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POEMS syndrome presents with a distended abdomen: A case report

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Abstract

POEMS syndrome is a rare, serious, multisystem disorder and its diagnosis is frequently missed due to its varied clinical presentation. We report here, a 69-year-old woman with initial complaints of distended abdomen, who was misdiagnosed with tuberculosis but failed anti-tuberculosis treatment. Further examinations showed peripheral neuropathy, monoclonal plasma cell disease, sclerotic bone lesions, an elevated serum vascular endothelial growth factor (VEGF) concentration, lymph node hyperplasia, endocrine abnormalities, and skin hyperpigmentation. A diagnosis of POEMS syndrome was made and the patient responded to lenalidomide-based chemotherapy.

Keywords

Ascites, peripheral neuropathy, plasma cell disease, sclerotic bone lesions, POEMS syndrome

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Background

POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes) syndrome is a rare, serious, multisystem disorder.[1] Signs and symptoms may include progressive sensorimotor polyneuropathy, organ enlargement, endocrine disorders, a monoclonal plasma cell proliferative disorder, sclerotic bone lesions, lymph node hyperplasia, elevated vascular endothelial growth factor (VEGF) levels, oedema, darkening of the skin (hyperpigmentation) and papilledema.[1] Diagnosis can be missed because its signs and symptoms mimic those of other disorders. We describe here, a patient who presented with abdominal distention and ascites and was initially misdiagnosed with peritoneal tuberculosis. By sharing our experience of this case, we hope to make clinicians aware of this rare disorder.

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Case report

A 69-year-old woman who had been experiencing generalized weakness and leg swelling for a year presented to the clinic. Over the past 10 months she had developed a distended abdomen and her hands and feet were numb and cold. She also reported that her mouth and eyes felt dry at times. She had lost 5 kg in weight over the past 12 months but had not experienced any fever or night sweats. Her medical history included hypertension and diabetes, but these were well controlled. Family history showed that her husband had been treated for tuberculosis (TB) 33 years ago.

Six months previously, she had visited the clinic of a local hospital and underwent an ultrasonographic examination that showed ascites. She underwent paracentesis and was prescribed diuretics but had a poor response. Two months later, an abdominal computed tomography (CT) scan showed multiple lymph node swellings with high calcified shadows, and a CT-guided peritoneal lymph node biopsy showed lymphatic tissue and granuloma formations. At that time, a diagnosis of TB was made. The patient was prescribed triple anti-tuberculotic treatment (i.e., isoniazid 300 mg qd, ethambutol 0.75 g qd, and rifapentine 0.6 g bi-weekly). One month later, because of persistent ascites, 1 g pyrazinamide qd and 10 mg prednisolone qd were added to her treatment regimen, but her response was poor.

At the current clinic visit, physical examination showed normal vital signs, but she had several 0.2–0.4-cm red nodules on her forehead, chest, and abdominal wall (Figure 1). The patient also had perioral hyperpigmentation (Figure 2) and enlarged lymph nodes in the axillary areas, but her heart and lung examinations were unremarkable. Abdominal examination showed a distended abdomen, slight epigastric tenderness, and shifting dullness, with no rebound tenderness. Bowel sounds were heard four times/minute, and there was pitting oedema in both legs. Neurological examination showed slight weakness, with a muscle strength of 4/5 in her four extremities. The patient's laboratory, biopsy, and image results are shown in Table 1. The patient also exhibited the following: signs of nerve damage; slowed nervous transmission; IgG λ type M protein positivity; numerous sclerotic bones with increased densities (Figure 3); VEGF level of 1595 pg/ml; multiple lymph node swellings. An axillary lymph node biopsy showed clustered plasma cells (Figure 4). Elevated cortisol levels, subclinical hypothyroidism, hyperpigmentation, paracentesis, and pitting oedema in both of legs were also noted.

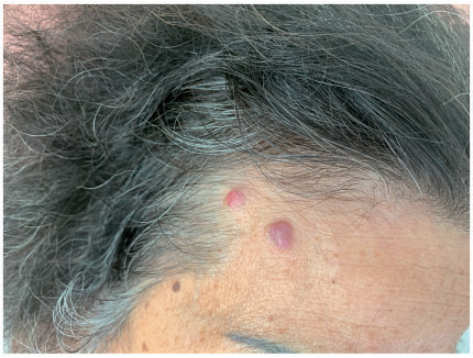

Figure 1. Forehead haemangiomas. Multiple 0.2–0.4-cm red nodules were observed on the patient's forehead.

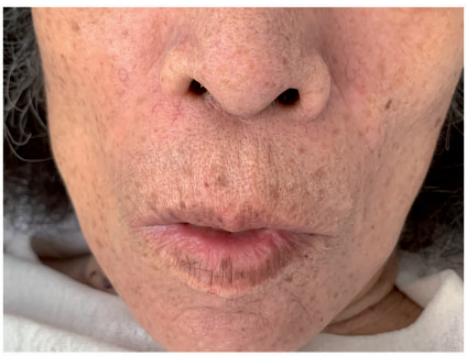

Figure 2. Perioral hyperpigmentation.

