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Waldenstrom's Macroglobulinemia Presenting With Spinal Cord Compression: A Case Report

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Waldenstrom's macroglobulinemia (WM) is a rare lymphoplasmacytic lymphoma characterized by a wide range of clinical presentations related to direct tumor infiltration and the production of IgM. Most commonly it presents with cytopenia, hepatosplenomegaly, lymphadenopathy, constitutional symptoms, and hyperviscosity syndrome. We report a case of WM in an 81-year-old man who initially presented with severe back pain. The patient had no peripheral lymphadenopathy or hepatosplenomegaly and his peripheral blood smear was normal. MRI of the spine revealed an epidural mass causing spinal cord compression at T9. Surgical decompression was performed and pathological analysis of the mass revealed a lymphoproliferative B-cell process. The diagnosis of WM was established after cytomorphologic and immunohistochemical analysis of the patient's bone marrow revealed the presence of a lymphoid/lymphoplasmacytoid-like bone marrow infiltrate along with an elevated serum IgM level. The patient responded both clinically and serologically to local radiotherapy. This case is unusual because the patient lacked all common clinical features of WM. This is the first reported case of epidural spinal cord compression as the initial manifestation of WM, adding to the spectrum of clinical presentations seen in this disease. Am. J. Hematol. 81:955–958, 2006. © 2006 Wiley-Liss, Inc.

Key words: Waldenstrom's macroglobulinemia; spinal cord compression; epidural space; radiotherapy

INTRODUCTION

Waldenstrom's macroglobulinemia (WM) is an uncommon B-cell lymphoproliferative neoplasm accounting for only 6% of all B-cell malignancies [1,2]. Recently it has been considered a unique clinicopathologic entity characterized by lymphoplasmacytic bone marrow and tissue infiltrate, as well as the production of serum monoclonal immunoglobulin M (IgM) [3]. This disease has a wide range of clinical presentations with symptoms attributable either to tissue infiltration by neoplastic cells or to the quantity and immunological properties of the monoclonal IgM produced. However 27% of patients diagnosed with WM are asymptomatic, presenting with an elevated IgM level (> 3,000 mg/dL) and lymphoplasmacytic infiltration of the bone marrow only [4].

Epidural metastasis causing spinal cord compression in lymphoid neoplasms is well described [5]; this however has not been reported in the context of WM. We report an unusual case of epidural spinal cord compression as the initial presentation of underlying WM. The diagnosis was based on the presence of a lymphoid/lymphoplasmacytoid bone marrow infiltrate and an elevated serum immunoglobulin M level. This case outlines the possibility of epidural metastasis in WM.

CASE REPORT

An 81-year-old Caucasian man with a past medical history of type 2 diabetes, hypertension, and osteoarthritis presented to the emergency department with a 1 week history of progressively worsening severe, constant left-sided low back pain radiating to the

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abdominal wall above the umbilicus. The patient had no bowel or bladder problems and his pain was not associated with motor or sensory neurological deficits at presentation. Upon physical examination he had paravertebral tenderness over the lower thoracic spine; his neurological exam was normal. There was no demonstrable Raynaud's phenomenon. No cutaneous lesions, lymphadenopathy, or hepatosplenomegaly were noted on examination. Initial laboratory investigations revealed a white blood cell (WBC) count of 7,200/μL, hemoglobin of 10.8 g/dL, and platelet count of 288,000/μL. The patient had a history of chronic low hemoglobin that ranged between 9.5 and 11.0 g/dL in the 10-year period before this presentation (normal 13–18 g/dL). A peripheral blood smear was normal showing no circulating atypical cells. Kidney function tests were normal with a creatinine level of 1.07 mg/dL (normal 0.6–1.2 mg/dL) and urea nitrogen level of 12.8 mg/dL (normal 7–18 mg/dL). Additional laboratory tests revealed elevated LDH at 263 IU/L (normal 110–220 U/L), calcium of 9 mg/dL (normal 8.5–10.5 mg/dL) and normal liver function tests.

Magnetic resonance imaging of the thoracic and lumbar spine was done showing a 7-cm enhancing posterior epidural mass spanning levels T8–T10 (Fig. 1A), impinging on the left T9 nerve root and causing spinal cord compression at the level of the T9 vertebra (Fig. 1B). Total body imaging with CT scan did not reveal any organ involvement or adenopathy. Despite initial management with glucocorticoids, the pain persisted and the patient underwent a decompressive laminectomy at T9. Postoperatively the patient developed weakness and lower motor neuron findings attributed to a subdural hematoma. He continued on glucocorticoids and received a course of palliative external beam radiotherapy to the lower thoracic spine.

