CASE REPORT/*OPIS PRZYPADKU*

Guillain-Barré syndrome as the first manifestation of POEMS syndrome

Zespół Guillaina-Barrégo jako pierwsza manifestacja zespołu POEMS

Monika Sójka[1], Agata Gajos[1,2], Justyna Pigońska[1,2], Marek Bogucki[1], Krzysztof Tyfa[3], Andrzej Bogucki[1,2]

[1]Kliniczny Oddział Neurologii z Pododdziałem Chorób Układu Pozapiramidowego, III Szpital Miejski im. dr. Karola Jonschera w Łodzi
[2]Klinika Chorób Pozapiramidowych, Uniwersytet Medyczny w Łodzi
[3]Zakład Radiologii, III Szpital Miejski im. dr. Karola Jonschera w Łodzi

Neurologia i Neurochirurgia Polska 2012; 46, 3: 284-287
DOI: 10.5114/ninp.2012.29136

Abstract

POEMS syndrome is a rare multisystem disorder, characterized by the presence of polyneuropathy, 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 polyneuropathy 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, polyneuropathy, monoclonal protein.

Streszczenie

Zespół POEMS należy do rzadkich chorób układowych, charakteryzujących się występowaniem polineuropatii, organomegalii, endokrynopatii, obecnością białka monoklonalnego i zmian skórnych. Różnorodny obraz kliniczny oraz niewystępowanie głównych objawów w jednym czasie znacznie utrudniają i opóźniają diagnostykę.
W pracy przedstawiono przypadek 42-letniego mężczyzny z obwodową polineuropatią, u którego początkowo nie stwierdzono obecności białka monoklonalnego i rozpoznano zespół Guillaina-Barrègo. Później ujawniły się inne objawy i ostatecznie rozpoznano zespół POEMS.

Słowa kluczowe: zespół POEMS, polineuropatia, białko monoklonalne.

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, polyneuropathy) [1-3]. The acronym POEMS refers to major components of this syndrome: polyneuropathy, 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 osteoscle-

Correspondence address: Monika Sójka, Kliniczny Oddział Neurologii z Pododdziałem Chorób Układu Pozapiramidowego, III Szpital Miejski im. dr. Karola Jonschera w Łodzi, ul. Milionowa 14, 93-113 Łódź, e-mail: mosojka@go2.pl
Received: 2.04.2011; accepted: 29.09.2011

rotic (60%) and mixed (30%) myeloma. It can also coexist with systemic diseases such as systemic lupus erythematosus [6].

Heterogeneous clinical onset without the simultaneous occurrence of symptoms significantly interferes with diagnosis and makes diagnosis of POEMS difficult.

Case report

A 42-year-old man was hospitalized for the first time following a five-week history of persistent paraesthesias of the hands and feet and progressive weakness of the lower limbs. His medical history was unremarkable. On admission, neurological examination revealed diminished upper limb tendon reflexes, paraparesis (more pronounced distally – 3/5, than proximally – 4/5; the patient required an aid to walk), impaired superficial sensation in the feet and abolished tendon reflexes in the lower limbs.

The results of laboratory tests (blood count, biochemistry, coagulogram, proteinogram, serum thyroid hormones, and vitamin B_{12} levels) were normal. Cerebrospinal fluid albumin-cytological dissociation was present (protein 144 mg/dL, cytosis – 2 cells/μL). No monoclonal protein was found in serum or spinal fluid.

Lumbo-sacral spine magnetic resonance imaging (MRI) showed mild bulges of L4/L5 and L5/S1 intervertebral 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 atelectatic 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 mU/L, normal = 0.27-4.2) and

Table 1. Nerve conduction study results

Motor nerve conduction				
Nerve	**Distal latency (ms)**	**Conduction velocity (m/s)**	**Amplitude (mV)**	**F wave min. latency (ms)**
Right median	4.0	35.5	4.9	43.8
Right ulnar	3.4	38.1	5.4	42.7
Left peroneal		no response		
Left tibial		no response		
Sensory nerve conduction				
Nerve		**Conduction velocity (m/s)**		**Amplitude (μV)**
Right median		44.8		7.4
Right ulnar		34.3		2.3
Left sural		34.1		2.5

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 B_{12} 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)-1-β, 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

1. Koike H., Sobue G. Crow-Fukase syndrome. *Neuropathology* 2000; 20: 69-72.
2. Lizis-Kolus K., Kowalska A., Nowakowska-Domagała M. The POEMS syndrome with coexisting endocrinopathy – case report. *Pol J Endocrinol* 2007; 58: 238-243.

3. Dispenzieri A., Kyle R.A., Lancy M.Q., et al. POEMS syndrome: definitions and long-term outcome. *Blood* 2003; 101: 2496-2506.
4. Gandhi G.Y., Basu R., Dispenzieri A., et al. Endocrinopathy in POEMS syndrome: The Mayo Clinic experience. *Mayo Clin Proc* 2007; 82: 836-842.
5. Vital C., Vital A., Ferrer X., et al. Crow-Fukase (POEMS) syndrome: a study of peripheral nerve biopsy in five new cases. *J Peripher Nerv Syst* 2003; 8: 136-144.
6. Murphy N., Schumacher H.R. Jr. POEMS syndrome in systemic lupus erythematosus. *J Rheumatol* 1992; 19: 796-799.
7. Asbury A.K., Cornblath D.R. Assessment of current diagnostic criteria for Guillain-Barré syndrome. *Ann Neurol* 1990; 27 (Suppl): S21-S24.
8. Laurenti L., Matteis S., Sabatelli M., et al. Early diagnosis followed by front-line autologous peripheral blood stem cell transplantation for patients affected by POEMS syndrome. *Leuk Res* 2008; 32: 1309-1312.
9. Dispenzieri A. POEMS syndrome. *Blood Rev* 2007; 21: 285-299.
10. Yilmaz M., Okan V., Pehlivan M., et al. A case of POEMS syndrome developing during the clinical course of immune trombocytopenic purpura. *Platelets* 2007; 18: 540-542.
11. Sharabi Y., Raanani P., Shenkar A., et al. Plasma cell dyscrasia with polyneuropathy – POEMS syndrome presenting with vasculitic skin lesions and responding to combination chemotherapy. *Leuk Lymphoma* 2000; 40: 209-213.
12. Lee M.R., Choi H.J., Lee E.B., et al. POEMS syndrome complicated by extensive arterial thromboses. *Clin Rheumatol* 2007: 26: 1989-1992.
13. Nakajima H., Ishida S., Furutama D., et al. Expression of vascular endothelial growth factor by plasma cells in the sclerotic bone lesions of a patent with POEMS syndrome. *J Neurol* 2007; 254: 531-533.
14. Mineta M., Hatori M., Sano H., et al. Recurrent Crow-Fukase syndrome associated with increased serum levels of vascular endothelial growth factor: a case report and review of the literature. *Tohoku J Exp Med* 2006; 210: 269-277.
15. Gajos A., Kielis W., Szadkowska I., et al. Nabyte neuropatie obwodowe w przebiegu gammapatii monoklonalnych. *Neurol Neurochir Pol* 2007; 41: 169-175.
16. Lozeron P., Adams D. Monoclonal gammopathy and neuropathy. *Curr Opin Neurol* 2007; 20: 536-541.
17. Herskovitz S., Scelsa S.N., Schaumburg H.H. Peripheral neuropathies in clinical practice. *Oxford University Press*, New York 2010, pp. 113-126.