CASE REPORT

POEMS syndrome: a rare cause of exudative ascites and chronic peripheral neuropathy

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SUMMARY

POEMS syndrome (Peripheral neuropathy, Organomegaly, Endocrinopathy, M protein, Skin changes) is a rare plasma cell disorder with multisystem involvement. A 40-year-old man with a chronic history of unexplained peripheral neuropathy, presented with exudative ascites. He was found to have an incidental osteolytic lesion of the sacrum proven to be a plasmacytoma. Immunoelectrophoresis for monoclonal protein was negative.

In addition, the patient was found to have hepatosplenomegaly, erectile dysfunction, hyperprolactinaemia and hypothyroidism. The patient, was given steroid along with lenalidomide, and showed a good clinical response.

BACKGROUND

Although ascites is not an uncommon finding in POEMS (Peripheral neuropathy, Organomegaly, Endocrinopathy, M protein, Skin changes) syndrome, POEMS syndrome itself is a rare cause of ascites and often not considered in the differential diagnosis. By reporting this case our objective is to draw attention to this condition and to emphasise the importance of a holistic approach towards common symptoms particularly if unexplained.

CASE PRESENTATION

A 40-year-old man presented to the Accident and Emergency Department with a 3-month history of worsening abdominal distension and bilateral lower limb oedema. His history started in 2013, with bilateral pedal oedema after which he visited his family physician. Investigations revealed normal liver, kidney and cardiac functions and so he was reassured and advised for leg elevation. In June 2014, he developed progressive left leg and foot weakness for which he visited a private hospital. A lumbosacral MRI was requested and revealed an extradural lesion compressing the dural sac, which was subsequently excised and histopathology showed angiolipoma. He was started on regular limb physiotherapy but his symptoms did not improve.

One month later, he developed paraesthesia and worsening weakness which progressed over 8 months to involve the right leg after which he became paraplegic. Few months later, he started to have gradual abdominal distension associated with worsening bilateral lower limbs oedema until his presentation to our hospital in June 2015. He

had no significant past medical history apart from impaired glucose tolerance. On further history, he had an 8-month history of erectile dysfunction, and a 2-month history of unexplained hyperhidrosis. The rest of the systematic review is unremarkable. He is working as a businessman, is not a smoker and consumes alcohol occasionally.

On presentation, his vital signs were normal. He had no signs of jaundice, anaemia, cyanosis or lymphadenopathy, however there was marked pitting oedema in the lower limbs. Chest and cardiovascular examination were unremarkable. Abdominal examination revealed abdominal distension with shifting dullness suggestive of ascites, and hepatosplenomegaly, but no stigmata of chronic liver disease. Neurological examination revealed normal cranial nerves and no cerebellar signs, however there was significantly diminished power in the distal muscles (3/5), and to a lesser extent in the proximal muscles (4/5). Lower limb reflexes were absent, with downgoing plantars bilaterally. Sensation was diminished in both lower limbs in a stocking pattern. Upper limb examination was unremarkable.

INVESTIGATIONS

His blood tests revealed a normocytic normochromic anaemia (Hb=11.2 g/dL, mean corpuscular volume =82 fl, mean corpuscular haemoglobin =28 pg), with a high platelet count (609). His haematinics revealed a low vitamin B₁₂ (143 pg/mL (ref 187–883)). His erythrocyte sedimentation rate was normal, as were his bone profile, renal and liver function tests. Hepatitis and HIV serology tests were negative, as was a full autoimmune screen (including rheumatoid factor, antinuclear antibody, anti-dsDNA). Hormonal analysis revealed several abnormalities—including primary hypothyroidism, hyperprolactinaemia and hypergonadotropic hypogonadism. Serum immune electrophoresis did not reveal monoclonal protein, and urine Bence Jones protein was negative.

HORMONAL PROFILE RESULTS

T3=3.0 (ref 3.5–6.5 PMOL/L)

T4=7.5 PMOL/L (ref 11.5–22.7)

Thyroid stimulating hormone=16.92 uiu/mL (ref 0.55–4.78 UIU/ML)

Prolactin=990 mIU/L (ref 187–883)

Testosterone 1.0 nmol/L (ref 9.9–27.8)

Follicular stimulating hormone=8.4 mIU/mL (ref 1.5–12.4)

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Figure 1 CT scan of abdomen showing hepatosplenomegaly and ascites.

