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CASE REPORT

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HaNDL Syndrome Presenting With Confusion: A Rare Case Report

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ABSTRACT

HaNDL syndrome *(Syndrome of Transient Headache and Neurologic Deficit with Cerebrospinal Fluid Lymphocytosis)* characterized by sudden onset headache, transient neurological deficits, and cerebrospinal fluid (CSF) lymphocytosis, is a self-limited clinical entity that is rarely seen. In this article, we present a case with HaNDL syndrome in a 28-year-old male patient who presented with confusion and agitation after sudden onset of headache, right hemiparesis, and lymphocytosis pleocytosis.

Keywords: HaNDL Syndrome, confusion, headache

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INTRODUCTION

HaNDL syndrome is a rare clinical manifestation with good prognosis usually diagnosed with headache, neurological deficit, and presence of lymphocytosis in CSF. For the first time, Bartleson et al. (1) identified seven cases, in 1981, diagnosed with HaNDL syndrome with migraine like attacks associated with CSF lymphocytosis. With the publication of the following case series, International Classification of Headache Disorders (ICHD) defined and classified it by the definition of 'syndrome of transient headache and neurological deficits with CSF lymphocytosis' (HaNDL)' (2). In this definition, confusion has not been a characteristic symptom of the disease. In recent years, although there were cases with the presence of confusion as a distinctive feature of this syndrome, it has not been considered by the Committee of the International Headache Society as a clinical spectrum of the neurological symptoms (3). Although HaNDL syndrome has been attempted to be associated with stroke or migraine, its etiology has not been clearly clarified yet (4). In this article, we present a HaNDL syndrome, which is a very rare condition presented with confusion and agitation following headache.

CASE

A 28-year-old male patient had severe headache one week before his own wedding ceremony, but he and his relatives did not admit to the hospital by attributing this headache to stress due to his previous migraine attacks. During this period, the patient had experienced periods of occasional decrease and increase in headache. At the end of one week, headache became more severe and the patient's relatives noticed his confusion. Upon failure to establish any communication with the patient and his developing aggression, he has been brought to the emergency room of our hospital by his relatives.

In his medical history, the patient had no disease except migraine. In his neurological examination, his general status was moderate, he was confused, noncooperated, disoriented, had no neck stiffness, the cranial nerves were intact, and his muscle strength were 2/5 in the right upper and lower extremities. His vital signs were stable, and his hemogram and biochemistry were normal. There was no acute or chronic lesion in cranial tomography (BCT) of the patient. Diffusion magnetic resonance imaging (MRI) did not show any diffusion restriction. Lumbar puncture (LP) was decided in case of an intracranial infection. In LP, CSF was found to be clear, opening pressure was 17 cm H_2O, and 190/mm^3 lymphocytic pleocytosis, 67 mg/dL glucose level and 155 mg/dl protein level was found. Cranial MRI and MR venography showed no acute lesions. All microbiological examinations performed on blood and CSF were negative. Patient's electroencephalography (EEG) was normal.

On the first day of hospitalization of the patient, his confusion and hemiparesis completely recovered after hydration and analgesic treatment. The control LP performed three days later showed 130/mm^3 lymphocytic pleocytosis and 95 mg/dL of protein level. On the eighth day of hospitalization, no cell was detected in the LP and he was discharged with full recovery.

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DISCUSSION

Although the prevalence of HaNDL syndrome is not clear, it is more common in males aged 15-40 years than females. Approximately 26% of patients had a history of migraine in their medical history (5-7). The majority of the patients describes a severe, throbbing headache that they have never experienced before. The localization of the pain is usually bilateral and lasts from one hour to one week. Headache may be accompanied by photophobia-phonophobia (8,9). Neurological deficits including sensory, motor, or speech impairment can be seen in each patient. Some patients may have a history of viral disease before the onset of symptoms. In addition to 10-760/mm3 lymphocytosis in CSF, protein increase is seen 96% of patients (1). Confusion, papilledema, cranial nerve palsy and epileptic seizures can be rarely seen in patients (10,11). In our case, there was a confusion and agitation clinic following headache.

According to the 2nd edition of the ICHD classification, brain imaging methods, among the diagnostic criteria, should be within the normal range (2). However, in a study by Bıçakcı et al. (12), a patient presented with confusion and a lesion on cranial MRI has been presented and it has been emphasized that ICHD-II criteria could be restrictive.

Several different opinions have been proposed for the etiology of HaNDL syndrome. Bartleson et al. (1), who defined the disease for the first time, suggested that both headache and pleocytosis develop in the same process rather than the CSF pleocytosis developed secondary to headache. The hypothesis of Day et al. (13) suggests that a sensitizing agent triggers vascular permeability and inflammatory reaction. Apart from these hypotheses, they emphasized that a viral infection may activate the immune system and initiate HaNDL syndrome. The most important finding supporting this hypothesis is that some patients have had a viral infection before the onset of symptoms (8,9,14). After detecting human herpes virus type 7 (HHV-7) PCR positivity in the CSF examination of a patient in a recent study by Stelten et al. (15), it has been stated that viral infection may play a role in the etiology of this disease. According to a recent hypothesis, HaNDL syndrome may have a more comprehensive pathophysiology. The authors concluded that the pathophysiology of HaNDL syndrome is holistic and that this confusion may be a clinical indicator of the disease, based on the agitation and confusion findings, excluding other causes (11).

There are some studies evaluating the potential relationship of HaNDL syndrome with migraine. In particular, Nakashima (16) stated that although this syndrome is rare and its prognosis is good, it should be considered in differential diagnosis especially in the presence of severe headache and neurological deficit. Moavero et al. (17) reported that the pathophysiology of this disease may be associated with migraine because of the presence of migraine in all three patients with HaNDL syndrome who presented with confusion. In some studies, the relationship of HaNDL syndrome with acute ischemic stroke has been investigated. However, despite prolonged neurological deficits in these studies, diffusion-weighted MRI was found to be normal in all patients (18-20). Epilepsy, encephalitis, meningitis, neurobrucellosis, neurosyphilis, reversible posterior leukoencephalopathy syndrome and central nervous system vasculitis should be considered in the differential diagnosis, apart from acute stroke and migraine (2,7,21). In our case, all microbiological tests were normal in diffusion MRI, MR angiography, cranial MRI, EEG, serum and CSF examinations.

As in our case, a few studies have been published that present some evidence of confusion and agitation associated with headache (10,11).

CONCLUSION

In the light of the literature, we believe that the acute confusion state may be a part of the HaNDL syndrome and that it may be included in the differential diagnosis of HaNDL syndrome when all other clinical conditions are excluded for all confusional clinical pathologies.

Ethics Committee Approval: Ethics committee approval is not required as it is a retrospective case evaluation, this study was carried out in accordance with the Helsinki Declaration.

Informed Consent: Patient informed consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept –TA; Design – BAA; Supervision –TA;Source- MK; Materials – YGA; Data Collection and/or Processing – TA, BAA, MK; Analysis and/or Interpretation – YGA; Literature Search – TA; Writing Manuscript – TA; Critical Review – BAA.

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