Journal of Korean Medical Science
Vol 7, No. 1, 79-84 March 1992

POEMS Syndrome

— A Case Report —

Jae Woo Kim, M.D., Sang Kun Lee, M.D., Kyung Min Ha, M.D.
Ki Ho Kim, M.D.* Gwang Yeol Joh, M.D.*, Hyo Jin Kim, M.D.**
Seoung-Oh Yang, M.D.***, Sook Hee Hong, M.D.****

Department of Neurology, Dermatology, Internal Medicine***
*Diagnostic Radiology***, Pathology****
College of Medicine, Dong-A University

POEMS syndrome is a multisystem disorder associated with polyneuropathy, organomegaly, endocrinopathy, a monoclonal protein (M-protein), and skin changes. The authors describe a patient with POEMS syndrome who had osteosclerotic myeloma confirmed by open bone biopsy.
Magnetic resonance imaging (MRI) showed discrete lesions of low signal intensity in both T1 and T2-weighted images. This patient is now being successfully treated with melphalan and prednisone with much improvement in skin thickening and sensory change in the lower extremities.

Key Words: *POEMS syndrome, Monoclonal protein, Osteosclerotic myeloma*

INTRODUCTION

POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) syndrome is a rare multisystemic disorder characterized by a combination of polyneuropathy, hemangioma, hyperpigmentation and hypertrichosis of the skin, variable endocrine disturbances, generalized edema, organomegaly, and a plasma cell dyscrasia with an M-protein often associated with myeloma. The pathogenesis of this syndrome has not been fully explained. In Korea only a few cases have been reported (Joo et al., 1987; Lee et al., 1987).

We describe a patient with POEMS syndrome along with a review of the literature.

CASE REPORT

A 43-year-old male had been admitted to the Department of Neurology, Dong-A University Hospital because of polyneuropathy and weight loss. He had been healthy until 12 months earlier, when he began to notice numbness in his feet and weight loss. During the 3 months before admission, slowly worsening ascending peripheral neuropathy developed and did not respond to medication.

On physical examination there was a generalized wasting of axial and limb musculature, but weakness was not noted. A few well-defined, dome-shaped nodules were scattered on the trunk and extremities (Fig. 1). Increased hair growth on the perineum, thickening of skin in the lower legs, and hyperpigmentation were also noted.

Neurological examination revealed that the cranial nerves were normal. Decreased sensation of all modalities was noted in distal parts of the upper and lower extrimities. Deep tendon reflexes were absent in the lower extremities.

On admission, white blood cell count was 13,400/mm^3. Platelet count was 625,000/mm^3. Proteinuria and Bence-Jones protein were not noted. Serum protein was 8.2g (albumin 4.5g and globulin 3.7g) and IgG was 3095mg/dl (800-1700). A CSF examination disclosed 36.5mg/dl of IgG and 128mg/dl of protein but no cells. Serum and CSF protein electrophoresis and immunoelectrophoresis showed a monoclonal spike of IgG-lambda. Serum testosterone was 2.84ng/ml (0.15-1.1) but ACTH, cortisol, growth hormone, prolactin, LH and FSH were normal. Liver scan showed hepatosplenomegaly without dysfunction

Address for correspondence: *Jae Woo Kim, Department of Neurology, College of Medicine, Dong-A University, 1, 3-Ga Dongdaesin-dong, Seo-gu, Pusan 602-103, Korea (Tel: 240-5261)*

