Guillain-Barré syndrome as the first manifestation of POEMS syndrome

Zespół Guillain-Barrégo jako pierwsza manifestacja zespołu POEMS

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Abstract

POEMS syndrome is a rare multisystem disorder, characterized by the presence of polynuropathy, organomegaly, endocrinopathy, monoclonal protein and skin changes. The variety of clinical pictures and asynchronous manifestation of dominant features make diagnosis difficult.

We report a case of a 42-year-old man with polynuropathy who was initially negative for monoclonal protein and so Guillain-Barré syndrome was diagnosed. Other signs and symptoms, including monoclonal gammopathy, developed later in the course of the disease and finally POEMS syndrome was diagnosed.

Key words: POEMS syndrome, polynuropathy, monoclonal protein.

Introduction

POEMS syndrome is a rare systemic disease. Other names for the disease are Crow-Fukase syndrome, Takatsuki syndrome, and PEP osteosclerotic myeloma (plasma cell dyscrasia, endocrinopathy, polynuropathy) [1-3]. The acronym POEMS refers to major components of this syndrome: polynuropathy, organomegaly, endocrinopathy, monoclonal gammopathy (M protein) and skin lesions. The term POEMS was used for the first time by Bardwick in 1980 [4,5].

The highest risk of POEMS is in the fourth to sixth decades of life, with men almost three times more likely to be affected. The mean age of onset is 48 for men and 59 for women. Five-year survival is observed in approximately 60% of patients.

POEMS syndrome is one of the paraneoplastic syndromes. It develops most often in the course of osteoscler-
vertebral discs without clinical significance. Previously performed MRI of the thoracic spine revealed no abnormalities. Electroneurography showed signs of demyelination as well as of axonal lesion of motor and sensory nerves of upper and lower limbs (Table 1).

The patient fulfilled the clinical (progression of paraparesis beyond 4 weeks), electrophysiological (prolonged distal latencies and slowing of motor conduction velocities) and laboratory (spinal fluid albumin-cytological dissociation) criteria for Guillain-Barré syndrome [7]. Plasma exchange was introduced (five sessions) but without any benefit. The patient was referred to the rehabilitation department for further treatment.

Four months later, the patient was once again admitted to the Department of Neurology due to progressing weakness of the lower and upper limbs and recurrent dyspnoea. Neurological examination revealed symmetrical weakness of the upper (2/5) and lower (0/5) limbs, lack of tendon reflexes in all extremities and diminished superficial sensation in the hands and feet. Fundus examination showed bilateral papilloedema. Numerous skin lesions of telangiectasia type as well as hyperpigmentation on the chest and upper limbs were present. Severe oedema of the legs was observed. The patient was subfebrile. A chest computed tomography (CT) scan revealed bilateral aplectatic and inflammatory changes, bilateral hydrothorax and enlarged mediastinal lymph nodes. Antibiotics were administered and – as shown by a subsequent CT – pneumonia faded away, but some fluid in both pleural cavities and enlargement of the mediastinum persisted. An ultrasound of the abdomen revealed hepatosplenomegaly and ascites. Cerebrospinal fluid total protein level was significantly increased (418 mg/dL), but the cytosis was normal (3 cells/μL). At that time, immunofixation showed the presence of monoclonal protein (IgA, lambda light chains) in serum, cerebrospinal fluid and urine. The findings raised the suspicion of POEMS syndrome. Expanded diagnostics toward endocrinopathies disclosed an elevated level of serum TSH (thyroid stimulating hormone) (9.2 mIU/L, normal = 0.27-4.2) and

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**Table 1. Nerve conduction study results**

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Distal latency (ms)</th>
<th>Conduction velocity (m/s)</th>
<th>Amplitude (mV)</th>
<th>F wave min. latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right median</td>
<td>4.0</td>
<td>35.5</td>
<td>4.9</td>
<td>43.8</td>
</tr>
<tr>
<td>Right ulnar</td>
<td>3.4</td>
<td>38.1</td>
<td>5.4</td>
<td>42.7</td>
</tr>
<tr>
<td>Left peroneal</td>
<td>no response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left tibial</td>
<td>no response</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Nerve</th>
<th>Conduction velocity (m/s)</th>
<th>Amplitude (μV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right median</td>
<td>44.8</td>
<td>7.4</td>
</tr>
<tr>
<td>Right ulnar</td>
<td>34.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Left sural</td>
<td>34.1</td>
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an increased level of free thyroid hormones FT4 (6.4 pmol/L, normal = 12-22) and FT3 (2.67 pmol/L, normal = 3.95-6.8). The substitution treatment of hypothyroidism was started. The cause of the lower leg oedema was not identified: lower limbs venal ultrasonography was unremarkable, and total serum protein and albumins were within the normal range.

