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CASE REPORT

Parosteal osteosarcoma with a manifestation of subperiosteal low-grade central osteosarcoma

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Abstract
We report the peculiar case of a parosteal osteosarcoma arising beneath the periosteum in a 12-year-old boy. He complained of difficulty in left knee flexion. Plain radiography showed a uniformly dense mineralized mass in the bone cortex and parosteal ossified nodules at the metaphysis and diaphysis of the left distal femur. Periosteal reaction was not evident. Uniquely, plain radiography had a smooth outline and revealed gradually thickening mass toward the center. Histologically, the tumor showed a proliferation of spindle-shaped cells with parallel-oriented dense bone trabeculae and hyaline cartilaginous tissue disclosing mild atypia. The periosteum was inverted along the polypoid mass, but there was no periosteum at the top. Immunohistochemically, the spindle cells, including those at the top of the polypoid mass, and cartilaginous cells were positive for MDM2 and CDK4. MDM2 gene amplification was detected in these cells by fluorescence in situ hybridization. Despite the peculiar feature of plain radiography, the lesion was diagnosed as parosteal osteosarcoma. This case report presents a case of parosteal osteosarcoma arising beneath the periosteum, although it is postulated to arise in the outer layer of the periosteum. The unique radiographic findings in this case suggest an association of parosteal osteosarcoma with vigorous bone growth before closure of the growth plate.

Keywords Parosteal osteosarcoma · MDM2

Introduction

Parosteal osteosarcoma and periosteal osteosarcoma are subtypes of surface osteosarcoma, which are typically of low to intermediate histological grade. Historically, they were referred to as juxtacortical osteosarcoma. They occur in young adults, peaking in incidence in the third decade of life. It has been postulated that parosteal osteosarcoma arises from the outer layer of the periosteum, while periosteal osteosarcoma originates from the deep layer of the periosteum or surface of the cortex [1]. When surface osteosarcoma exhibits a high nuclear grade, it is called high-grade surface osteosarcoma [1]. Plain radiographs of parosteal osteosarcoma show dense mineralization with lobulated outlines. Parosteal osteosarcoma is not accompanied by a periosteal reaction, so it is postulated to arise from the outer layer of the periosteum [1]. In the current report, we present a case of low-grade surface osteosarcoma arising beneath the periosteum with parallel trabecular bone formation, a proliferation of spindle cells, and cartilaginous differentiation accompanied by MDM2 gene amplification. Although the imaging findings were unusual, we diagnosed this peculiar case as parosteal osteosarcoma based on the histological and genetic features. This case report presents a case of parosteal osteosarcoma arising beneath the periosteum, although it is postulated to arise in the outer layer of the periosteum. The unique radiographic findings in this case suggest an association of parosteal osteosarcoma with vigorous bone growth before closure of the growth plate.

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Case report

A 12-year-old boy presented with a limited range of motion in his left knee joint, which he had experienced for 1 year. Tenderness, pain, and local heat were not evident. A small

solid protuberance on the posterior aspect of the left distal thigh was palpable. The patient did not have any relevant medical history. Plain radiography showed a lesion with homogeneous dense ossification in the posterior bone cortex from the distal diaphysis to the metaphysis of the femur. The margins of the lesion were smooth and the lesion gradually thickened as it approached the center. No periosteal reaction was evident. Extracortical nodular lesions with calcification were also observed posteroinferior to the cortical lesion, but continuity of calcification between the lesions was not apparent (Fig. 1). Computed tomography (CT) showed homogenous calcification along the posterior bone cortex of the distal femur, consistent with the findings on plain radiography (Fig. 2). The lesion was irregularly marginated and bordered indistinctly at depth, suggesting bone marrow involvement, but no periosteal reaction was evident. Continuity of ossification between the parosteal calcified nodules and the cortical lesion was not evident on CT.

Although chronic osteomyelitis and myositis ossificans were considered on imaging findings, the possibility of osteogenic bone tumors, including osteosarcoma, could not be ruled out. To evaluate the extent and malignancy of the lesion and to determine the site of biopsy, an [^{18}F]-2-fluoro-2-deoxy-D-glucose positron emission tomography/magnetic resonance imaging (^{18}F-FDG PET/MRI) scan was performed. The cortical lesion in the posterior femur showed a low signal on T1-weighted images (T1WI) and mostly a low signal on fat-suppressed T2WI, but there was a high signal area in the deep bone marrow, which suggested infiltration and edema. Fat-suppressed T2WI also depicted a low-signal polypoid mass, corresponding to the parosteal calcified mass found in the plain radiography and CT, contiguous with the femoral cortex lesion via high-signal stalk-like soft tissue. Foci of FDG accumulation were found in the stalks of the polypoid lesion, and the maximum standardized uptake value (SUV_{max}) was 3.35 (Fig. 3). Laboratory data showed no significant abnormality. The imaging findings suggested a relatively low-grade bone tumor, and parosteal osteosarcoma and periosteal osteosarcoma were listed in the diagnosis, but the possibility of conventional osteosarcoma and chronic osteomyelitis remained.

