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Distinguishing Osteomyelitis From Ewing Sarcoma on Radiography and MRI

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Abstract

OBJECTIVE—The purpose of this study was to determine whether clinical and imaging features can distinguish osteomyelitis from Ewing sarcoma (EWS) and to assess the accuracy of percutaneous biopsy versus open biopsy in the diagnosis of these diseases.

MATERIALS AND METHODS—Three radiologists reviewed the radiographs and MRI examinations of 32 subjects with osteomyelitis and 31 subjects with EWS to determine the presence of 36 imaging parameters. Information on demographic characteristics, history, physical examination findings, laboratory findings, biopsy type, and biopsy results were recorded. Individual imaging and clinical parameters and combinations of these parameters were tested for correlation with findings from histologic analysis. The diagnostic accuracy of biopsy was also determined.

RESULTS—On radiography, the presence of joint or metaphyseal involvement, a wide transition zone, a Codman triangle, a periosteal reaction, or a soft-tissue mass, when tested individually, was more likely to be noted in subjects with EWS ($p = 0.05$) than in subjects with osteomyelitis. On MRI, permeative cortical involvement and soft-tissue mass were more likely in subjects with EWS ($p = 0.02$), whereas a serpiginous tract was more likely to be seen in subjects with osteomyelitis ($p = 0.04$). African Americans were more likely to have osteomyelitis than EWS ($p = 0$). According to the results of multiple regression analysis, only ethnicity and soft-tissue mass remained statistically significant ($p = 0.01$). The findings from 100% of open biopsies (18/18) and 58% of

percutaneous biopsies (7/12) resulted in the diagnosis of osteomyelitis, whereas the findings from 88% of open biopsies (22/25) and 50% of percutaneous biopsies (3/6) resulted in a diagnosis of EWS.

CONCLUSION—Several imaging features are significantly associated with either EWS or osteomyelitis, but many features are associated with both diseases. Other than ethnicity, no clinical feature improved diagnostic accuracy. Compared with percutaneous biopsy, open biopsy provides a higher diagnostic yield but may be inconclusive, especially for cases of EWS. Our findings underscore the need for better methods of diagnosing these disease processes.

Keywords

Ewing sarcoma; MRI; osteomyelitis; radiography

Ewing sarcoma (EWS) is the second most common malignant bone tumor in children and young adults, occurring in approximately 2.9 per million individuals in the United States [1]. A cure is possible for approximately two thirds of patients who have localized EWS; however, the prognosis for patients with metastatic disease is poor [1]. Therefore, prompt diagnosis is essential to initiating appropriate therapy and preventing distant metastasis. Most patients with EWS present with symptoms of localized pain or swelling, and radiographs show permeative bone destruction. Clinical and laboratory findings can often help narrow the differential diagnosis; however, definitively distinguishing between small round blue cell tumors and osteomyelitis may be difficult [2–10]. In particular, the features of EWS and osteomyelitis are similar on imaging, and there are numerous reports of EWS being misdiagnosed as osteomyelitis on imaging studies [3–10]. Even biopsy findings may be inconclusive, resulting in a delay in diagnosis and curative therapy [11–13].

Although an abundance of literature describes the imaging features of osteomyelitis and EWS, few studies directly compare the imaging features of large cohorts of these patients, and to our knowledge, none have compared the imaging and clinical findings of such patients to determine whether they differ [14–18]. Therefore, we sought to determine whether there are specific clinical or imaging features that are predictive of the correct diagnosis and whether correlating clinical and imaging features improved our predictive ability. We also assessed the optimal approach to diagnosing these diseases by investigating the diagnostic accuracy of open and percutaneous biopsies.

Materials and Methods

A waiver of consent for this retrospective study was approved by our institutional review board, and the study was deemed HIPAA compliant. Patients with EWS or osteomyelitis who were treated between January 1995 and January 2012 and who underwent radiography, MRI, or both procedures at the primary investigational site at the time of diagnosis were identified using departmental databases containing information on solid tumors, infectious diseases, and diagnostic imaging. The treatment time interval was chosen to optimize sample size. Efforts were made to match anatomic sites of disease between the two patient groups so that equal numbers of patients with disease affecting the appendicular versus axial skeleton

were included. For subjects who had more than one bone lesion, only the primary or symptomatic bone lesion was analyzed.

Imaging studies were deidentified and reviewed by a panel of three pediatric radiologists with 4, 16, and 34 years of experience at the beginning of the study period. Reviewers were blinded to each subject's diagnosis, clinical characteristics, and results of other imaging examinations, but they were aware of age and ethnicity.