Luteinising hormone=12.2 mIU/mL(ref 1.7–8.6)

A CT scan of abdomen and pelvis showed hepatosplenomegaly with severe ascites (figure 1) and intra-abdominal lymphadenopathy with osteolytic lesion in the sacrum (figure 2). The ascites was subsequently tapped and analysis revealed an exudative picture (with WBC 152 (99 % lymphocytic), protein 4.6 g/dL with serum ascitic albumin gradient of 0.7 g/dL). Ascitic adenosine deaminase (ADA) level was normal and acid fast Bacilli stain and culture as well as tuberculosis PCR tests were negative.

Following neurology review, nerve conduction studies were requested revealing a severe mixed sensorimotor neuropathy affecting all limbs, though much more pronounced in the lower limbs.

A positron emission tomography (PET) scan was requested to evaluate the sacral lesion: it showed intense metabolic activity (SUV max of 12.5) at the left aspect of the sacral bone (around L5–S1), strongly suggesting a neoplastic process (figure 3).

A CT-guided biopsy of sacral lesion was then performed, with cytological analysis revealing sheets of moderately differentiated plasma cells positive for CD138, with monoclonal expression of λ Ig light chains and no expression of CD45 or CD20 (figure 4). This confirmed the diagnosis of plasmacytoma.

Figure 2 CT scan of pelvis showing an osteolytic lesion at the left aspect of the sacral bone.

Figure 3 PET scan showing intense metabolic activity (SUV max of 12.5) at the left aspect of the sacral bone.

Subsequently a bone marrow biopsy was obtained showing a mildly hypercellular bone marrow for age with trilineage haematopoiesis and subtle infiltrate of plasma cells. The plasma cells were highlighted by CD138 immunostaining and showed monoclonal expression of λ Ig light chain consistent with plasma cell dyscrasia (figure 5). Of note, cytogenetic analysis of the bone marrow sample showed a normal male karyotype and the additional FISH probe panels for multiple myeloma were negative.

Further blood tests were done for vascular endothelial growth factor (VEGF), tumour necrosis factor α (TNF- α) and interleukin (IL) 6, which were all high: VEGF=5594 pg/mL(ref 62–707), TNF- α 11.7 pg/mL(ref up to 8.1), IL-6=26.3 pg/mL(ref up to 7.0).

DIFFERENTIAL DIAGNOSIS

The presence of exudative ascites raised the suspicion of possible different causes like tuberculosis, malignancy and connective tissue disease, but the negative test for ascitic ADA had excluded

Figure 4 Biopsy of the sacral bone lesion showing sheets of moderately differentiated plasma cells positive for CD138, with monoclonal expression of λ Ig light chains and no expression of CD45 or CD20.

Figure 5 Bone marrow biopsy showing mildly hypercellular bone marrow for age with trilineage haematopoiesis and subtle infiltrate of plasma cells. The plasma cells were highlighted by CD138 immunostain and showed monoclonal expression of λ Ig light chain.

the possibility of tuberculosis in addition to a negative serological test for connective tissue disease. Also a CT scan of the body didn't reveal any underlying malignancy.

The finding of an osteolytic lesion in this patient along with the presence of peripheral neuropathy made the suspicion of multiple myeloma highly likely as an underlying cause but immunoelectrophoresis didn't reveal monoclonal protein.

TREATMENT

The patient was initially given supportive therapy with daily regular limb physiotherapy and regular diuretic therapy for ascites and lower limb oedema while results of his investigations were awaited. Therapeutic paracentesis was done on several occasions to relieve his tense ascites, but despite these measures the patient continued to be symptomatic. Also he was given L-thyroxine for the hypothyroidism and vitamin B replacement.

After the conclusive results of an underlying POEMS syndrome, the patient was referred to the haematologist and was given both dexamethasone and lenalidomide.

OUTCOME AND FOLLOW-UP

Two months after receiving treatment with dexamethasone and lenalidomide, the patient's disability reduced and he could walk with walking frames; also there was a reduction in the volume of ascites and lower limb oedema. VEGF also showed a slight reduction in its level.

