

## POEMS Syndrome – A Case for More Aggressive Treatment

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### Abstract

**Introduction:** Patients with POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal or M-protein and skin changes) syndrome exhibit a wide range of clinical manifestations and are often seen by a variety of specialists prior to diagnosis. **Clinical Picture:** We describe a case of POEMS syndrome that first presented with significant neuropathy but progressed to develop further manifestations of the condition, including marked gastrointestinal symptoms. **Treatment:** The patient was commenced on localised radiotherapy and chemotherapy in addition to immunomodulatory therapy for the neuropathy. **Conclusion:** We highlight several learning points that may benefit physicians from varied specialties. This case is also unique for its marked gastrointestinal manifestation. To our knowledge, this is the second reported case in the literature with this feature.

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### Introduction

POEMS syndrome is a rare, multisystem disorder originally characterised by the presence of polyneuropathy, organomegaly, endocrinopathy, monoclonal or M-protein and skin changes. Bardwick proposed the acronym in 1980.<sup>1</sup> With a wide array of features, this condition can present to a variety of medical subspecialties. We report a patient who presented with neurological and gastrointestinal symptoms from which several learning points were highlighted.

### Case Report

A 56-year-old man complained of a six-month history of progressive weakness and paresthesia of the lower limbs. Simultaneously, he had profuse watery non-bloody diarrhoea that had resulted in significant weight loss. He did not complain of abdominal discomfort. Examination revealed a distal and limb girdle weakness of both lower limbs (MRC Grade 4) with bilateral foot drop. Proprioception and vibration sense were intact. There were no objective sensory findings. He was globally areflexic. There was evidence of peripheral oedema but no organomegaly or lymphadenopathy.

Nerve conduction studies revealed evidence of a demyelinating polyneuropathy with marked conduction slowing in peroneal, median and ulnar nerves bilaterally. Sural responses were absent and tibial nerves inexcitable. The cerebrospinal fluid was acellular with a raised protein level of 1 g/L (reference range, 0.1 to 0.4).

He underwent endoscopic evaluation of his gastrointestinal tract. There was macroscopic evidence of mild colitis affecting the rectosigmoid and descending colon, and histological examination of the affected tissue showed moderately extensive lymphoplasmacytic infiltrate of the lamina propria. There was no evidence of amyloid deposition. A xylose absorption test was within normal limits, as was examination for faecal fat. Serial stool cultures including tests for *Clostridium difficile* toxin were negative. There were bilateral pleural effusions and ascites on computed tomography (CT) but no hepatosplenomegaly or evidence of intra-abdominal malignancy.

Full blood count, renal function and calcium level were normal. B2-microglobulin level was elevated at 3003 µg/L (reference range, 0 to 1900). Initial serum protein electrophoresis was unremarkable. However, immunofixation revealed a faint IgG lambda band in serum and

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urine. A skeletal survey revealed a solitary osteosclerotic lesion in the fifth lumbar vertebral body. MRI of thoracic and lumbosacral spine showed that in addition to this lesion (Fig. 1), there was a smaller lesion in the second sacral vertebral body. There were no osteolytic lesions. A bone marrow trephine and aspirate showed normal cellularity. There were no plasma cell aggregates. A CT-guided biopsy of the lesion was performed and histology was consistent with a plasmacytoma. Hormonal profile testing revealed decreased testosterone level of 2.46 nmol/L (reference range, 9.9 to 27.80) with a normal study of the pituitary axis. In view of the constellation of a demyelinating polyneuropathy, osteosclerotic plasmacytoma, extravascular volume overload and endocrinopathy, the patient was diagnosed with POEMS syndrome.

Prior to this diagnosis, the patient had been diagnosed with chronic inflammatory demyelinating polyneuropathy. He had been treated with a course of plasmapheresis and maintained on oral steroid therapy. There had been a subjective initial partial response before his symptoms progressed. Following the diagnosis of POEMS, a course of radiotherapy to the bone lesions was completed. There was no objective improvement and he progressed to develop severe global weakness in his upper and lower limbs. In addition, he suffered unremitting diarrhoea despite a trial of mesalazine for the presumptive colitis. Six months after the diagnosis, a repeat bone marrow trephine showed mild hypocellularity with adequate megakaryocytosis. However, repeat spinal imaging showed that the original bone lesions showed no change in size and appearances and new bony lesions were seen in the sacral vertebral bodies. He was commenced on cyclical oral cyclophosphamide and dexamethasone therapy, with only a marginal improvement in limb function. He remained bed-bound and succumbed to sepsis and multi-organ failure a month later.