Images were reviewed using a PACS (Syngo, Siemens Healthcare), and workstation tools such as magnification, window, and level were used at the discretion of the reviewer. The radiographic examination included obtaining two orthogonal radiographs of the affected bone. In most MRI examinations, 3- to 5-mm-thick unenhanced T1-weighted and STIR coronal images and T2-weighted axial images were obtained. Contrast-enhanced MRI generally included fat-suppressed T1-weighted axial and coronal images. Coronal MR images of the lesions of the extremities included the entire bone from the proximal to the distal joint. For each subject, the panel first reviewed all radiographs, then the MR images, and then both types of images together, during separate review sessions that occurred, on average, 8 months apart, to avoid recall bias from prior image reviews. Also, because the images may have been reviewed by a study radiologist during clinical management, we allowed an average of 6 months to elapse between the time of admission of the patient to the institution and image review.

Table 1 shows the 36 imaging parameters evaluated, and the definitions of these parameters are provided in Appendix 1. The presence of each parameter was determined by panel consensus before each reviewer independently predicted whether the diagnosis would be EWS, osteomyelitis, or indeterminate. Discrepancies in predictions were resolved by consensus. Table 2 presents information on demographic characteristics, baseline laboratory results, and clinical history that we collected from medical records.

Information on the type (percutaneous or open), number, and results of biopsies and cultures was recorded. Until March 2012, percutaneous biopsies were performed by an experienced interventional radiologist with the use of a variety of commercially available handheld biopsy needles ranging from 13 to 18 gauge. After that time, a biopsy drill (OnControl biopsy needle system, Vidacare) with an 11-gauge bit was used. Open biopsies were performed by an experienced orthopedic or general surgeon, and all specimens were examined by an experienced pathologist. For subjects who underwent repeat biopsy, the time (measured in days) between admission to our institution and definitive diagnosis was recorded to determine the delay in diagnosis.

Statistical analyses were performed using SAS software (version 9.3, SAS Institute). For demographic characteristics, primary site of involvement, and clinical and laboratory findings, chisquare or Fisher exact tests were used to determine whether categorical variables were different between disease cohorts. Two-sample *t* tests or Wilcoxon rank-sum tests were used to determine whether continuous variables were different between groups. Fisher exact test was used to determine whether disease prediction accuracy based on radiography or MRI was different by independent or consensus review. For radiographic and MRI

parameters, differences between cohorts were evaluated by chi-square test or Fisher exact test. Multiple regression analyses were performed by fitting logistic regression models to explore the association between diagnosis and demographic characteristics, primary site of involvement, clinical and laboratory findings, and imaging parameters that were significantly different between the cohorts. Statistical significance was denoted by $p < 0.05$.

Results

Demographic Characteristics and Laboratory and Clinical Findings

Seventy patients were initially identified as being eligible for participation in the study. Seven patients who had imaging performed at an institution other than the study institution were excluded from the study because the images they provided were poor-quality digitized copies or did not show the entire bone. Of the remaining 63 patients, 31 had EWS and 32 had osteomyelitis. There was no difference between the two cohorts in terms of age, sex, or primary site of disease (Table 2).

Ethnicity was a statistically significant predictor of diagnosis ($p = 0$), according to the Fisher exact test: African Americans were significantly more likely to have osteomyelitis ($n = 17$) than EWS ($n = 2$). Of note, 18% of African Americans with osteomyelitis (3/17) had sickle cell disease. There was no statistically significant difference ($p = 0.07$) in any laboratory or other clinical finding between the two groups (Table 2).

Of the 31 subjects with EWS, 25 underwent open biopsy and six underwent needle biopsy of the primary tumor. The diagnosis was confirmed in 88% of patients who underwent initial open biopsies (22/25) and in 50% of patients who underwent initial percutaneous biopsies (3/6). A single repeat biopsy confirmed the diagnosis for six patients for whom findings were initially inconclusive: five diagnoses were confirmed by open biopsy and one by percutaneous biopsy. The average delay in diagnosis for these six subjects was 10 days (range, four to 21 days).

