated neuro-Behçet with migraine-like headache in childhood. Migraine-like headache may be a sign of NBD as in our patient. Our patient has been presented to remind the role of brain MRI in the differential diagnosis of headache in childhood, and the possibility of NBD.

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