Multimodality Imaging Including PET/CT in a Patient with Amyloid Arthropathy and Multiple Myeloma

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Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography

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Abstract

We report a case of amyloid arthropathy in a patient with multiple myeloma. Amyloid arthropathy is a very rare condition that may be associated with multiple myeloma. It presented in our patient as soft tissue masses around joints and eroding into adjacent bones. We found it to be hypermetabolic on fused positron emission tomography and computed tomographic scanning.

Case Report

A 57-year-old man with chronic hepatitis B and C was found in 2000 to have abnormal paraprotein in the blood and abnormal renal function, which worsened until April 2007 when he required dialysis. He also had light-chain monoclonal protein in the urine, and a bone marrow biopsy showed mild proliferation of plasma cells, which was thought to be related to chronic hepatitis B and C. In August 2007 his lumbar MRI showed several spotty marrow lesions consistent with multiple myeloma, associated with abnormalities of his serum calcium and alkaline phosphatase. On that basis he started treatment for multiple myeloma with bortezomib in January of 2008.

In May 2008 he was admitted for pain control at an outside institution and complained of soft tissue masses growing in the right humerus, left distal clavicle, posterior wrist and left scapular area. Biopsies of the soft tissue masses were nondiagnostic.

In August 2008, he presented to our institution with paresthesias in the right arm due to the mass in the area of the shoulder, and a weight loss of 70 pounds. The patient was wheelchair bound, with decreased range of motion in the right arm and weakness in both lower extremities and right arm. He had palpable masses including a 7.0 cm mass on the proximal right humerus, 3.0 cm mass on his left distal clavicle, small masses on both wrists, and asymmetry between his left and right scapula. Bone marrow biopsy showed 20% plasma cells. A bone survey obtained at that time showed large lucencies around the hips and shoulders (Fig 1 and 2) that were suspected to be due to myeloma.

PET/CT was then performed partly to evaluate for any other lymphoproliferative disorder that might explain the patient's weight loss better than multiple myeloma and partly to look for plasmacytomas or other focal disease. The PET/CT demonstrated increased metabolic activity in thickened soft tissues surrounding both hips (maximum SUV 3.6 on the left and 2.9 on the right) and shoulders (maximum SUV 6.2 on the left and 5.9 on the right). There was also hypermetabolic activity at the wrists, in the low lumbar spine, in the cervical spine, and at the knees (Fig 3). A cystic collection along the right biceps was not hypermetabolic but was surrounded by a hypermetabolic rim. The associated noncontrast CT obtained in conjunction with PET/CT imaging showed osseous erosions of both femoral heads and the left acetabulum. Synovial thickening was present at both hip joints, and on the left created a large mass. Small calcifications were present in the left-sided mass. CT through the shoulders revealed bilateral erosions of the glenoid fossa and humeral head as well as numerous calcifications in lumpy soft tissue masses (Fig 4 and 5). There were hypermetabolic erosions at the wrists, small erosions at the knees, and in the lumbar spine and cervical spine. More suggestive of multiple myeloma than of amyloidosis were two small lytic lesions in the bony pelvis, one 14 mm and the other 5 mm in diameter. Neither of these was noticeably hypermetabolic.

Right hip arthroplasty was then undertaken both for pain relief and to prevent pathologic fracture. In the days just after this procedure, and before the associated pathology results were known, MRI was performed of the pelvis and of the right humerus to evaluate further the masses in those locations. At both hips and at the right shoulder, there were masses of thickened synovium that expanded the joints and eroded the adjacent bones. At the shoulder, it extended into the tendon sheath of the tendon of the long head of the biceps brachii muscle, which was distended by cyst-like pockets of fluid. The thickened synovium was approximately isointense to muscle on T1 weighting and was slightly brighter on T2 weighting.

