CASE REPORT

Polyarteritis Nodosa in Association with Subarachnoid Hemorrhage

Masahiro Oomura, Takemori Yamawaki, Hiroaki Naritomi, Tadashi Terai, and Koji Shigeno

Abstract

We report a 65-year-old man with classic polyarteritis nodosa (PAN) who developed subarachnoid hemorrhage. Polyarteritis nodosa was strongly suspected, however, the biopsy specimens of kidney and sural nerve showed no findings of vasculitis and the serum titer of antmyeloperoxidase-antineutrophil cytoplasmic autoantibody (MPO-ANCA) was negative. Cranial magnetic resonance angiography showed no findings of aneurysms. He developed subarachnoid hemorrhage (SAH) during the course and died. Autopsy confirmed fibrinoid necrosis in the medium-sized artery of multiple organs. To our knowledge, this is the first report of a case of classic PAN accompanied by SAH in which MPO-ANCA proved negative.

Key words: polyarteritis nodosa, subarachnoid hemorrhage, intracranial aneurysm, ANCA

(DoI: 10.2169/internalmedicine.45.1632)

Introduction

Polyarteritis nodosa (PAN) is a rare multisystem disease characterized by systemic necrotizing arteritis of small- and medium-sized arteries (1). The skin, joints, kidneys, gastrointestinal tract, and peripheral nerves are most commonly involved (1). It is reported that the prevalence of central nervous system (CNS) complication ranges from 20% to 45% and the most common CNS involvement is diffuse encephalopathy (2). Although aneurysmal formation in visceral arteries is common in patients with PAN, aneurysms are rarely found in intracranial arteries (1, 2). We report a PAN patient who developed fatal subarachnoid hemorrhage (SAH) probably due to rupture of intracranial aneurysm.

Case Report

A 65-year-old man was admitted to our department in September 2002, complaining of gait disturbance and fever. He had been in good health until January 2002, when he noticed painful cutaneous eruptions in both legs. Eight months before admission, he started to complain of gait disturbance and leg pain. Angiography of the legs showed no specific changes suggestive of macroangiopathy. Two months before admission, gait disturbance had exacerbated to the extent that he could not walk by himself. One week before admission, he became febrile.

On admission, his body temperature was increased to 37.1°C, his heart rate was 94 beats per minute, and blood pressure, 120/70 mmHg. Livedo reticularis was observed in the trunk and four extremities. His face lost spontaneous expression. Neurological examination disclosed slight muscle weakness in the four extremities and decreased deep tendon reflexes in the legs. There was no definite involvement of the cranial nerves. There was no rigidity or tremor noted in the extremities. Pain and touch sensations were intact. No ataxia was noted in the extremities. He had unstable gait and bradykinesia

Received for publication November 4, 2005; Accepted for publication March 17, 2006
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creased to 13.4 mg/dl (<0.5). The findings of cerebrospinal fluid included increased protein to 78 mg/dl (<45) and IgG to 13.5 mg/dl (<4), respectively. There was no pleocytosis in cerebrospinal fluid. There were no definite conduction blocks in the extremities by evoked electrophysiological test, although sural nerve was not evoked bilaterally. Transthoracic echocardiography showed no vegetation in the cardiac valves. Magnetic resonance (MR) image and MR angiography obtained on the 7th day of hospitalization detected no abnormal lesion including cerebral aneurysms except for mild ischemic change in the white matter (Fig. 1A). The ischemic change was considered to be due to atherosclerotic change. The basal ganglias were free from infarction. Biopsy specimens were obtained from the sural nerve, kidney, and skin of the left leg. No apparent vasculitis was found in these biopsied specimens. Although there was no pathological confirmation, we strongly suspected PAN based on clinical and laboratory findings. We administered methylprednisolone 1,000 mg/day intravenously for 3 days, then prednisolone 60 mg/day orally. Although the serum CRP level decreased after steroid administration, the gait disturbance remained unchanged. On the 42nd day of hospitalization, he suddenly became comatose and the respiration stopped. Cranial computed tomography disclosed a high density area in the basal cistern corresponding to SAH (Fig. 1, B and C). The SAH was prominent in the infratentorial area. The coma and respiratory arrest were considered to be caused by brainstem involvement due to SAH. He was placed on a mechanical ventilator. Because of severe neurological states, surgical treatment was not indicated. Finally, he died on the 49th day of hospitalization. Permission to perform an autopsy was obtained. Grossly, the brain showed edema and congestion. SAH was observed around the cerebellum and brainstem. Microscopic examination demonstrated fibrinoid necrosis, which is characteristic of PAN, in the medium-sized arteries of the kidneys (Fig. 1D), peritoneum (Fig. 1E), esophagus, stomach, jejunum, ileum, gallbladder, and adrenal glands. This vasculitic change was rarely observed in the arterioles, capillaries, and venules. Crescent formation was not observed in the glomeruli. Because of severe brain damage due to long-term artificial respiration, microscopic examination of brain could not be performed.

Discussion

PAN is a rare multisystem disease characterized by necrotizing arteritis of small- and medium-sized arteries (1). The most commonly affected sites include the skin, joints, kidneys, gastrointestinal tract, and peripheral nerves (1). The neurological manifestations of PAN are protean and can mimic almost any clinical syndromes. The most common neurological manifestation of PAN is mononeuropathy multiplex caused by vasculitis of the vasa nervosum (1). The involvement of the central nervous system is less common and
tends to occur later in the disease. Involvement of the central nervous system in patients with PAN reported previously includes diffuse encephalopathy, cerebral infarction, and epilepsy, all of which are considered to be caused by vasculitis of intracranial arteries (2).

