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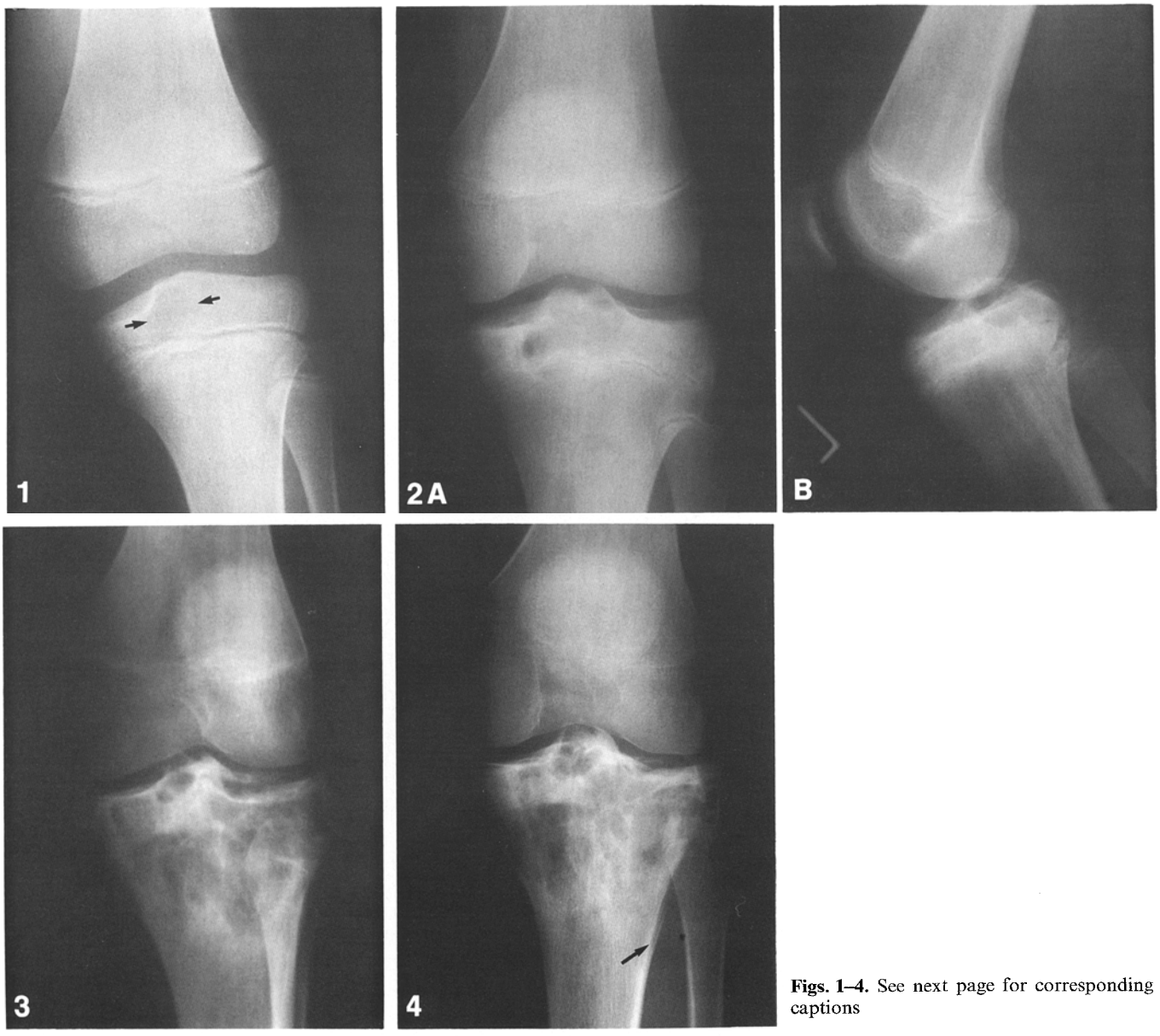
Skeletal Radiology

Case report 730

Michaela A.I. Giudici, M.D.[1], Kathleen D. Eggli, M.D.[1], Richard P. Moser, Jr., M.D.[1], James S. Roloff, M.D.[2], Elizabeth E. Frauenhoffer, M.D.[3], and Mark J. Kransdorf, L.T.C., M.C., U.S.A.R.[4]

