INTERNAL MEDICINE

□ CASE REPORT □

M-protein-negative Myeloma Mimicking Lumbar Disc Herniation

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Abstract

A 60-year-old man was referred to us with high levels of aspartate aminotransferase and lactate dehydrogenase (LDH). He did not complain of any symptoms; however, he had been diagnosed with lumbar disc herniation, even though his back pain improved only to half of its previous level with pregabalin. Thus, we asked about the red flag of back pain and confirmed that he had involuntary body weight loss, which led us to diagnose truly non-secretory multiple myeloma, a variant of multiple myeloma that is associated with M-protein negativity and a normal serum free light chain level.

Key words: truly non-secretory multiple myeloma, M-protein, red flags

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Introduction

In patients with non-secretory multiple myeloma (NSMM), which accounts for approximately three percent of all multiple myeloma (MM) cases (1), the results of protein electrophoresis and the immunofixation of serum and urine are normal. Furthermore, the 2-4% of NSMM patients who also have normal serum free light chain (FLC) ratios are diagnosed as having truly NSMM (1).

Truly NSMM, which is a variant of multiple myeloma, is difficult to diagnose because it has no specific measurable biomarkers: the patients are M-protein-negative and show normal serum free light chain levels. We herein report the case of patient who showed a symptom consistent with lumbar disc herniation, but in whom red flags helped in the detection of truly NSMM.

Case Report

A 60-year-old man visited an orthopedist in July 2015 after experiencing low back pain and numbness of the right leg at the L4 dermatome for two weeks. Based on the symptoms, the patient was diagnosed with lumbar disc herniation on the basis of the magnetic resonance imaging (MRI) findings. The patient's pain level was reduced by 50% after pregabalin treatment. Screening tests revealed that he had increased levels of aspartate aminotransferase (AST) and lactate dehydrogenase (LDH); he was therefore referred to our department after seven weeks.

His medical history was unremarkable. He took no regular medications other than pregabalin and mecobalamin. He had experienced an unintended weight loss of 4% (from 70 kg to 67.5 kg) in the two previous months. The results of a physical examination were normal. The blood examination findings were as follows: white blood cell count, 5,400/μL; hemoglobin level, 10.3 g/dL; mean corpuscular volume, 100.3 fL; reticulocyte count, 78,000/μL; and platelet count, 120,000/μL. The abnormal laboratory findings on the initial tests included total protein (6.1 g/dL), AST (122 U/L) and LDH (977 U/L) levels, with the LDH isoenzymes composed of LDH-1, 13.1% (reference range, 20.0-31.0%); LDH-2, 35.2% (reference range, 28.8-37.0%); LDH-3, 33.2% (reference range, 21.5-27.6%); LDH-4, 14.7% (reference range, 6.3-12.4%); and LDH-5, 3.8% (reference range, 5.4-13.2%). The patient's albumin, alanine aminotransferase, bilirubin, creatine kinase, and C-reactive protein levels were within the reference ranges. Neither kidney dysfunction nor hypercalcemia was detected. M-protein was not detected in the diagnostic tests, electrophoresis or immunofixation of the pa-

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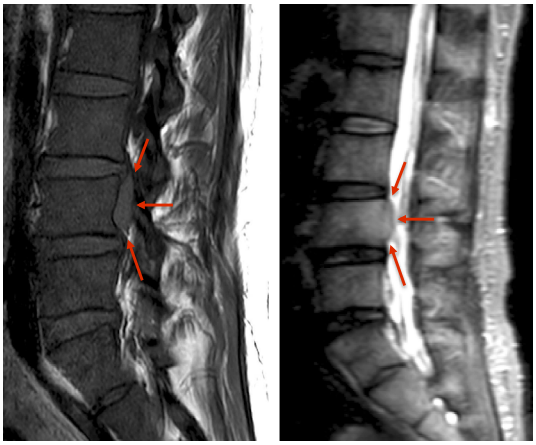

