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CASE REPORT

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Microscopic correlation of radiographically disparate appearing well differentiated osteosarcoma

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Abstract Well differentiated (low grade) osteosarcomas are often unrecognized and inadequately treated. We report on a patient with a well differentiated osteosarcoma of the tibia that radiographically presented with two strikingly dissimilar appearing juxtaposed lesions. Proximally, the lesion was sclerotic, and distally, osteolytic. The distal lytic half of the lesion showed focal cortical disruption on MR imaging. Microscopic correlation of the resected specimen suggested that the sclerotic component of the lesion had more fibrous dysplasia-like tissue with fewer features of well differentiated osteosarcoma, and the lytic component, features suggestive of well differentiated osteosarcoma. We believe this microscopic interpretation explains the disparate radiographic appearance as all belonging to well differentiated osteosarcoma with varying amounts of fibrous dysplasia-like tissue rather than the development of well differentiated osteosarcoma in fibrous dysplasia.

Keywords Tibia · Fibrous dysplasia · Well differentiated osteosarcoma radiographs · MRI

Abbreviations *LGIOS* Low grade intraosseous-type osteosarcoma · *MRI* Magnetic resonance imaging

Introduction

Low grade intraosseous-type osteosarcoma (LGIOS) is rare and frequently difficult to recognize, resulting in delayed or inadequate treatment [1]. They represent 1.9 percent of all osteosarcomas in the Mayo Clinic files (Rochester, MN) and 1 percent of all osteosarcomas recorded in the Rizzoli Institute in Bologna, Italy [1, 2]. Histologically, these tumors are often confused with fibrous dysplasia, but the combination of an infiltrative pattern microscopically and radiographic features atypical for fibrous dysplasia allows distinction between the two entities. When treated with wide excision, the tumor almost never recurs. When treated with local excision, the tumor always recurs, and 15 percent of these recurrences are in the form of a higher grade of osteosarcoma [1]. We present a patient in whom the radiographic features suggested fibrous dysplasia (Fig. 1). The MR fea-