Departments of [1] Radiology, [2] Pediatrics, and [3] Pathology, Penn State University Hospital, The Milton S. Hershey Medical Center, Hershey, Pennsylvania, and [4] Department of Radiologic Pathology. Armed Forces Institute of Pathology, Washington, D.C., USA



Figs. 1–4. See next page for corresponding captions

Radiological studies

Fig. 1. Anteroposterior radiograph of the left knee obtained in 1985 demonstrates a subtle, lytic lesion (*arrows*) in the proximal tibial epiphysis, near the medial tibial spine. No evidence of metaphyseal involvement or periosteal reaction is apparent

Fig. 2A, B. Taken in March 1989, anteroposterior (**A**) and lateral (**B**) radiographs of the left knee reveal a sharply demarcated, lobulated, lytic lesion in the posterior segment of the proximal tibial epiphysis. Although this lesion has increased in size considerably since 1985 (Fig. 1), no evidence of metaphyseal involvement or periosteal reaction is noted

Fig. 3. Taken in March 1990, this oblique radiograph of the left knee shows dramatic enlargement of the lytic lesion, which is engulfing most of the proximal tibial epiphysis and extending through the metaphysis into the upper diaphysis. Depression of the lateral tibial plateau is present due to pathological fracture following a motor vehicle accident and impact of the left knee against the dashboard. Despite the dramatic growth since the films from 1985 (Fig. 1), the lesion remains sharply marginated and without evidence of periosteal reaction

Fig. 4. In June 1990, the radiograph revealed metadiaphyseal periosteal reaction (*arrow*) attributed to "healing" of the tibial plateau fracture. Otherwise, there has been no significant radiographic change in the lytic lesion since 3 months earlier (Fig. 3)

Clinical information

This 16-year-old white male sustained minor trauma to his left knee in 1985. At that time, no evidence of fracture was noted. In retrospect, radiographs (Fig. 1) revealed a subtle radiolucency in the proximal tibial epiphysis near the medial tibial spine, although this lesion was not recognized until 4 years later. Between 1985 and 1987, the patient complained of recurrent pain in the left knee. Follow-up radiographs were obtained in 1987 but were underpenetrated, precluding assessment of interim change in the proximal tibial lesion. A left medial meniscectomy was performed in 1988, but intermittent joint pain and effusions persisted.

In 1989, a third set of radiographs (Fig. 2) was obtained which clearly revealed a sharply demarcated, lobulated lytic lesion in the mid-posterior part of the proximal tibial epiphysis. Periosteal reaction was absent. As noted above, in retrospect the lytic lesion was present on radiographs from 1985 (Fig. 1). Unmistakable radiographic enlargement of the tibial lesion between 1985 and 1989 had taken place.

In March 1990 the patient was involved in a motor vehicle accident, during which he jammed his left knee into the dashboard of his car. Radiographs (Fig. 3) obtained at that time revealed further enlargement of the lytic lesion, which now involved the majority of the epiphysis of the proximal tibia and extended through the metaphysis and into the upper diaphysis. A new depression of the lateral tibial plateau was noted due to pathological fracture, in the region of the lytic lesion. Radiographs obtained in June 1990 (Fig. 4) showed no significant change in the size of the lytic lesion since 3 months earlier, but along the metadiaphysis of the proximal tibia, a lamellated periosteal reaction, attributed to reparative healing of the pathological fracture, was noted.

In August 1990, following a biopsy performed elsewhere, the patient was referred to our hospital where physical examination revealed marked atrophy of the left lower extremity. Analysis of range of motion of the left knee revealed deficits of 20° full flexion and 15° full extension. Laboratory studies were within normal limits.

Address reprint requests to: Richard P. Moser, Jr., M.D., Department of Radiology, Penn State University Hospital, The Milton S. Hershey Medical Center, Hershey, PA 17033, USA

Diagnosis: Malignant large cell lymphoma of tibial epiphysis

Grossly, the biopsied tissue weighed 10 g, was tan and fleshy with calcifications, and contained an identifiable bony fragment measuring $1.7 \times 1.1 \times 0.6$ cm.