Of the 32 subjects with osteomyelitis, 18 underwent open biopsy, 12 underwent percutaneous biopsy, and two underwent abscess drainage without biopsy (one open abscess drainage vs one percutaneous abscess drainage). All open biopsies (18/18) and 58% of initial percutaneous biopsies (7/12) yielded a diagnosis: findings for three specimens were considered inadequate or inconclusive on histopathologic review. Histopathologic findings for the remaining 27 specimens identified the following diagnoses: chronic osteomyelitis ($n = 8$), chronic and acute osteomyelitis ($n = 4$), osteomyelitis not specified as chronic or acute ($n = 4$), chronic recurrent multifocal osteomyelitis ($n = 4$), acute osteomyelitis ($n = 3$), normal bone ($n = 3$), and subacute osteomyelitis ($n = 1$). Thirty-one biopsy specimens were obtained for culture, and culture isolated the following bacterial pathogens in 14 of these specimens: methicillin-susceptible *Staphylococcus aureus* ($n = 4$), coagulase-negative *S. aureus* ($n = 3$), methicillin-resistant *S. aureus* ($n = 2$), gram-positive cocci not otherwise specified ($n = 1$), *Staphylococcus intermedius* ($n = 1$), *Pseudomonas fluorescens* ($n = 1$), *Prevotella intermedia* ($n = 1$), and *Propionibacterium acnes* ($n = 1$).

Five subjects who had osteomyelitis underwent a second biopsy (four open biopsies and one percutaneous biopsy) because the findings from initial histologic analysis of the specimens were negative or inconclusive, the culture findings were negative, or both. Histopathologic analysis of specimens obtained during repeat biopsies indicated the following diagnoses: chronic osteomyelitis ($n = 2$), chronic recurrent multifocal osteomyelitis ($n = 1$), acute and chronic osteomyelitis ($n = 1$), and nondiagnostic findings ($n = 1$). Specimens from four biopsies were obtained for culture, and methicillin-susceptible *S. aureus* was isolated from one of these four specimens. For the five subjects with osteomyelitis who underwent a second biopsy, the average delay until diagnosis was 57 days (range, 4–251 days). Because increasing pain and swelling occurred in the affected area, one subject with presumed chronic recurrent multifocal osteomyelitis underwent a repeat biopsy 251 days after initial results of biopsy and culture were negative. Repeat biopsy resulted in diagnoses of acute and chronic osteomyelitis, and coagulase-negative *S. aureus* was isolated from the culture specimen.

Imaging Findings

There were 60 evaluable radiographic examinations (30 EWS subjects and 30 osteomyelitis subjects) and 55 evaluable MRI examinations (29 EWS subjects and 26 osteomyelitis subjects). The discrepancy in the numbers of evaluable radiographic and MRI examinations resulted from the poor quality of images obtained at institutions other than our own or from imaging that did not include the entire bone. Table 3 summarizes the imaging parameters that univariate analysis found to be significantly different for EWS and osteomyelitis. According to findings from our multiple logistic regression model, two features remained statistically significant: African Americans are more likely to have osteomyelitis than EWS ($p = 0.01$), and a soft-tissue mass is more likely to occur in association with EWS than with osteomyelitis ($p = 0.002$). No other clinical or imaging features were predictive of the diagnosis. Although not statistically significant, permeative cortical involvement was more commonly observed in association with EWS ($n = 21$) than with osteomyelitis ($n = 13$) on radiography (Fig. 1).

Other nonpredictive radiographic parameters that we observed in subjects with osteomyelitis and that have been reported as being typical of this diagnosis [14, 16] included a cavity in bone and cortical sequestrum; however, few subjects had these findings. Lamellar periosteal reaction was seen in 13 subjects with EWS and five with osteomyelitis, spiculated periosteal reaction was seen in five subjects with EWS and one with osteomyelitis, and a serpiginous medullary or cortical tract (i.e., a longitudinally oriented tortuous medullary or cortical lucency seen on radiographs or signal abnormality seen on MR images traversing the medulla and cortex) was seen in none of the subjects with EWS and in four subjects with osteomyelitis.

Noteworthy nonpredictive MRI parameters included cortical thinning (in 17 subjects with EWS and seven subjects with osteomyelitis) ($p = 0.08$), spiculated periosteal reaction (in five subjects with EWS and in none of the subjects with osteomyelitis) ($p = 0.06$), and a cavity in bone (in one subject with EWS and three subjects with osteomyelitis) ($p = 0.33$). Two of the three cavities in bone in patients with osteomyelitis (67%) showed the penumbra

sign (a peripheral hyperintense layer on unenhanced T1-weighted images that shows intense enhancement on contrast-enhanced images) (Fig. 2), whereas one cavity in bone in a patient with EWS did not (Fig. 3). On MRI, a Codman triangle was present in only two subjects with EWS and one subject with osteomyelitis. A wide transition zone was seen in 23 subjects with EWS (Figs. 1, 3, and 4) and 25 with osteomyelitis. Cortical saucerization (excavation of the outer cortical surface) was present on MRI examination in four subjects with EWS and in none of the subjects with osteomyelitis, and it was observed on radiographic examination in six subjects with EWS and one with osteomyelitis. All seven subjects with radiographic saucerization had a soft-tissue mass and medullary involvement noted on MRI (Figs. 4 and 5). The subject who had osteomyelitis was thought to have had a longstanding primary soft-tissue infection with secondary involvement of bone.

