CASE REPORT

Getting a handle on complicated migraine

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SUMMARY

We describe a case of a 45-year-old man who presented with a transient syndrome consisting of headache with neurological deficits. Neuroimaging including brain angiography was normal. Cerebrospinal fluid (CSF) analysis revealed an elevated protein and lymphocytic pleocytosis. The diagnosis of a syndrome of Headache and Neurological Deficits with CSF Lymphocytosis (HaNDL) was made after excluding all the other possible causes for the patient's presentation. He made an excellent recovery following a short course of naproxen sodium.

BACKGROUND

Headache and Neurological Deficits with cerebrospinal fluid Lymphocytosis (HaNDL) was initially described in 1980.¹ It remains a diagnosis of exclusion. Therefore, extensive microbiological tests should be performed to exclude the broad range of conditions that might give a similar clinical picture.

A review article by Nelson² concluded that the pathophysiology of HaNDL is not entirely known, and it has a possible relationship with migraine. In particular, there is evidence for spreading cortical depression and reduced radionuclide uptake on single photon emission CT (SPECT), suggestive of hypoperfusion in both conditions. However, while the two conditions may have analogous pathophysiology, the major discriminating factors are the monophasic nature of HaNDL as well as the presence of cerebrospinal fluid (CSF) lymphocytosis, which are not typically features of migraine.

CASE PRESENTATION

A 45-year-old right-handed man presented to the hospital with gradually evolving throbbing right-sided headache of moderate-to-severe intensity, nausea, nominal aphasia and transient left hand weakness. The symptoms resolved completely after 7 h.

The onset of headache was preceded by right hemiparaesthesia evolving over 10 min, and transient visual blurring causing impaired peripheral vision bilaterally and lasting less than 5 min. There was no associated photophobia or phonophobia, and no symptoms of autonomic dysfunction.

The patient reported two similar stereotypical episodes occurring in the previous 2 weeks, with full recovery between attacks. The patient had no viral or febrile illness prior to the onset of the symptoms.

There was no history of migraine in the patient or his family. No vascular risk factors were identified.

On admission, the vital signs were normal; the patient was alert and fully oriented. No focal

neurological deficit or signs of meningeal irritation were identified. Fundoscopic examination was normal.

No formal neuropsychological evaluation was performed as the patient was entirely normal at the time of examination. However, bedside testing did not reveal any deficits in language, writing or cognition.

INVESTIGATIONS

Laboratory investigations, including full blood count, coagulation profile and kidney function, were unremarkable. The inflammatory markers were normal with an erythrocyte sedimentation rate of 11 mm/h and a C reactive protein of 2.1 mg/L. Anti-N-methyl-D-aspartate receptor antibodies (anti-NMDA) were negative.

A CT of the brain was normal. MRI of the brain and MR angiography were unremarkable; including diffusion weighted imaging (DWI).

CSF analysis revealed elevated protein at 100 mg/dL, 88 white cells/ μ L (100% lymphocytes) and normal glucose. No oligoclonal bands were detected. Microscopy and culture were negative, including mycobacterial. Testing for herpes simplex, varicella zoster and enteroviruses by PCR was negative. Serological testing for HIV, *Mycoplasma* and *Borrelia* was negative.

DIFFERENTIAL DIAGNOSIS

The patient presented with a recurring paroxysmal syndrome comprising focal neurological symptoms and headache. Migraine with aura presents in broadly this fashion, but there are some atypical features: the patient is presenting with his first 'migraine' in his midforties; the aura also is atypical for migraine in that visual symptoms are minimal in contrast to evanescent sensorimotor symptoms. The aura in this patient lasts several hours in contrast to the migrainous aura, which typically fades in under an hour. Additionally, the presence of a reactive CSF would be against migraine.

