Knee Pain in a 9-year-old Girl

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History and Physical Examination

A 9-year-old girl presented to her pediatrician with 2 months of right knee pain with insidious onset and no trauma. She was an active, multisport athlete. A diagnosis of overuse tendinitis was made, and activity modification, ice, and NSAIDs were prescribed. After 1 month, she showed no improvement and radiographs were taken (Fig. 1), after which MRI (Fig. 2) and a technetium bone scan (Fig. 3) were completed, and orthopaedic oncology referral was made.

On presentation to our clinic, the patient described intermittent pain exacerbated with activity localized to the inferior pole of the patella. She had a history of Lyme disease, which was diagnosed and treated earlier in the same year without sequelae.

Physical examination showed a well-appearing, alert girl who appeared her stated age. She ambulated with an antalgic gait. Musculoskeletal examination showed her right lower extremity to have normal neurologic and vascular findings. Her knee was without effusion and she had full extension and flexion compared with the contralateral side;

the principal knee ligaments were intact. She had mild tenderness with palpation of the lateral, distal femur. The remainder of her examination and complete blood count and inflammatory markers were normal.

Imaging Interpretation

Radiographs revealed a well-circumscribed lesion in the lateral, distal femoral epiphysis with decreased radiopacity compared with surrounding bone. The lesion did not appear to cross the physis or enter the joint. Review of her MR images showed a lesion abutting the physis and the articular cartilage with low signal on proton-density sequences (Fig. 2A), high signal on T2-weighted sequences (Fig. 2B), and heterogeneous contrast uptake on gadolinium-enhanced sequences (Fig. 2C). Peripheral marrow edema was not seen on the T2-weighted MRI (Fig. 2B); gadolinium-enhanced MRI sequences showed heterogeneous enhancement (Fig. 2C). A technetium-99m bone scan showed no increase in osteoblast activity in the lesion (Fig. 3).

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All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request. 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. This work was performed at Boston Children's Hospital, Boston, MA, USA.

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

Differential Diagnosis

Chondroblastoma
Giant cell tumor of bone
Chondromyxoid fibroma
Osteomyelitis
Enchondroma
Eosinophilic granuloma
Clear cell chondrosarcoma

An image-guided needle biopsy of the lesion was performed through a lateral approach, and samples were sent for histologic analysis (Fig. 4).

Fig. 1A–B (A) AP and (B) lateral radiographs of the knee show an epiphyseal lesion of the distal, lateral femoral epiphysis.

Histology Interpretation

On low-power microscopy, histologic analysis of the patient's lesion showed mature blue-gray cartilage in a partially nodular configuration without other constituent tissues (Fig. 4A). On higher power, chondrocytes were small and nondescript with intermittent spacing and low cellularity; no mitoses were seen (Fig. 4B).

Fig. 3A–B (A) Anterior and (B) posterior views of the whole-body technetium-99m bone scan show no enhancement at the lesion.

Fig. 2A–C Sagittal MR images of the knee show cross-sections of the epiphyseal lesion with the (A) proton density, (B) T2-weighted, and (C) T1-weighted with gadolinium contrast techniques. The lesion abuts the physis and the articular cartilage with low signal on the proton density

sequence, high signal on the T2-weighted sequence, and heterogeneous contrast uptake on the gadolinium-enhanced sequence. Peripheral marrow edema is not seen on the T2-weighted MRI. Heterogeneous mass enhancement is seen on the gadolinium-enhanced MRI sequence.

Fig. 4A–B (A) A photomicrograph shows a hyaline cartilage lobule with overall homogenous, low cellularity (Stain, hematoxylin and eosin; original magnification, $\times 200$). (B) Scattered throughout the field are benign-appearing chondrocytes (Stain, hematoxylin and eosin; original magnification, $\times 400$).

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

Diagnosis

Epiphyseal enchondroma

Discussion and Treatment

Symptoms of epiphyseal enchondroma are nonspecific but, unlike conventional metadiaphyseal enchondromas, epiphyseal lesions often produce pain in the absence of trauma or other insult [11]. Our patient's radiographs showed a radiolucent lesion with a narrow zone of transition, indicating a benign etiology. Increased signal on T2-weighted MRI

indicated high water content, consistent with a cartilage lesion, but lacking the peripheral edema characteristic of chondroblastoma. Her bone scan showed no increase in metabolic activity in the lesion, also consistent with an indolent diagnosis. Finally, histologic analysis of her biopsy specimen showed normal-appearing cartilage without hypercellularity, atypia, or components of osseous, fibrous, or myxoid tissues, all consistent with a benign epiphyseal enchondroma [3]. Although focal myxoid change and degeneration may be seen on rare occasion in these tumors, those features were not seen here.