Pathological analysis of soft tissue fragments recovered from the epidural lesion revealed an atypical, moderately dense, and diffuse lymphoid infiltrate, consisting of small, round lymphocytes admixed with larger round to oval cells with irregular nuclear contours and distinct nucleoli (see Fig. 2). They were predominantly B cells staining positively for CD 20 and CD 79a. Clusters of CD-138-positive plasma cell were also noted. These morphologic and immunophenotypic characteristics were suggestive of the presence of an indolent B-cell lymphoproliferative process. This was further investigated by a bone marrow biopsy which revealed a hypo- to normocellular marrow with a CD-138-positive plasma cell infiltrate mainly occupying the intertrabecular space and constituting 10–15% of marrow cellularity. The infiltrate consisted of mature plasma cells admixed with smaller immature (lymphoid/lymphoplasmacytoid-like) atypical cells (see Fig. 3). Immunohistochemical staining of these cells was positive for CD 20, CD 79a, and partially for CD 10, negative for CD 5, CD 43, and CD 23. Staining for kappa and lambda immunoglobulin light chains revealed kappa light chain predominance (10:1 ratio). Further hematological and immunologic workup revealed an elevated IgM serum level of 2,113 mg/dL

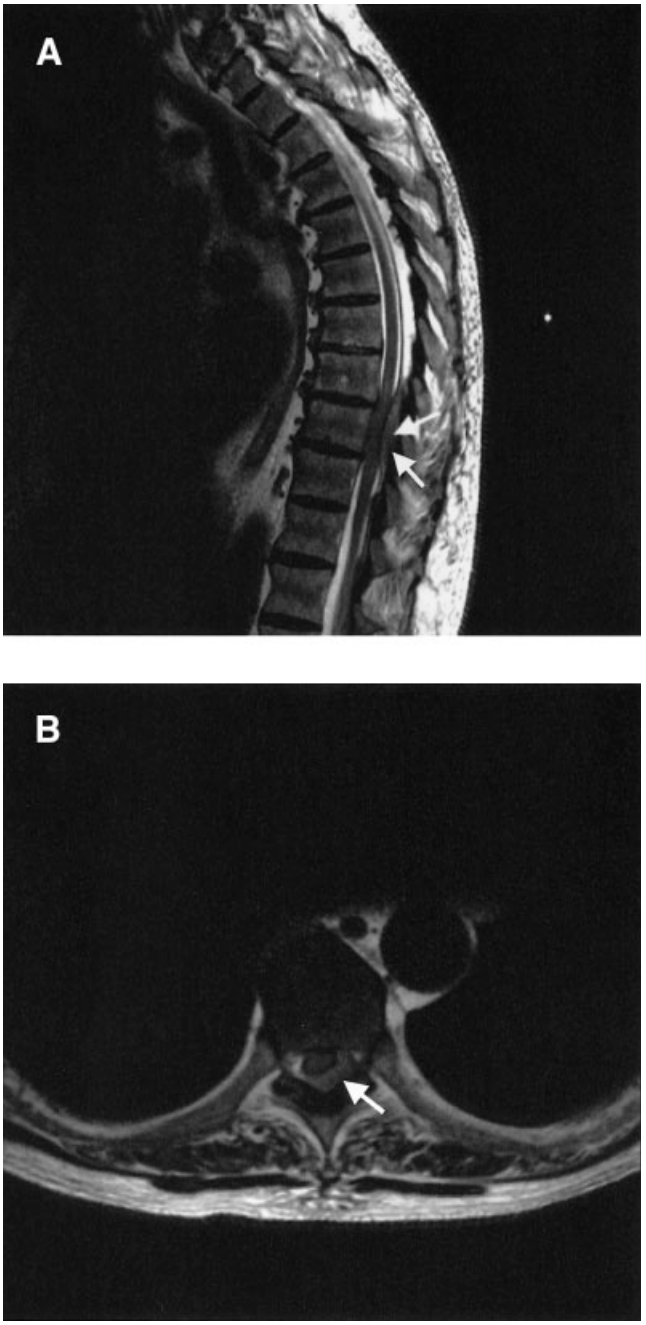

Fig. 1. (A) Magnetic resonance imaging of the spine shows an enhancing epidural mass (arrows) from T8 to T10. (B) Axial imaging reveals the mass is predominantly on the left and is causing spinal cord compression at T9.

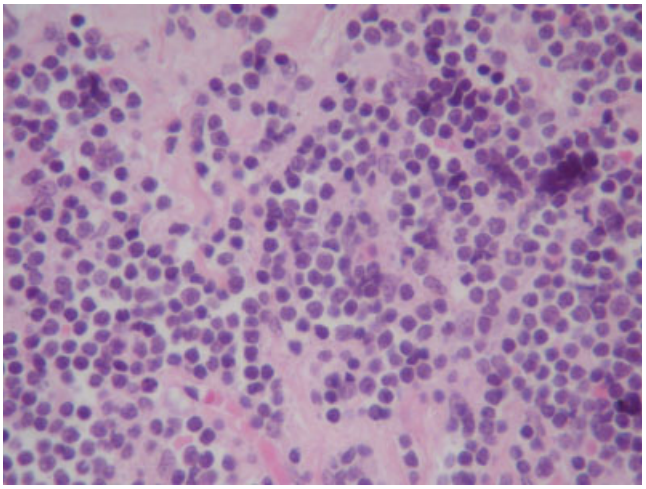

Fig. 2. Epidural soft tissue mass histopathology shows a dense atypical lymphoid infiltrate (H&E, original magnification x100).