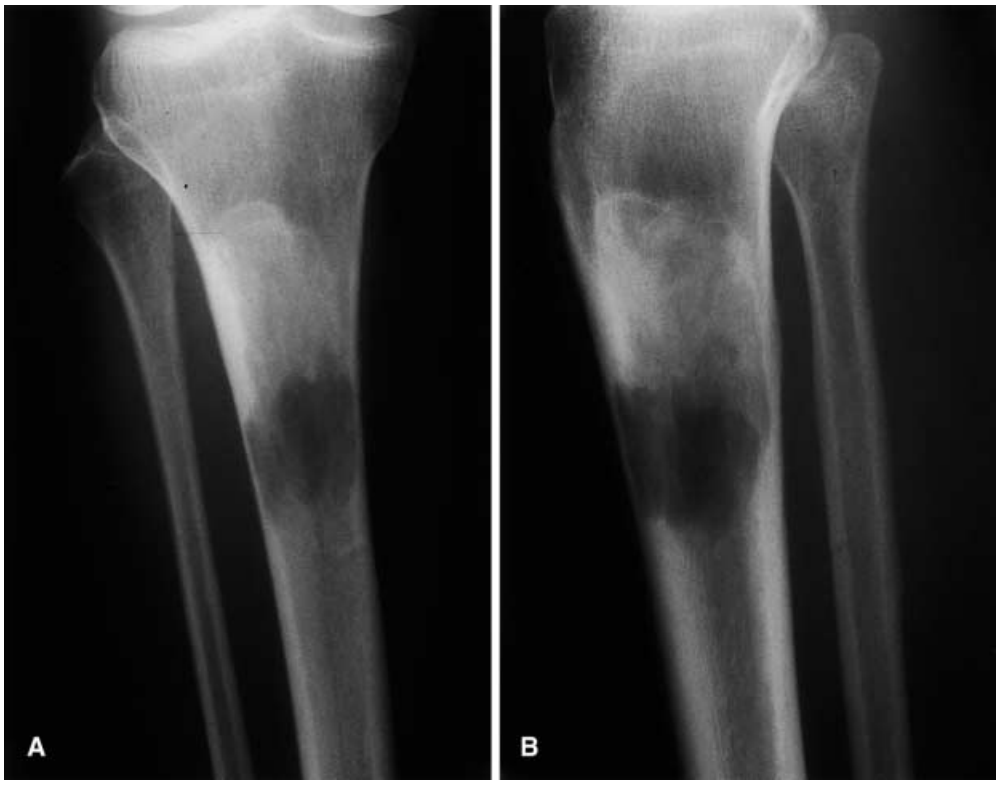


Fig. 1 AP (**A**) and lateral (**B**) conventional radiographs of the proximal tibia demonstrate a mixed lytic and sclerotic lesion in the proximal tibial diaphysis. The proximal 1/2 of the lesion is predominately osteosclerotic with a well-defined sclerotic rim. The distal 1/2 of the lesion is purely osteolytic with associated endosteal erosion and cortical thinning, most marked anteriorly. There is a small focus of benign periosteal new bone formation along the posterior aspect of the lesion. The margin of the lytic component of the lesion is less well defined inferiorly

tures, however, were atypical for that diagnosis leading to biopsy and resection (Fig. 2, 3). The microscopic features of the resected specimen were indicative of well differentiated osteosarcoma (Fig. 4). The radiograph was striking in the clear demarcation of the matrix between the juxtaposed sclerotic proximal and distal osteolytic components of the lesion (Fig. 1). Careful microscopic correlation with the radiographic findings suggested the likely explanation for the disparate radiographic appearance in a tumor diagnosed as a well differentiated osteosarcoma and is further discussed.

Case Report

A 56-year-old otherwise healthy female presented with leg pain. Radiographs of the left leg revealed a lesion approximately 8 cm in length with the proximal half moderately sclerotic and the distal half entirely osteolytic (Fig. 1). Minimal endosteal thinning anteriorly and posteriorly with a small posterior benign appearing solid periosteal reaction was noted. The favored radiographic diagnosis was fibrous dysplasia. Because of the atypical pain not associated with any recent trauma and without clear evidence of fracture on the radiograph, magnetic resonance imaging (MRI) of the lesion was performed. The MR images showed in the distal portion of the lytic component of the lesion disruption of the cortex anteriorly and laterally without an extraosseous mass (Fig. 2). The cortical destruction resulted in a reversal of the radiographic diagnosis of fibrous dysplasia, and the possibility of a low grade sarcoma was raised. The possibility of a low grade sarcoma arising in fibrous dysplasia was also considered. A biopsy of the lytic component of the lesion was performed. The biopsy material suggested a fibrous hypocellular spindle-shaped lesion (not shown), which viewed in conjunction with the radiographs suggested either desmoplastic fibroma or low grade fibrosarcoma. The tumor was resected by a wide margin (Fig. 3),and the limb reconstructed with a bone allograft. Microscopic examination of the resected specimen showed features consistent with a diagnosis of LGIOS (Fig 4). Under low power, the proximal margin was well demarcated and showed a margin with reactive new bone formation. The lesion was composed of a hypocellular spindle cell proliferation with no obvious permeation. The spindle cells showed no cytologic atypia (Fig. 4A, B, C). The central portion showed similar features. The lesion abutted the cortex but did not permeate it. The distal portion was more cellular and showed permeation of marrow fat and cytologic atypia. Bone formation was minimal (Fig. 4D, E). The patient is well and disease free 2 years following the operation. No chemotherapy was administered.

Discussion

The elusive nature of the diagnosis of LGIOS and its microscopic confusion with fibrous dysplasia has been well recorded in two large series [1, 2]. The rarity of this tumor in comparison with the frequency of the lesion that it most closely mimics, fibrous dysplasia, probably further contributes to the uncertainly and delay in diagnosis. When faced between the two diagnoses, imaging aids to the diagnosis of LGIOS are poor margination and/or cortical destruction, which may be seen in 60 percent of patients with LGIOS [2].

