An Unusual Presentation of Multiple Myeloma

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Multiple myeloma (MM) is a disease characterized by the malignant proliferation of plasma cells of a single clone. Bone destruction is the hallmark of MM, and bone pain is the typical presenting feature. This article presents the case of a patient with typical symptoms of lateral epicondylitis that did not improve with conservative therapy. Further studies revealed the presence of MM. The presenting features of MM and approach to management are briefly reviewed.

CASE PRESENTATION

Initial Presentation

A 71-year-old man presented to his primary care doctor with complaints of right elbow pain. He stated that he was pulling a heavy object 1 week earlier and, since then, developed progressively intense pain in the right elbow. The patient gave a past history of asthma since childhood, hypertension, and recently diagnosed diet-controlled diabetes mellitus. Medications included salmeterol, diltiazem, and hydrochlorothiazide. He denied having allergies or using illicit drugs, alcohol, or tobacco. He was a school teacher with an active lifestyle. His blood pressure was 120/70 mm Hg, heart rate was 80 bpm, and respiratory rate was 14 breaths/min. His weight was 160 lb. He was afebrile. He had pain of the right elbow on flexion and extension of the forearm. The lateral epicondyle was tender to palpation.

The patient was diagnosed with lateral epicondylitis and was given nonsteroidal anti-inflammatory drugs (NSAIDs) and a compression wrap and was advised to rest his arm. He returned in 2 weeks with no improvement and was referred to physical therapy. Three months of conservative therapy failed to improve his symptoms of tennis elbow.

Subsequent Presentation and Clinical Course

At his presentation at 3 months, laboratory evaluation and imaging of the elbow were ordered. Laboratory data showed a mild normochromic, normocytic anemia (hemoglobin concentration, 10.9 g/dL [normal, 14.0–18.0 g/dL], hematocrit, 32.2% [normal, 42.0%–52.0%], normal values of mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration). Leukocyte and platelet counts were normal. Erythrocyte sedimentation rate was elevated (75 mm/h). Albumin level was normal, but the level of globulins was high, with a decreased albumin-to-globulin ratio. Results of the rest of the laboratory work-up were normal.

Radiography of the elbow showed a lytic lesion in the area of the right proximal radius (**Figure 1**). Magnetic resonance imaging (**Figure 2**) showed a large destructive, expansile mass within the medullary cavity of the proximal radial shaft, with a large soft tissue component that was enhanced in T_2-weighted images. A radiographic skeletal bone survey was ordered and showed lytic lesions at multiple locations, including the right humerus, proximal and distal bilateral femurs, and bilateral ischial bones. In addition, a compression deformity of the spine was seen at the level of T7.

Biopsy of the radial lytic lesion revealed a monomorphous population of plasma cells consistent with plasmacytoma. Serum protein electrophoresis showed a monoclonal spike in the immunoglobulin gamma region. Based on these findings, the patient was diagnosed with MM and was referred to an oncology clinic. He received radiation to his left forearm to help relieve his pain as well as chemotherapy (melphalan and prednisone). Three years later, he is doing well and is in remission.

DISCUSSION

Lateral Epicondylitis

Lateral epicondylitis, or tennis elbow, is a commonly encountered problem in today's active society. It is an overuse injury associated with many activities. Patients present with lateral elbow and forearm pain exacerbated

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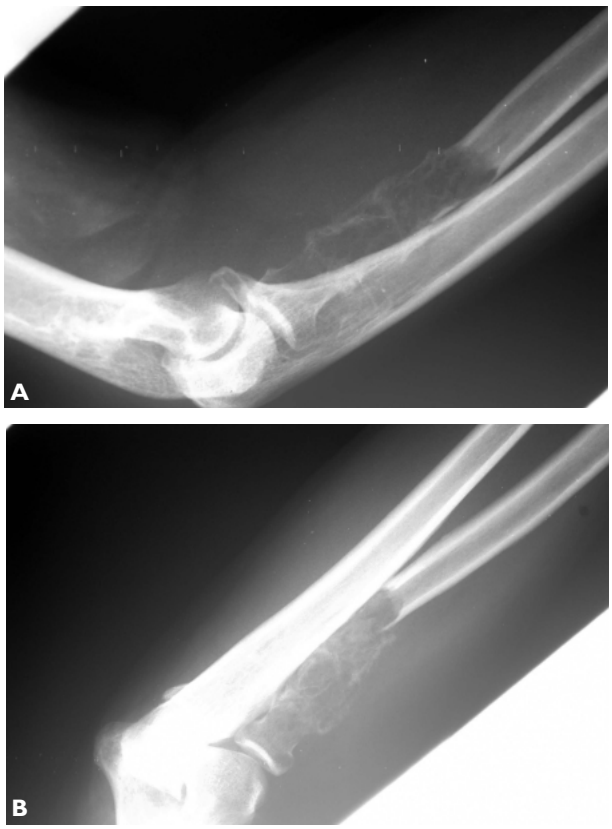


Figure 1. Radiographs of the case patient's right elbow. (**A**) Lateral view. (**B**) Anteroposterior view.

by use. The typical patient is a man or woman aged 35 to 55 years who either is a recreational athlete or one who engages in rigorous daily activities. Upon examination, the patient has a point of maximal tenderness just distal (5–10 mm) to the lateral epicondyle in the area of the extensor carpi radialis brevis muscle and tendon. Wrist extension or supination (but not flexion or pronation) against resistance with the elbow extended will provoke symptoms. Radiographs can be helpful in ruling out other disorders or concomitant intra-articular pathology (eg, osteochondral loose body, posterior osteophytes).

