

POEMS SYNDROME: A CASE REPORT AND DISCUSSION

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Introduction

POEMS syndrome, also known as the Crow-Fukase syndrome, was first reported in 1956.¹ It is characterized by the association of polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes. The acronym POEMS was derived by Bardwick and colleagues² using these five features.

Case Description

A 46-year-old African American man presented with weakness and numbness in both legs and pain in the left upper chest of 3 weeks' duration. He noted no change in urinary or bowel habits, but he had anorexia with more than 30 pounds of weight loss over 3 months. He had no fever or night sweats and no cardiac, respiratory, or gastrointestinal symptoms, but he recalled having generalized painless lymphadenopathy for

more than 20 years with no recent change. He was intermittently followed by a physician for diabetes mellitus, hypertension, lymphadenopathy, and impotence. The patient had no risk factors for HIV infection.

Physical examination revealed multiple widespread lymph nodes that were nontender, firm, mobile, and 1-2 cm in size. They were most prominent in the cervical areas. He had reduced (4/5) power in both legs. Touch and pain sensation were also impaired. The cranial nerves and rectal sphincter tone were normal. His hemoglobin and white blood cell levels were normal, but his platelet count was elevated at 846,000/mm³. His renal function and serum calcium level were normal. Other laboratory findings included total protein 7.2 g/dL, albumin 3.1 g/dL, and lactate dehydrogenase 307 U/L. A chest radiograph demonstrated an expansile lesion in the first rib (Fig 1).



Fig 1. — Chest radiograph demonstrating expansile lesion in the first rib.

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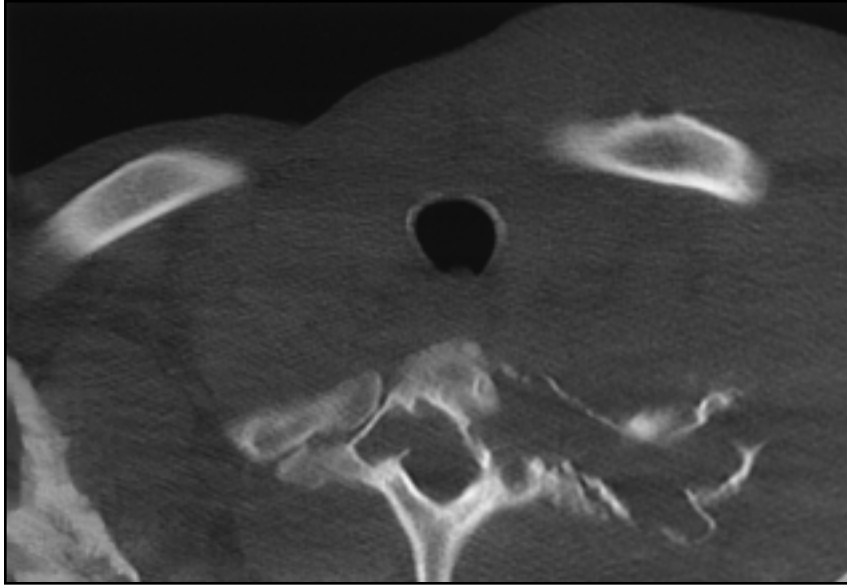