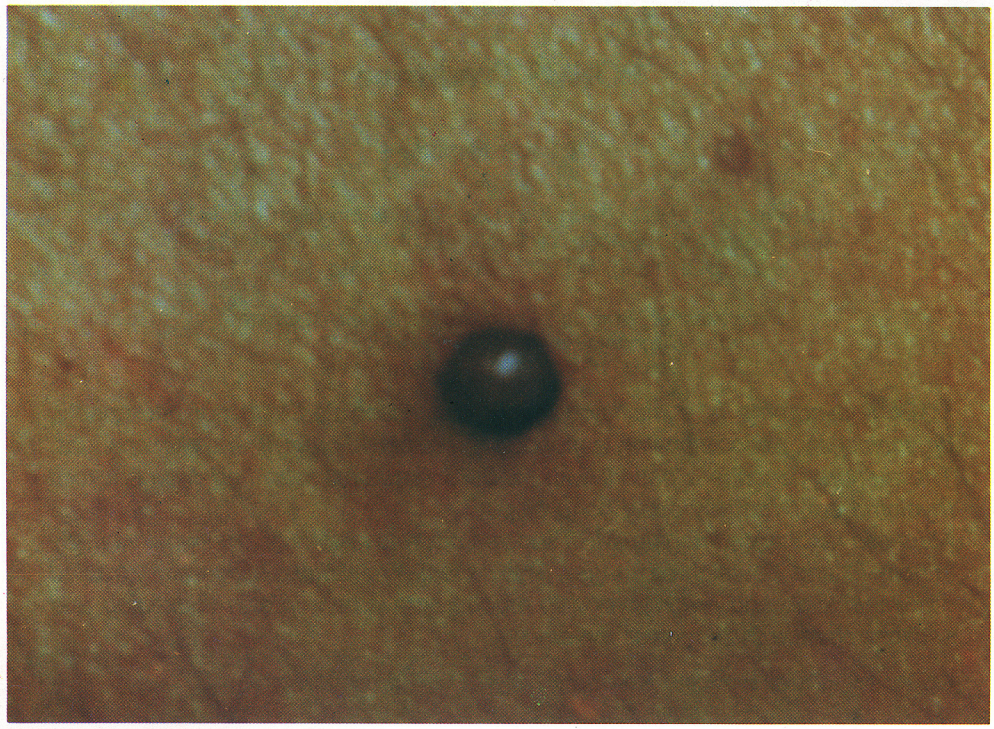

Fig. 1. Cherry hemangioma on the trunk.

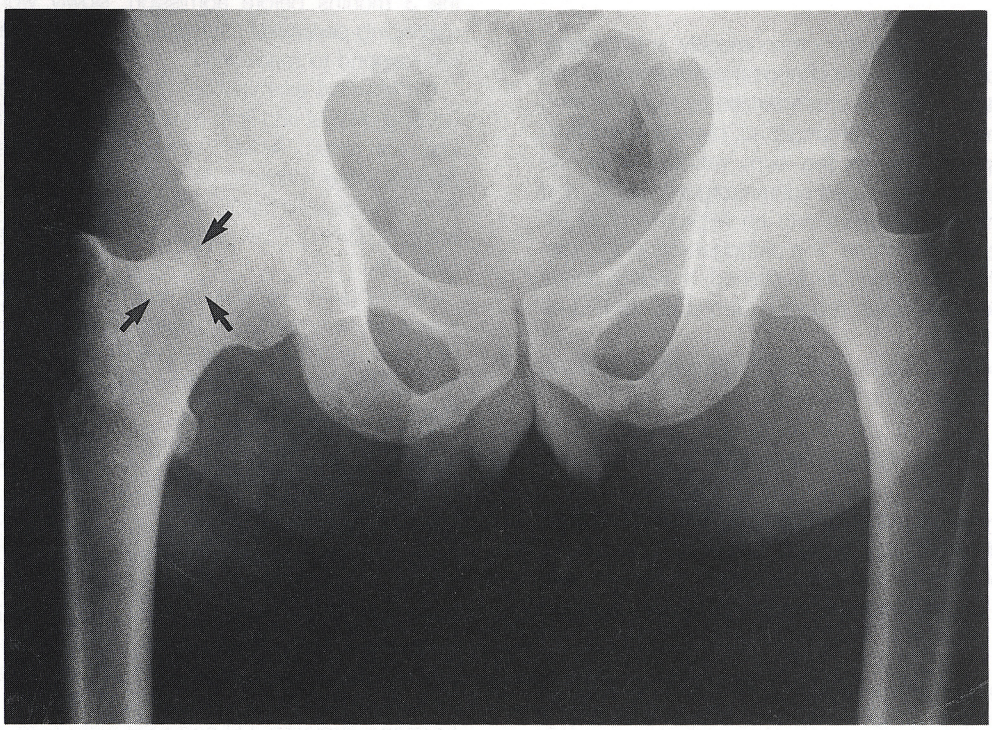

Fig. 2. A small osteosclerotic lesion seen at the right femur neck (arrows).