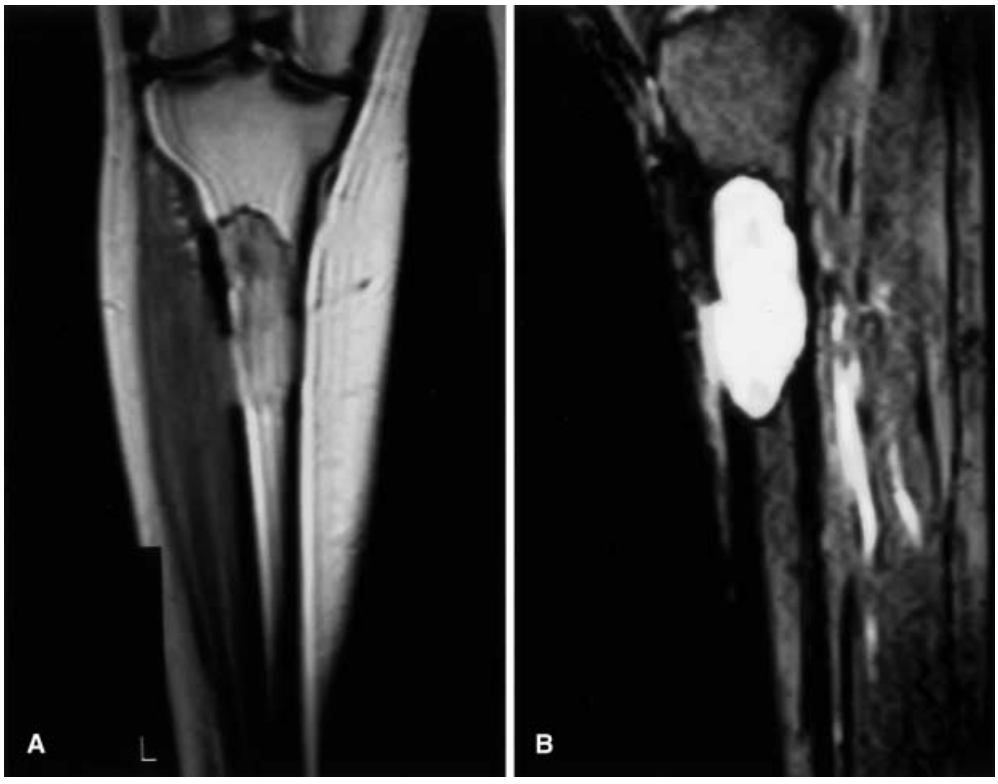
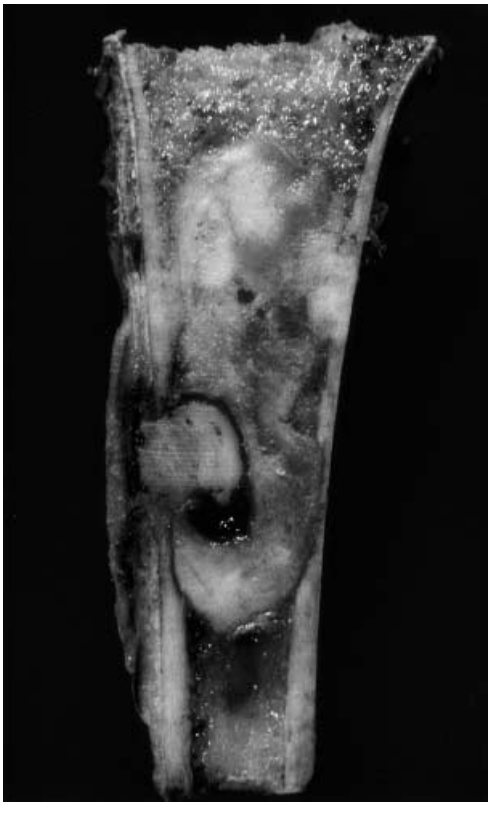


Fig. 2 Coronal T1-weighted **A** and sagittal T2-weighted **B** MR images show a large intramedullary lesion in the proximal tibial diaphysis with homogeneous high signal intensity on T2-weighted and heterogeneous low and intermediate signal intensity on T1-weighted images. Although the T1-weighted images show slightly lower signal intensity proximally in the lesion, overall the signal intensity of the intramedullary lesion does not reflect the disparate pattern of bone destruction revealed on the conventional radiographs. There is evidence of abnormal signal penetrating the tibial cortex anteriorly and laterally with a thin linear focus of signal abnormality adjacent to the cortex consistent with periosteal new bone formation or soft tissue thickening



