Orthopaedic Case of the Month

Medial Knee Pain in a 69-year-old Man

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Received: 25 June 2010 / Accepted: 30 September 2010 / Published online: 19 October 2010
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History and Physical Examination

A retired 69-year-old man was referred with a recent exacerbation of right medial knee pain. The pain had been gradually progressive for 3 years, with marked deterioration in the previous 6 months. There was no history of trauma or preceding infection. His pain was exertionally related; he was able to walk approximately 150 m before resting to relieve the pain. Deep knee flexion exacerbated his symptoms. He had occasional night pain after an active day but no other symptoms.

His medical history was positive for Type 1 insulin-dependent diabetes, chronic renal failure, coronary artery disease treated with one left anterior descending stent, first

metatarsophalangeal joint gout, and retinal detachment. There was no positive personal or familial cancer history.

Physical examination showed a mild effusion with no skin changes, deformity, or mass. There was medial femoral condylar tenderness at and just proximal to the joint line. ROM was 0° to 130°. No ligamentous abnormalities or neurovascular deficits were noted. His hip and spine examinations were normal.

Abnormal blood results confirmed his chronic renal failure with a creatinine level of 329 µmol/L, gout with a plasma urate level of 544 µmol/L, and poorly controlled diabetes with a glucose level of 10.7 mmol/L.

After plain film evaluation (Figs. 1, 2), the patient underwent MRI of the right knee at his referring hospital (Figs. 3–5).

Based on the history, physical examination, laboratory studies, and imaging studies, what is the differential diagnosis at this point?

Imaging Interpretation

Plain film evaluation (Figs. 1, 2) showed an osteolytic, subarticular, eccentrically located 3.5- by 4-cm ovoid lesion in the medial femoral condyle. An irregular subchondral bone plate was observed with multiple points of intraarticular and extraarticular breach. Proximally, the lesion had a narrow zone of transition with a sclerotic margin. There were also mild degenerative changes in the medial femoral tibial joint.

MRI showed a 4.2- (AP) × 3.6- (mediolateral) × 1.7-cm (craniocaudal) proton density weighted intermediate signal and heterogeneous intermediate signal T2 subarticular lesion in the medial femoral condyle (Fig. 3). There was marked chondral irregularity overlying the lesion with no

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Each author certifies that his or her institution approved the reporting of this case report, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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Fig. 1 An AP radiograph of the knee shows a subarticular medial femoral condylar lesion

Fig. 2 A lateral radiograph of the knee shows a distal cortical breach and sclerotic border proximally.

major surrounding bone marrow edema (Fig. 4). Cortical breakthrough with intraarticular spread laterally into the intercondylar notch abutting the PCL was noted (Fig. 5). There was also a horizontal oblique undersurface tear through the posterior horn of the medial meniscus extending from the body to the posterior root horn attachment. The lateral meniscus and ligamentous structures were intact. No bone scan was performed, as a diagnosis of malignancy had not been made.

Differential Diagnosis

Metastatic disease
Lymphoma

Fig. 3 A coronal proton density sequence shows the homogenous intermediate lesion eroding into the intercondylar notch and up to the medial collateral ligament.

Fig. 4 A sagittal proton density scan shows marked cartilaginous irregularity.

Osteochondral defect
Infection
Chondroblastoma
Giant cell tumor (GCT) of bone
Osteoarthritic, rheumatoid, or crystal arthropathy.

Given the juxtaarticular location of the lesion with an associated cortical breach and soft tissue extension, an open biopsy was conducted to obtain a histologic

Fig. 5 An axial fat-suppressed T2-weighted MR image confirms lateral cortical breakthrough with intraarticular spread into the notch abutting the PCL.

diagnosis. This was performed via a medial transosseous approach with image intensification assistance to ensure accurate curettage location. Intralesional hemorrhagic tan and gray tissue fragmented material was sent for histologic and microbiologic analyses (Figs. 6, 7).

Based on the history, physical examination, laboratory studies, imaging studies, and histologic picture, what is the diagnosis and how should the patient be treated?

Histology Interpretation

A frozen section suggested acellular debris showing refractile crystals. A sample of joint fluid was sent for cytologic assessment after this review. Microbiologic cultures all were negative.

Permanent sections showed a destructive inflammatory process characterized by sheets of histiocytes and fibrous tissue (Fig. 6A). Interspersed throughout the lesion were aggregates of acellular material, rimmed by foreign body-type multinucleated giant cells (Fig. 6B). Polarization of nonprocessed, frozen sections revealed the presence of negatively birefringent monosodium urate crystals (Fig. 7). In addition, cytologic examination of a needle aspirate from the knee confirmed the presence of crystals.

Diagnosis

Gout

Discussion and Treatment

Based on the presence of intraosseous, negatively birefringent monosodium urate crystals, a diagnosis of gout

Fig. 6A–B (A) A section from formalin-fixed paraffin-embedded tissue shows a gouty tophus with a brisk histiocytic infiltrate surrounding dissolved urate deposits (Stain, hematoxylin and eosin; original magnification, $\times 100$). (B) A higher-magnification image highlights the presence of foreign body-type multinucleated giant cells and mononuclear histiocytes rimming the urate deposits (Stain, hematoxylin and eosin; original magnification, $\times 400$).

