A Patient of Migraine-like Headache with Amnesia, Pleocytosis and Transient Hypoperfusion of Cerebral Blood Flow

Yukiko TADA, Kiyoshi NEGORO, Masaaki ABE, Jun-ichi OGASAWARA, Motoharu KAWAI and Mitsunori MORIMATSU*

Abstract

Pseudomigraine with pleocytosis (PMP) is an uncommon disease in Japan. The diagnostic criteria include at least one episode of transient neurological deficit accompanied or followed by migraine-like severe headache, cerebrospinal fluid (CSF) lymphocytosis, and normal neuroimaging. Both the etiology and the pathophysiology of PMP is not yet well defined. We report a 40-year-old man with a PMP-like syndrome. He came to our clinic because of severe throbbing headache and amnesia, and the examination showed CSF lymphocytosis of 23/mm³, a transient decrease of cerebral blood flow in the left thalamus. All the symptoms were completely resolved within 2 months.

(Key words: pseudomigraine with pleocytosis (PMP), syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL), amnesia, cerebral blood flow, triptan)

Introduction

In 1981, Bartleson et al (1) proposed pseudomigraine with pleocytosis (PMP) in 7 patients, and PMP is clinically characterized by 1) moderate or severe headaches with one or more transient neurological deficits, 2) the disappearance of attacks within 2 months, 3) pleocytosis with a negative reaction on a bacteriologic test, 4) the absence of neuroradiological abnormalities other than a transient decrease in cerebral blood flow, and 5) the absence of epileptic waves on electroencephalograms. In this study, we report a patient with migraine-like severe headache-associated amnesia, pleocytosis, and a transient decrease in cerebral blood flow, which resembled PMP.

For editorial comment, see p 690.

Case Report

A 40-year-old man without a contributory family history had a 10-year history of migraine attacks involving left occipital pain without aura, which had occurred once every 2 to 3 months; he had received a commercially available analgesic agent. Since July 20, 2002, a marked tight sensation involving the entire head had persisted, and pulsating occipital pain with nausea and vomiting had frequently appeared, therefore, the patient consulted the outpatient clinic in our department on August 5. There were no findings suggesting inflammation, neurological findings including meningeal irritation, or abnormalities on cephalic MRI, and tizanidine hydrochloride, etizolam, and zolmitriptan were prescribed. Thereafter, oral administration of zolmitriptan rapidly improved headaches (the detailed data are unclear; however, there is a possibility that the patient continuously received 6 tablets of zolmitriptan in a short duration). On August 9 at 7:00 PM, the patient repeatedly inquired his family at home about the date of, and consulted our department at 8:00 PM as an emergency case; however, at this time, the symptom had improved, and neither consciousness disorder nor memory disorder was observed, suggesting transient global amnesia (TGA). Thereafter, the patient also repeatedly inquired something, and on August 13 (holiday), his family brought him to our department as he had telephoned his office several times, and he was admitted.

On admission he was 171 cm tall and weighted 86 kg. His...
vital signs showed a body temperature of 36.6°C and blood pressure of 140/95 mmHg, with a 88/min pulse rate. There was memory disorder, mild disorientation, and reduction of calculation ability, and the patient scored 13 (date-1 point, calculation-2 points, counting the numbers backward-1 point, additional counting-6 points, five articles-2 points, name of vegetables-5 points) according to a revision of Hasegawa’s Intelligence Scale (HDS-R); however, there were no other abnormal findings including meningeal irritation. Hematology on admission showed increases in the erythrocyte and leukocyte counts (RBC: 5,710,000/µl, WBC: 11,100/µl, Ht: 52.9%, CRP: 0.01 mg/dl) and a slight increase in the fibrinogen level (396 mg/dl); however, there were no other abnormal findings. Electroencephalography did not reveal any abnormal findings including epileptic abnormal waves. Brain magnetic resonance imaging (MRI) did not reveal any abnormal findings on T1-weighted or T2-weighted images, diffusion-weighted images, fluid-attenuated inversion recovery (FLAIR) images, or MR angiograms on admission and 3 days after admission. 99mTc-HMPAO-single photon emission computed tomography (SPECT) on admission revealed a decrease in blood flow in the left frontal and temporal lobes and the left thalamus; however, 3 days later, additional examination showed improvement of blood flow in the left thalamus (Fig. 1). A cerebrospinal fluid test was delayed because informed consent could not be obtained from the patient, but was performed on August 23. The mononuclear cell count was slightly increased (23/mm³). In addition, pressure was normal, and the levels of protein and sugar were 29 mg/dl and 63 mg/dl, respectively.

After admission, intravenous drip of low molecular weight dextran was started, considering the possibility of cerebral infarction; however, on August 16, the patient was discharged based on the patient’s desire. Thereafter, he consulted the outpatient clinic twice, and according to the HDS-R, scores were 18 on August 23 and 20 on August 30, showing gradual improvement in memory disorder. About 2 months after the appearance of migraine-like headaches, the patient returned to his job with the complete disappearance of the symptoms.