Because this was a painful, epiphyseal lesion in a 9-year-old child, chondroblastoma was considered the most likely diagnosis. Although radiographs supported this diagnosis, her symptoms were primarily mechanical and MRI lacked the peripheral edema characteristic of chondroblastoma. Histologic analysis would have shown increased cellularity, an epithelioid appearance, and mitoses, none of which was present [13]. Giant cell tumor, another common epiphyseal lesion, is rare in the first decade, lacks a sclerotic margin, and has giant cells observed on microscopy [2]. Similar to our patient's lesion, chondromyxoid fibroma is known to have a narrow, sclerotic transition zone and low and high signal on T1- and T2-weighted MRI sequences, respectively [4]. Chondromyxoid fibromas, however, are usually lobular and eccentric and may cross into the epiphysis but are not confined to it. Similarly, our patient's histologic specimen lacked any myxoid or fibrous components, further excluding chondromyxoid fibroma from consideration [3]. Our patient lacked constitutional and nonmechanical symptoms, elevated inflammatory markers, and peritumoral edema consistent with osteomyelitis [12]. Eosinophilic granuloma may have a variable appearance on radiographs but generally lacks a sclerotic margin on radiographs and also has characteristic peripheral edema and elevation of inflammatory markers [4]; microscopy showed no eosinophils.

Enchondroma is one of the most frequently encountered benign bone lesions and is a common impetus for orthopaedic oncologic referral. Enchondromas are not considered true neoplasms but are instead lesions resulting from deposition of physal cartilage in the metaphyseal bone during longitudinal growth [1, 9]. Because of the direction of growth, cartilage deposition is unlikely to occur on the opposite, or epiphyseal, side of the physis [11]. Traditional teaching emphasizes three lesions that may affect the epiphysis: chondroblastoma, giant cell tumor, and clear cell chondrosarcoma [8].

Jaffe and Lichtenstein [9] described the enchondroma as resulting from migration of otherwise normal chondrocytes from the physis during growth, leading to their metaphyseal placement. This hypothesis has since been corroborated by Brien et al. [1]; mutant parathyroid hormone leading to constitutive activation of Indian hedgehog, a primary gene

driving chondrocyte differentiation from stem cells, also has been linked to enchondroma formation [7]. Epiphyseal enchondromas are thought to result from dislodgement of chondrocytes from the secondary ossification center [11]. Solitary, epiphyseal enchondromas and enchondromatosis of the epiphyses have been documented [5, 6, 10].

Enchondromas of the long bones differ histologically from enchondromas of the hands and feet, the latter commonly show hypercellularity. Neither should show extensive bony destruction or soft tissue extension, however, which are considered malignant features. Older lesions may show extensive calcification with accompanying cystic degeneration, but no extensive myxoid change or tumor-type necrosis should be seen in this benign lesion [14, 15].

During a 55-year period at two tertiary musculoskeletal oncology centers, there were only 33 reported cases of epiphyseal enchondroma [11]. The conditions of presentation for the epiphyseal lesions described by Potter et al. [11], however, were quite different from those for conventional lesions, which are usually incidental findings. In the series of Potter et al. [11], 23 of 33 patients presented with pain, three had pathologic fractures, and two had expansile lesions with palpable masses.

Enchondromas typically are managed with observation. In the series of Potter et al. [11], 26 lesions were curetted and grafted, six patients had resection of the involved physis after skeletal maturity, and one underwent en bloc excision of the distal fibula. Potter et al. [11] conceded that the treatments were likely more aggressive than required, but all of the patients were suspected of having chondroblastoma and were treated accordingly. Pain is uncommon for metadiaphyseal enchondromas and often is considered a harbinger of malignant transformation. No differences were detected in the biologic activity of these lesions compared with typical, metadiaphyseal enchondromas and the authors thought the presenting symptoms were likely the result of their epiphyseal location rather than a difference in natural history. The findings of Potter et al. [11] suggest, that while many metadiaphyseal enchondromas likely go undetected, epiphyseal lesions are more likely to be diagnosed owing to accompanying symptoms and these symptoms should not be interpreted with overt concern.

In our patient, we recommended against surgery because of incongruities between the imaging characteristics and the initially presumed diagnosis of chondroblastoma. Our patient's lesion had no malignant radiographic features and was consistent with a cartilage lesion but lacked the marrow edema seen typically with chondroblastoma (Fig. 5). The family was counseled that the lesion most likely was an atypical, indolent chondroblastoma, and confirmatory needle biopsy was performed. After permanent analysis revealed a benign cartilage lesion consistent with a solitary, benign enchondroma, a discussion occurred with the

Fig. 5 A sagittal T2-weighted image of the knee of a pediatric patient with chondroblastoma of the proximal tibial epiphysis shows substantial marrow edema characteristic of this diagnosis, which was absent in the current case.

Fig. 6A–B (A) AP and (B) lateral radiographs of the knee 1 year after biopsy show minimal interval change.

patient and family and it was elected to observe the lesion. By 1 year after biopsy, the patient had returned to playing multiple sports without knee symptoms (Fig. 6).

Epiphyseal enchondromas are rare lesions and usually are mistaken for chondroblastoma [11]. In a pediatric patient presenting with an epiphyseal lesion but without symptoms and MRI findings characteristic of chondroblastoma, enchondroma should be considered in the differential diagnosis and unnecessary treatment may be avoided.

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