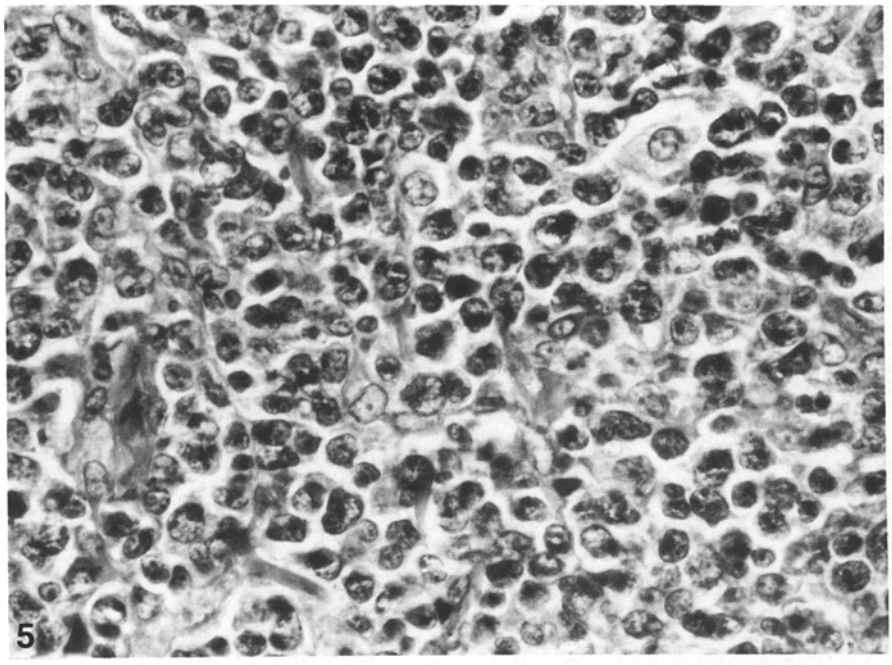
Microscopically, the lesion was a malignant large cell lymphoma composed entirely of large dyscohesive cells with open vesicular, sometimes irregular nuclei and prominent nucleoli (Fig. 5). Immunoperoxidase stains (leukocyte common antigen and L26, a pan-B cell marker) confirmed the lymphocytic nature of the neoplasm and showed the majority of the cells to be of B-cell lineage (Fig. 6). Neoplastic cells were seen infiltrating bone and soft tissues.

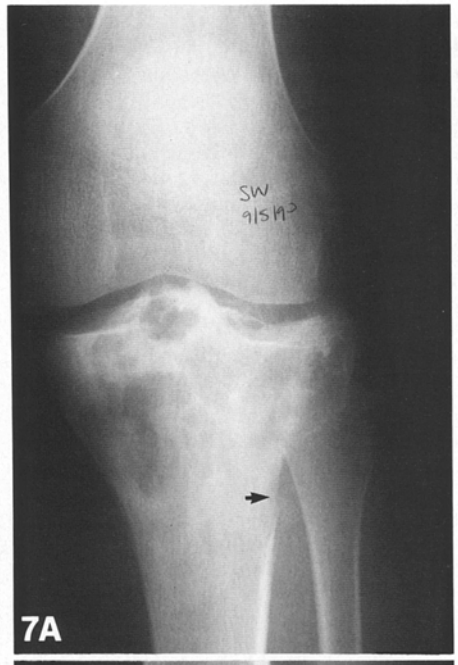
During the staging procedure, an extensive evaluation was undertaken (Fig. 7), including bone marrow aspiration and cerebrospinal fluid (CSF) evaluation. The patient's chest radiograph was unremarkable, and abdominal computed tomography (CT)

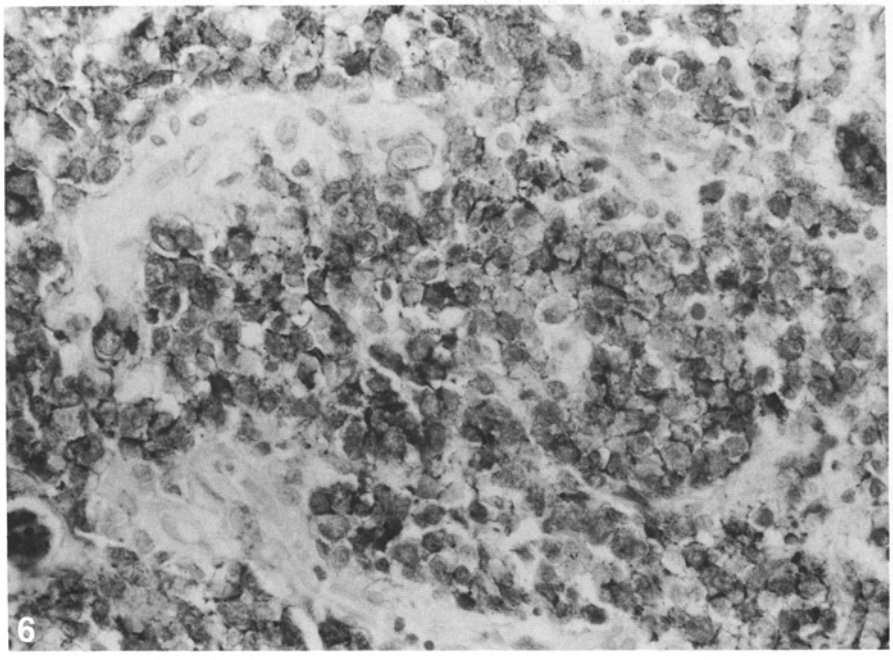
Fig. 5. Numerous, large, dyscohesive cells with irregular, vesicular nuclei, characteristic of large cell lymphoma (H & E, ×160)