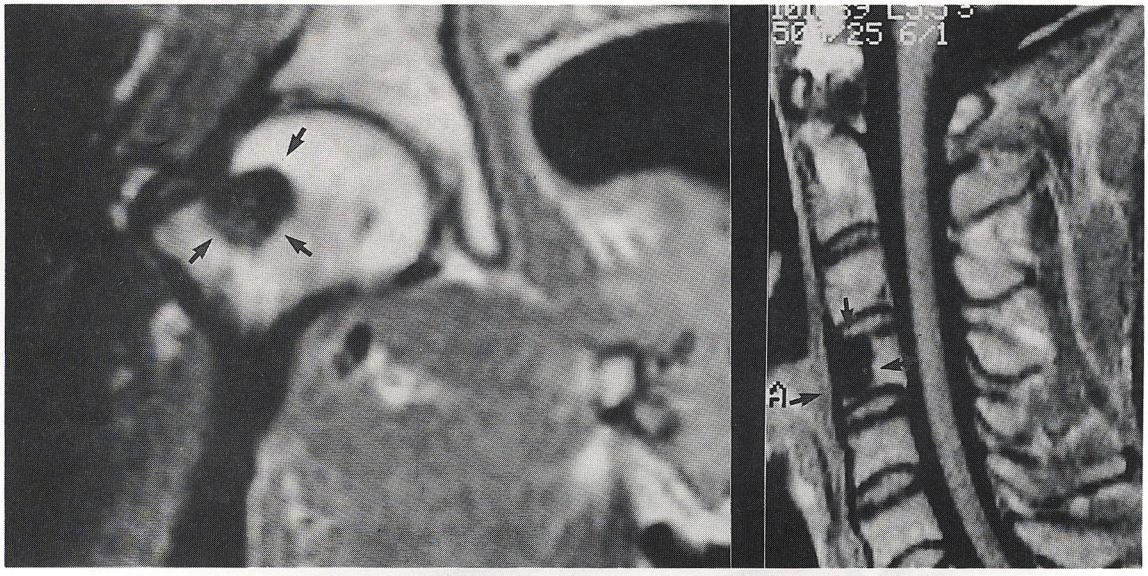

Fig. 3. Coronal and sagittal T1-weighted (TR/TE = 700/25 and 500/25) images of the right femur neck and cervical spin demonstrate well-defined, low signal intensity arease indicating osteosolerotic myelomatous lesions (arrow).

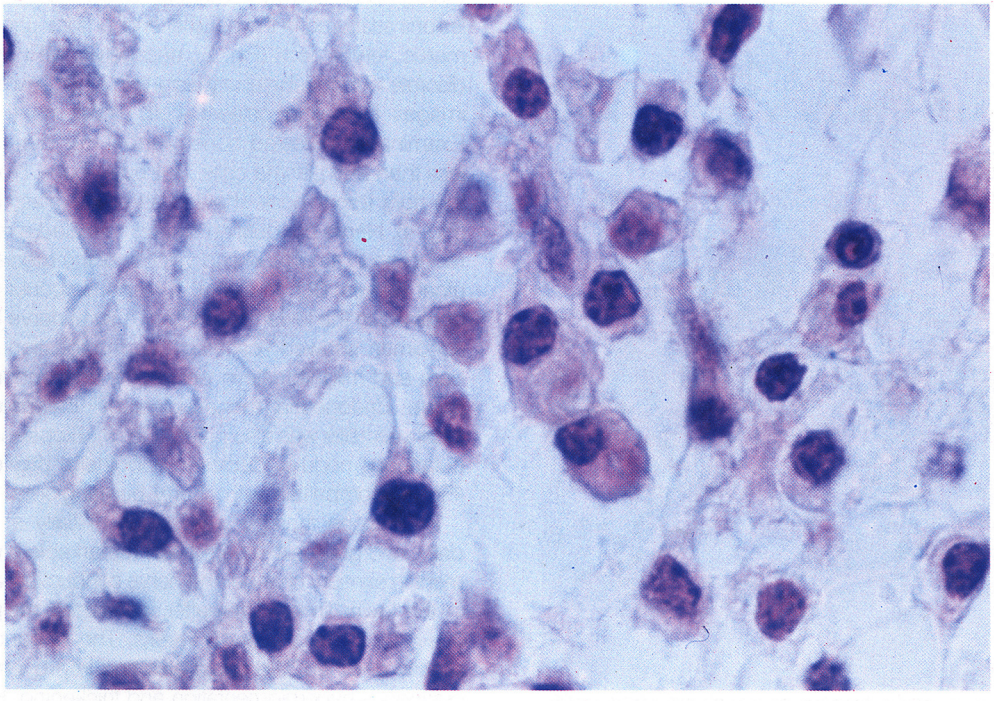

Fig. 4. Biopsy of the osteosclerotic lesion in the right femur neck shows a nest of plasma cells (H&E, ×1000).