Table 4 summarizes panel predictions based on radiography and MRI. Reviewers were more likely to misdiagnose osteomyelitis as EWS than vice versa. Consensus review slightly improved the ability to correctly predict the diagnosis but also increased the number of indeterminate predictions.

Discussion

Our study was prompted by the observation that, at our large children's cancer center, it is often difficult for radiologists to distinguish osteomyelitis from osseous EWS on imaging studies. In our study, radiologists were more likely to misdiagnose osteomyelitis as EWS than vice versa. This may be because the consequences of misdiagnosing a malignancy as a nonmalignant process are graver than the consequences of misdiagnosing an infection that is treatable even if originally missed. Even so, the ability of the radiologist to independently and correctly diagnose EWS was limited; only 70% of cases of EWS were correctly predicted by radiography, and 76% were correctly predicted by MRI. A consensus review of imaging modestly improved the predictive ability of both modalities, but it also increased the number of indeterminate predictions. Therefore, the value of securing an opinion from a second radiologist in these difficult cases is debatable. Clearly, better methods are needed to improve our ability to interpret the imaging findings for these two distinctly different pathologic processes.

Consistent with prior reports, we found that the problem may be compounded by nondiagnostic biopsy procedures [11–13, 19–21]. We found that only 58% of percutaneous biopsies (7/12) yielded a diagnosis for subjects with osteomyelitis, and diagnostic accuracy was even lower (50%; 3/6) for diagnosis of EWS. Interestingly, open biopsies were diagnostic for 100% of subjects with osteomyelitis (18/18) but for only 88% of those with EWS (22/25). Therefore, although open biopsy may provide a better diagnostic yield, it also has limitations, particularly in patients with EWS. Our findings suggest that when open biopsy is nondiagnostic, it is not prudent to monitor these patients with additional imaging and empirical treatment because such patients are more likely to harbor a malignancy than an infection. In such cases, we recommend promptly performing a repeat biopsy to initiate appropriate therapy.

Ethnicity was a significant predictor of diagnosis. African American subjects were far more likely to have osteomyelitis ($n = 17$) than EWS ($n = 2$) ($p = 0$). This finding agrees with prior reports showing that the incidence of EWS is much lower in African Americans than in whites. It is postulated that this finding occurs at least partially because intron 6 near the translocation breakpoint region of *EWSR1* (found in approximately 85% of EWS tumors) is 50% smaller in African Americans than whites [1, 22]. We also found that whites were twice as likely to have EWS ($n = 27$) than osteomyelitis ($n = 14$). Therefore, it is essential for the radiologist to be aware of the ethnicity of a patient when interpreting findings on bone images. Strikingly, there was no difference between the two cohorts in terms of laboratory findings or clinical history, including local erythema, fever, pain, and weight loss. According to multivariate analysis, only ethnicity and the presence of a soft-tissue mass remained as significant predictors of the diagnosis. In a study comparing the MRI features of 18 subjects with EWS and 10 subjects with osteomyelitis, Henninger et al. [23] also found that a soft-tissue mass was more common in subjects with EWS than in those with osteomyelitis ($p = 0.01$). However, in that study, the most significant distinguishing MRI feature was the transition zone: all subjects with EWS had a narrow transition zone, but none of the subjects with osteomyelitis had this feature ($p < 0.0001$). In contrast, we found that most subjects with EWS or osteomyelitis had a wide transition zone on MRI and that this feature did not predict the diagnosis. The reason for the discrepancy between our results and those of Henninger et al. is not clear, and additional work is needed to clarify the value of the transition zone as a predictor of these diagnoses.