DISCUSSION

We describe a 40-year-old man who presented to us with ascites and pedal oedema. Preceding this presentation he had a history suggestive of polyneuropathy, and of endocrinopathy which had not been properly diagnosed. By reporting this case we want to highlight that in POEMS syndrome, the diagnosis is often delayed because the condition is rare, and due to the diversity of organ involvement, patients may seek a number of specialist consultations before someone thinks of this condition.

POEMS syndrome is a rare multisystem disease which is a result of underlying plasma cell disorder.¹

It consists of polyneuropathy, organomegaly, endocrinopathy, monoclonal protein and skin changes.¹

The diagnosis is based on the presence of two mandatory major criteria along with one major and one minor criteria and not on a single presentation.²

Presence of ascites is a minor criterion from among a number of other minor criteria.

In our case the presentation at the time of diagnosis was with ascites. Ascites is a described complication seen in POEMS syndrome. The incidence is variably reported between 23% and 48%.^{3,4} Differences also exist because of the modality used to assess the presence of ascites. What needs to be emphasised is that the presence of ascites often poses a diagnostic challenge, so that a number of specialist opinions are sought to determine the possible aetiology. Among them are hepatologists, pathologists and infectious disease specialists.

The differentials for ascites are vast-ranging from transudative ascites (left ventricular failure, hypoalbuminaemia, nephrotic syndrome, etc) to exudative causes (inflammatory, infective, malignant causes).¹ With POEMS syndrome, the ascites is typically exudative as was the case with our patient and it is important to rule out other causes of exudative ascites. Cases have been described in literature where patients had other co-existent causes for their ascites like hepatitis B⁵ and also where tuberculous polyserositis was considered and treated due to a positive TB-DNA⁶ and eventually diagnosed as POEMS. Both these cases highlight the diagnostic difficulty in patients with POEMS syndrome particularly if ascites is one of the initial manifestations of the syndrome.

In a recent review of cases from China, 40% of patients with POEMS syndrome had ascites.¹ The cases they described had a low serum ascites albumin gradient similar to our case, indicating non-portal hypertension. The authors report elevated levels of complement components and TNF- α indicating immune activation as the possible mechanism of ascites in these patients.

Apart from ascites, our patient had a long history of undiagnosed peripheral neuropathy, which showed the typical findings usually seen in neuropathy of POEMS syndrome on electrophysiological study in the form of delayed nerve conduction velocity, prolonged distal motor latencies and severe reduction of compound muscle action potentials.

Peripheral neuropathy is a mandatory major criteria and is characterised by distal, ascending and symmetrical involvement. It usually starts with sensory involvement followed by motor symptoms.³

With regards to bony lesion in POEMS syndrome, about 47% had only sclerotic lesions, 51% had mixed sclerotic and lytic lesions, while lytic lesions without evidence of sclerosis were seen in only 2% of the patients,³ which is the case in our patient.

Treatment depends on whether the patient has limited or widespread disease. Those with limited disease with only few bone lesions without evidence of bone marrow involvement can be treated with localised radiotherapy, while those with evidence of bone marrow involvement or multiple bone lesion are treated with chemotherapy with or without autologous haematopoietic cell transplantation.¹

Contributors All the authors were involved in patient care and management and contributed to writing the case report. OFAA-M: diagnostic workup, investigation and discussing the plan, and writing about the investigation part. HALS: diagnostic blood and radiological investigations, acquisition and interpretation of the collected

Learning points

- ▶ POEMS (Peripheral neuropathy, Organomegaly, Endocrinopathy, M protein, Skin changes) syndrome should be considered in the differential diagnosis of unexplained exudative ascites after excluding the most common causes.
- ▶ The presence of an osteolytic lesion in a patient with peripheral neuropathy is not necessarily related to multiple myeloma or other related paraproteinaemia.
- ▶ The presence of multiple system involvement with no clear diagnosis after thorough investigation should alert the physician to an underlying particular syndrome.

relevant patient's data and manuscript submission. WAO: daily review of the patient in the round and writing the history and examination part of the case report. MKJ: an opinion regarding the lower limb weakness, the nerve conduction study and writing the discussion part of the case.

Competing interests None declared.

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