Transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (Handl Syndrome): A case report

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Abstract

The syndrome of headache with neurologic deficits and cerebrospinal fluid lymphocytosis (HaNDL) is a rare entity. This disease has been related with migrainous headaches. It is a benign disorder, self-limited, and characterized by fluctuating neurological symptoms and cerebrospinal fluid (CSF) lymphocytosis. A small proportion of patients develop intracranial hypertension as a consequence of the illness. Confusional state may be also observed.

We describe a case of a 29 years old man with acute onset of headache, dysthermia sensation, vomits, aphasia, and difficulty to perform daily activities such as unlocking the mobile phone. Blood tests as well as computed tomography (CT) and magnetic resonance imaging (MRI) were normal. Cerebrospinal fluid analysis revealed a lymphocytic pleocytosis (47 cells/µl, 100% lymphocytes). Electroencephalogram showed moderate slow rhythm in the left hemisphere, with frontotemporal predominance, and without epileptiform activity. With the diagnosis of HaNDL syndrome the patient was accepted in the Department of Neurology and discharged asymptomatic without treatment.

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While approximately 75% of HaNDL cases have a monophasic course, to self-limit in few hours [11]. Neurologic deficits typically last 15-120 minutes with moderate-severe intensity. Its duration is variable, although it is usual to self-limit in few hours [11]. Neurologic deficits include hemiparesis and hemisensory deficits (which often migrate in a fashion consistent with a cortical spreading depression), aphasia (HANDL hemiparesis and hemisensory deficits (which often migrate in a fashion consistent with a cortical spreading depression), aphasia (HANDL), elevated intracranial pressure (ICP) and papilledema [1], and photopsia/photophobia), and less commonly, acute confusional state (including decreased vision, homonymous hemianopsia, and cortical spreading depression-associated cerebral oligoemia has been observed during HaNDL attack, and may play a significant role [8,16].

Diagnosis of HaNDL syndrome is confirmed after having ruled out other diseases of the central nervous system according to the diagnostic criteria showed in Table 1. CSF pressure and protein are generally elevated at the time of diagnosis, and neuroimaging is usually normal. EEG during the acute symptoms may show slowed rhythm, like our case [11,14]. Some authors suggested to perform a CT angiography in patients affected of HaNDL syndrome, neuroimaging tests normal, and suspected diagnosis of vasculitis [8,11,16].

Table 1. Diagnostic criteria of the syndrome of transient headache and Neurologic deficits with cerebrospinal fluid lymphocytosis, according to the International Headache Society [4].

| A. Episodes of migraine-like headache fulfilling criteria B and C |
|---------------------------------------------------------------|
| - Accompanied or shortly preceded by the onset of at least one of the following transient neurological deficits lasting > 4 hours |
| a. Hemiparesis |
| b. Dysesthesia |
| c. Hemiparesis |
| - Associated with cerebrospinal fluid (CSF) lymphocytic pleocytosis (>15 white cells/μL) with negative etiological studies |

| B. Both of the following: |
|--------------------------|
| a. Associated with cerebrospinal fluid (CSF) lymphocytic pleocytosis (>15 white cells/μL) with negative etiological studies |

| C. Evidence of causation demonstrated by either or both of the following: |
|-----------------------------------------------------------------------|
| - Headache and transient neurological deficits have developed or significantly worsened in temporal relation to the CSF lymphocytic pleocytosis or led to its discovery |
| - Headache and transient neurological deficits have significantly improved in parallel with improvements in the CSF lymphocytic pleocytosis |
| - Not better accounted by another International Classification of Headache Disorders, 3rd edition diagnosis |

In conclusion, HaNDL, a rare disease with diverse clinical manifestations, remains a diagnosis of exclusion. It may be explained on the basis of migrainous or post-viral/inflammatory pathophysiology. The prognosis of this illness is benign and the treatment is symptomatic. However, symptoms including elevated IPC, papilledema and brain herniation may be observed, recquiring urgent treatment. We describe a HaNDL case trying to improve the knowledge of this pathology.

Conflicts of interest

No conflict of interest shown in the realization of this writing.

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Discussion

The syndrome of headache with neurologic deficits and cerebrospinal fluid lymphocytosis (HaNDL) is a rare entity comprising sudden onset migrainous headaches (generally in headache-naïve individuals) accompanied by a constellation of fluctuating neurological symptoms and CSF lymphocytosis. Neurological symptoms include hemiparesis and hemisensory deficits (which often migrate in a fashion consistent with a cortical spreading depression), aphasia (HANDL favours the left hemisphere), nausea, vomiting, visual disturbance (including decreased vision, homonymous hemianopsia, and photopsia/photophobia), and less commonly, acute confusional state [9,10], elevated intracranial pressure (ICP) and papilledema [11], and cerebral herniation [8], which worsen the prognosis.

The headache, observed frequently after the neurological symptomatology, may be hemicranial or holocranial, pulsatile, and moderate-severe intensity. Its duration is variable, although it is usual to self-limit in few hours [11]. Neurologic deficits typically last 15-120 minutes, although a range of 5 minutes to 3 days has been reported. While approximately 75% of HaNDL cases have a monophasic course, repeated attacks that occur for weeks or even months following the initial attack have been reported. When repeated attacks are observed, neurological deficits may vary due to the involve of different brain regions [2,3,5].

HaNDL is most frequently observed during the third and fourth decades of life, with no consistent gender predominance identified [3,5,6]. However, some case reports are observed in adolescents and childhood [12,13]. The etiopathogenesis of HaNDL is poorly understood. Some patients report a preceding non-specific viral prodromal illness [6,14], but studies have failed to provide a definite viral association [2,3]. The presence of antibodies directed against the CACNA1H subunit of the T-type voltage-gated calcium channel in one small study supported the inflammatory or autoimmune hypothesis [15]. Cortical spreading depression-associated cerebral oligoemia has been observed during HaNDL attack, and may play a significant role [8,16].

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Figure 1. Magnetic resonance imaging (MRI) showing any disturbs.
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