Nonsurgical treatment is the mainstay of care for patients with lateral epicondylitis, including rest of the affected arm, use of a counterforce brace, and NSAIDs. Wrist splinting and/or corticosteroid injections often are useful. Surgery is reserved for patients in whom several months of conservative therapy has not been helpful.

Clinical Manifestations of Multiple Myeloma

Bone destruction is the hallmark of MM, with roughly 70% to 80% of patients having bone involvement. Bone pain is the main presenting symptom in patients with MM or solitary bone plasmacytoma (SBP). In large series, approximately one third to two thirds of patients with myeloma present with bone pain at the time of diagnosis.[1,2] The pain may present acutely and lead to a diagnosis in a few weeks; however, patients often experience symptoms for several months before a diagnosis is reached. The case patient had symptoms for 3 months before the diagnosis was made. In addition to bone pain and pathologic fractures, symptoms of peripheral neuropathy (motor, sensory or mixed) may precipitate a diagnosis.[3] The **Table** summarizes the criteria for diagnosis of MM.[4,5]

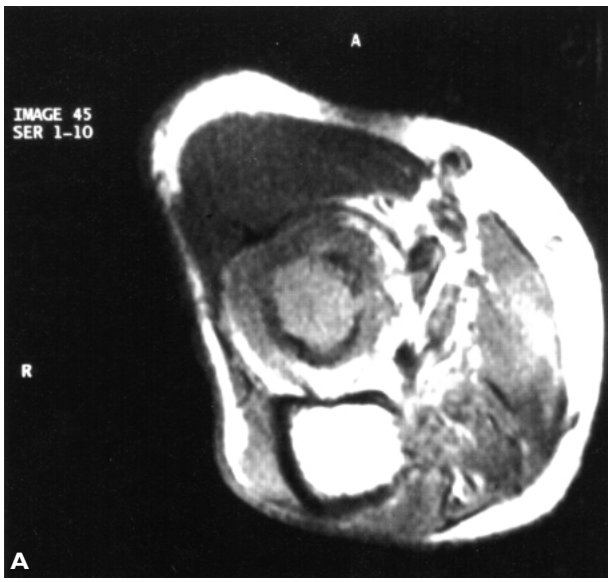
Bone destruction in plasma cell disorders is mediated through normal osteoclasts, which respond to local osteoclast-activating factors produced by myeloma cells or by other cells in the local microenvironment. Bone formation is markedly suppressed in myeloma bone disease and remains decreased even when patients are in remission.[1] Nevertheless, the variant of solitary or diffuse osteosclerosis in myeloma bone disease is well described, although its etiology is obscure.[6]

Myeloma in bone almost always occurs as multiple discrete foci or as a diffuse medullary infiltration.[7] The preliminary diagnosis of SBP involves the exclusion of myeloma elsewhere and should include a bone marrow biopsy, a radiologic skeletal survey, analysis of the serum proteins, and urine examination for Bence Jones protein. Establishing a diagnosis of SBP rests on careful long-term follow-up.[8] Several authors agree that most cases that initially present as a single lesion eventually disseminate—approximately two thirds within a decade.[8,9]

The bony areas most frequently involved in MM are the spine, skull, proximal long bones, and ribs. Presenting symptoms arise more frequently from the back and ribs. Pathologic fractures of the spine and femoral neck are not uncommon in the initial presentation of MM. In addition, mass lesions may develop and become palpable, especially on the skull, clavicles, and sternum.[10] Extra-axial involvement other than the proximal long bones is encountered much less frequently.

Diagnostic Evaluation

Radiologic manifestations of MM at diagnosis may include osteopenia, lytic ("punched out") lesions, and fractures. These manifestations may occur singly or in conjunction with each other. In addition, as many as 27% of cases have no radiologic evidence at diagnosis.[2,11] Lesions of the pelvis and long bones may be expansile (as in the case patient) with a "soap bubble" appearance, commonly leaving the cortex intact and showing no periosteal reaction. The soft tissue extension seen in