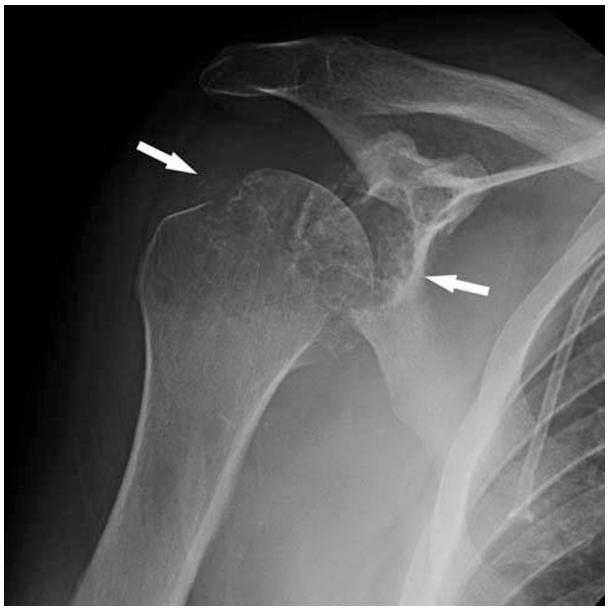

Figure 1. Right shoulder radiograph. Frontal view of the right shoulder demonstrates large lucencies in the humeral head and glenoid (arrow), subluxation of the glenohumeral joint and small calcifications in the soft tissues (thin arrow).

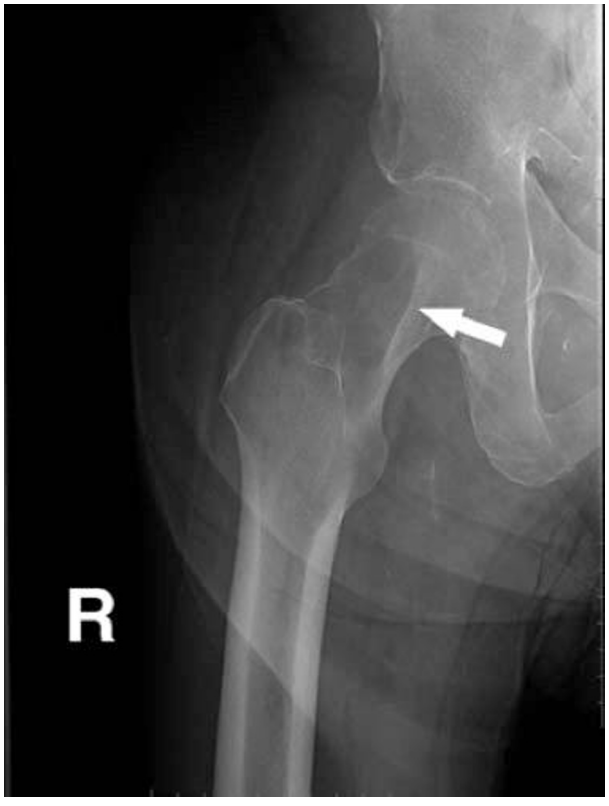

Figure 2. Right hip radiograph. Frontal view of the right hip shows a large lucency in the femoral neck and upper intertrochanteric area (arrow).

When results of histology became available, amyloid arthropathy was diagnosed in the pathologic specimen of the right hip. Biopsies of the right humerus soft tissue mass and of the left hip mass were also consistent with amyloid deposition secondary to multiple myeloma.

Treatment, other than the hip arthroplasty to prevent pathologic fracture, has been aimed at controlling the patient's multiple myeloma. The patient had a very good initial response to bortezomib and cyclophosphamide combination therapy, with a reduction in free kappa light chain from 4200 mg/L to 323 mg/L. However, he progressed after 3 cycles of chemotherapy and is currently receiving melphalan with dexamethasone and thalidomide. It is too early to know his response to this therapy. He is still wheelchair bound due to pain but able to ambulate with physical therapy assistance.

