Ewing’s sarcoma/primitive neuroectodermal tumor of the proximal humeral epiphysis

Parisa Morris, MD; Paul S. Dickman, MD; Matthew J. Seidel, MD

Abstract

Ewing’s sarcoma/primitive neuroectodermal tumor (ES/PNET) of bone is a rare childhood tumor most commonly located in the metadiaphysis. In skeletally immature patients, lesions of the epiphysis are rarely malignant, with the most common diagnosis being chondroblastoma. This article presents a case of ES/PNET of the proximal humeral epiphysis in a 12-year-old boy. To the authors’ knowledge, this is the first reported case of epiphyseal ES/PNET confirmed with molecular testing. Radiographs of the patient’s painful shoulder showed a well-defined lytic lesion within the humeral epiphysis. Magnetic resonance imaging suggested a chondroid tumor with surrounding edema. Based on the imaging characteristics, the patient’s age, and the lesion’s location, a preliminary diagnosis of chondroblastoma was made. A trochar biopsy of the lesion demonstrated a small, round, blue cell tumor on frozen section. Subsequently, immunohistochemical staining was uniformly positive in a membrane pattern for CD99, and molecular diagnostic testing demonstrated a EWSR1/FLI1 fusion transcript, confirming the pathologic diagnosis of ES/PNET. Although metadiaphyseal locations for ES/PNET are most common, this case adds to previously reported cases of epiphyseal ES/PNET, suggesting that the diagnosis be considered for pediatric epiphyseal tumors. This case also demonstrates why following rigorous oncologic treatment algorithms by obtaining a limited trochar biopsy, even in the case of a confident radiographic diagnosis, is critically important; the biopsy results can lead to a major change in treatment and avoid contamination of a larger area of soft tissue and bone.

The authors are from the Department of Orthopaedic Surgery (PM, MJS), the Department of Pediatrics (PSD), and the Department of Pathology (PSD), University of Arizona, Tucson, the Orthopaedic Surgical Oncology of Arizona at Specialty Orthopedic Surgery (MJS), Orthopaedic Oncology, Piper Cancer Center, Scottsdale Healthcare (MJS), Scottsdale, the Department of Pathology (PSD), Phoenix Children’s Hospital, the Department of Child Health, University of Arizona College of Medicine, Phoenix, Arizona.

Drs Morris and Dickman have no relevant financial relationships to disclose. Dr Seidel is a paid consultant for Wright Medical Technology, Inc, is employed by Orthopaedic Surgical Oncology of Arizona, and does paid presentations for Biomet.

Correspondence should be addressed to: Matthew J. Seidel, MD, Orthopedic Surgical Oncology of Arizona, 9700 N 91st St, Ste B108, Scottsdale, AZ 85258 (mseidel@oso.md).

doi: 10.3928/01477447-20121217-29
The differential diagnosis of epiphyseal bone lesions in children includes chondroblastoma, infection, and, more rarely, giant cell tumor, clear cell chondrosarcoma, enchondroma, and Langerhans cell histiocytosis. Malignant lesions of the epiphysis are rare. A large series of 2758 tumor cases from a German tumor registry in 1996 found no cases of primary malignant bone tumor of the epiphysis and fewer than 10 cases of primary osteosarcoma of the epiphysis.1

Ewing’s sarcoma/primitive neuroectodermal tumor (ES/PNET) of bone is the second most common primary malignant bone tumor of childhood and adolescence, with an incidence of 2 to 3 cases per million children annually in the United States.3 Most patients are Caucasian, with a slight male predilection. Ewing’s sarcoma/primitive neuroectodermal tumor has been widely studied, and a classic constellation of imaging and histologic, cytogenetic, and molecular diagnostic findings has been identified. Ewing’s sarcoma/primitive neuroectodermal tumor can occur in the axial skeleton but is more commonly seen in the appendicular skeleton. Long-bone disease typically involves the femur, tibia, humerus, or fibula. Lesions are usually found in the metadiaphysis.4

This article presents a case of primary ES/PNET of the proximal humeral epiphysis in a 12-year-old boy. Only 2 prior reports of the epiphyseal ES/PNET family of tumors (ESFT) exist, and it has rarely been described in larger studies of ES/PNET. To the authors’ knowledge, the current report is the first reported case of epiphyseal ES/PNET confirmed with molecular testing.

CASE REPORT

A 12-year-old boy was referred to the authors’ institution with a left proximal humerus epiphyseal lesion and shoulder pain. The patient played club baseball as a left-handed thrower and initially noted pain during play 6 months prior to presentation. His parents were concerned about overuse and took him out of baseball to rest his arm. On returning to throwing, he had an immediate recurrence of pain and weakness, which progressed over 6 weeks. He was evaluated by his primary care provider and underwent a 4-week course of physical therapy without improvement. Radiographs and magnetic resonance imaging of the shoulder revealed a lesion within the proximal humeral epiphysis. He was then referred to the author’s institution.