Figure 1. **Sagittal T1-weighted (left) and STIR (right) MRI images of the vertebrae showing broad reduced (left) and hyperintense (right) signals of the lumbar bones in comparison to the signals of the adjacent disk and paravertebral muscles, and a tumor involving the L4 vertebrae (arrow).**

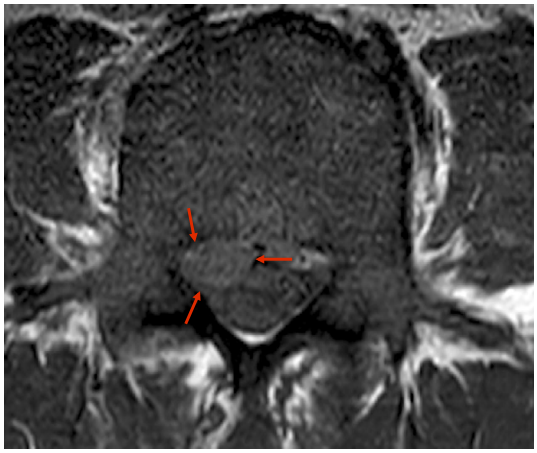

Figure 2. **An axial T1-weighted MRI image of the vertebrae showing a tumor constricting the vertebrae foramen (arrow).**

tient's serum and urine protein. A free light chain (FLC) assay also revealed a normal κ/λ ratio. However, the β_2 microglobulin level was high (6.5 mg/L; reference range, 0.8-1.8 mg/L), and the immunoglobulin (Ig) levels were low for IgG (622 mg/dL; reference range, 870-1,700 mg/dL), IgA (78 mg/dL; reference range, 110-410 mg/dL), and IgM (13 mg/dL; reference range, 35-220 mg/dL), while the IgD level was normal (<0.6 mg/dL). Lumbar MRI, which was performed by his previous doctor, showed broad reduced T1-weighted signals and hyperintense short tau inversion recovery (STIR) signals of the lumbar bones in comparison to the signals of the adjacent disk and paravertebral muscles, and a tumor that involved the L4 vertebrae (Fig. 1, 2). Positron-emission tomography/computed tomography (PET/CT) also showed the uptake of fluorodeoxyglucose (FDG) by the tumor in the L4 vertebral body. The bone marrow biopsy showed hyperplasia of the atypical plasma cells (65.5%) (Fig. 3). An immunohistochemistry study of a bone marrow biopsy specimen showed that the plasma cells were negative for CD20, CD79a, CD138, CD3, CD5, cyclin D1, κ and λ. A cytogenetic analysis by fluorescent *in situ* hybridization (FISH) detected neither t(4;14) (p16;q32), t(14;16) (q32;q23), nor del(17p13) (TP53). Based on these findings, the patient was diagnosed with "truly NSMM" of the non-producer type, which was classified as stage 3 according to the International Staging System (ISS) and IIIA according to the Durie-Salmon staging system. The patient was treated with bortezomib, cyclophosphamide, and dexamethasone chemotherapy. After four cycles of chemotherapy, the patient experienced pain relief, the normalization of his AST and LDH levels, a decrease in the accumulation of FDG, and a >90% reduction in his bone marrow plasma cells.

Discussion

According to the consensus statement from the International Myeloma Workshop (1), the workup for all newly diagnosed myeloma patients includes, protein electrophoresis, serum and urine immunofixation, and serum FLC. However, the results of protein electrophoresis and serum and urine immunofixation are normal in patients with NSMM, which accounts for approximately 3% of all MM cases (1). Furthermore, 2-4% of NSMM patients have normal serum FLC ratios; these patients are considered to have truly NSMM (1). Although not specific, hypogammaglobulinemia, which is found in 92% of NSMM patients (2), might be a clue that can help to make an early diagnosis of NSMM, if combined with myeloma defining events (hypercalcemia, renal insufficiency, anemia, and/or bone lesions [CRAB]). Thus, when a patient shows hypogammaglobulinemia and a CRAB event without any abnormalities in the specific biomarkers for myeloma, NSMM should be considered and specimens should be collected from the patient's bone marrow or suspicious lesions for the diagnosis. A caveat, however, would be that both a bone marrow and tumor biopsy specimens can be negative. In this situation, lesions containing plasmacytosis (detected by PET/CT) should be biopsied (3).