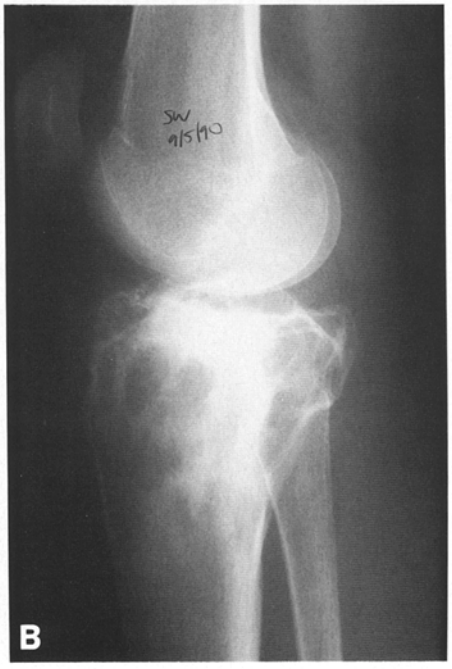
Fig. 6. Lymphoma cells expressing cytoplasmic membrane positivity for L26 antigen (pan-B cell marker), confirming B-cell lineage of lymphoma (immunoperoxidase staining with hematoxylin counterstain, ×100)

Fig. 7A, B. A tibial biopsy was performed in August 1990. Anteroposterior (**A**) and lateral (**B**) radiographs obtained in September 1990 suggested further diaphyseal extension of the lesion. The site of prior left tibial biopsy (**A**, *arrow*) is noted in the lateral metadiaphysis of the proximal tibia









study revealed chronic, bilateral renal scarring, but no evidence of adenopathy or other focal lesion. Bone scintigram (Fig. 8) showed increased radionuclide activity in the solitary proximal left tibial lesion. Magnetic resonance imaging (MRI) (Fig. 9) demonstrated abnormal signal in the proximal end of the left tibia corresponding to the neoplastic tissue and revealed cortical disruption and extension into the adjacent anterolateral soft tissues. Since these studies failed to uncover evidence of lymphomatous involvement beyond the vicinity of the proximal left tibia, it was concluded that the patient was afflicted with primary lymphoma of bone. This conclusion was reinforced by the imaging sequence which demonstrated a lytic lesion of at least 5 years' duration in the proximal tibial epiphysis.

By the end of 1990, the patient had completed four courses of chemotherapy. Subjectively, he felt considerably better than prior to the onset of treatment, and on physical examination, objective improvement was documented since the range of motion of the left knee had returned to normal. When compared with pretherapy films, follow-up radiographs revealed minimally increased sclerosis in the proximal tibial lesion.

Discussion

Based on the original radiographs from 1985 (Fig. 1) which showed a small, sharply demarcated, lytic le-

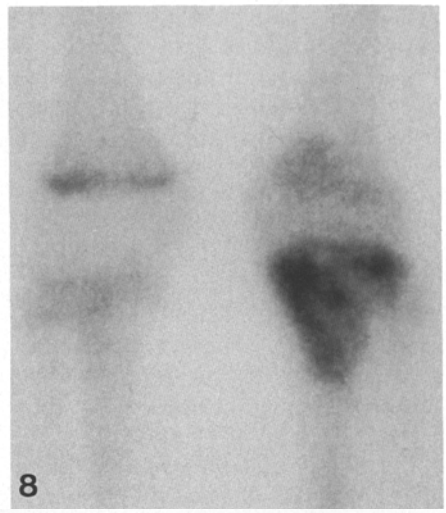


Fig. 8. Technetium 99m methylene diphosphonate scintigram showed inhomogenous increased radionuclide activity in the proximal left tibia, corresponding to the radiographic abnormality. Also noted is asymmetry in tracer uptake in the distal left femoral epiphyseal plate, attributed to premature fusion