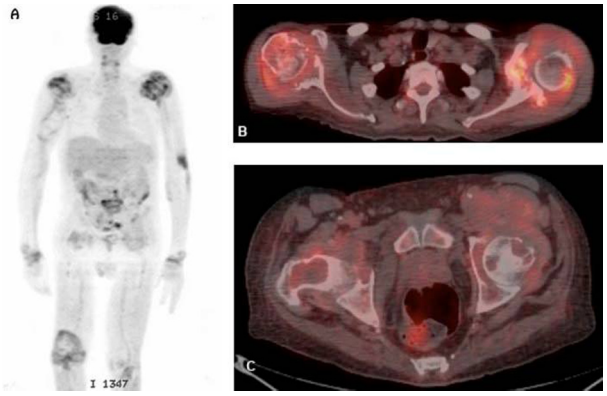

Figure 3. A. Maximum intensity projection. B Axial image through the shoulders. C Axial image through the hips. There is increased metabolic activity in the thickened soft tissues surrounding both hips and shoulders with associated osseous erosions. Increased activity is also present at both knees, wrists, and in the low lumbar spine.

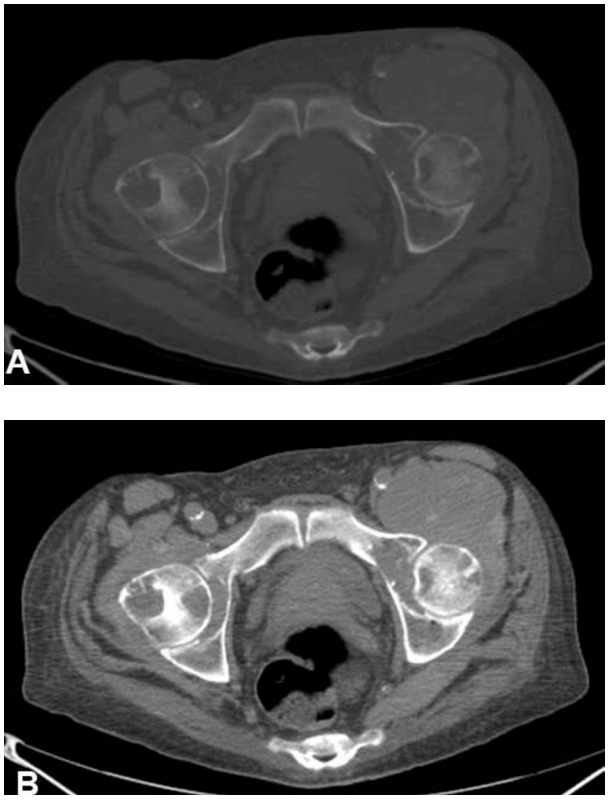

Figure 4. Noncontrast CT obtained in conjunction with PET/CT imaging at the level of the hips, Fig 4a filmed on bone window and Fig 4b filmed on soft tissue window. Bilateral osseous erosions involve both femoral heads and the left acetabulum.

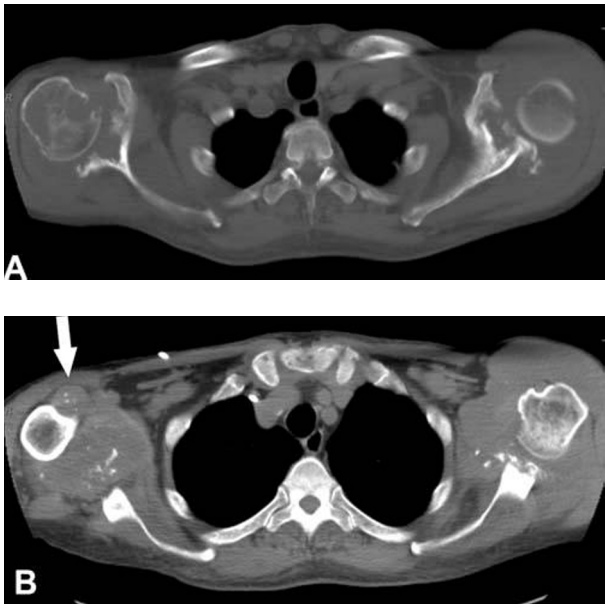

Figure 5. CT at the level of the shoulders, Fig 5a filmed on bone window and Fig 5b filmed on soft tissue window, a few centimeters caudal to Fig 5a. There are bilateral osseous erosions and numerous calcifications in soft tissue masses. Note the calcifications in the distended right tendon sheath of the long head of the biceps brachii muscle (arrow).