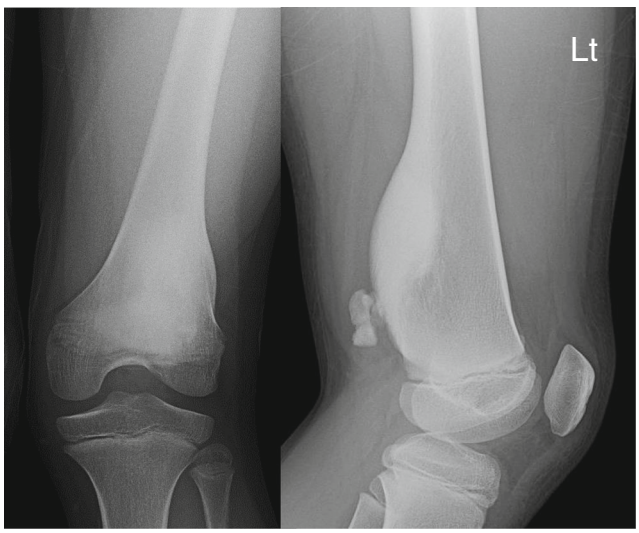


Fig. 1 Plain radiography showed a lesion with homogeneous dense ossification in the posterior bone cortex from the distal diaphysis to the metaphysis of the femur. The margins of the lesion were smooth, and the lesion gradually thickened as it approached the center. No periosteal reaction was evident. Extracortical nodular lesions with calcification were also observed posteroinferior to the cortical lesion, but the continuity of calcification between the lesions was not apparent

An open biopsy was conducted. The biopsy specimen revealed the proliferation of spindle-shaped cells with parallel bone formation. Immunohistochemically, the tumor cells were positive for MDM2. MDM2 gene amplification was detected by fluorescence in situ hybridization (FISH) (Fig. 4d). Based on histological and molecular features, the lesion was diagnosed as parosteal osteosarcoma. Wide resection was carried out. Gross findings and a reconstructed image of hematoxylin and eosin staining of the resected specimen are shown in Fig. 5a,b. In the polypoid mass, the lesion showed a proliferation of spindle-shaped cells with parallel fashion of bone formations. In the medullary lesion, loose cellular proliferation of spindle-shaped cells with parallel bone trabeculae was also observed. Spindle-shaped tumor cells revealed fibroblast-like morphology and low-grade nuclear atypia (Fig. 5c,d). Cartilaginous cells were found in the stalk of the polypoid mass (Fig. 5e,f). The periosteum was inverted along the polypoid mass (Fig. 5g). However, there was no periosteum at the top of the polypoid mass (Fig. 5h). Immunohistochemically, the spindle-shaped cells were positive for MDM2 and CDK4 (Fig. 5i,j) and the cartilaginous cells were also positive for MDM2 (Fig. 5k). Spindle cells at the top of the polypoid mass were also positive for MDM2 (Fig. 5l). A histological overview is presented in Fig. 5m. The tumor cells proliferated more on the proximal side than on the distal side. The tumor was widely resected and the femur was reconstructed using vascularized fibula. The patient has been free of local recurrence after surgery for 2 years.

Discussion

We experienced a case of parosteal osteosarcoma arising beneath the periosteum. Parosteal osteosarcoma is a low-grade bone-forming neoplasm that arises predominantly on the surface of the long bone in an exophytic pattern; it constitutes about 3% of all osteosarcomas. It more commonly arises at the distal femur, rather than the proximal tibia and humerus. Its incidence peaks during the third

