Uncommon, sinister vertebral fracture

Early-onset multiple myeloma

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Multiple myeloma (MM) is a neoplastic disorder caused by clonal proliferation of plasma cells derived from B cells in bone marrow. These proliferating myeloma cells increase production of osteoclast-activating factors, which leads to skeletal destruction, pathologic fractures, osteoporosis, and severe bone pain. Multiple myeloma is the third most common hematologic malignancy in Canada, with 6 new cases per 100 000 people in 2007[1] and an estimated 2500 new cases in 2013.[2] It affects men more than women, with a lifetime risk ratio of 1.3 to 1 in Canada.[2] Population-based studies on ethnicity have reported MM as the most common hematologic malignancy in people of African descent, with the rate in this ethnic group being 2 to 3 times that in white patients; Asian (specifically Japanese) and Mexican populations report lower rates.[3]

Onset of MM before the age of 60 years is rare, with a median age at diagnosis of 66 years. Only 10% of patients are younger than 50 at diagnosis.[4] A large study of more than 10 000 patients demonstrated that cases diagnosed before the age of 50 had fewer comorbidities, which foretells better survival with appropriate therapy, thereby highlighting the importance of early recognition.[5] Primary care providers should be aware of the possibility of MM in this age group, and carefully note unusual presentations or red flags that might point to a diagnosis.

Case

An otherwise healthy 47-year-old labourer of Latin American descent with chronic low back pain presents with an exacerbation of pain despite ongoing physiotherapy. He has full lumbosacral range of motion and normal findings on neurologic examination but limited lifting capacity. Over the next 4 weeks, he derives mild improvement and symptom relief from physiotherapy and modified duties at work, but reports pain at night interrupting his sleep.

At the end of the month, he falls on his driveway from standing height and aggravates his back. He presents with severe pain and guarded movement and is started on nonsteroidal anti-inflammatory drugs. The patient is also advised to ice the area and intensify his physiotherapy regimen. The patient's mobility continues to decline over the next 2 weeks. At the next follow-up visit, he is walking with a cane and reports constant, severe pain (8 out of 10) during the day and

EDITOR'S KEY POINTS

- Nocturnal back pain, pathologic vertebral fracture after a normal fall, and worsening mobility in a healthy middle-aged patient should be considered to have a malignant cause until proven otherwise.
- Multiple myeloma (MM) is the third most common hematologic malignancy in Canada. Although it commonly presents in patients older than 60 years of age, 10% of MM cases occur in patients younger than 50 years of age.
- Younger patients with MM have better morbidity and mortality outcomes if diagnosis and treatment initiation are timely.
- Diagnosis of MM requires an elevated monoclonal serum or urine protein level, 10% or greater clonal bone marrow plasma cells, and presence of related organ or tissue impairment (anemia, renal failure, hypercalcemia, or osteolytic bone lesions).

POINTS DE REPÈRE DU RÉDACTEUR

- Il faudrait envisager une cause maligne jusqu'à preuve du contraire dans le cas de douleurs lombaires nocturnes, de fractures vertébrales pathologiques à la suite d'une chute banale et d'une réduction de la mobilité chez des patients d'âge moyen en santé.
- Le myélome multiple (MM) est le troisième cancer hématologique le plus commun au Canada. Quoiqu'il se présente habituellement chez les patients de plus de 60 ans, 10 % des cas de MM se produisent chez des personnes de moins de 50 ans.
- Les patients plus jeunes ont de meilleurs résultats sur les plans de la morbidité et de la mortalité si le diagnostic et l'amorce du traitement sont faits en temps opportun.
- Le diagnostic du MM se base sur des niveaux de protéines monoclonales sériques ou urinaires élevés, 10 % ou plus de clones plasmocytaires dans la moelle osseuse et la présence d'une déficience organique ou tissulaire connexe (anémie, insuffisance rénale, hypercalcémie ou lésions osseuses ostéolytiques).

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night. A lumbar spine x-ray scan conducted that day indicates abnormal appearance of L5, demonstrating a generalized mild compression fracture with 25% loss of height and ill-defined margins suggestive of an underlying pathologic lesion.