We found that, on radiographic examination, metaphyseal involvement is more common in subjects with EWS than in those with osteomyelitis. This is perhaps surprising because EWS has been described as a tumor that may involve only the diaphysis, sparing the metaphysis, whereas osteomyelitis typically originates in the highly vascular metaphysis and later spreads through the Haversian canals into the subperiosteum, through the medullary space into the diaphysis, or across the physis into the epiphysis [1, 24–26]. Although not statistically significant, an interesting finding was the presence of cortical saucerization on the radiographic images of six subjects with EWS but only one subject with osteomyelitis. This uncommon feature has been described in subjects with EWS and in adults with bone metastases resulting from bronchogenic carcinoma [27–29]. Bone marrow involvement and soft-tissue masses were seen on MR images of all seven subjects with this finding in our study. The subject with osteomyelitis had atypical findings because there was a large soft-tissue process that we thought was the primary infectious focus but that probably spread to bone secondarily. We conclude that cortical saucerization is at least partially the result of the pressure effect of the associated soft-tissue mass on the bone. Although uncommon, this imaging feature may help distinguish EWS from primary osteomyelitis.

In our study, two of three intramedullary cavities in subjects with osteomyelitis showed the penumbra sign on MRI. This penumbra sign results from a discrete layer of highly vascular granulation tissue surrounding an abscess cavity. The granulation layer is hyperintense to the main abscess on T1-weighted images and has intense rapid enhancement after administration of gadolinium [30–32]. This feature has been reported to be 27% sensitive but 96% specific for the diagnosis of bone infection [33]. Therefore, although uncommon, the penumbra sign is likely to be useful in discriminating between infection and neoplasm.

Our study has several limitations. We may have overestimated the tendency for radiologists to misdiagnose osteomyelitis as EWS because we work in a cancer center and have a heightened suspicion of cancer in general. We also acknowledge that the rate of biopsies for which results are positive will depend on the local practice environment and will be influenced by the experience of interventional radiologists, surgeons, and pathologists. Regarding the significance of imaging features, several rare features for which statistical significance was not reached may be predictive of the diagnosis when examined in a larger cohort. Also, there was the potential for recall bias based on prior imaging review by a study radiologist. We controlled for this by allowing an adequate amount of time to pass between the date of admission of the subject and the date that images were reviewed for study purposes. Finally, there may have been a referral bias because the majority of our cohort who had osteomyelitis had evidence of chronic infection on pathologic inspection. Therefore, the findings that we report may not be as relevant to patients who present with acute infection. However, our cohort is representative of patients for whom obtaining a diagnosis is more difficult, and our findings should be useful to radiologists who encounter such patients in their daily practice.

In conclusion, we found that the ability of radiologists to accurately distinguish EWS from osteomyelitis was limited. Consistent with prior reports, several MRI and radiographic features were predictive of the correct diagnosis, but many overlap. Ethnicity was the only clinical parameter that was a significant predictor of diagnosis. African Americans are far more likely to have osteomyelitis than EWS, and EWS was twice as common as osteomyelitis in whites. Therefore, radiologists should be aware of patient ethnicity when interpreting images of bone disease. When all imaging and clinical features were considered together, only ethnicity and the presence of a soft-tissue mass were predictive of the diagnosis. Although open biopsy provided a higher diagnostic yield, we still support performing percutaneous biopsy first to avoid the risk of morbidity associated with surgical procedures. We recommend that a surgical consultation be obtained before percutaneous biopsy to ensure that the patient quickly undergoes an open procedure if the results of the initial biopsy are inconclusive. When the results of open biopsy are indeterminate, we recommend that repeat biopsy be performed without delay, because only subjects with EWS in our study had inconclusive results of open biopsy. It is clear that better pathologic and radiologic methods of distinguishing EWS from osteomyelitis are needed to reduce the anxiety of patients and patient guardians and to avoid delays in the management of these diseases. In the future, novel imaging techniques, such as diffusion-weighted MRI, PET-MRI, or the use of tumor-specific radiotracers, may allow us to better distinguish between these distinctly different entities [34].

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APPENDIX 1: Definitions of Imaging Parameters Used by Radiologist Reviewers to Distinguish Osteomyelitis from Ewing Sarcoma

I. Zone of transition

- A. Wide: on radiographs, tumor margins are poorly defined and not sharp; on MR images, tumor margins infiltrate underlying normal marrow and lack a sharp edge on all sequences
- B. Narrow: on radiographs, tumor margins are sharp and well defined; on MR images, there is a sharp contrast between the tumor and normal marrow on all sequences

II. Soft-tissue involvement

- A. Mass: on radiographs, a mass is a lobular, abnormal density in soft tissue; on MR images, a mass is a lobular or infiltrative structure located in soft tissue that contains solid material (is not completely fluid on a water-sensitive sequence) and has areas that enhance after gadolinium administration
 1. Deep: abuts bone
 2. Superficial: subcutaneous only; does not abut bone
 3. Both: involves subcutaneous tissue and abuts bone