Bone marrow biopsy gave no evidence of any myeloproliferative disorder. Abdominal CT revealed a tumour, probably metastatic, destroying the sacral bone. The patient did not agree to a tumour biopsy. He was referred for palliative treatment.

**Discussion**

To diagnose POEMS syndrome, it is necessary to confirm the presence of polyneuropathy and monoclonal gammopathy (both are considered to be major diagnostic criteria). Moreover, at least one of the following minor criteria must be present: sclerotic bone changes, organomegaly, endocrinopathy, Castleman disease, papilloedema, peripheral oedema, skin changes, hydrothorax or ascites [1,2,4,8].

The presented patient finally fulfilled five minor diagnostic criteria, in addition to two obligatory major ones.

Other symptoms often observed in POEMS syndrome, although not included in the diagnostic criteria, are blood disorders (thrombocytosis, polycythaemia), congestive cardiomyopathy, pulmonary hypertension, obstructive pulmonary disease, thromboembolism, vitamin B12 deficiency, weight loss, excessive sweating, diarrhoea and fever [9,10].

The pathomechanism responsible for the multiorgan involvement in POEMS remains unclear. The important role of vascular endothelial growth factor (VEGF) was suggested. Significantly elevated levels (in serum, but not in cerebrospinal fluid) of VEGF were found in patients with POEMS and it may be responsible for microangiopathy. Increased concentrations of proinflammatory cytokines such as interleukin (IL)-1β, IL-6 and tumour necrosis factor (TNF)-α were also observed [8,11-14].

Monoclonal gammopathy, a disorder caused by the uncontrolled proliferation of a single cell clone producing one class of immunoglobulin (M protein), is responsible for approximately 10% of chronic acquired peripheral neuropathies in adults. It is therefore very important that the panel of laboratory tests performed in patients with acquired neuropathies should also include serum proteins immunofixation. Multiple myeloma (with or without amyloidosis), osteosclerotic myeloma, primary systemic amyloidosis, Waldenström macroglobulinaemia and benign monoclonal gammopathy of undetermined significance (MGUS) are the most common disorders responsible for peripheral neuropathy related to monoclonal gammopathy [15,16]. Elevated CSF protein is usually present in cases of polyneuropathy due to sclerotic myeloma and it can be observed also in Waldenström macroglobulinaemia and MGUS [17]. In such cases with motor or mixed symptomatology, Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy may be suspected.

Polyneuropathy in POEMS begins with sensory symptoms and signs, most often affecting distal parts of the upper and lower limbs. Later, ascending motor deficits develop. Electrophysiological testing reveals both demyelinating and axonal loss of motor and sensory fibres.

In the presented case, the acute onset as well as the results of clinical, electrophysiological and laboratory evaluation, at first, strongly supported the diagnosis of Guillain-Barré syndrome. At that time, monoclonal protein was not found in serum and cerebrospinal fluid.

In patients with POEMS syndrome, monoclonal protein is present primarily in serum (90-95%), rarely in cerebrospinal fluid. It is an IgA or IgG class protein consisting exclusively or almost exclusively of lambda light chains [1,4,8]. The appearance of monoclonal protein in serum or other body fluids varies from case to case and it is sometimes considerably delayed in relation to other systemic symptoms. On the other hand, the disappearance of monoclonal protein in serum may lead to the withdrawal of POEMS symptoms.

In reported cases of POEMS, it was a rule that when clinical symptoms of neuropathy developed, monoclonal gammopathy was always present. It was exceptional in our patient that during the initial evaluation, in spite of severe incapacitating polyneuropathy, monoclonal protein was not found.

**Disclosure**

Authors report no conflict of interest.

**References**