While a bone scan and magnetic resonance imaging (MRI) of his spine are organized, he is sent to an emergency department in view of his rapidly declining mobility. He returns to the office the next day unchanged, with a prescription for narcotics and further physiotherapy. The following day, an urgent MRI finds "ill-defined L5, diagnosis between a sub-acute traumatic compression fracture and more sinister pathology ... a pathological fracture due to spondylitis or metastatic disease cannot be excluded." A bone scan also confirms recent fractures of the L5 vertebral body and left seventh costochondral joint.

Two days after the MRI, the patient returns completely immobile, using a wheelchair. Blood tests are taken, with results showing normocytic anemia with a hemoglobin level of 100 g/L, a leukocyte level of 5.9×109/L with a normal differential count, and a platelet level of 273×109/L. Test results for human leukocyte antigen B27 and rheumatoid factor are negative, erythrocyte sedimentation rate (ESR) is 1 mm/h, and liver transaminase, creatinine, lactate dehydrogenase, calcium, and alkaline phosphatase levels are all normal. A key finding comes from his serum protein electrophoresis and immunofixation, which measures an elevated total protein level of 105.0 g/L and a spike in the g-globulin region measuring 61.6 g/L (normal range is 5.1 to 13.2 g/L). The patient is referred and admitted to hospital.

Inpatient testing confirms a diagnosis of stage 2 MM. Repeat MRI reveals new compression fractures of T12 to L5 vertebral bodies. Bone marrow biopsy shows 25% to 30% plasma cells, consistent with MM. While serum free light-chain assay is not performed, a urine test is negative for Bence-Jones proteins. The patient is started on dexamethasone and thalidomide while awaiting radiation therapy for symptomatic treatment of his back pain and autologous stem cell transplant.

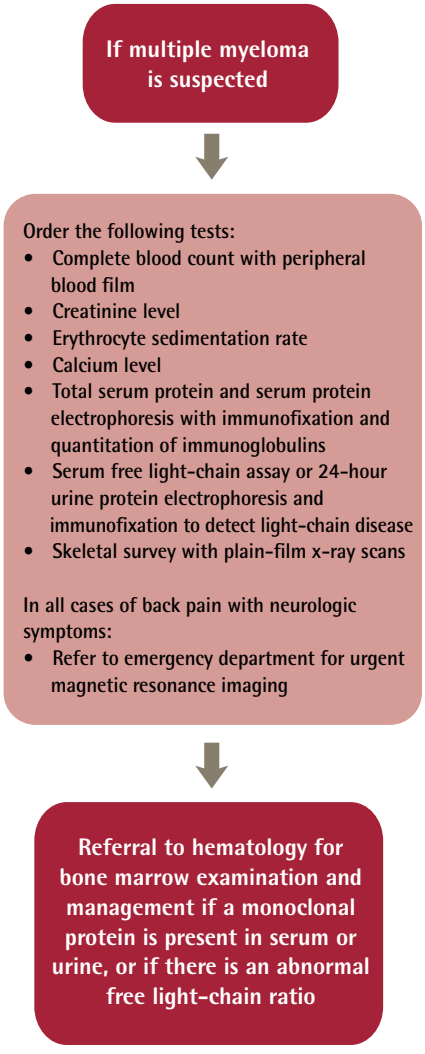
Discussion

We reviewed the relevant UpToDate articles for MM, including all references cited in the articles "Clinical Features, Laboratory Manifestations, and Diagnosis of Multiple Myeloma"[6] and "Staging and Prognostic Studies of Multiple Myeloma."[7] We then conducted nested PubMed searches combining the MeSH term *multiple myeloma* with 1 of 5 key word searches for *case studies*, *reviews*, *epidemiology*, *diagnosis* or *clinical features*, or *treatment* or *management*. Abstracts for English-language articles published in the past 10 years were hand-searched, with clinically relevant articles selected for review.

Traditionally, areas of active hematopoiesis such as the vertebral bodies, skull, thoracic cage, pelvis, and proximal humeri and femora are most commonly affected in MM.[4] Our patient presented after a fall, with lumbar pain, stiffness, and limited mobility, suggesting a likely diagnosis of acute or chronic lumbar strain. Other possibilities included arthritic changes, ankylosing spondylitis, and MM. Patients with MM often describe severe bone pain around the affected area precipitated by movement, and uncommonly occurring at night. Other clinical features can include fatigue, weight loss, infections, and generalized weakness.[8] **Figure 1** outlines key initial investigations in the diagnosis of MM.

