Are the Comments on HaNDL Syndrome in the ICHD-II Sufficient?

ICHD-II'ya göre HaNDL Sendromunun Yorumları Yeterli mi?

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ABSTRACT

A 33-year-old man was admitted to our emergency department for severe frontal headache followed by a state of consciousness disturbance and right-sided hemiparesis. No previous febrile disease, head trauma, vascular risk factor, and medication for any systemic disease were defined in his history. He had experienced a similar disorder three years ago and had recovered completely. Cerebrospinal fluid (CSF) analysis revealed pleocytosis and electroencephalography (EEG) showed diffuse slow wave activity. Hyperintense foci on T2 and FLAIR sequences representing bilateral cortical ischemia, prominent on the right hemisphere, were seen on MRI. Contrast-enhanced T1 images showed marked leptomeningeal thickening with enhancement. The patient was considered as having CSF lymphocytosis (HaNDL syndrome) due to temporary headache with neurologic deficit and CSF pleocytosis. Diagnostic criteria have been identified for this syndrome according to the International Classification of Headache Disorders, 2nd edition (ICHD-II). According to these criteria, neuroimaging should be normal. Positive neuroimaging findings and impairment of consciousness have been reported in a limited number of HaNDL cases so far. Diversity of neurological signs, duration and distinctness from migraine headache have been described in comment section under the diagnostic criteria. Comments are inadequate in this regard. (*Archives of Neuropsychiatry 2014; 51: 178-180*)

Key words: HaNDL Syndrome, headache, criteria, MRI lesions

ÖZET

Otuz bir yaşında erkek hasta frontal bölgede şiddetli baş ağrısı, bilinç bozukluğu ve sağ hemiparezi nedeniyle acile başvurdu. Öncesinde ateşli hastalık, kafa travması vasküler risk faktör, sistemik hastalık tanımlanmıyordu. Üç yıl önce benzer bir durum ve tam düzelme öyküsü vardı. Beyin omurilik sıvısı (BOS) analizinde pleositoz ve elektroensefalografi (EEG)'de diffuz yavaş aktivite belirlendi. MR görüntülemesinde T2 ve FLAIR sekanslarında sağ hemisferde daha belirgin olmak üzere kortikal iskemiyeye bağlı hiperintens odaklar görüldü. Kontrastlı T1 ağırlıklı görüntülerde belirgin leptomeningial tutulum ve kalınlaşma saptandı. Olgu geçici ve nörolojik defisitli geçici baş ağrısı ve BOS'da pleositoz nedeniyle HaNDL sendromu olarak değerlendirildi. HaNDL sendromu için Baş ağrısı Bozukluklarının Uluslararası Sınıflaması 2. Basım'a göre tanı ölçütleri belirlenmiştir. Bu kriterlere göre beyin görüntüleme normal olmalıdır. HaNDL sendromunda pozitif nörogörüntüleme bulguları ve bilinç bozukluğu varlığı sınırlı sayıda olguda bildirilmiştir. Nörolojik belirtiler, süresi ve migren baş ağrısı farklılıkları, çeşitliliği tanı kriterleri altında yorum bölümünde tarif edilmiştir. Yorumlar bu bağlamda yetersiz kalmaktadır. (*Nöropsikiyatri Arşivi 2014; 51: 178-180*)

Anahtar kelimeler: HaNDL sendromu, baş ağrısı, ölçütler, MRI lezyonları

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Introduction

Transient headache and neurological deficit along with the presence of lymphocytes in cerebrospinal fluid (CSF) is defined as CSF lymphocytosis (HaNDL syndrome). In the International Classification of Headache Disorders, 2nd edition (ICHD-II), the syndrome is under the topic of 'Headache attributed to nonvascular intracranial disorder'. According to ICHD-II, the diagnostic criteria are as the following: (A) Episodes of moderate or severe headache lasting hours, (B) CSF pleocytosis with lymphocytic predominance and normal neuroimaging, CSF culture and other tests for aetiology, (C) Episodes of headache accompanied by transient neurological deficits, and (D) Episodes of headache and neurological deficits recur over <3 months (1). It is a benign syndrome. Aggressive treatment is not required and most patients recover spontaneously with supportive treatment. Nonspecific abnormal electroencephalography (EEG), single-photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI) findings have been demonstrated (2,3,4,5,6,7,8,9,10,11). In this study, we present the radiological improvement period which continued longer compared to clinical findings in a male patient with HaNDL. The patient had very severe pulsatile headaches followed by agitation, confusion, impaired consciousness, visual hallucinations, and mild left hemiparesis. Our aim was to emphasize the limitations of the criteria for HaNDL by presenting this case