The patient reported pain with activity, mainly throwing, and occasional night pain. He had also noticed decreased force and velocity with throwing. His symptoms were somewhat alleviated by ibuprofen and acetaminophen with codeine. He described only moderate limitation in activity. He reported no constitutional symptoms, and his history was negative for prior malignancy or systemic illness. At presentation, the patient was tender to palpation over the anterior humeral head. He had symmetric upper-extremity bulk and tone. His range of motion was normal with the exception of limited external rotation. He also had 4/5 strength in external and internal rotation compared with the contralateral side. Sensation was intact throughout the extremity in all dermatomes.

Radiographs revealed a lesion within the central humeral epiphysis that appeared well defined and slightly lytic (Figure 1). Magnetic resonance imaging was interpreted as a chondroid tumor of the epiphysis with surrounding edema (Figure 2).

Based on the imaging characteristics, the patient’s age, and the lesion’s location, a presumptive diagnosis of chondroblastoma was made. The patient was taken to the operating room with the plan for a confirmatory trochar biopsy of the lesion via frozen section, followed by curettage and bone grafting. However, frozen section evaluation performed on 2 specimens demonstrated a small, round, blue cell tumor, most likely ES/PNET. The procedure was terminated, and the specimen was submitted for complete pathologic evaluation.

The initial pathology diagnosis was ES/PNET. Photomicrographs revealed
uniform cells with round to oval nuclei and little cytoplasm (Figure 3). Immunohistochemical staining was uniformly positive in a membrane pattern for CD99 (Figure 4) and negative for CD45, CD56, epithelial membrane antigen, myogenin, terminal deoxynucleotidyl transferase, and tyrosine hydroxylase. Molecular diagnostic testing demonstrated an EWSR1/FLI1 fusion transcript by reverse transcription deoxyribonucleic acid amplification, consistent with type 1 fusion transcript, confirming the pathologic diagnosis of ES/PNET.6

The patient is currently undergoing neoadjuvant chemotherapy, and wide resection of the lesion with reconstruction is planned.

Discussion

Ewing’s sarcoma/primitive neuroectodermal tumor of bone is a rare childhood tumor accounting for approximately 3% of all malignant childhood tumors and 10% of primary bone malignancies.6 It is most common in the second decade of life. Patients present with pain, swelling, and a mass, especially when the tumor is located in an extremity.7,8 Recent advances in treatment protocols have led to improvements in survival. Five-year event-free and overall survival for patients with localized disease has been reported at 71% and 77%, respectively,9 with up to 39% survival at 5 years for those with metastatic disease at the time of diagnosis.3,6 Ten-year overall survival for localized disease is approximately 63%, and 32% for metastatic disease.3

Ewing’s sarcoma/primitive neuroectodermal tumor can involve any bone in the axial or appendicular skeleton, with approximately 30% of cases involving the pelvis and approximately 50% occurring in long bones.10 Long-bone lesions typically arise in the diaphysis or metaphysis.1,6 The Intergroup Ewing’s Sarcoma Study 7299 group identified 206 patients with ES/PNET of bone; of these, approximately 57% were located in the metaphysis and approximately 35% presented in the diaphysis.4 Only 1 (0.5%) patient presented with a lesion in the epiphysis.4

Minimal discussion of cases of primary epiphyseal ES/PNET is found in the literature. A 1993 report of 5 patients with ES/PNET found that 1 patient had transphysal spread of disease that involved the epiphysis.11 However, this was a case of primary Ewing’s sarcoma in the distal femoral metaphysis that then spread distally into the epiphysis.11 In 2003, a report of 1 case of epiphyseal osteosarcoma and 1 case of epiphyseal ES/PNET was published.2 The ES/PNET patient presented with knee pain and eventually had immunohistochemical confirmation of ES/PNET of the proximal tibial epiphysis.2 A second report was recently published of primitive neuroectodermal tumor of the epiphysis in a 5-year-old patient with a lytic lesion in the distal femoral epiphysis, again confirmed with immunohistochemical findings.5 To the current authors’ knowledge, their patient is the first instance in the literature presenting with a proximal humeral epiphyseal lesion that was confirmed to be ES/PNET on microscopic, immunohistochemical, and molecular testing.

Historically, the differential diagnosis for pediatric epiphyseal lesions has included almost entirely benign lesions, with the most common being chondroblastoma.1 Treatment for chondroblastoma is typically curettage and bone grafting, followed radiographically for complete healing and resolution.12 The treatment protocol for malignant bone tumors is radically different and must be performed by a multidisciplinary oncology team. The current case demonstrates the importance of strict adherence to diagnostic strategies in dealing with bone lesions of unspecified nature.

This case report is important in 2 regards. First, although metadiaphyseal locations for ES/PNET are most common, epiphyseal disease is possible. This case adds to the limited but mounting evidence that ES/PNET should be considered in the differential diagnosis of pediatric epiphyseal tumors. Second, this report demonstrates why following standard oncologic treatment algorithms, even in the case of a confident radiographic diagnosis, is critically important. For this patient, proceeding with a limited trochar biopsy led to a major change in treatment and avoided contamination of a larger area of soft tissue and bone. This will allow the eventual wide resection of this tumor to be completed in a straightforward fashion that will not require excessive resection of a contaminated scar, muscle, or extra bone and should not require complex plastics closure or coverage.

References