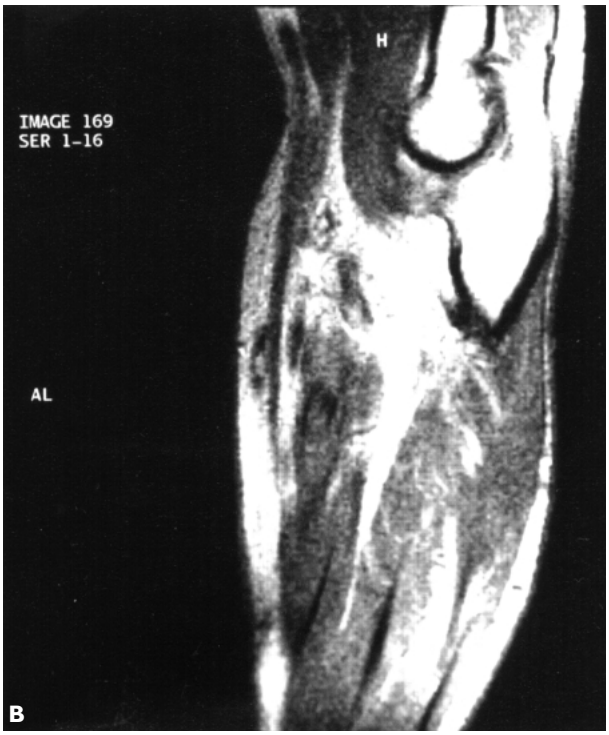


Figure 2. T_2-weighted magnetic resonance images of the case patient's right elbow. (**A**) Cross section. (**B**) Longitudinal section.

the case patient also is quite common. Spinal lesions tend to be purely destructive and less expansile. They may cross the disk into adjacent vertebral bodies with concurrent development of paraspinous masses, mimicking tuberculous spondylitis.[8]

Besides the above-mentioned common radiographic patterns, osteosclerosis may be seen, either intermingled with areas of radiolucency or diffuse.[6] Diffuse sclerosis is considered extremely rare, with an estimated frequency of 1% to 3%.[12] Rarely, an expansile polycystic bone lesion in multiple myeloma reflects amyloid deposition (amyloidoma).[6] Metaplastic formation of cartilage or bone may occur in amyloidoma, further altering the radiographic appearance.[13]

Traditionally, plain radiographs (a skeletal bone survey) have been used both to diagnose and to evaluate treatment response in patients with multiple myeloma.[1] As bone formation is significantly impaired, bone scintigraphy will be abnormal in a minority of myeloma patients with active bone disease and, therefore, is not routinely recommended.[14] Magnetic resonance imaging has been shown to be much more sensitive than a radiographic bone survey in detecting asymptomatic bone disease[15] and also more sensitive in detecting bone marrow involvement in patients with otherwise presumed SBP.[16] Positron emission tomography using the emitter ^{18}F-fluorodeoxyglucose appears especially sensitive for detecting osteolytic bone disease and could prove useful in the evaluation of multiple myeloma.[17] Dual energy X-ray absorptiometry scanning may uncover significant osteopenia in multiple myeloma patients with apparently normal radiographs.[18] Finally, technetium-99m-sestamibi scanning

Table. Criteria for diagnosis of multiple myeloma

Major criteria:

1. Plasmacytomas on tissue biopsy
2. Bone marrow plasmacytosis (30% plasma cells)
3. Monoclonal immunoglobulin spike on serum electrophoresis: IgG > 3.5 g/dL or IgA > 2.0 g/dL; κ or λ light-chain excretion > 1.0 g/d on 24-h urine protein electrophoresis

Minor criteria:

a. Bone marrow plasmacytosis (10%–30% plasma cells)
b. Monoclonal immunoglobulin spike present but of lesser magnitude than listed above
c. Lytic bone lesions
d. IgM < 50 mg/dL, IgA < 100 mg/dL or IgG < 600 mg/dL

Any of the following sets of criteria will confirm the diagnosis:

Any 2 major criteria

Major criterion 1 plus minor criterion b, c, or d

Major criterion 3 plus minor criterion a or c

Minor criteria a, b, and c or a, b, and d

Adapted from Durie and Salmon.[4,5]

seems promising in terms of sensitivity and cost effectiveness.[1]

Treatment

Treatment of myeloma bone disease traditionally has included radiation therapy (especially for SBP, in which the intent is curative[1]) and surgery for impending or pathologic fractures, sometimes with the use of polymethylmethacrylate, a component of bone cement normally used in orthopedic procedures. Chemotherapy is implemented if there is evidence of disseminated disease. The use of oral sodium fluoride in large doses to produce fluorosis has not been shown effective in reducing bone pathology and is not recommended.[1] Intravenous bisphosphonates are routinely used in the vast majority of patients with MM. By inhibiting osteoclast activity, bisphosphonates significantly reduce the rate of pathologic fractures, the need for radiotherapy and surgery, and improve bone pain and quality of life.[1]

CONCLUSION

To our knowledge, MM presenting with symptoms of lateral epicondylitis has been reported only once, by Benedict et al.[8] Physicians should suspect myeloma in patients with joint symptoms that are resistant to treatment, and radiographic evaluation should be pursued. **HP**

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