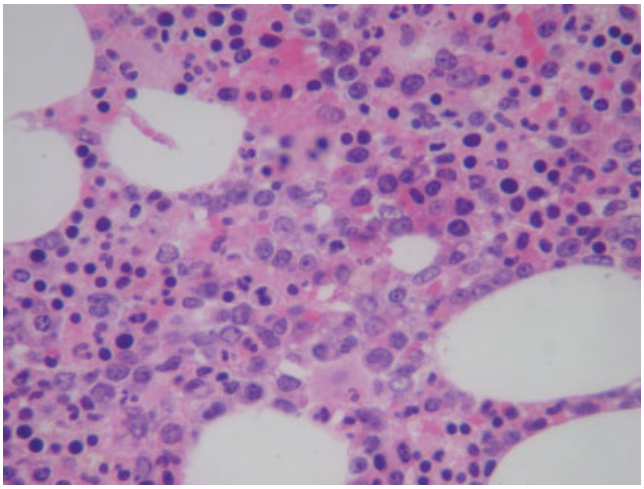

Fig. 3. Bone marrow biopsy reveals a lymphoid infiltrate consisting of mature plasma cells admixed with smaller immature (lymphoid/lymphoplasmacytoid-like) atypical cells (H&E, original magnification x100).

(normal 60–250 mg/dL). Serum immunofixation showed presence of a large IgM kappa and 2 small IgG kappa bands. The Coombs' and cold agglutinin tests were negative. These results supported the diagnosis of WM.

DISCUSSION

Symptoms in WM are caused by tissue infiltration and the production of immunoglobulin M. Patients usually present at a median age of 63 years usually with constitutional symptoms such as fatigue (66%), fever (15%), anorexia (25%), and weight loss (17%) which are caused by tumor infiltration and clonal expansion [6].

Anemia (hemoglobin < 12 g/dL) is the most common finding in patients with symptomatic WM (63%). It is generally caused by bone marrow infiltration, which less frequently can lead to thrombocytopenia (16%) and leukopenia (4%). Infiltration of the liver, spleen, and lymph nodes leads to hepatomegaly in 20% of patients, splenomegaly in 19%, and lymphadenopathy in 15%. Involvement of other organs such as the lung, kidney, gut, and skin are rare [6,7].

The circulation, tissue deposition, and autoimmune properties of IgM monoclonal proteins are responsible for an array of clinical manifestations in WM [8]. The most characteristic of these is hyperviscosity syndrome which is caused by the increasing serum concentrations of IgM, resulting in aggregation of red cells and increased serum viscosity. It is seen in 15% of WM patients at diagnosis and is clinically characterized by oronasal hemorrhage, visual defects, and multiple neurological abnormalities [9,10]. Other presenting symptoms related to monoclonal IgM include cryoglobulinemia and cold agglutinin hemolytic anemia occurring in 5% of patients [11], peripheral neuropathies in 5–10% [12], and amyloidosis in 2% [13].

Up to 25% of patients with WM experience neurologic complications through the course of their disease [14–16]. The most common of these is peripheral demylating neuropathy which is caused by the autoimmune activity of monoclonal IgM. Increased serum viscosity and vascular disorders account for other neurological manifestations such as ischemic and hemorrhagic strokes, as well as subarachnoid hemorrhages. Malignant lymphoid infiltration of the central nervous system (CNS) is rare. When it occurs, it is responsible for the Bing-Neel syndrome [14,15]. Clinical manifestations of this syndrome depend on the type of infiltrate, which can be diffuse or tumoral. Patients with a tumoral infiltrate usually present with seizures or focal neurological signs related to the site of infiltration. In the diffuse form, infiltration of the leptomeningeal spaces, peri-ventricular white matter, pons, and medulla are common; and patients frequently demonstrate symptoms of confusion and encephalopathy [14,15,17]. Spinal cord or cauda equina complications of WM are rare. Isolated cases of myelopathy, cauda equina amylosis, and spinal canal impingement from vertebrolysis have been reported in patients known for WM [15,18].