As our case evolved with changing diagnoses, several management issues developed. If not for the atypicality of the pain in this patient with a presumptive radiographic diagnosis of fibrous dysplasia, it is unlikely that an MR examination would have been performed, and it is therefore also unlikely that the patient would have been biopsied. The decision to biopsy was largely made on the basis of the MR findings (Fig.°2A, B), which showed focal cortical destruction, untenable with the radiographic diagnosis of fibrous dysplasia, and which also presumably accounted for the patient's symptoms. The presumptive biopsy diagnoses of desmoplastic fibroma or low grade fibrosarcoma were not entirely tenable with the radiographic findings. The large area of sclerosis seen in the proximal portion of this lesion is a feature that is not consistent with either of these two diagnoses. However, because the biopsy had been obtained from the site that showed the greatest aggression on imaging studies, it was felt that this was representative of the most aggressive aspect of the tumor, based on which two decisions were made: (1) Performance of a wide resection of the tumor, (2) No chemotherapy to precede the

Fig. 3 Resected tumor specimen. Biopsy site through disrupted cortex into lytic area of lesion. Morphologically some dissimilarity is noted between the proximal and distal components of the tumor

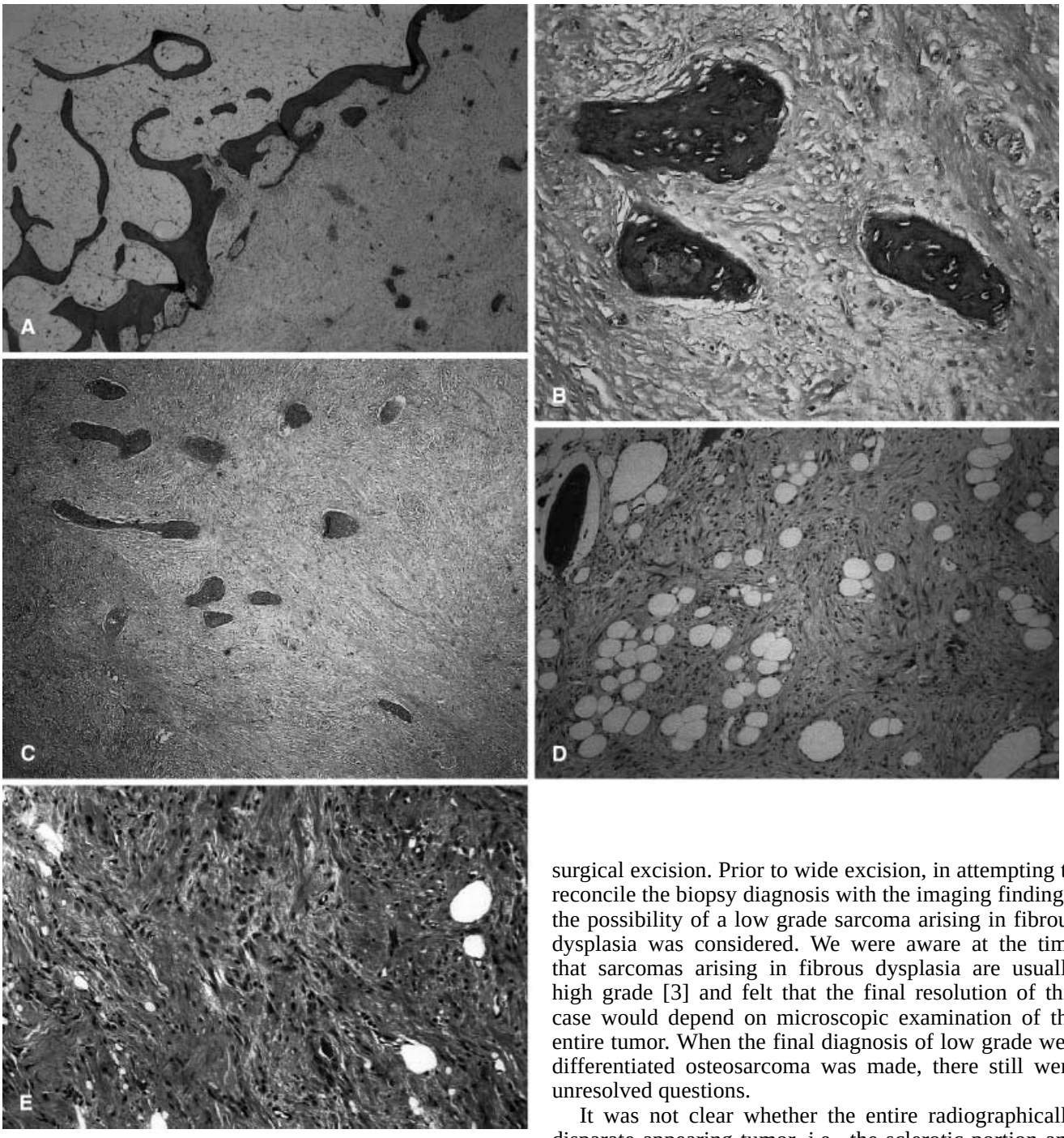


Fig. 4 A–C Proximal component of the tumor (sclerotic on radiographs) shows a circumscribed hypocellular spindle cell lesion containing scattered small irregular spicules of bone consistent with fibrous dysplasia. Marrow fat is separated from the spindle cell lesion by a thin rind of bone. **D** Distal portion of fibro-osseous lesion shows increased cytologic atypia of the stromal cells, which on higher magnification (**E**) demonstrates nuclear enlargement and hyperchromasia

surgical excision. Prior to wide excision, in attempting to reconcile the biopsy diagnosis with the imaging findings, the possibility of a low grade sarcoma arising in fibrous dysplasia was considered. We were aware at the time that sarcomas arising in fibrous dysplasia are usually high grade [3] and felt that the final resolution of this case would depend on microscopic examination of the entire tumor. When the final diagnosis of low grade well differentiated osteosarcoma was made, there still were unresolved questions.