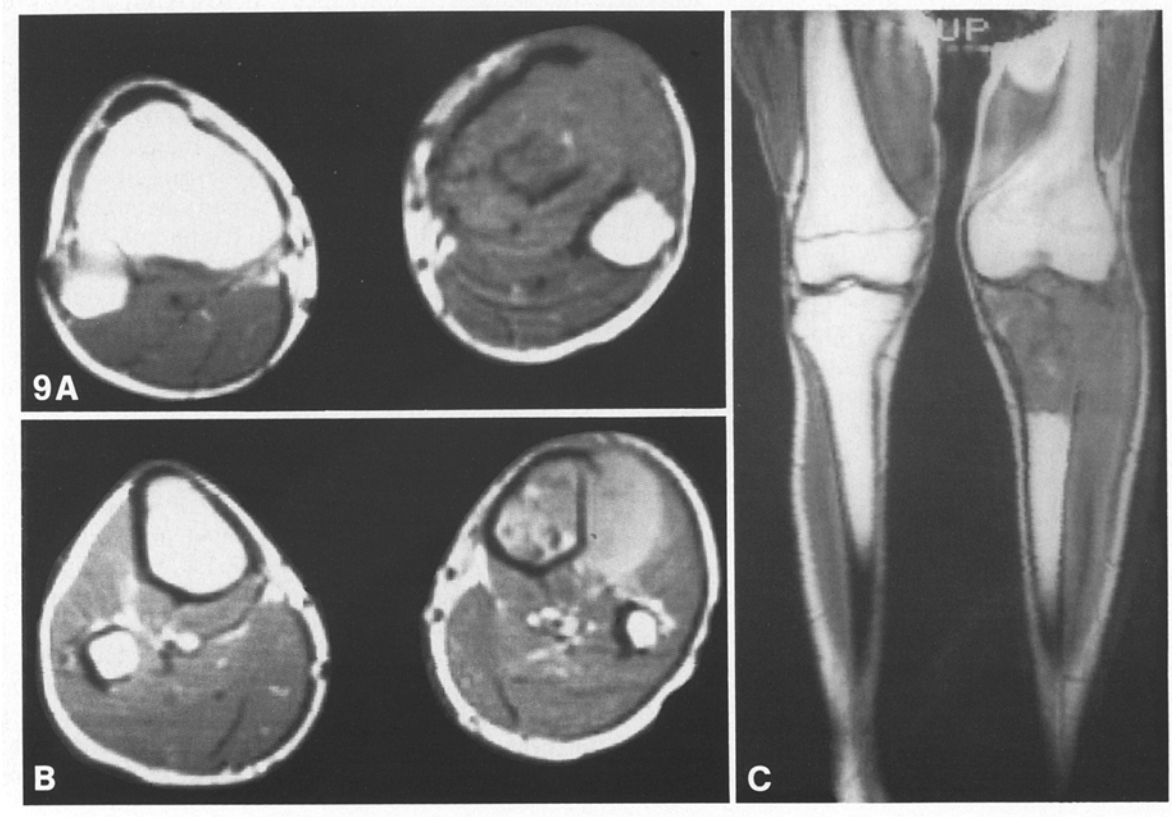


Fig. 9A–C. Magnetic resonance images obtained in October 1990. **A** Axial T1-weighted image (TR 600/TE 15) shows abnormal signal throughout the marrow of the proximal left tibia. Anterolateral tibial cortical disruption was also noted. However, the significance of this latter alteration is unclear due to the prior biopsy at this site. **B** Axial T2-weighted image (TR 2200/TE 25) exquisitely delineated the soft-tissue component of the lesion which extended anterolaterally from the left tibia. **C** Coronal T1-weighted image (TR 600/TE 15) showed the extent of the tumor in the proximal tibia and correlated nicely with the radiographs (Fig. 5)

sion (confined to the proximal tibial epiphysis) without evidence of matrix mineralization or periosteal reaction, the following differential diagnosis is appropriate: chondroblastoma (i.e., Codman's tumor), bone abscess, eosinophilic granuloma, and subchondral cyst [4].