On the other hand, in most who receive primary care for acute lower back pain, the pain is thought to have a mechanical cause involving the spine and surrounding structures (4). However, lower back pain in conjunction with red flags, including pain for more than one month, >50 years of age, and unexplained weight loss, indicates a more serious cause. In our case, the elevation of LDH levels with anemia and hypogammaglobulinemia implied a hematological malignancy. Thus, we reassessed the MRI scan and identified lower T1-weighted and hyperintense STIR signals of the spinal marrow, and a mass involving the L4 vertebrae that extended into the vertebral foramen, both of which indicated a hematologic malignancy such as MM (5). Although electrophoresis and the immunofixation of serum and urine proteins did not reveal the M-protein, we further pursued of MM and finally reached a diagnosis of truly NSMM.

Truly NSMM, which has no specific measurable biomark-

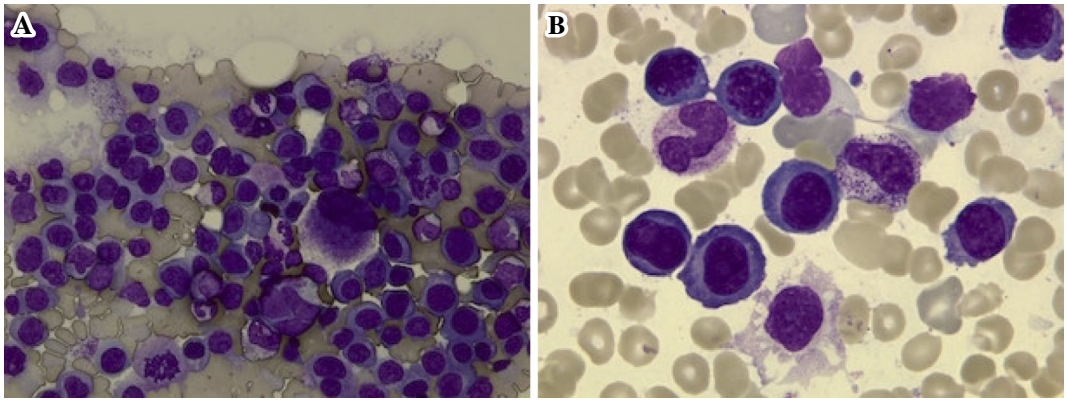

Figure 3. **A bone marrow aspiration specimen showing marked plasma cell proliferation. May-Grünwald Giemsa staining: (A) ×400, (B) ×1,000.**

ers, tends to be diagnosed at an advanced stage (6). However, the red flags and hypogammaglobulinemia with some CRAB events might indicate this rare type of MM.

The authors state that they have no Conflict of Interest (COI).

References

1. Lonial S, Kaufman JL. Non-secretory myeloma: a clinician's guide. Oncology **27**: 924-928, 930, 2013.
2. Kyle RA, Gertz MA, Witzig TE, et al. Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin Proc **78**: 21-33, 2003.
3. Orchard K, Barrington S, Buscombe J, Hilson A, Prentice HG, Mehta A. Fluoro-deoxyglucose positron emission tomography imaging for the detection of occult disease in multiple myeloma. Br J Haematol **117**: 133-135, 2002.
4. Atlas SJ, Deyo RA. Evaluating and managing acute low back pain in the primary care setting. J Gen Intern Med **16**: 120-131, 2001.
5. Hanrahan CJ, Shah LM. MRI of spinal bone marrow: part 2, T1-weighted imaging-based differential diagnosis. Am J Roentgenol **197**: 1309-1321, 2011.
6. McConnaughey D, Thornton JD, Wu D. Disorientation and vertebral fractures. Lancet **353**: 1848, 1999.