Discussion

Recently, the number of patients with migraine-like attacks with neurological symptoms complicated by pleocytosis has been increasing. Previous case reports of PMP (1–6) are summarized in Table 1. Migraine more frequently develops in women, whereas the incidence of PMP is relatively higher in men, and most man patients do not have a history of migraine. The proportion of patients with findings suggesting inflammation, such as fever, cold-like precursory symptoms, and leukocytosis, is relatively high, although the grade is mild. Concerning the feature, moderate to severe pulsating headaches have been reported, and the proportion of patients with nausea/vomiting or light/sound hypersensitivity was also high. It has been reported that approximately 60% of the patients have bilateral headaches, and that the mean duration of headaches is 19 hours. As for neurological symptoms, the incidences of paresthesia, aphasia, and hemiplegia are high, whereas the incidences of meningeal irritation and optic agnosia as the aura of migraine are low. There is no case report in which the main symptom is amnesia, as observed in the present patient, in the literature. The mean duration of neurological symptoms was 5 hours, and the mean treatment period was 49 days. Cerebrospinal fluid findings included an increase in the mononuclear cell count (10–760/mm³), an increase in pressure, and an increase in the protein level in a large number of patients.

In the new International Classification of Headache Disorders (ICHD-II) (7), PMP is defined as “Syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL)” in the section “Part two: The secondary headaches. 7. Headache attributed to nonvascular intracranial disorder”, and is distinguished from migraine. Familial hemiplegic migraine (FHM) mainly causes hemiplegia and severe pulsating headaches, and has been clarified to be associated with abnormalities in the gene (CACNA1A) determining a P/Q type Ca channel α1A subunit, which is present in the short arm of the No. 19 chromosome (19p13) (8). It has been reported that patients with migraine rarely show a cerebrospinal fluid cell count of 5 to 15/mm³ or more (2, 9). In most patients with FHM, pleocytosis is observed (10), and such cases are difficult to differentiate from PMP. A recent study performed gene investigation in 8 patients in whom clinical findings suggested PMP, and reported that there were no abnormalities in the CACNA1A gene as observed in patients with FHM (11). In addition, diseases such as viral meningoencephalitis, granulomatous meningitis, neural syphilis, central infection with Borrelia or Mycoplasma, collagen disease-related angiitis, cancerous meningitis, and Mollaret meningitis should be differentiated from PMP (2, 3).

The etiology and pathogenesis of PMP remain to be clarified; however, there are two hypotheses: viral infection activates immune response, stimulating the trigeminal terminal of the pachymeninx blood vessel, or aseptic inflammation in the meningeal vascular system causes transient vascular headaches and neurological symptoms via a mechanism resembling cortical spreading depression (12). In the present patient, pleocytosis and a decrease in cerebral blood flow at the area associated with neurological symptoms were also observed, and the clinical course suggested a similar pathogenesis.

Migraine is considered as a strong etiology of TGA as well as an epileptic or vascular mechanism. There are several studies which investigated the association between migraine and TGA (13, 14). In the present patient, the characteristic symptom of repeating the same question also suggested TGA early after onset; however, amnesia persisted for 24 hours or more after onset, and TGA was ruled out. Triptan preparation-induced TGA has been reported in 1 patient (15); a 54-year-old woman continuously received an ergotamine...
Figure 1. SPECT findings in the present our patient. On admission (A), a decrease in blood flow in the left frontal and temporal lobes and the left thalamus was observed (arrows); however, additional examination 3 days after admission (B) showed improvement of blood flow in the left thalamus (arrowhead).
preparation and sumatriptan succinate at migraine attacks, and showed TGA as a clinical symptom, whereas imaging revealed thalamic infarction. In the present patient, it was also speculated that vasospasm related to excessive administration of zolmitriptan was etiologically involved in protracted neurological symptoms; however, the state of taking the agent was not clarified, and the association was unclear.

References


Table 1. A Summary of Representative Cases of Pseudomigraine with Pleocytosis

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient No. (man/woman)</th>
<th>Age (mean)</th>
<th>Personal history of migraine</th>
<th>Infectious sign</th>
<th>Duration of syndrome</th>
<th>Neurological symptoms</th>
<th>CSF lymphocytes (/mm$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartleson et al (Neurology, 1981)</td>
<td>7 (3/4)</td>
<td>16–50</td>
<td>0%</td>
<td>57%</td>
<td>7–84 days</td>
<td>sensory&gt;motor</td>
<td>33–188</td>
</tr>
<tr>
<td>Berg et al (Neurology, 1995)</td>
<td>36 (27)</td>
<td>7–52</td>
<td>24%</td>
<td>40% (cold)</td>
<td>1–84 days</td>
<td>sensory&gt;visual</td>
<td>16–350</td>
</tr>
<tr>
<td>Gómez-Aranda et al (Brain, 1997)</td>
<td>50 (28)</td>
<td>14–39</td>
<td>26%</td>
<td>22% (fever)</td>
<td>6 h–49 days</td>
<td>sensory&gt;aphasia</td>
<td>10–760</td>
</tr>
<tr>
<td>Caminero et al (Headache, 1997)</td>
<td>4 (3)</td>
<td>26–44</td>
<td>0%</td>
<td>25% (fever)</td>
<td>1–10 days</td>
<td>motor&gt;visual</td>
<td>75–590</td>
</tr>
<tr>
<td>Nomura et al (Clin Neurol, 2002)</td>
<td>1 (woman)</td>
<td>28</td>
<td>(–)</td>
<td>(leukocytosis)</td>
<td>2 months</td>
<td>left hemiparesis, visual symptom</td>
<td>14</td>
</tr>
<tr>
<td>Tsukamoto et al (Clin Neurol, 2003)</td>
<td>1 (woman)</td>
<td>20</td>
<td>(+)</td>
<td>(cold)</td>
<td>5 days</td>
<td>right hemiparesis, aphasia</td>
<td>50</td>
</tr>
<tr>
<td>Present case</td>
<td>1 (man)</td>
<td>40</td>
<td>(+)</td>
<td>(leukocytosis)</td>
<td>2 months</td>
<td>amnesia</td>
<td>23</td>
</tr>
</tbody>
</table>

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