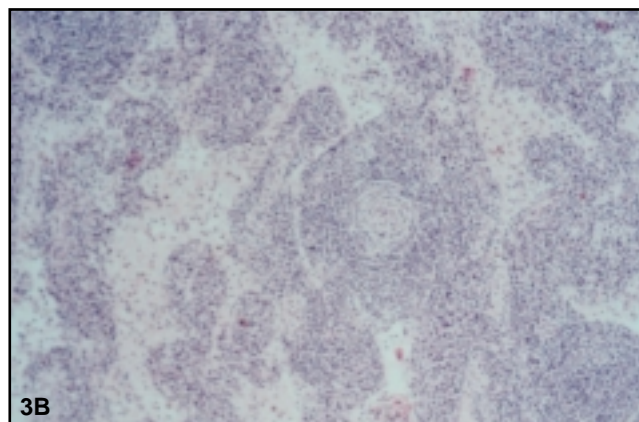
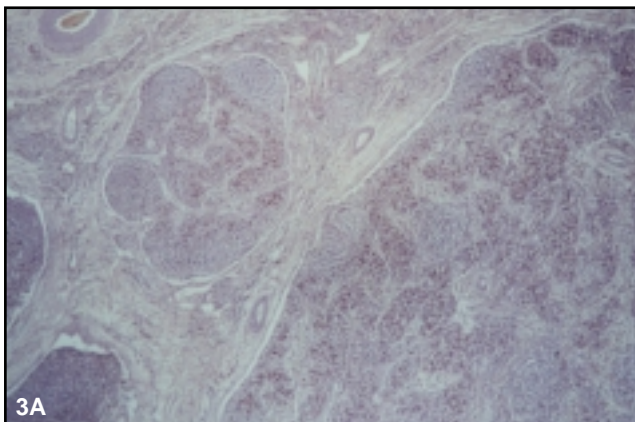
Fig 2. — Computed tomography scan of the chest showing generalized lymphadenopathy, a moderate left pleural effusion, hepatosplenomegaly, and a mixed lytic and sclerotic lesion in the left first rib.

Further workup revealed a monoclonal gammopathy of the IgG λ type (2,740 g/dL.). Computed tomography (CT) of the chest showed generalized lymphadenopathy, a moderate left pleural effusion, hepatosplenomegaly, and a mixed lytic and sclerotic lesion of the left first rib (Fig 2). Bone scan showed increased uptake in the

skull, the left scapula, and the left second and third posterior ribs. Radiographic bone survey demonstrated lytic changes in the posterior parietal bone and an expansile lytic area in the posterior aspect of the left first rib. A cervical lymph node biopsy demonstrated dense plasmacytic infiltrate consistent with Castleman's disease, plasma

cell variant (Figs 3A-B). Bone marrow aspiration and biopsy showed 10%-15% plasmacytosis. Biopsy of the first rib revealed sheets of plasma cell infiltration (Fig 4). The vitamin B₁₂ level was low (141 pg/mL) as was the testosterone level (1.67 ng/mL.). Electromyography (EMG) was consistent with a demyelinating polyneuropathy. HIV testing was negative, and interleukin 6 (IL-6) level was not estimated.

A diagnosis of multiple myeloma with POEMS syndrome was made. The patient was treated with 43.75 Gy of radiation therapy for the painful areas in the first rib and supraclavicular fossa and is currently undergoing chemotherapy with L-phenylalanine mustard (melphalan) and prednisone. The bulky disease over the first rib regressed after the radiation therapy. He has also responded to the systemic treatment with improvement of the neuropathy and shrinkage of lymph nodes. The serum IgG level has fallen from 2,740 g/dL to 1,700 g/dL.



Figs 3A-B. — Lymph node showing dense plasmacytic infiltrate consistent with Castleman's disease, plasma cell variant. A - magnification 4x, B - magnification 10x.