Chondroblastoma. In the case reported here, the radiographic appearance (Fig. 1) of the proximal tibial lesion in 1985 is most consistent with chondroblastoma [4]. The clinical and radiographic findings of this entity have been well described [1, 4, 9]. Chondroblastoma is an uncommon, benign neoplasm of immature cartilage. Some 70% of patients afflicted with chondroblastoma present during the 2nd decade of life (the patient described in this case was 16 years of age at the time of initial presentation). The chondroblastoma most commonly arises in the epiphysis of a long bone, and 50% occur in the knee (23% distal femur, 19.4% proximal tibia, 6.5% patella). Radiographically, the chondroblastoma is a round or oval lytic lesion with a sharply demarcated border. Between 40% and 50% of these lesions are confined to the epiphysis, while the remainder extend from their epiphyseal origin into the adjacent metaphysis. Exclusive metaphyseal involvement is extremely rare. Approximately 40% of chondroblastomas are radiolucent, while the remainder demonstrate a mottled density due to mineralization of the chondroid matrix. Associated periosteal reaction, representing reparative bone formation, has been variably reported in from 15% to 60% of cases [4]. Uncommonly, chondroblastoma behaves aggressively and invades adjacent structures or even metastasizes distantly. In our case, the patient's later images (Figs. 3, 4, 7–9) suggested (incorrectly) a diagnosis of chondroblastoma which, over a 5-year period, had become aggressive (or even malignant).

Bone abscess. The radiographic appearance of the proximal tibial lesion in 1985 (Fig. 1) is compatible with a bone (Brodie's) abscess, except for the epiphyseal location, but neither clinical nor laboratory evidence supported an infectious etiology. In addition, protracted clinical/radiographic course between 1985 and 1990 is inconsistent with infection.

Eosinophilic granuloma (EG) is a "mimicker" of many skeletal lesions, including both benign and malignant entities. Futhermore, EG of bone can demonstrate dramatically dissimilar radiographic appearances, varying from malignant-appearing, ill-defined, motheaten or permeative bone destruction with coexistent, lamellated, periosteal reaction. The appearance radiologically may be indistinguishable from osteomyelitis or Ewings's sarcoma. EG may also be a benign-appearing, sharply demarcated, solitary, lytic lesion (radiographically indistinguishable from bone cyst, non-mineralized enchondroma, etc). However, it is exceedingly rare to encounter skeletal EG as a solitary focus confined to the epiphysis.

Subchondral cyst. This consideration is easily excluded due to the young age at initial presentation (16 years) and the absence of coexistent degenerative arthritis or juvenile rheumatoid arthritis. Typically, subchondral cysts are encountered in older individuals in moderately to markedly osteoarthritic joints.

In our case report, based on the 5 year history, the epiphyseal origin of the lesion, and the initial benign radiographic appearance over a several year period, skeletal lymphoma was somewhat of a "surprise" diagnosis. Oberling is generally credited with the first description of primary lymphoma of bone in 1928 [6, 16]. Since that time, there have been many articles dealing with primary lymphoma of bone, which is an uncommon entity, accounting for less than 5% of all primary bone tumors [7, 11]. Over the years, there has been considerable controversy about the nomenclature/subclassification of lymphoma [2, 3, 5, 16]. Nevertheless, most authorities agree that primary lymphoma of bone is a distinct entity [5, 11, 13, 15]. To the best of our knowledge, however, primary lymphoma of bone arising in the epiphysis (of a skeletally immature individual) has not been reported previously.

Osseous involvement is more frequent in non-Hodgkin's lymphoma (NHL) than in Hodgkin's disease [2]. The following three criteria are necessary to establish a diagnosis of primary lymphoma of bone [6, 12]: (a) On presentation, the patient demonstrates a primary focus in a single bone; (b) histological proof in obtained from the skeletal focus (not from a metastasis); (c) the onset of symptoms of the primary skeletal lesion precedes the appearance of distant metastases by at least 6 months. The case reported here definitely satisfied these three criteria.