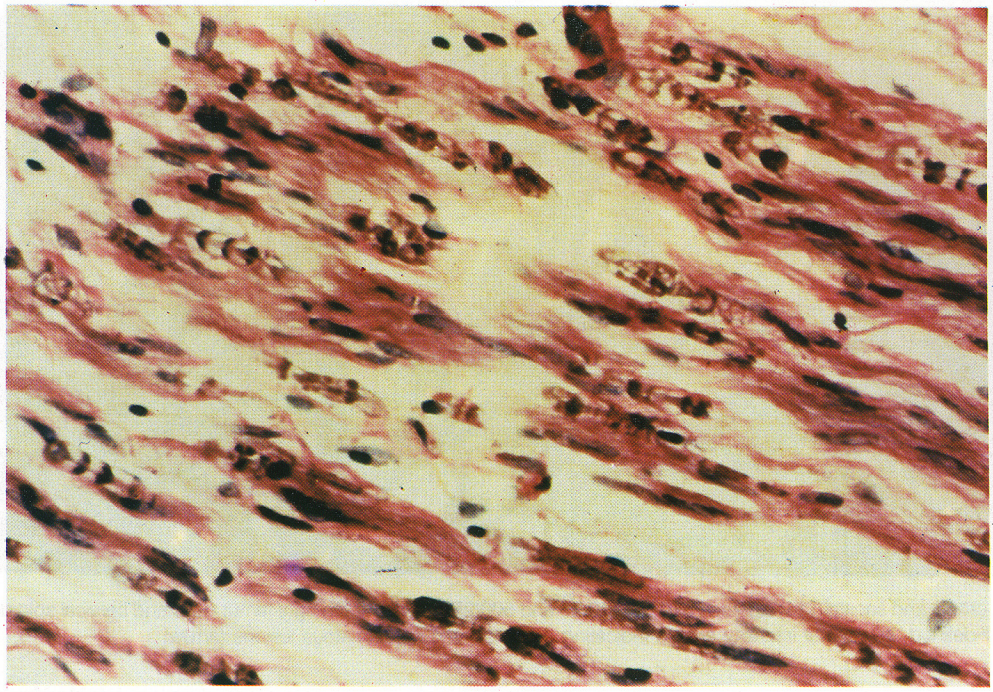

Fig. 5. Sural nerve biopsy specimen shows scattered myelin digestion chambers and mild fibrosis (H&E, ×400).

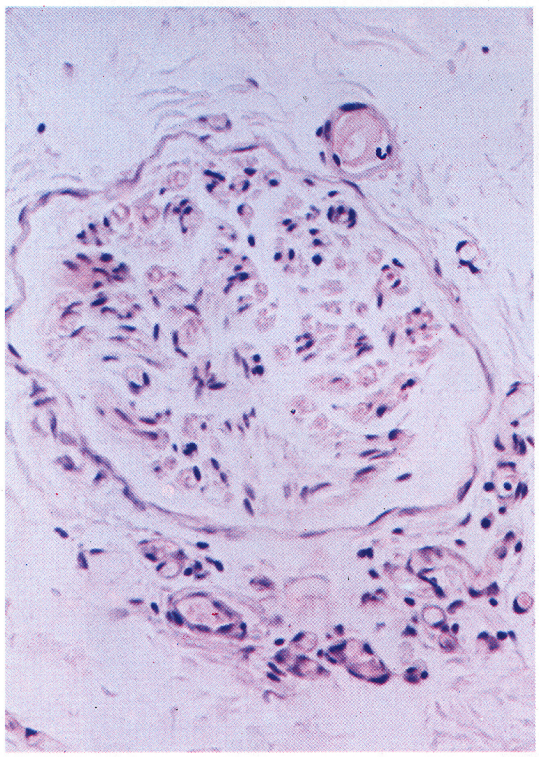

Fig. 6. Biopsy of a cutaneous nodule shows intravascular endothelial prolifertion (H&E, ×400).