Initial blood work is the mainstay of MM diagnosis. Specific tests include complete blood count, peripheral blood film, creatinine level, calcium level, ESR, albumin level, total serum protein level, and serum

Figure 1. Key initial investigations in the diagnosis of multiple myeloma



protein electrophoresis with immunofixation and quantitation of immunoglobulins. In 15% to 20% of MM cases, only an abnormal proliferation of light-chain proteins occurs owing to lack of expression of the immunoglobulin heavy chain (ie, Bence-Jones proteins). Traditionally, 24-hour urine protein electrophoresis and immunofixation was performed to identify these patients. However, serum free light-chain assays have been increasingly used to detect these patients owing to the ease of testing and the improved sensitivity compared with urine protein electrophoresis.[9] The serum free light-chain assay measures levels of κ and λ light chains and provides a κ to λ ratio. An abnormal ratio would suggest higher proportions of κ or λ light chains caused by MM.

Our patient's diagnosis of MM was strongly suggested by normocytic anemia and the finding of an elevated monoclonal protein on electrophoresis. Notably, our patient did not present with the traditional findings of elevated ESR, elevated creatinine level, or hypercalcemia. Preserved renal function confers a more favourable MM prognosis; renal insufficiency arises from the development of light-chain tubular casts, leading to interstitial nephritis (myeloma kidney). Nephropathy can also result from hypercalcemia-induced volume depletion leading to prerenal azotemia, light-chain deposition disease, kidney stones, amyloidosis, and the use of nephrotoxic medications (eg, nonsteroidal anti-inflammatory drugs for pain).

A skeletal survey of possible affected sites is also important in MM diagnosis. On plain-film x-ray scans, MM can appear as osteopenic bones with "punched-out" osteolytic lesions and pathologic fractures. Other types of imaging are important adjuncts: bone scans help determine how recently a fracture occurred and, if available, MRI or computed tomography can detect earlier, subtle lesions undetectable by x-ray scans.[4,8] Urgent MRI referral should always be made if neurologic abnormalities such as weakness, paresthesias, and bowel or bladder dysfunction are present along with the pain, in order to assess for cord compression. In our patient's case, sinister back pain prompted a lumbar x-ray scan, with MRI and a bone scan following identification of substantial pathology. Of interest, the identification of a rib fracture on bone scan represented a plasmacytoma: a proliferation of plasma cells distant from the primary MM site.

All patients with findings suggestive of MM should be immediately referred to the hematology department for bone marrow examination and management, where the definitive diagnosis is made through the finding of 10% or greater clonal plasma cells on bone marrow aspiration and biopsy.[4]

The prognosis for MM is highly heterogeneous, based on a range of factors, and treatment is tailored to each individual case.[10] The philosophy of treatment is aimed at symptom control and is stratified based on whether the patient is a candidate for high-dose chemotherapy followed by autologous stem cell transplantation. Treatment regimens involve steroids in combination with an immunomodulator (lenalidomide or thalidomide), a proteasome inhibitor (bortezomib), or chemotherapy (eg, melphalan, cyclophosphamide). Eligibility for autologous transplantation is assessed by age, stage of myeloma, and other laboratory test results.[11] Bone disease can be treated with analgesics, palliative radiation, bisphosphonates, and occasionally with kyphoplasty or vertebroplasty.

Conclusion

A 47-year-old man presenting with a pathologic lumbar vertebral fracture after a fall from his own height suggests potentially sinister pathology. Other red flags specific to this case included progressively impaired mobility and rapidly increasing nocturnal back pain of a different quality than his pre-existing chronic mechanical low back pain.

Despite MM having a usually advanced age of onset, unusual presentations of this nature in younger patients should push clinicians to include the possibility of MM in their differential diagnosis. This is especially important to consider in light of the substantial survival benefit younger patients have over older patients with MM, provided MM is diagnosed early and treated appropriately in a timely fashion.

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Competing interests
None declared

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