In most studies, primary lymphoma of bone affects young adults between the ages of 25–40 years, with a slight male predominance [3]. In their review of 12 cases of primary lymphoma of bone, Pettit et al. reported in their patients an age range of 16–80 years (mean 41 years) with a male:female ratio of 1:1 [11]. The most common site of involvement is the appendicular skeleton, particularly in the lower extremity [6, 14]. The most frequent symptom is bone pain, although painless swelling has also been reported.

Patients afflicted with primary lymphoma of bone typically present in overall good physical condition. This contrasts dramatically with the poor condition of those patients with disseminated lymphoma which has metastasized to bone. Not surprisingly, therefore, the prognosis is better for those patients afflicted with primary lymphoma of bone rather than lymphoma metastatic to bone [3, 10, 11].

The radiographic appearance of lymphoma of bone is most commonly osteolytic, but predominantly sclerotic and mixed patterns have also been described [2, 3, 14]. Unlike the case reported herein, the radiographic margins of primary lymphoma of bone are usually poorly defined, motheaten, or permeative [6, 7, 14]. An inconstant associated finding is periosteal reaction [2]. Primary lymphoma of bone most commonly occurs in the metaphysis of a lower extremity long bone, especially the femur or tibia [14]. Extension of the lesion from the metaphysis into the epiphysis has been reported, but iso-

lated epiphyseal involvement is distinctly uncommon.

In *summary*, we present a case of primary lymphoma of bone arising in the proximal tibial epiphysis of a 16-year-old boy. To the best of our knowledge, primary lymphoma of bone has not been described previously as a mimicker of chondroblastoma. This case report is intended to increase awareness among clinicians and radiologists that primary lymphoma of bone can present with a long clinical prodrome and initially benign radiographic appearance. Early recognition of this unusual presentation will (hopefully) increase the likelihood of cure. However, it is recognized that in children, primary lymphoma of bone is a rare diagnosis and associated with a poor prognosis unless aggressive treatment is utilized [8].

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References

1. Bloem JS, Mulder JD (1985) Chondroblastoma: a clinical and radiological study of 104 cases. Skeletal Radiol 14:1
2. Bragg DG, Colby TV, Ward JH (1986) New concepts in the non-Hodgkin lymphomas: radiologic implications. Radiology 159:289
3. Braunstein EM, White SJ (1980) Non-Hodgkin lymphoma of bone. Radiology 135:59
4. Brower AC, Moser RP, Gilkey FW, Kransdorf MJ (1990) Chondroblastoma in cartilaginous tumors of the skeleton. In: Davidson AJ (ed) AFIP atlas of radiologic-pathologic correlations, fascicle II. Hanley & Belfus, p 74
5. Coles WC, Schulz MD (1948) Bone involvement in malignant lymphoma. Radiology 50:458
6. Coley BL, Higinbotham NL, Groesbeck HP (1950) Primary reticulum-cell sarcoma of bone – summary of 37 cases. Radiology 55:641
7. Dinshaw KA, Advan SH, Nair CN, et al. (1984) Primary non-Hodgkin's lymphoma of bone. Indian J Cancer 20:275
8. Miller DR (1989) Hematologic malignancies: leukemia and lymphoma. In: Miller DR, Baehner RL, Miller LP (eds) Blood disease of infancy and childhood. CV Mosby, St. Louis; p 689
9. Moser RP, Brockmole DM, Vinh TN, et al. (1988) Chondroblastoma of the patella. Skeletal Radiol 17:413
10. Pear BL (1974) Skeletal manifestations of the lymphomas and leukemias. Semin Roentgenol 9:229
11. Pettit CK, Zukerberg LR, Gray MH, et al. (1990) Primary lymphoma of bone. Am J Surg Pathol 14(4):329
12. Phillips WC, Kattapuram SV, Doseretz DE, et al. (1982) Primary lymphoma of bone: relationship of radiographic appearance and prognosis. Radiology 144:285
13. Raymond AK, Unni KK (1982) Case report 194: primary non-Hodgkin lymphoma of bone. Skeletal Radiol 8:153
14. Resnick D, Niwayama G (1988) Diagnosis of bone and joint disorders. WB Saunders, Philadelphia, p 2471
15. Rodman D, Raymond AK, Phillips WC (1982) Case report 201: primary lymphoma of bone (PLB) – left fibula. Skeletal Radiol 8:235
16. Sweet DL, Mass DB, Simon MA, et al. (1981) Histiocytic lymphoma (reticulum-cell sarcoma) of bone; current strategy for orthopedic surgeons. J Bone Joint Surg [Am] 63:79