of reticuloendothelial cells. A bone survey with simple radiography showed variable sized osteosclerotic lesions scattered in the cervical and lumber spines, humerus, femur neck (Fig. 2), and pelvis. MRI showed discrete low signal intensity lesions in T1 & T2 weighted images indicating osteosclerotic myeloma (Fig. 3). Examination revealed bone marrow was normal with less than 2% plasma cells. But open bone biopsy of the right femur neck showed sheets of plasma cells (Fig. 4). Nerve conduction studies revealed a marked reduction in amplitude and velocity of the median and ulnar nerves. But an electrical response could not be obtained in the lower extremities. A sural nerve biopsy specimen showed scattered myelin digestion chambers and mild fibrosis in perineurial and endoneurial tissue. Endoneurial mononuclear cell infiltration with focal vasculitis was also noted (Fig. 5). Biopsies of two cutaneous nodules disclosed endothelial proliferation (Fig. 6) compatible with cherry hemangioma.

Prednisone therapy was begun, initially at 60mg daily, and gradually tapered with remarkable improvement in sensory change and nerve conduction velocity in the lower limbs. Thereafter we started melphalan 6 mg for 7 days every 6 weeks. The M-band level slightly declined. We could also find improvement in cutaneous hyperpigmentation and thickening. He has remained well up to the time of writing.

DISCUSSION

In this unique syndrome abnoprmalities occur in the central and peripheral nervous systems, the integument, the endocrine glands, the skeleton and the reticulo-endothelial and immunohematopoietic systems. The pathophysiological interrelationships among these systems are obviously complex and not well understood, but are possibly related to the plasma cell tumors often present in these patients (Bardwick et al., 1980). Moreover, the relationship of conventional multiple myeloma, solitory myeloma of bone and osteosclerotic myeloma to each other and to the POEMS syndrome is unclear. Although osteosclerotic myeloma is a rare disorder, one out of 200 patients with myeloma in one series and three out of 90 in another (Evison and Evans, 1967), almost half of the 59 cases reviewed by Iwashita et al, had sensorimotor polyneuropathy and 15 to 36% of them had one or more POEMS features (Iwashita et al., 1977). In contrast to conventional multiple myeloma, osteosclerotic myeloma occurs at an earlier age, and patients rarely complain of bone pain. The bone marrow is rarely infiltrated with plasma cells, and M-components are small in the serum and rarely appear in the urine (Kelly et al., 1983). In our case also, CBC, serum calcium, phosporus, and renal function were all normal. No Bence-Jones protein was found and bone marrow aspirate of the iliac crest revealed less than 2% plasma cells. M-components were IgG-lambda and the level was 3095 mg% in the serum.

No clues to the etiology of the neuropathy have come from histopathological studies of the peripheral nerves. A spectrum of results has been reported in the literature, from normal histology to degeneration of myelin sheaths and axons-the degree of axonal damage being roughly proportional to the myelinsheath damage (Aguayo et al., 1964; Hesselvik, 1969; Morley and Scheiger, 1967).

An intriguing possibility is that an abnormal immunoglobulin, or fragment thereof, produced by the neoplastic plasma cells is responsible for the neurologic lesions by binding to specific antigens in the peripheral nervous system. Latov et al. (1981), using a complement fixation assay, first demonstrated that the M-protein had antimyelin activity and the antigenic determinant within myelin was later identified as a myelin-associated glycoprotein (MAG) (Melmed et al., 1983; Nemni et al., 1983). Recent studies by Ilyas et al. (1985) and Freddo et al. (1985) have shown that the M-protein binds not only to MAG, but also to a glycolipid of the peripheral nervous system and it is likely that binding is to the same or closely related carbohydrate epitopes shared by a number of glycoprotein and glycolipids (Freddo et al. 1985). Of several speculative pathogeneses of angioma in this syndrome, the angiogenic role of "toxic" substances secreted by plasma cells is highly hypothetioal (Dereure et al., 1990). Cutaneous angiomas have been reported at a 26-44% incidence in this rare syndrome (Feddersen et al., 1989). In about 25% of patients with sclerotic myeloma and polyneuropathy, however, no serum or urine monoclonal protein is detectable, and a radiologic skeletal survey is essential for evaluation. The individual lesions may be completely sclerotic, mixed sclerotic and lytic, or cystic and may be present for many years before or after diagnosis with little apparent progression radiologically. As in our case and many previously reported cases, radioistope bone scans are usually less sensitive than radiographic skeletal surveys (Read and Warlow, 1978), probably because of the indolent nature of the osteosclerotic lesions. In this case MRI demonstrated well-demarcated bone lesions, so we expect that MRI will play an important role in confirmation of osteosclerotic myeloma. The involvement of multiple endocrine glands in patients with this syndrome is striking. The two most prominent endocrine manifestations are gonadal failure and diabetes mellitus. Gynecomastia is frequent and prolactin levels are elevated frequently in women with amenorrhea and in males with hypogonadism. In this case the only abnormal endocrine function was elevated serum testosterones, the meaning of which is uncertain. Although elevated testosterone level may account for hypertrichosis in this patient, most previously reported cases demonstrated low testosterone in spite of the skin lesions. Hepatomegaly, splenomegaly, and generalized lymphadenopathy are often discovered.