Table 1. Laboratory analyses, biopsies, and imaging results.

Tests	Results
Laboratory tests	
Routine blood tests	CRP, 13.3 mg/l; WBC, 5.41×10^9/l; Hb, 10^5 g/l; platelets, 221×10^9/l; albumin, 28 g/l
Tumour markers	CA125, 45.3 IU/ml
Immunity testing	ANA and ANCA (−)
Tuberculosis test	T-spot (−)
Serum immune electrophoresis	IgG λ type M protein (+)
VEGF	1595 pg/ml (reference 0–142 pg/ml)
Endocrine-related examinations	Elevated cortisol (18.1 μg/dl, reference 2.9–17.3 μg/dl). Subclinical hypothyroidism (TSH, 6.6 μIU/ml; reference 0.4–5.0 μIU/ml)
Procedure and biopsies	
Paracentesis	Yellow clear fluid, serum ascites albumin gradient >11 g/l, without acid-fast bacilli
Bone marrow biopsy	Hyperplastic bone marrow; possible plasma cells, 0.5%
Axillary lymph node biopsy	Clustered plasma cells
Forehead nodule biopsy	Haemangioma
Thyroid left lobe nodule fine-needle puncture biopsy	Benign
Imaging studies	
Electromyography	Nerve damage and slow nervous transmission
Leg Doppler ultrasonography	Right venous thrombosis
Lymph node ultrasonography	Multiple lymph node swellings
Chest and abdominal contrast-enhanced CT	Multiple sclerotic bones with increased densities

ANA, Antinuclear antibody; ANCA, Antineutrophil cytoplasmic antibody; CRP, C-reactive protein; Hb, haemoglobin; TSH, thyroid-stimulating hormone; VEGF, Vascular endothelial growth factor; WBC, white blood cell count.

A diagnosis of POEMS syndrome was made because the patient had two mandatory criteria (i.e., peripheral neuropathy and monoclonal plasma cell disease), three major criteria (i.e., sclerotic bone lesions, an elevated VEGF level, and lymph node hyperplasia disease), and three minor criteria (i.e., endocrine abnormalities, skin hyperpigmentation, and ascites and leg edema).[1] After determining the diagnosis, we initiated lenalidomide-based chemotherapy (i.e., lenalidomide 25 mg qd for three weeks and dexamethasone 40 mg weekly for four weeks). The patient was also prescribed diuretics for her oedema and 25 μg levothyroxine od for subclinical hypothyroidism. Three months after the two courses of treatment, the patient's ascites had gradually reduced and her body weakness had improved significantly, although she still experienced slight numbness in her hands and feet. At her most recent follow-up examination, her condition was stable.

This case study was approved by Medical Ethics Committee of the Aerospace Center Hospital in Beijing, China and signed informed consent was obtained from the patient for publishing her anonymised data. The reporting of this study conforms to CARE guidelines.[2]

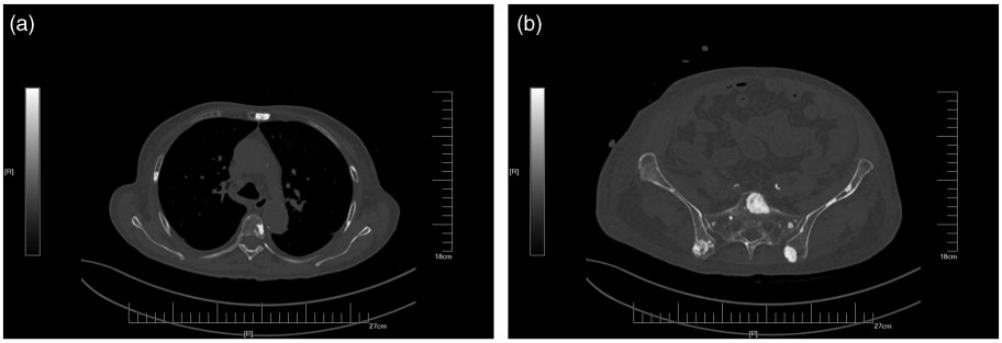

Figure 3. Computed tomography scan shows multiple sclerotic bones with increased densities. (a) Sternum bone density shadow and (b) sacrum and ilium bone density shadow.

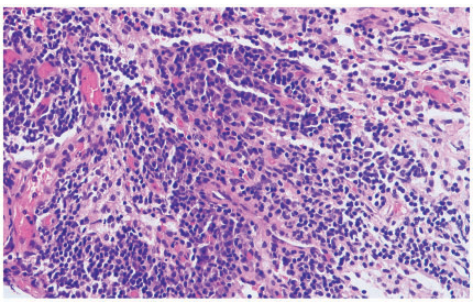

Figure 4. Axillary lymph node biopsy shows clustered plasma cells.