Perhaps the patient is having transient ischaemic attacks (TIAs)? Several aspects of the history argue against this hypothesis: the lack of a single vascular distribution to explain the symptoms; the gradual onset of symptoms; the duration of symptoms and their stereotypical nature all make TIA a less likely diagnosis. Stereotypical events are unlikely to be due to TIA, and alternatives such as migraine or focal seizures should be considered. However, rarely, focal hypoperfusion due to critical arterial stenosis can cause TIA, often stereotyped and related to upright posture. Although, originally, TIAs are defined as a sudden onset of focal

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neurological symptoms/signs lasting less than 24 h, TIAs nearly always last less than an hour.³

Seizures should be considered in the differential, but this is unlikely because of absence of prominent positive phenomena. In addition, the course of the symptoms is too prolonged and evolutionary for a seizure disorder.

An emerging central nervous system vasculitis deserves consideration, but it is unlikely given the evanescent nature of the syndrome, and absence of MRI abnormalities and absence of progression of deficits.

Hashimoto's encephalopathy could also feature bouts of paroxysmal cortical dysfunction with a reactive CSF profile, though spontaneous resolution without corticosteroids would be unlikely.

Although the CSF is consistent with an aseptic meningitis, there are no clinical signs of meningism and no systemic features to suggest an infectious or inflammatory process. In addition to this, the patient was not taking medications that could induce an aseptic meningitis.

A recent observation is that incomplete forms of anti-NMDA receptor encephalitis may mimic HaNDL.⁴ However, anti-NMDA antibodies were not detected in our patient, making this an unlikely diagnostic consideration.

We are left with HaNDL as the only plausible explanation for the patient's presentation.

TREATMENT

The patient was treated with a short course of naproxen sodium 250 mg two times per day with an excellent response. He has remained well without recurrence of symptoms 9 months from the initial presentation.

DISCUSSION

HaNDL is characterised by episodes of transient neurological deficits accompanied or followed by moderate-to-severe headache. The average duration of the transient neurological deficits is 5 h. Sensory symptoms are common (78%), followed by aphasia (66%) and motor deficits (56%). Visual symptoms occurred in only 12% of episodes.⁵

Antecedent viral illness has been reported in 25–40% of cases.^{5 6} This has led to the hypothesis of viral infection triggering an autoimmune process with production of autoantibodies capable of inducing an aseptic inflammation of cranial vessels. However, the exact pathogenesis remains unclear.

MRI including DWI is usually normal. However, few reports have demonstrated global hemispheric or focal regions of hypoperfusion that matched with neurological deficits in acutely symptomatic patients with HaNDL.^{7 8} Ictal SPECT may show focal area of decreased uptake. Cerebral angiography is normal in the vast majority of cases, however, it has been found to trigger the episodes in some cases.⁹ EEG shows transient focal slowing in the affected hemisphere in three-quarters of the patients.^{5 10}

On CSF analysis, elevated opening pressure (up to 400 mm H₂O) was found in 56% of cases, high-protein levels (up to 250 mg/dL) in more than 90% and lymphocytosis (10–760 cells/mL), normal glucose and no oligoclonal bands are identified.⁵

SPECT can be used to differentiate HaNDL from other conditions, such as focal meningoencephalitis, where an increase in radionuclide uptake is expected.¹¹ SPECT does not differentiate between HaNDL and migraine, as there is reduction in radionuclide uptake in both conditions.

Learning points

- ▶ Detailed history taking is essential in the evaluation of patients who present with headache.
- ▶ Headache and Neurological Deficits with cerebrospinal fluid Lymphocytosis (HaNDL) is a monophasic, self-limiting condition that resolves usually within a few months from onset without any neurological consequences.
- ▶ It mimics migraine with the notable exception of the prolonged aura, the prominence of sensorimotor aura over visual symptoms and the presence of a reactive cerebrospinal fluid.
- ▶ HaNDL remains a diagnosis of exclusion. The differential diagnosis is very broad and therefore extensive investigations should be carried out to exclude the other possibilities.

Competing interests None declared.

Patient consent Obtained.

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