- 4. Circumferential: completely surrounds bone
 - B. Walled-off fluid collection: cannot be determined by radiography; on MR images, it appears very dark on T1-weighted sequences, is bright on water-sensitive sequences, and shows only a rim of enhancement after administration of gadolinium
 - C. Edema: on radiographs, has poorly defined density obliterating normal tissue planes between muscle and fat; on MR images, has infiltrative signal abnormality that blurs normal tissue planes, follows water signal on all sequences, and may enhance after gadolinium administration
- III. Periosteal reaction
 - A. Single layer: only one layer of abnormal new periosteal bone
 - 1. Thick: larger than or equal to 2 mm
 - 2. Thin: smaller than 2 mm
 - 3. Both: has both thick and thin areas
 - 4. Uniform: all new periosteal bone has same density
 - 5. Nonuniform: Some areas of new periosteal bone are irregular, diminished, or variable
 - B. Lamellar: Two or more layers of new periosteal bone
 - 1. Irregular thickness: layers have both thin and thick areas
 - 2. Regular thickness: all layers are the same thickness
 - 3. Uniform spacing: all layers are the same distance apart
 - 4. Nonuniform spacing: layers are not evenly spaced apart
 - C. Spiculated: periosteal new bone is at right or acute angles to underlying bone from which it arises
- IV. Subperiosteal component: present if there is distance of 3 mm or more between periosteal new bone and underlying cortex
 - A. Fluid: cannot be determined accurately on radiographs; on MR images, subperiosteal component follows water signal on all sequences and does not enhance after administration of gadolinium
 - B. Solid: cannot be determined accurately on radiographs; on MR images, subperiosteal component does not follow water signal on all sequences and enhances after gadolinium administration
- V. Codman triangle: on radiographs and on MR images, elevation of periosteum at margins of bone abnormality, creating a triangle composed of underlying cortex, periosteum, and an open side
- VI. Cortical involvement: any abnormality involving the cortex

- A.** Focal: involving less than 33% of entire bone cortex
 - B.** Diffuse: involving 33% or more of entire bone cortex
 - C.** Thinned: involved cortex is thinner than normal cortex
 - 1.** Uniform: all involved cortex is thinned
 - 2.** Nonuniform: only some of involved cortex is thinned
 - D.** Thickened: involved cortex is thicker than normal cortex
 - 1.** Uniform: all involved cortex is thickened
 - 2.** Nonuniform: only some of involved cortex is thickened
 - E.** Permeative: on radiographs, mixed lucent and dense areas infiltrate the cortex; on MR images, poorly defined, inhomogenous signal diffusely infiltrates the cortex
 - F.** Destroyed: on radiographs and MR images, the cortex is partially or completely invisible in affected area
 - 1.** Focally: involved cortex is destroyed in one or a few focal areas
 - 2.** Diffusely: involved cortex is entirely destroyed; no intact cortex
 - G.** Intact: the involved cortex is intact; no destroyed area
 - H.** Sequestrum: on radiographs and MR images, a calcification (appearing as a dark signal on all MR sequences) within a sharply circumscribed lucency or a signal abnormality that is separate from the surrounding normal bone is seen
 - I.** Saucerization: excavation of the outer cortical surface of a long bone
- VII.** Medullary involvement: any abnormality involving the medullary canal
- A.** Matrix
 - 1.** On radiographs
 - a.** Cartilaginous matrix appears as rings and arcs, popcornlike, focal stippled, or flocculent
 - b.** A fibrous matrix appears as ground glass
 - c.** Osteoid matrix appears as a trabecular ossification, cloudlike, or an ill-defined and amorphous calcification
 - 2.** On MR images
 - a.** Cartilaginous matrix follows cartilage signal intensity on all sequences

Fig. 1. 19-year-old woman with Ewing sarcoma

A, Radiograph with external rotation view of humerus shows permeative cortical process (*arrow*).

B and C, Sagittal T1-weighted (**B**) (TR/TE, 360/14) and STIR (**C**) (TR/TE, 3825/30) MR images show cortical thickening (*arrows*). Note wide transition zone on both sequences and mild deep soft-tissue edema.

D, Axial contrast-enhanced T1-weighted (TR/TE, 1080/14) image shows abnormal marrow and abnormal enhancement (*arrow*) in intact cortex and surrounding soft-tissue edema.

Fig. 2. 3-year-old boy with osteomyelitis of distal radius

A, Anteroposterior radiograph shows cavity (*arrow*) in distal radial metaphysis.