Discussion

POEMS syndrome reflects a combination of symptoms due to multi-organ disorders. Mandatory diagnostic criteria include peripheral neuropathy and monoclonal plasma cell disease, with the latter almost always of the λ-light-chain type.[1] Other diagnostic criteria for the syndrome include, sclerotic bone lesions, elevated VEGF levels, and lymph node hyperplasia with prevalence rates of 97%, 68%, and 15%–25%, respectively.[1] There is also a requirement to meet at least one minor diagnostic criteria (i.e., endocrine abnormalities [67%]; skin changes [68%]; organ enlargement [50%]; excess vascular capacity [29%]; thrombocytosis/polycythaemia [50%] visual nipple oedema [29%]).[1] A diagnosis of POEMS syndrome is confirmed when both of the mandatory criteria, one of the three major criteria, and at least one of the six minor criteria are fulfilled.[1]

As her main complaint, our patient presented with a distended abdomen that was unresponsive to paracentesis and diuretics; peritoneal lymph node biopsy had shown granulomas, suggesting tuberculosis but anti-TB treatment was ineffective. Further evaluations showed numerous plasma cells at lymph node biopsy. In addition, she manifested peripheral neuropathy, elevated VEGF levels, subclinical hypothyroidism, serum-positive M protein, hyperpigmentation, and ascites. These signs and symptoms supported a diagnosis of POEMS syndrome. Moreover, her positive response to lenalidomide-based chemotherapy was consistent with a diagnosis of this disorder.

A possible reason for the initial misdiagnosis of TB, is that, POEMS syndrome is a rare condition and so clinicians are unfamiliar with its signs and symptoms which can mimic those of TB (i.e., cough, lymphadenopathy, fever, weight loss, tuberculous peritonitis). Extravascular capacity overload is one of the main clinical presentations of POEMS syndrome. A study conducted in the USA, showed that while 24% of patients with POEMS syndrome had peripheral

oedema, only 7% had ascites and 3% had pleural effusion.[1] Although the pathogenesis of POEMS syndrome is unknown, pro-inflammatory factors and VEGF are thought to be responsible for the microvascular disease, oedema, fluid accumulation, increased vascular permeability, and neuropathy.[3–5] Indeed, patients with POEMS syndrome tend to exhibit serum VEGF levels 5–10 times higher than normal controls or individuals with other neurological disorders.[6,7] In a study of 105 patients that included, 29 with POEMS syndrome, and 76 with other disorders, investigators reported that at a VEGF level >200 pg/ml showed a diagnostic sensitivity of 68% and specificity of 95% in support of a POEMS diagnosis.[8]

Symptoms usually begin with tingling and perceived coldness in the extremities. Over 50% patients develop severe muscle weakness that can lead to difficulty in climbing stairs, rising from a chair, or gripping objects.[9] Patient physical examinations shows symmetrical sensory motor neuropathy, with muscle weakness being more obvious than sensory loss and electromyography shows slow nerve conduction.[1] Bone sclerosis is a major feature that distinguishes POEMS syndrome from TB, sarcoidosis, multiple myeloma, and lymphoma. In the US study, routine radiographic examinations showed 97% patients with sclerotic bone damage.[1] Of the patients with bone damage, 51% manifested sclerotic damage together with soluble bone damage, and only 2% showed soluble damage alone; the pelvis, spine, ribs, and distal extremities are frequently affected.[10,11] The constellation of λ-restricted monoclonal gammopathy, plasma cell rimming around lymphoid aggregates, and megakaryocytic hyperplasia in a bone marrow biopsy is highly suggestive of POEMS syndrome, especially in the context of a peripheral neuropathy.[12] Lymph node hyperplasia is another feature associated with POEMS syndrome, and a series of case studies confirmed the presence of lymph node hyperplasia in 25 of 43 lymph node biopsy specimens.[13,14]

Endocrine abnormalities vary, with an overall incidence of 84%.[15] In a study of 170 patients with POEMS syndrome, hyperprolactinemia, male breast development, hypothyroidism and mildly elevated thyroid-stimulating hormone levels were observed in 10, 10, 14, and 14 patients, respectivley.[15] Skin changes (i.e., hyperpigmentation, haemangioma, and capillary dilation) have been reported in approximately two-thirds of patients, with up to 30% patients experiencing thrombosis.[1]

There is currently no standard treatment for POEMS syndrome.[16–18] Targeted radiotherapy is preferred when patients manifest 1–3 isolated bone lesions without bone marrow involvement, and systemic lenalidomide-based chemotherapy is preferred in patients with extensive osteoporotic lesions or bone marrow involvements.[18,19] Two small, prospective studies of lenalidomide combined with dexamethasone showed a remission rate of over 70% and a three-year progression-free survival rate of 60–75%.[20,21] Consistent with these findings, our patient improved significantly after receiving lenalidomide-based treatment, and had reduced ascites with an improvement in her muscle weakness.

POEMS syndrome is a rare and serious disorder where affected patients can present with various initial complaints as a consequence of multisystem involvement. The collection of a detailed medical history, physical examination, and adequate knowledge regarding this rare disorder is critical for a timely diagnosis and appropriate treatment. We have reported this case with the aim of reminding clinicians about this rare disorder and so prevent misdiagnosis.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

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