

HaNDL syndrome: transient headache and neurological deficits with cerebrospinal fluid lymphocytosis

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ABSTRACT

We report the case of a 54-year-old woman with multiple presentations to the emergency department with severe headache, transient variable neurological deficits and normal investigations aside from CSF lymphocytosis. This represents a rare but under-diagnosed condition, transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL) syndrome.

HaNDL is an important differential diagnosis for headache. We summarise the current knowledge about its clinical course, diagnosis and typical investigation findings.

Case report

A 54-year-old woman presented to an emergency department (ED) out-of-area with several days of bilateral headache, mild meningism, nausea and vomiting. She had several short-lived episodes of migratory neurology; suffering patches of bilateral asymmetrical numbness, slurred speech, blurred vision and confusion, which lasted from minutes to hours. There was no viral prodrome. She had a past medical history of infrequent migraine with aura. She had no regular medications, reported minimal alcohol use and had no risk factors for immunosuppression or atypical infections. On initial presentation her obser-

vations, examination, blood tests (full blood count, renal and liver function, electrolytes, coagulation screen, CRP) and CT head were normal. Her symptoms settled with analgesia and she was discharged with a diagnosis of migraine.

She re-presented to the emergency department several days later with ongoing symptoms. She had since suffered several episodes of short-lived expressive dysphasia. Examination and blood tests were again normal. A lumbar puncture (LP) was performed for possible meningoencephalitis. This demonstrated a marked lymphocytosis, raised protein, minimal red cells and a normal glucose (Table 1).

Table 1: CSF results for patients with comparable normal values.

CSF component	Value	Normal range
Appearance	Clear and colourless	Clear and colourless
White cells	428x10 ⁶ /L	0–5x10 ⁶ /L
Lymphocytes	98%	N/A
Monocytes	2%	N/A
Red cells	1x10 ⁶ /L	0x10 ⁶ /L
Protein	2.03g/L	0.15–0.45g/L
Glucose	3.0mmol/L	2.8–4.4mmol/L
Gram stain	No organisms seen	Nil organisms
Culture	No growth after three days	Nil growth

Table 2: Differential diagnoses for recurrent severe headache, lymphocytosis and neurological symptoms.

Differential diagnoses for recurrent severe headache, lymphocytosis and neurological symptoms			
Migraine variants	Lyme disease	Neurosyphilis	Neurobrucellosis
Granulomatous and neoplastic arachnoiditis	Varicella-zoster/herpes simplex encephalitis	CNS vasculitis	Recurrent encephalitis (MELAS, anti-NMDA receptor encephalitis)
CNS mycoplasma infection	Benign recurrent lymphocytic meningitis	Neurolupus	HaNDL
Reversible cerebral vasoconstrictive syndrome	Drug-induced aseptic meningitis	Posterior reversible encephalopathy syndrome	

She was commenced on IV Aciclovir. CSF viral PCR was negative for HSV, VZV and enterococcus, therefore Aciclovir was stopped and the patient discharged after resolution of symptoms.

Unfortunately, her symptoms returned and she re-presented the next day with ongoing severe headache and new episodic transient right-sided hemiplegia. The differential diagnoses were therefore broadened (Table 2). An MRI of brain, HIV test, auto-immune screen and CSF immunoglobulins were also normal.

The otherwise normal investigations and symptoms led to the final diagnosis of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL) syndrome.

Discussion

HaNDL is a self-limiting headache disorder that typically lasts under three months¹ but may rarely recur over the space of many years.² It generally affects adults aged 30–40 years, though can occur at any age, including children.^{1,3}

It is characterised by:

- Episodic headaches, usually severe⁴
- Transient neurological deficits involving different neurovascular territories¹ including:
 - Sensory symptoms (78%)
 - Aphasia (66%)
 - Motor symptoms (56%)
 - Visual symptoms (8%)
 - Confusion (very rare)
- CSF lymphocytosis¹

- Normal neuroimaging, CSF culture and other tests for aetiology.⁵

Headaches typically last between several hours to days and are separated by symptom-free intervals.¹ Neurological deficits can occur prior to, during or after headache. Prodromal symptoms, including fever, may also be present. Previous migraine is reported in roughly a third of patients.¹ No long-term sequelae are seen.¹

Investigations demonstrate raised CSF protein, lymphocytosis, normal glucose with frequently raised opening pressures.^{1,5-6} Oligoclonal bands are absent.⁶ CSF changes resolve over time,⁵ and microbiological tests are typically normal.¹ MRI and CT-head are usually normal.^{1,5} EEGs show transient focal slowing in affected hemispheres in the majority of cases.^{6,7} Single-positron emission CT scans (SPECT) can show hypoperfusion of brain areas during both symptomatic and asymptomatic phases and hyperperfusion of previously symptomatic areas.^{6,8}

The aetiology of HaNDL remains unknown. Initially believed to be an atypical migraine,^{1,9} this view has fallen out of favour. Strong evidence is lacking for an infective cause, except rare inconsistent reports.^{1,10}

Conclusion

HaNDL is a rare and probably under-diagnosed disease. It should be considered in cases of recurrent presentations of previously presumed viral meningitis. Despite dramatic symptomology, it has an excellent prognosis and normally spontaneously resolves over several months. Its cause remains unknown.

Competing interests:

Nil.

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