B, Coronal unenhanced T1-weighted (TR/TE, 500/21) MR image windowed to show relatively hyperintense peripheral rim of multilocular penumbra (*arrows*).

C, Coronal contrast-enhanced T1-weighted (TR/TE, 550/14) MR image shows intense enhancement of highly vascularized penumbra (*arrows*).

Fig. 3. 6-year-old boy with Ewing sarcoma

A, Anteroposterior radiograph of left femur shows multiple cavities (*arrows*) in proximal diaphysis.

B, Unlike in patient with osteomyelitis shown in Fig. 2B, margins of cavities (*arrows*) in this patient are dark on T1-weighted (TR/TE, 431/11) MR image.

C, Coronal contrast-enhanced T1-weighted (TR/TE, 431/11 ms) MR image shows heterogeneous marrow enhancement and wide transition zone. Note, in contrast to Fig. 2C, that there is no peripheral enhancement of cavities. Substantial deep soft-tissue edema is present.

Fig. 4. 10-year-old boy with Ewing sarcoma

A, Anteroposterior radiograph shows cortical saucerization (*arrow*) along distal lateral femur.

B and **C**, Coronal STIR (**B**) (TR/TE, 4845/30) and axial contrast-enhanced T1-weighted (**C**) (TR/TE, 1080/14) MR images show small soft-tissue mass (*arrows*) and medullary tumor in area of cortical abnormality. Note wide transition zone on coronal image.

Fig. 5. 13-year-old boy with osteomyelitis

A, Lateral radiograph of distal femur shows sharply defined cortical saucerization (*curved arrow*) and subtle lucency (*straight arrow*) in medullary canal.

B, Sagittal contrast-enhanced T1-weighted (TR/TE, 710/15) MR image shows enhancing mass (*arrow*) that was thought to have arisen primarily from soft tissue with secondary involvement of subperiosteum. Pus was drained, and *Staphylococcus aureus* was isolated from culture.

TABLE 1**Imaging Parameters Evaluated on Radiographic and MRI Examination of Subjects with Ewing Sarcoma or Osteomyelitis**

Location in bone
Diaphyseal, metaphyseal, or epiphyseal (for appendicular tumors)
Near a synchondrosis or growth plate equivalent (for axial tumors)
Joint
Involves more than 33% of bone
Zone of transition: wide, narrow, or indeterminate
Soft-tissue involvement
Mass
Deep, superficial, or both
Circumferential: yes, no, or indeterminate
Completely solid: yes, no, or indeterminate
Walled-off fluid collection: yes, no, or indeterminate
Edema: yes (deep, superficial, or both) or no
Periosteal reaction
Single layer
Thick, thin, or both
Uniform or nonuniform
Lamellar
Irregular thickness or regular thickness
Uniform spacing or nonuniform spacing
Spiculated: yes or no
Subperiosteal component: fluid, solid, or indeterminate
Codman triangle: yes or no
Cortical involvement
Focal or diffuse
Thinned or thickened
Uniform, nonuniform, or indeterminate
Permeative: yes, no, or indeterminate
Destroyed (focally or diffusely), intact, or indeterminate
Sequestrum: yes or no
Saucerization: yes or no
Medullary involvement
Matrix: yes, no, or indeterminate
Cartilaginous, fibrous, osteoid, or indeterminate
Skip lesion: yes, no, or indeterminate
Cavity in bone: yes, no, or indeterminate
Penumbra: yes, no, or indeterminate
Well defined, ill defined, or indeterminate
Medullary, cortical, or both

Serpiginous tract: yes, no, or indeterminate

Medullary, cortical, or both

Note—Definitions provided in Appendix 1.

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TABLE 2

Demographic Characteristics, Primary Site of Involvement, and Clinical and Laboratory Findings of 31 Subjects With Ewing Sarcoma and 32 Subjects With Osteomyelitis