Acknowledgements

The authors would like to thank Dr. Je G. Chi for his helpful comments on pathologic findings from the sural nerve.

REFERENCES

Aguayo A, Thompson DW, Humphrey JG: *Multiple myeloma with polyneuropathy and osteosclerotic lesions. J Neurol Neurosurg Psychiat 27:562, 1964.*

Bardwick PA, Zvafler NJ, Gill GN, Newman D, Greenway GD, Resnick DL: *Plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M protein, and skin*

changes: The POEMS syndrome. Medicine 59:311-322, 1980.

Dereeure O, Gillot B, Dandurand M, Bataille R, Chertok P, Donadio D, Blotman F, Barneon G, Guilhou JJ: *Cutaneous lesions in POEMS syndrome. Ann Dermatol Venereol 117(4):283-290, 1990.*

Feddersen RM, Burgdorf W, Foucar K, Elias L, Smith SM: *Plasma cell dyscrasia: A case of POEMS syndrome with a unique dermatologic presentation. J Am Acad Dermatol 21:1061-1068, 1989.*

Evison G, Evans KT: *Bone sclerosis in multiple myeloma. Br J Radiol 40:81, 1967.*

Freddo L, Ariga T, Saito M, Macala LC, Yu RK, Latov N: *The neuropathy of plasma cell dyscrasias: binding of IgM M protein to peripheral nerve glycolipid. Neurology 35:1420-1424, 1985.*

Hesselvik M: *Neuropathological studies on myelomatosis. Acta Neurol Scand 45:95, 1969.*

Ilyas AA, Quarles RH, Dalakas MC, Fishman PH, Brady RD: *Monoclonal IgM in a patient with paraproteinemic polyneuropathy binds to gangliosides containing disalosyl group. Ann Neurol: 655-659, 1985.*

Iwashita H, Ohnishi A, Asada M, Kanasawa Y, Kuroiwa Y: *Polyneuropathy, skin hyperpigmentation, edema, and hypertrichosis in localized osteosclerotic myeloma. Neurology 27:675, 1977.*

Joo SJ, Kang YK, Bang YJ, Choi SJ, Klm BK, Kim NK, Chi JG, Kim CW, Lee KW, Cho KH: *A case report of POEMS syndrome. The Korean Journal of Internal Medicine 33:539-547, 1987.*

Kelly JJ, Kyle RA, Miles JM, Dyck PJ: *Osteosclerotic myeloma and peripheral neuropathy, Neurology 33:202-210, 1983.*

Latov N, Braun PE, Gross RB, Sherman WH, Penn AS, Chess L: *Plasma cell dyscrasia and peripheral neuropathy: identification of the myelin antigens that react with human paraproteins. Proc Natl Acad Sci USA 78:7139-7142, 1981.*

Lee MS, Sunwoo IN, Kim KW, Chi JG: *A case report of the POEMS syndrome. The Journal of Korean Neurological Association 6:75-80, 1987.*

Melmed C, Frail D, Duncan I, Braun P, Danoff D, Finlayson M, Steward J: *Peripheral neuropathy with IgM kappa monoclonal immunoglobulin directed against myelin-associated glycoprotein. Neurology 33:1397-1405, 1983.*

Morley JB, Schweiger AC: *The relation between chronic polyneuropathy and osteosclerotic myeloma. J Neurol Neurosurg Psychiat 30:432, 1967.*

Nemni R, Glassi G, Latov N, Sherman WH, Olarte MR, Hays AP: *Polyneuropathy in nonmalignant IgM plasma cell dyscrasia: a morphological study. Ann Neurol 14:43-54, 1983.*

Read D, Warlow C: *Peripheral neuropathy and solitary plasmacytoma. J Neurol Neurosurg Psychiat 41:177-184, 1978.*