Case

A 33-year-old male patient was admitted to the emergency room with a very severe headache followed by consciousness disturbance. He did not describe any previous febrile disease, head trauma, vascular risk factor, and medication for any systemic disease. He had a similar clinical disorder 3 years ago, and was followed by another center for headache and consciousness disturbance without fever. He had recovered in two days without a specific treatment. According to his previous medical data, diffuse slow activity was found in EEG, whereas MRI findings were normal. He had the diagnosis of encephalitis. Lumbar puncture was not performed and no antiviral medication was given. It was reported that both the case and the first degree relatives had migrainous headaches. Agitated confusion state and subtle left hemiparesis were detected in neurological examination. Ophthalmologic examination was normal. Signs of meningeal irritation were not obtained. Non-contrast computed tomography (CT) images were normal. In lumbar puncture, the initial CSF pressure was normal and there was pleocytosis (45 leukocyte/mm³, 95% monocyte, 5% lymphocyte). Biochemical tests of CSF revealed normal values of protein, glucose, sodium, chloride and lactate (protein:37.3 mg/dL, glucose:84 mg/dL, lactate:2.85 mg/dL, chloride:128 mEq/L, LDH 42%). Complete blood count (CBC) erythrocyte sedimentation rate, CRP level, liver and kidney functioning tests were also normal. HbsAg, Anti-HCV, CMV, Toxoplasma, Borrelia, VDRL, HIV, Brucella antibodies, Antinuclear antibody (ANA) and Antineutrophil cytoplasmic autoantibody (cANCA, pANCA) were negative. B12 level, thyroid function tests, antibody measurements and serum and CSF immunoglobulin analysis were normal. CSF was negative

for oligoclonal bands. There was no fungal or bacterial growth in CSF culture. Cytologic investigation was negative twice and PCR test for tuberculosis was also negative. Urine analysis revealed no pathologic findings. On MRI, bilateral cortical ischemic foci, more widespread on the right side, were detected on T2-weighted and FLAIR images. Significant leptomeningeal thickening with contrast enhancement were detected on T1-weighted images (Figure 1 A,B). Magnetic resonance angiogram (MRA) in the first 24 hours was normal. EEG showed diffuse slow wave activity without any epileptic focus. Electrocardiogram and echocardiography tests were normal. Antiviral medications were given and a tranquilizer was administered for agitations. Neurological findings began to improve 24 hours after hospitalization. On the third day, the clinical state recovered entirely. After the third day, his medication was stopped. Repeat lumbar puncture one week later revealed no cell in CSF and no biochemical characteristic feature. EEG returned to normal. During the clinical observation, fever, nausea and vomiting were not seen. He was discharged. He had no complaint in the follow-up examination after the 3rd week. He had only rare headaches that responded to nonspecific analgesics. On the second follow-up examination after 2 months, he was back to his work and MRI findings significantly regressed. In the sixth month, MRI was entirely normal (Figure 2). He was observed for two years when he had no complaints except for rare migraine attacks and he not used any medication.

Discussion

The case was defined as HaNDL syndrome based on the clinical and laboratory findings. HaNDL syndrome was described as a diagnosis of exclusion. This syndrome was suspected in our case after excluding other diagnoses. Due to recurrent characteristics of hypertensive encephalopathy, chronic bacterial and fungal infections of the central nervous system, a current cerebrovascular accident and central nervous system vasculitis, and meningeal carcinomatosis were investigated. There were no

Figure 1. a) Contrast enhanced axial T1 images showed marked leptomeningeal enhancement. b) Hyperintense foci on coronal FLAIR sequences representing bilateral cortical ischemia, prominent on the right hemisphere were seen on MRI.

Figure 2. Six month later, MRI was normal

significant data except for CSF pleocytosis. The clinical status improved rapidly independent from the medication and there was no exacerbation when the medication ceased. During follow-up, there were no concomitant findings such as increased acute-phase reactants, fever and anemia, or alterations in pulse, blood pressure and rhythm. CNS vasculitis was excluded due to normal MRA findings in the first 24 hours and spontaneous recovery of both attacks. Dural enhancement was considered to be related to lumbar puncture. No clues for a new neurologic and systemic disease, vasculitis, chronic CNS infection and neoplasm were detected during follow-up. Follow-up MRI controls were also normal.

The exact etiology of HaNDL syndrome remains unknown and it is included in nonvascular intracranial disturbances in headache classification. According to ICHD-II - HaNDL syndrome, the clinical course begins with headache. The diagnostic criteria include neurological disturbances accompanying headache episode, CSF pleocytosis, normal test results in culture, imaging and other tests, vanishing of headache and neurological episode in 3 months. Rare situations have been emphasized in addition to the diagnostic criteria in ICHD-II (1). Diversity of neurological signs, duration and distinctness from migraine headache have been described in the comments section under the diagnostic criteria. Symptom-free periods between the attacks have been reported (1). There were two asymptomatic periods following two attacks in our case. According to ICHD-II, neurological manifestations were most commonly sensory symptoms (78% of episodes), aphasia (66%), or motor deficits (56%). Visual symptoms, which are common in migraine with aura, were not often observed (18%). Confusion has not been identified in the reports. Indeed, confusion occurs more frequently than other neurological signs (4,12). It stands out as a major sign in our case during the attacks.