Characteristic	Subjects With Ewing Sarcoma (n = 31)	Subjects With Osteomyelitis (n = 32)	p
Age (y), mean (range)	11.7 (2.0–20.0)	9.8 (2.0–22.0)	0.1
Sex, no. (%)			0.4
Female	10 (32)	14 (44)	
Male	21 (68)	18 (56)	
Ethnicity			0.000
African American	2 (6)	17 (53)	
Native American	0	1 (3)	
White	27 (87)	14 (44)	
Other	2 (6)	0	
Anatomic sites			0.7
Femur	11 (35)	14 (44)	
Tibia or fibula	9 (29)	9 (28)	
Hand	3 (10)	0	
Humerus	3 (10)	2 (6)	
Forearm	2 (6)	3 (9)	
Pelvis	2 (6)	1 (3)	
Foot	1 (3)	2 (6)	
Clavicle	0	1 (3)	
History or physical findings			
Fever	7 (23)	13 (41)	0.12
Local erythema	1 (3)	2 (6)	1
Local pain	27 (87)	29 (91)	0.71
Local swelling	16 (52)	20 (63)	0.38
Local tenderness	7 (23)	14 (44)	0.08
Recent trauma	7 (23)	7 (22)	0.95
Weight loss	1 (3)	6 (19)	0.1
Sickle cell disease	0	3 (9)	0.2
Anemia (other than sickle cell disease)	6 (19)	5 (16)	0.7
Diabetes	0	0	
Laboratory findings, mean (range)			
Alkaline phosphatase (U/L)	202 (61–386)	234 (76–440)	0.11
Lactate dehydrogenase (U/L)	465 (3–1028)	352 (61–730)	0.08
WBC count ($\times 10^9$ cells/L)	7 (4–12)	9 (5–20)	0.07
Absolute neutrophil count ($\times 10^9$ neutrophils/L)	4.11 (1.4–8.6)	5.4 (1.4–18.7)	0.28
Polymorphonuclear leukocytes (%)	56 (16–82)	56 (29–93)	0.84
Erythrocyte sedimentation rate (mm/h)	30 (3–86)	32 (10–99)	0.75

Note—Except where otherwise indicated, data are number of patients with percentage in parentheses.

TABLE 3

MRI and Radiographic Parameters That Were Found to Be Significantly Different for Ewing Sarcoma and Osteomyelitis by Chi-Square Test or Fisher Exact Test

Imaging Modality, Parameter, and Finding	Ewing Sarcoma	Osteomyelitis	<i>p</i>
Radiography (<i>n</i> = 60)			
Joint involvement			0.05
Yes	5 (17)	0	
No	24 (83)	28 (100)	
Metaphyseal involvement			0.03
Yes	23 (77)	15 (50)	
No	7 (23)	15 (50)	
Transition zone			0.05
Wide	28 (97)	24 (83)	
Narrow	0	5 (17)	
Both	1 (3)	0	
Codman triangle			0.03
Yes	8 (27)	1 (3)	
No	22 (73)	29 (67)	
Periosteal reaction			0.05
Yes	25 (83)	18 (60)	
No	5 (17)	12 (40)	
Soft-tissue mass			0.002
Yes	18 (90)	5 (36)	
No	2 (10)	9 (64)	
MRI (<i>n</i> = 55)			
Cortical involvement			0.02
Yes	29 (100)	20 (80)	
No	0	5 (20)	
Permeative cortical involvement			0.02
Yes	23 (82)	10 (50)	
No	5 (18)	10 (50)	
Soft-tissue mass			0.0002
Yes	22 (76)	6 (25)	
No	7 (24)	18 (75)	
Serpiginous tract			0.04
Yes	0	4 (100)	
No	28 (60)	19 (40)	

Note—Data are number (%) of patients. Numbers vary for parameters within each modality because of indeterminate or nonapplicable findings that were excluded from analysis.

TABLE 4

Predictions by Panel Reviewers Regarding Diagnosis of Ewing Sarcoma and Osteomyelitis by Radiography and MRI

Review Type, Imaging Modality, Diagnosis	Correct ^a	Incorrect ^b	Indeterminate ^c	<i>p</i>
Independent				
Radiography				0.1
Osteomyelitis (<i>n</i> = 30)	14 (47)	15 (50)	1 (3)	
Ewing sarcoma (<i>n</i> = 30)	21 (70)	9 (30)	0	
MRI				0.2
Osteomyelitis (<i>n</i> = 26)	15 (58)	11 (42)	0	
Ewing sarcoma (<i>n</i> = 29)	22 (76)	7 (24)	0	
Consensus				
Radiography				0.009
Osteomyelitis (<i>n</i> = 30)	13 (43)	10 (33)	7 (23)	
Ewing sarcoma (<i>n</i> = 30)	24 (80)	2 (7)	4 (13)	
MRI				0.002
Osteomyelitis (<i>n</i> = 26)	17 (65)	9 (35)	0	
Ewing sarcoma (<i>n</i> = 29)	23 (79)	1 (3)	5 (17)	

Note—Data are number (%) of patients.

^a All three reviewers gave the correct prediction.

^b At least one reviewer gave the wrong prediction.

^c All three reviewers gave an indeterminate prediction.