His gait disturbance was considered attributable to bradykinesia and myalgia. Myalgia is a common complaint in patients with PAN but it is unlikely that inflammatory myopathy occurred because pathological findings of myositis were lacking and the serum level of CPK was within normal limits. He had no facial expression and bradykinesia. Although the description of Parkinsonian symptoms in patients with PAN is rare, it is possible to consider that the masked face and bradykinesia encountered in our patient were attributable to PAN (3).

Generally, a combination of prednisone and cyclophosphamide is recommended to treat PAN cases in the active phase (1). In the present case, cyclophosphamide was not administered. We considered that the toxic side effects of cyclophosphamide could not counterbalance its therapeutic effect because there was no pathological confirmation of PAN.

Visceral aneurysms such as in the gastrointestinal system and kidney are common in patients with PAN, whereas aneurysms of intracranial arteries are exceptionally rare (1, 2). To our knowledge, only eight cases have been reported previously (Table 1) (4-11). Of these eight cases, six developed SAH and another developed intracerebral hemorrhage. In the present case, postmortem examination could not identify intracranial aneurysms because of severe brain damage caused by long-term artificial respiration. It is, however, considered definitive that the abundant SAH in the infratentorial space was caused by rupture of aneurysm in the vertebral or basilar arteries. Of the above-mentioned eight PAN cases with intracranial aneurysms, three cases had aneurysms in infratentorial arteries (8, 9, 11). In these three cases, aneurysms were located in the superior cerebellar, anterior inferior cerebellar, or intracranial vertebral arteries. The size of aneurysms was small in two of them (8, 9).

Table 1. Reported Cases of Polyarteritis Nodosa with Intracranial Aneurysms

<table>
<thead>
<tr>
<th>References</th>
<th>Age</th>
<th>Gender</th>
<th>Type of Stroke</th>
<th>Location of AN</th>
<th>Size of AN</th>
<th>MPO-ANCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gherardi et al (1967)</td>
<td>26</td>
<td>female</td>
<td>SAH</td>
<td>ACA</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>Leonhardt et al (1972)</td>
<td>16</td>
<td>male</td>
<td>no hemorrhagic stroke</td>
<td>multiple</td>
<td>small</td>
<td>N.D.</td>
</tr>
<tr>
<td>Travers et al (1979)</td>
<td>N.D.</td>
<td>N.D.</td>
<td>SAH</td>
<td>MCA, ICA</td>
<td>2mm</td>
<td>N.D.</td>
</tr>
<tr>
<td>Beattie et al (1995)</td>
<td>50</td>
<td>male</td>
<td>SAH</td>
<td>Acom, ICA</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>Munn et al (1998)</td>
<td>20</td>
<td>male</td>
<td>SAH</td>
<td>SCA, VA, ICA, MCA</td>
<td>5mm</td>
<td>N.D.</td>
</tr>
<tr>
<td>Oran et al (1999)</td>
<td>10</td>
<td>male</td>
<td>ICH</td>
<td>AICA, SCA</td>
<td>small</td>
<td>N.D.</td>
</tr>
<tr>
<td>Takahashi et al (2002)</td>
<td>70</td>
<td>male</td>
<td>SAH</td>
<td>ACA</td>
<td>N.D.</td>
<td>positive</td>
</tr>
<tr>
<td>Thompson et al (2003)</td>
<td>38</td>
<td>female</td>
<td>SAH</td>
<td>VA</td>
<td>N.D.</td>
<td>positive</td>
</tr>
<tr>
<td>This case</td>
<td>65</td>
<td>male</td>
<td>SAH</td>
<td>probably VA</td>
<td>unknown</td>
<td>negative</td>
</tr>
</tbody>
</table>

Abbreviations: AN, aneurysm; SAH, subarachnoid hemorrhage; ICH, intracerebral hemorrhage; ACA, anterior cerebral artery; ICA, internal carotid artery; MCA, middle cerebral artery; Acom, anterior communicating artery; SCA, superior cerebellar artery; AICA, anterior inferior cerebellar artery; VA, vertebral artery; N.D., not described; MPO-ANCA, antomyeloperoxidase antineutrophil cytoplasmic autoantibodies.
they are small in size. In the present case, MR angiography on the 7th day of hospitalization failed to detect aneurysm. The reason for this can be explained by three possibilities: First, the aneurysm was too small to be detected by MR angiography, second the location of the aneurysm was out of the range of interest on MR angiography, and third the aneurysm developed after MR angiography. Because the SAH developed 35 days after the MR angiography was obtained, the third possibility is considered to be unlikely. MR angiography on the 7th day of hospitalization did not cover the vertebral arteries. It is considered likely that the aneurysm was not detected by MR angiography because of its location in the vertebral artery or its small size.

Recently, PAN is classified into two types, one the classic PAN in which medium-sized arteries are mainly involved, and the other the microscopic PAN in which small-sized vessels are mainly involved with or without the involvement of medium-sized arteries (14). MPO-ANCA, autoantibody for myeloperoxidase in neutrophil, is highly positive in patients with microscopic PAN and negative in patients with classic PAN (14). The present case is categorized as classic PAN on the basis of the pathological findings showing predominant involvement of medium-sized arteries and a negative MPO-ANCA titer.

The diagnosis of classic PAN is rather difficult because of lack of specific signs, symptoms or diagnostic serologic tests. The diagnosis is often established on the basis of vasculitic findings in biopsied specimen (1). In our case, however, biopsied specimen failed to show fibrinoid necrosis, and the definite diagnosis of classic PAN could be made only by the autopsy. In patients with suspicion of PAN, cerebral angiography should be considered even if MR angiography indicates no association of aneurysm, since fatal SAH may result from the rupture of small aneurysms in supra- and infra-tentorial arteries.

References


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