EEG and SPECT scans may show focally abnormal areas consistent with the focal neurological deficits (5,6,8,11). Nakashima et al. detected a decrease of radionuclide involvement in cerebral SPECT scans in these patients (8). EEG abnormalities were detected in most of patients in HaNDL syndrome (10). Diffuse slow activity was identified in our case on EEG, which subsided in a week. In HaNDL syndrome's comments, CT, MR and MRA have always been reported to be normal. However, later studies demonstrated abnormal findings on these imaging methods (2,3,4,5,6,7,8,9,11). Yılmaz et al detected hypoperfusion in right parieto-occipital lobes on perfusion imaging, and edema in gray matter, particularly in the right hemisphere (4). Segura et al. suggested that MRI would prevent

these patients to take aggressive medication due to misdiagnosis of acute ischemia. Therefore, MRI might be the primary imaging method in these patients (9) Kurtuncu et al described left fronto-parietal leptomeningeal enhancement on MRI, left temporal and parietal lobe hypoperfusion. Arteriolar vasomotor changes during attacks have also been shown in HaNDL patients on MRI (13).

Confusion and pathologic MRI findings were the challenging aspects for HaNDL diagnosis in our case, since no data regarding these findings do not exist on ICHD-II. We suggest that these should be emphasized on ICHD-II under the comments section. This might be helpful to the clinician in differential diagnosis and in avoiding aggressive treatment.

References

1. Headache Classification Subcommittee of the International Society. The international classification of headache disorders, 2nd edn, Cephalgia 2004; 24(Suppl 1):9-160.
2. Gómez-Aranda F, Cañadillas F, Martí-Massó JF, Díez-Tejedor E, Serrano PJ, Leira R, Gracia M, Pascual J. Pseudomigraine with temporary neurological symptoms and lymphocyte pleocytosis, A report of 50 cases. *Brain* 1997; 10:1105-1113.
3. Lansberg MG, Woolfenden AR, Norbash AM, Smith DB, Albers GW. Headache with neurological deficits and CSF lymphocytosis: a transient ischemic attack mimic. *J Stroke Cerebrovasc Dis* 1999; 8:42-44.
4. Yılmaz A, Kaleagasi H, Dogu O, Kara E, Ozge A. Abnormal MRI in a patient with 'headache with neurological deficits and CSF lymphocytosis (HaNDL). *Cephalalgia* 2010; 30:615-619.
5. Caminero AB, Pareja JA, Arpa J, Vivancos F, Palomo F, Coya J. Migrainous syndrome with CSF pleocytosis. SPECT findings. *Headache* 1997; 37:511-515.
6. Fuentes B, Díez Tejedor E, Frank A. Syndrome of headache with neurological deficits and CSF lymphocytosis: a spreading depression mechanism? The role of SPECT. *Headache* 1998; 38:324.
7. Vallet AE, Desestret V, Tahon F, Cho TH, Nighoghossian N. Acute perfusion MR imaging in a HaNDL-like syndrome. *Cerebrovasc Dis* 2010; 29:98-100.
8. Nakashima K. Syndrome of Transient Headache and Neurological Deficits with Cerebrospinal Fluid Lymphocytosis: HaNDL. *Internal Medicine* 2005; 44:690-691.
9. Segura T, Hernandez-Fernandez F, Sanchez-Ayaso P, Lozano E, Abad L. Usefulness of multimodal MR imaging in the differential diagnosis of HaNDL and acute ischemic stroke. *BMC Neurology* 2010; 10:120-124.
10. Case of syndrome of headache with neurological deficits and cerebrospinal fluid lymphocytosis (HaNDL) with focal slowing on electroencephalogram. *Intern Med J* 2012; 42:944-947.
11. Kurtuncu M, Tuzun E, Kaya D, Icoz S, Baslo B, Ertas M, Akman-Demir G, Eraksoy M: Anti-neuronal antibodies associated with headache with neurological deficits and cerebrospinal fluid lymphocytosis. *J Headache Pain* 2008; 9:333-335.
12. Parissis D, Ioannidis P, Balamoutos G, Karacostas D. Confusional State in the Syndrome of HaNDL. *Headache* 2011; 51:1285-1288.
13. Kappler J, Mohr S, Steinmetz H. Cerebral vasomotor changes in the transient syndrome of headache with neurologic deficits and CSF lymphocytosis (HaNDL). *Headache* 1997; 37:516-518.