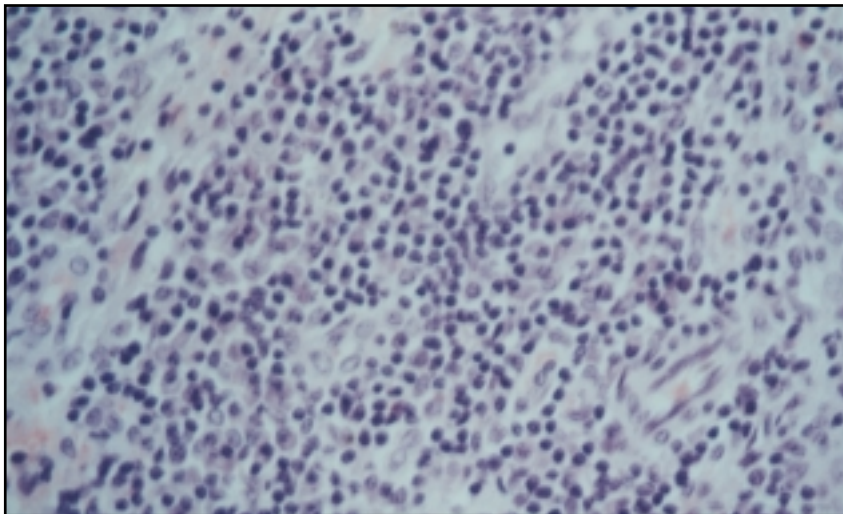


Fig 4. — Biopsy of the first rib revealed plasma cell infiltration.

Discussion

POEMS syndrome is rarely reported in Caucasians. A retrospective study of 25 cases reported in 1994 by Soubrier et al³ indicated that there is appreciable symptomatic diversity in POEMS syndrome. No definite criteria are available for the diagnosis. Most of the reports include patients who have at least four of the five features of the syndrome. However, the prognosis remains unchanged for patients who have fewer than four characteristic features.⁴

Minute changes in the vessel wall leading to increased vascular permeability have been suggested as the basic pathophysiology.⁵ This is probably mediated by cytokines. No unique cytokine has been identified and no uniform change has been described to explain the above hypothesis.⁶ Elevated levels of IL-6, a cytokine originating in lymph nodes that induces final maturation of activated B cells into

immunoglobulin-producing cells, have been noted in the serum and cerebrospinal fluid (CSF) of patients with the syndrome. The levels are correlated with the treatment response and progression of the disease. The origin of increased levels of IL-6 in the CSF is not clear. Other cytokines that are associated with POEMS syndrome include IL-1 β , tumor necrosis factor (TNF), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor- β (TGF- β).⁷

Although the five syndrome components are essential for absolute diagnosis of POEMS syndrome, varying combinations of symptoms are present in many reported cases. Polyneuropathy is the most common symptom. Most patients with this symptom have symmetrical motor and sensory deficiency in the extremities. It usually starts in the lower extremities with progressive proximal extension. Decreased deep tendon

reflexes associated with various combinations of sensory symptoms are found. EMG shows signs of both demyelination and axonal degeneration.^{1,4}

Organomegaly involving the liver occurs with varying nonspecific pathologic features.⁸ Spleen and lymph node tissue may show normal histology or features of Castleman's disease.⁹⁻¹¹ Endocrinopathy usually manifests as impotence and gynecomastia.^{8,12} Other disturbances include diabetes mellitus, hypothyroidism, hyperprolactinemia, and amenorrhea.⁸

A monoclonal serum protein spike with varying types of plasma cell dyscrasias is seen. It ranges from a monoclonal gammopathy of unknown significance (MGUS) to plasmacytoma with osteolytic, osteosclerotic, or mixed bone lesions.^{3,12,13} The immunoglobulin subtypes can be IgG or IgA. The majority of patients have a λ light chain.¹⁴ A polyclonal gammopathy can also occur.

Skin lesions vary from local to generalized hyperpigmentation. Skin biopsy may show inflammation, fibrosis, or nonspecific changes. Skin angiomas are reported in Asian patients.¹⁵ Other less common manifestations include anasarca, peripheral edema, pleural effusion, ascites, thrombocytosis, polycythemia, fever, and vitamin B₁₂ deficiency.³

Therapy for solitary bone lesions consists of local surgical excision or radiation therapy or both.³ Systemic symptoms are

being treated with chemotherapy as used for multiple myeloma,¹⁶ but neurotoxic agents should be avoided.³ The prognosis is better for patients with a solitary plasma cell lesion presenting with the syndrome.³ All the elements of the syndrome tend to improve when the underlying plasma cell dyscrasia responds to treatment.

Conclusion

POEMS syndrome is a distinct pathological entity with diverse clinical manifestations. Our patient exhibited four of the five main components of the syndrome, as well as other nonclassical manifestations. He was treated with radiation therapy to the expansile lesion in the rib, followed by systemic chemotherapy, with clinical improvement.

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