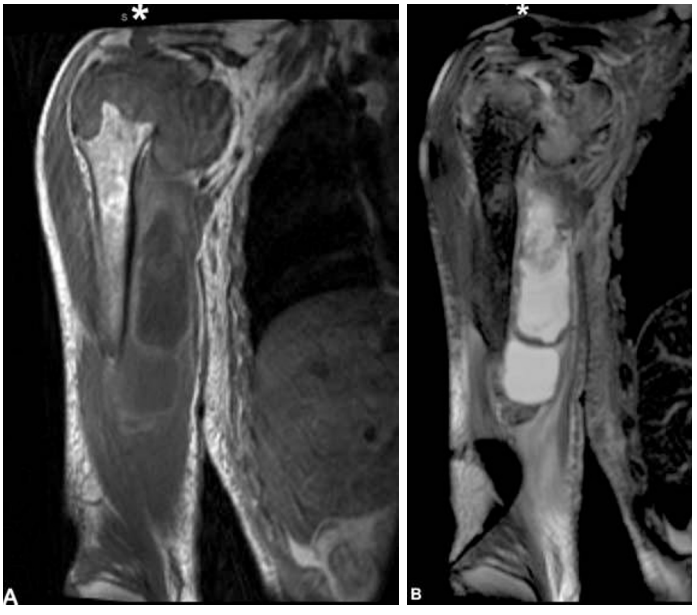

Figure 6. MRI of the right humerus. Coronal T1 (TR 500/TE 13) and coronal T2 (TR 4350 /TE 82) -weighted MR images of the right humerus. Thickened synovium expands the shoulder joint and erodes the humeral head and glenoid fossa (arrow Fig 6b). The tendon sheath of the tendon of the long head of the biceps brachii muscle is distended by cyst-like pockets of fluid.

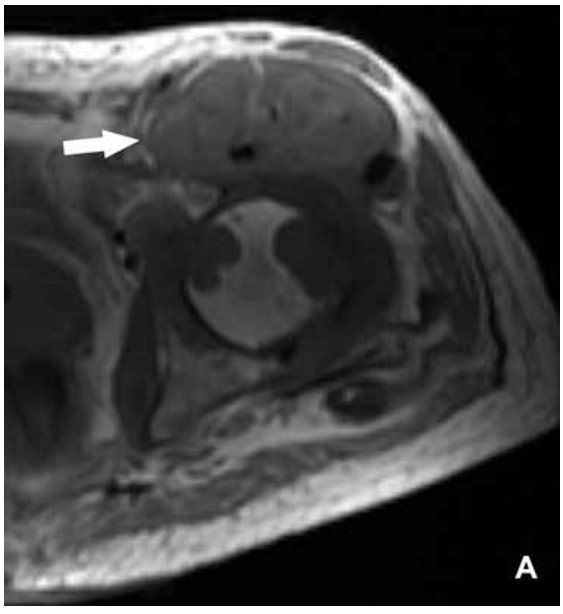

Figure 7. MRI of the pelvis. Axial T1 (TR 566 /TE 13) -weighted MR image of the pelvis. Thickened synovium erodes the left femoral head. The iliopsoas muscle is thickened (arrow).