Fig. 7 A fresh-frozen tissue section shows negatively birefringent needle-shaped crystals (Polarized light, $\times 630$).

was made. Knee pain is a common complaint and, in this age group, most likely would be attributable to a degenerative intraarticular process, such as knee osteoarthritis or meniscal attrition. When associated with a focal osteolytic defect located in the juxtaarticular or subarticular region, a more aggressive list of differential diagnoses becomes possible. This patient had known gout but believed his pain was of a different nature and type compared with his prior great toe pain. There were no episodes of knee erythema. The plain films were not typical of the classic punched-out periarticular lesions with an overhanging edge, as this lesion had a more central location in the femoral condyle. Infection, metastatic disease, a large osteochondral lesion, a subarticular cyst or geode all were possible, more common, diagnoses at this stage of his investigations. His pain was over a period of 3 years, making an aggressive lesion less likely. Metastatic disease or lymphoma, although possible, was not radiographically typical. Although the lesion was osteolytic, it had a more sclerotic, rather than absent, border. Infection also was considered, but with a 3-year history, the lack of erythema, absence of systemic symptoms, and primarily mechanical pain, was clinically less suspected.

MR appearances were consistent with a subarticular lesion including GCT, chondroblastoma, lymphoma, synovial inflammatory, or a degenerative-based disease process. His age made GCT and chondroblastoma less likely. GCT was even less likely given the purely epiphyseal location of the lesion, but MR signal characteristics may have resembled this tumor. The absence of edema on T2 weighting also made infection and chondroblastoma lower on the list of differentials. No chondroid matrix was visible in the lesion as typically noted with chondroblastoma. The absence of a large soft tissue mass made lymphoma unlikely. Atypical infections are always possible, therefore, the importance of obtaining samples for typical and atypical microbiologic evaluation. These results were negative. The lack of hyperintense signal on T2 weighting was not consistent with a geode or an osteoarthritic degenerative cyst.

The histologic findings revealed urate deposits with a concomitant inflammatory response. Polarization of non-processed frozen tissue confirmed the presence of negatively birefringent crystals. Cytologic analysis from the joint aspirate additionally confirmed the presence of crystals. These observations correlated with MRI, which showed a soft tissue, tophaceous extension. The diagnosis of gout was made.

Numerous authors have reported intraosseous lytic lesions with soft tissue extension secondary to gout in the spine [3, 13], talus [4, 8, 15, 17], navicular [22], proximal tibia [6], and patella [11, 19], all mimicking aggressive malignant processes. There is one case report of gouty

tophus causing a patella fracture [16]. For lesions with an associated soft tissue mass, the differential diagnoses include malignant disorders and gout.

Gout affects 1% to 4% of adult Western men with a reported decreased incidence in women [1]. There appears to be a dietary etiologic link with higher consumption of meat, seafood, and fructose. In 1980, the prevalence of gout in China was very low. The syndrome became more common as dietary habits became more Westernized, producing an equivalent modern prevalence in 2008 of 1.14% [14]. There also seems to be a genetic factor in gout development [7] and elevated serum urate levels [23].

Most purine is produced endogenously in the liver, with an additional quantity provided by ingested purine-containing foods. Serum urate levels are balanced between intracellular turnover and degradation by xanthine oxidase. When the concentration exceeds the solubility limit of 380 mmol/L, the risk of monosodium urate crystal formation is increased. Normal serum urate levels are close to this limit because humans and higher primates are deficient of the enzyme uricase, which degrades urate to the highly soluble allantoin. The kidney excretes approximately $\frac{2}{3}$ of urate and a renal basis for hyperuricemia is noted in approximately 90% of patients [20]. The use of diuretics and initiation of gout therapy can raise urate levels.

The urate crystal-induced proinflammatory response typically causes the pain, swelling, and tenderness seen in an acute attack of gout [5, 12]. Acute attacks typically affect one joint, usually in the lower limb, and can mimic septic arthritis. The first metatarsophalangeal joint is the most commonly affected, followed by the midtarsal joints, ankles, and knees. Further acute episodes can lead to chronic tophaceous gout in 30% of untreated individuals [18].

These have numerous radiographic features. Chondrocalcinosis can be, but is not always, present. Cartilage thinning, multiple subchondral cysts, osteophytes, and an associated soft tissue swelling usually are observed on plain films. The MR appearances are characterized by erosions and tophi. The erosions are most commonly periarticular but also can be intraarticular. The tophi are homogeneous intermediate or low on T1 and variable on T2 weighting, although hemosiderin deposition may lower the T2 signal. Isolating monosodium urate crystals from either joint fluid or tophi soft tissue masses confirms the diagnosis.

Treatment is generally medical with surgery reserved for site-specific indications, including removal of large deposits causing substantial functional impairment or superimposed septic arthritis. Distinguishing between drugs used for treatment of acute attacks from those for long-term disease control is mandatory. Acute attacks are managed by rest, ice, and NSAIDs with or without

colchicine. Interleukin 1 β inhibitors [21], prednisolone [10], parenteral adrenocorticotrophic hormone [2], and intraarticular corticosteroids [24] also have been used for management of acute attacks. Xanthine oxidase inhibition by allopurinol is used as first-line therapy [24]. Probenecid, sulfinpyrazone, and benzbromarone are second-line uricosuric agents. Febuxostat is an emerging xanthine oxidase inhibitor used in patients intolerant to allopurinol [9].

This case illustrates a lytic intraosseous gouty tophi of the medial femoral condyle with intraarticular and periarticular extension diagnosed with a combination of imaging, histopathologic analysis, and joint fluid analysis. This was biopsied and, after frozen section analysis, curettaged. Given the relative small size of this lesion and the cortical breach into the joint, it was not packed with bone graft or cement. After the initial period of postoperative rehabilitation with protected weightbearing for 6 weeks, the patient's knee pain improved. He was commenced on NSAIDs for 4 weeks and then continued on 100 mg of allopurinol daily. Followup at 6 months confirmed that he had marked improvement in his symptoms, but he was not completely pain free. No consideration was given to joint replacement surgery at this stage given the absence of significant pain and the ability to perform activities of daily living, without marked restriction.

Acknowledgments We thank Drs Kurt Weiss, David Biau, and Jay Wunder for input in this case.

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