We report here a patient with WM presenting with spinal cord compression secondary to an epidural mass. Following the criteria described in the second international workshop on WM, the diagnosis of WM was made based on the presence of inter-

trabecular bone marrow infiltration by atypical lymphocytes showing plasma cell and plasmacytoid differentiation along with elevated serum IgM [2]. WM was considered the cause of the cord compression, as the epidural mass consisted of an infiltrate similar to that found in the bone marrow. This case is unusual, since the patient lacked all the common clinical features of WM. He was previously anemic and his hemoglobin remained stable above 10 g/dL after the diagnosis. The complaints related to the epidural disease were the only symptoms attributable to WM. The patient slowly recovered from his neurological deficit and has now been followed for 12 months without evidence of progressive disease. In the year following completion of palliative radiotherapy to the epidural mass, his serum IgM level has gradually dropped to 1,392 mg/dL. In this time, no systemic treatment for WM was initiated given what was felt to be the absence of clinical or laboratory indications.

Although rare, hematological neoplasms presenting as spinal cord compression have been described in the literature. These include Hodgkin's and non-Hodgkin's lymphoma, plasmacytoma, and multiple myeloma [19]. To our knowledge this is the first report of a patient with WM presenting with a spinal cord compression syndrome. This adds to the wide variety of CNS related clinical presentations of WM and points to the need for considering WM along with other lymphoid neoplasms in the differential diagnosis of spinal cord compression.

REFERENCES

1. Dimopoulos MA, Alexanian R. Waldenstrom's macroglobulinemia. Blood 1994;83:1452–1459.
2. Ghobrial IM, Gertz MA, Fonseca R. Waldenstrom macroglobulinaemia. Lancet Oncol 2003;4:679–685.
3. Owen RG, Treon SP, Al-Katib A, et al. Clinicopathological definition of Waldenstrom's macroglobulinemia: Consensus panel recommendations from the Second International Workshop on Waldenstrom's Macroglobulinemia. Semin Oncol 2003;30:110–115.
4. Alexanian R, Weber D, Delasalle K, Cabanillas F, Dimopoulos M. Asymptomatic Waldenstrom's macroglobulinemia. Semin Oncol 2003;30:206–210.
5. Gabriel K, Schiff D. Metastatic spinal cord compression by solid tumors. Semin Neurol 2004;24:375–383.
6. Gertz MA, Merlini G, Treon SP. Amyloidosis and Waldenstrom's macroglobulinemia. Hematology 2004:257–282.
7. Merlini G, Baldini L, Broglia C, et al. Prognostic factors in symptomatic Waldenstrom's macroglobulinemia. Semin Oncol 2003;30:211–215.
8. Dimopoulos MA, Kyle RA, Anagnostopoulos A, Treon SP. Diagnosis and management of Waldenstrom's macroglobulinemia. J Clin Oncol 2005;23:1564–1577.
9. Kwaan HC, Bongu A. The hyperviscosity syndromes. Semin Thromb Hemost 1999;25:199–208.
10. Gertz MA, Kyle RA. Hyperviscosity syndrome. J Intensive Care Med 1995;10:128–141.
11. Farhangi M, Merlini G. The clinical implications of monoclonal immunoglobulins. Semin Oncol 1986;13:366–379.
12. Vital A. Paraproteinemic neuropathies. Brain Pathol 2001;11: 399–407.
13. Gertz MA, Kyle RA, Noel P. Primary systemic amyloidosis: A rare complication of immunoglobulin M monoclonal gammopathies and Waldenstrom's macroglobulinemia. J Clin Oncol 1993; 11:914–920.
14. Delgado J, Canales MA, Garcia B, Alvarez-Ferreira J, Garcia-Grande A, Hernandez-Navarro F. Radiation therapy and combination of cladribine, cyclophosphamide, and prednisone as treatment of Bing-Neel syndrome: Case report and review of the literature. Am J Hematol 2002;69:127–131.
15. Massengo S, Riffaud L, Morandi X, Bernard M, Verin M. Nervous system lymphoid infiltration in Waldenstrom's macroglobulinemia. A case report. J Neurooncol 2003;62:353–358.
16. García-Sanz R, Montoto S, Torrequebrada A, et al. Waldenström macroglobulinaemia: Presenting features and outcome in a series with 217 cases. Br J Haematol 2001;115:575–582.
17. Hug A, Haas J, Storch-Hagenlocher B, Wildemann B. Leptomeningeale Tumorzellinfiltration als Erstmanifestation eines Immunozytoms (M. Waldenstrom). Nervenarzt 2004;75:1012–1015.
18. Liberato B, Riethmuller A, Comenzo RL, Lis E, Raizer JJ. Myelopathy from Waldenstrom's macroglobulinemia: Improvement after Rituximab therapy. J Neurooncol 2003;63:207–211.
19. Chahal S, Lagera JE, Ryder J, Kleinschmidt-DeMasters BK. Hematological neoplasms with first presentation as spinal cord compression syndromes: A 10-year retrospective series and review of the literature. Clin Neuropathol 2003;22:282–290.