## Discussion

POEMS syndrome is a rare, multisystem disorder originally characterised by the presence of polyneuropathy, organomegaly, endocrinopathy, monoclonal or M-protein and skin changes.<sup>1</sup> Recently, Dispenzieri et al<sup>2</sup> proposed that the diagnosis can be made when there is the occurrence of a monoclonal lymphoproliferative disorder in the presence of a peripheral polyneuropathy in addition to at least one of the following: sclerotic bone lesions, Castleman's disease, organomegaly, oedema, endocrinopathy, skin changes or papilloedema. Our patient presented mainly with symptoms from a neuropathy which was electrophysiologically demonstrated to be a severe demyelinating polyneuropathy. Further investigations revealed an isolated sclerotic bone lesion, which was histologically confirmed to be a plasmacytoma. While multiple myeloma is usually characterised by the development of lytic bone lesions,

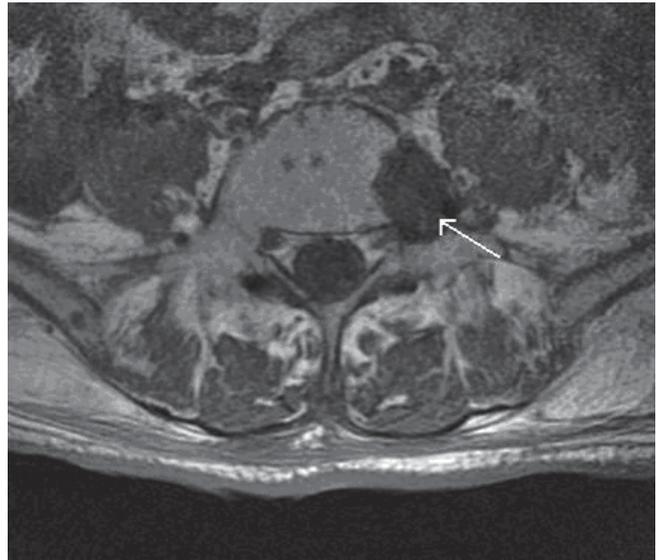


Fig. 1. Axial T1-weighted magnetic resonance imaging showing the osteosclerotic lesion on the left posterolateral aspect of the fifth lumbar vertebral body extending into the pedicle (white arrow).

there have been rare cases associated with widespread osteosclerotic lesions.<sup>3</sup> In our patient, distinction from multiple myeloma is based on the absence of dispersed plasma cells on bone marrow examination, the very low level of monoclonal protein and the absence of related organ or tissue impairment. It is interesting to note that the monoclonal M-protein was detected only on immunofixation and was not evident on electrophoresis. This is a recognised phenomenon that is reflective of the low magnitude of the protein spike in POEMS and should be borne in mind when investigating clinically suspected cases.<sup>2</sup>

The prominent gastrointestinal symptoms in our patient were investigated and revealed histological evidence of colitis. There was no malabsorption or amyloid deposition. To our knowledge, this is the second reported case of POEMS with these findings. The exact mechanism for this is unknown. Vascular endothelial growth factors have been implicated in the pathogenesis of POEMS. It is possible that the ensuing inflammatory response results in the development of colitis.<sup>4</sup>

The overall median survival of patients with POEMS was 13.7 years in a large series. Those with clubbing or extravascular volume overload had median survivals of 2.6 and 6.6 years respectively.<sup>2</sup> Our patient had extravascular volume overload but no clubbing and survived only a year. Patients with POEMS syndrome have limited response to plasmapheresis and intravenous immunoglobulin therapy.<sup>5</sup> Those with single or multiple osteosclerotic lesions in a limited area are usually treated with radiation and more

than 50% of patients will have some response.<sup>2</sup> Some patients with solitary osteosclerotic lesions respond to surgical excision.<sup>5</sup> There have been reports of patients responding to excision of larger lesions even in the presence of more diffused lesions with marked improvement in polyneuropathy.<sup>6</sup> In those who have not responded, high-dose chemotherapy and peripheral blood stem cell transplant have been suggested.<sup>2</sup> These options should be considered in patients who do not respond to standard therapy.

This case also illustrates the importance of immunofixation in detecting low levels of monoclonal protein when investigating a demyelinating polyneuropathy, the need for close monitoring, re-evaluation and consideration of aggressive surgical therapy and high-dose chemotherapy with stem cell support in patients with POEMS who do not respond to initial treatment.

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