Discussion

Amyloidosis may manifest as a wide range of diseases characterized by extracellular deposition of protein and protein derivatives. The disease becomes clinically significant when its diffuse form affects organ function or local deposition creates a mass, also called an amyloidoma [1]. Most cases of amyloidosis can be classified as either primary or secondary. Primary amyloidosis is related to amyloid light chain and involves mesenchymal structures including the heart, tongue, muscle, synovial membrane, or perivascular connective tissue [2]. Primary amyloidosis has a strong connection with multiple myeloma. At least 30% of patients with primary amyloidosis will eventually develop multiple myeloma [2], and 5 - 15 % of patients with multiple myeloma will develop amyloidosis [3-5]. In our patient's case the distribution of amyloid is that of primary amyloidosis associated with multiple myeloma [2]. Another form of amyloid deposition with B2-microglobulin may also cause polyarthropathy with pain and stiffness involving large joints as well as the wrists and spine. This form tends to occur in patients with long-term (over 5 years) dialysis [6,7].

Secondary amyloidosis is related to chronic inflammatory disease such as Crohn's disease, rheumatoid arthritis and other rheumatic or connective tissue disorders, chronic osteomyelites, tuberculosis, and lung diseases including bronchiectasis and cystic fibrosis [1]. It shows a predilection for the liver, spleen, kidney and adrenal glands [2], and it is associated with deposition of amino-acid terminus-SAA protein precursors [1].

In our patient's case, the clinical manifestation of amyloidosis was arthropathy involving predominantly the hips and shoulders, but there was also some involvement by PET/CT and conventional radiography of the low lumbar spine, knees, and wrists. The large lucent lesions created about the joints in patients with amyloid arthropathy can mimic intraosseous lesions of multiple myeloma on conventional radiographs, and this was the initial interpretation in our patient. Cross-sectional imaging helped clarify the situation by making it clear that the osseous lucencies were due not to intrinsic bony disease but to synovial thickening and extrinsic erosion of bone. This shifted the differential diagnosis to polyarticular arthritic conditions including rheumatoid arthritis and related

illnesses as well as indolent infections. Recognition of the small periarticular calcifications in the soft tissues was helpful, as calcifications may be seen in amyloidomas [8].

Primary amyloidosis is an uncommon disease, and amyloid arthropathy is even rarer. Fautrel et al described 11 cases [9]. In their series of cases, all of their patients had amyloid arthropathy in conjunction with pre-existing multiple myeloma [9], though there have been other cases in which amyloid arthropathy preceded the onset of multiple myeloma [10]. Frequent sites of involvement are the shoulders, wrists, hips, knees, and the carpal tunnel. Amyloid-related thickening of the soft tissues of the carpal tunnel can cause carpal tunnel syndrome, and shoulder involvement can give visibly evident thickening of the shoulders, termed the shoulder-pad sign [7, 9]. Because the clinical manifestations of amyloid arthropathy can be easily confused with other polyarticular forms of arthritis such as rheumatoid arthritis, the radiologist should consider this diagnosis, particularly in patients with multiple myeloma or other predisposing conditions.

On MRI amyloid arthropathy typically demonstrates homogenous low-to-intermediate signal intensity on both T1 and T2 weighted images, though some foci of low signal may be seen on T2-weighted images, and there can be high T2 signal in cyst-like areas. Periarticular amyloid may enhance mildly after gadolinium administration [3, 7, 11].

We have been able to find few reports of PET/CT in amyloidosis. Some reports have found increased metabolic activity in amyloid depositions in the lung [12-15], and one report described increased PET/CT activity in amyloid adenopathy [16]. Although other radionuclides including Tc 99m aprotinin [17] and Tc99m DMSA [18] may be of use and may be preferred for evaluation of amyloidosis, the increasing use of PET/CT for patients with multiple myeloma [19, 20] makes it important to recognize amyloid arthropathy as being among the causes of increased metabolic activity in periarticular soft tissues and bone. We report a case of moderately increased FDG uptake in numerous sites of amyloid deposition in the periarticular tissues of a patient with multiple myeloma as a predisposing condition.

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