It was not clear whether the entire radiographically disparate appearing tumor, i.e., the sclerotic portion and the osteolytic portion, all equally represented LGIOS, or whether LGIOS (distal portion) was fortuitously juxtaposed to an area of fibrous dysplasia, or if the hitherto unreported occurrence of a low grade sarcoma arising in fibrous dysplasia was the explanation. Careful microscopic correlation of the tumor in its upper, mid, and lower portions was performed, and the conclusions drawn were that the sclerotic portion represented fibrous dysplasia-like histological findings (Fig. 4A, B, C). The

distal lytic component of the lesion represented less fibrous dysplasia-like pattern and more features of well differentiated osteosarcoma (Fig. 4E). On balance, therefore, it was felt that the entire tumor represented well differentiated osteosarcoma, with suggestive features apparent in the radiographically lower lytic portion of the tumor and the upper sclerotic portion appearing more fibrous dysplasia-like. Neither histologically nor on MR was the difference between the superior and inferior portions of the tumor as dramatic as on the radiographs. This tumor, mimicking fibrous dysplasia or a low grade sarcoma arising in fibrous dysplasia, highlights the difficulties encountered in making the diagnosis of well differentiated osteosarcoma. A critically influential feature in making the diagnosis of well differentiated osteosarcoma was the presence of cortical destruction identified on MR imaging (Fig. 2). Another significant aspect influencing the management of the patient was the biopsy site, which suggested a low grade malignancy. A nonrepresentative biopsy sample could have adversely affected further management.

As a practical measure, we would like to mention that fibrous dysplasia is overwhelmingly a far more common entity than is well differentiated osteosarcoma. We believe that in most instances, fibrous dysplasia does not require imaging beyond the radiograph, and remains a well recognized ‘leave-me-alone’ lesion. When there are atypical features either in symptoms or on imaging such as cortical destruction or a soft tissue mass, the possibility of the lesion representing the rare LGIOS (well differentiated) might be considered. When the pathologist is faced with the uncertainty of fibrous dysplasia or LGIOS, careful scrutiny of the imaging studies for cortical disruption, soft tissue mass, or unequivocal poor margination ought to sway the diagnosis in favor of well differentiated osteosarcoma.

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