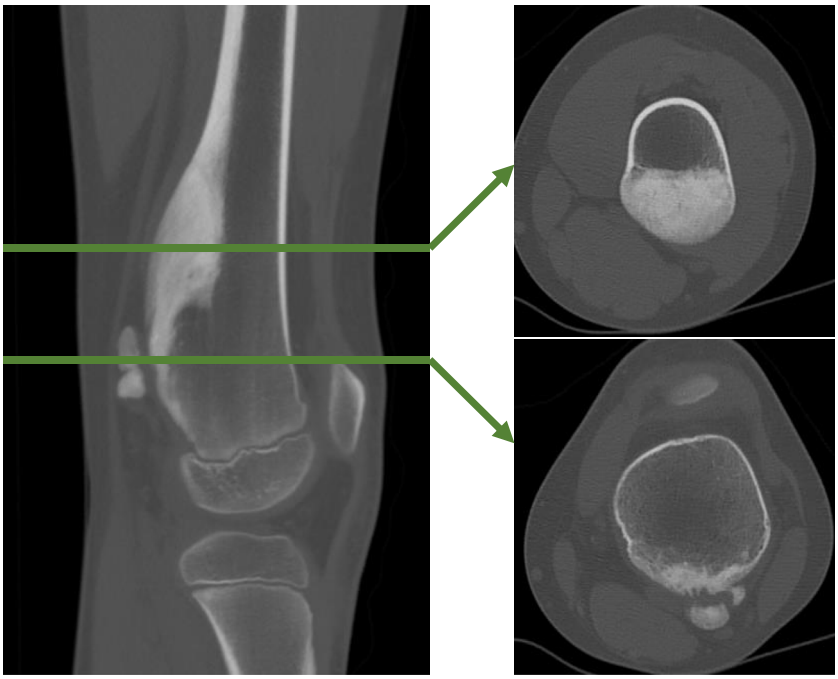


Fig. 2 Computed tomography (CT) showed homogenous calcificated mass along the posterior bone cortex of the distal femur, which was irregularly marginated and bordered indistinctly at depth, suggesting bone marrow involvement, but no periosteal reaction was evident. The continuity of ossification between the parosteal calcified nodules and the cortical lesion was not evident

and fourth decades. Histologically, the tumor shows spindle-shaped cells arranged in fascicles, which are hypocellular with minimal atypia and low mitotic activity. Bone trabeculae are well formed and arranged mostly in a parallel fashion. Cartilaginous differentiation, in the form of small scattered nodules or a cartilaginous cap, is also seen [1–3]. Generally, parosteal osteosarcoma is thought to be derived from the outer layer of the periosteum and grows without elevation of the periosteum [1]. MDM2 and CDK4 coamplification is also seen in this condition [4, 5]. Plain radiography of the parosteal osteosarcoma shows dense mineralization with lobulated outlines, mushroom-like growth with a space separating the tumor from the underlying cortex, and more mineralization in the

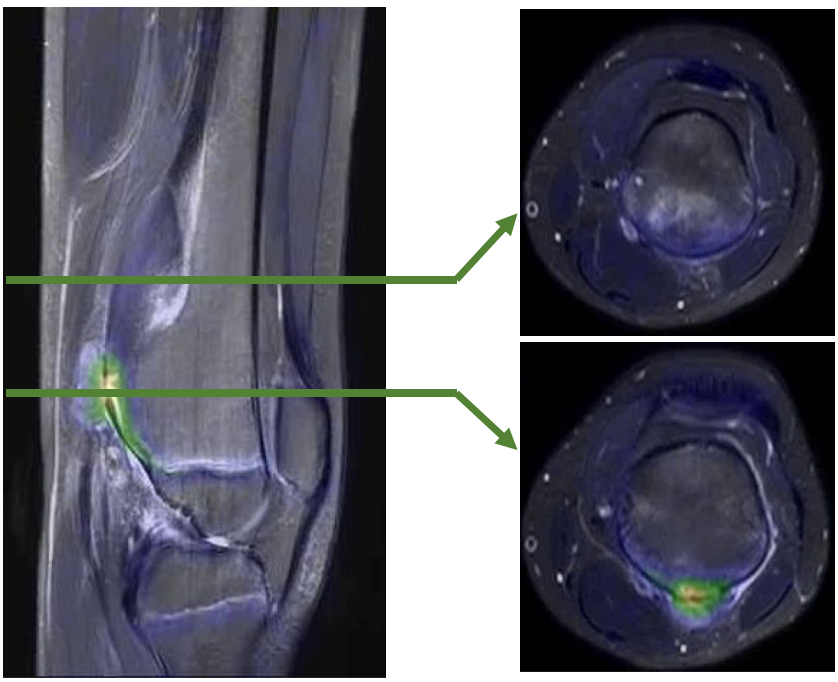


Fig. 3 Fusion images between ^{18}F-FDG PET and fat-suppressed T2WI acquired with a PET/MRI scanner are shown. The cortical lesion in the posterior femur showed mostly low signal on fat-suppressed T2WI, but there was a high signal area in the deep bone marrow, which suggested infiltration and edema. Fat-suppressed T2WI also depicted a low-signal polypoid mass, contiguous with the femoral cortex lesion via a high-signal stalk-like soft tissue. The foci of FDG uptake were found in the stalks of the polypoid lesion, and the maximum standardized uptake value (SUV_{max}) was 3.35

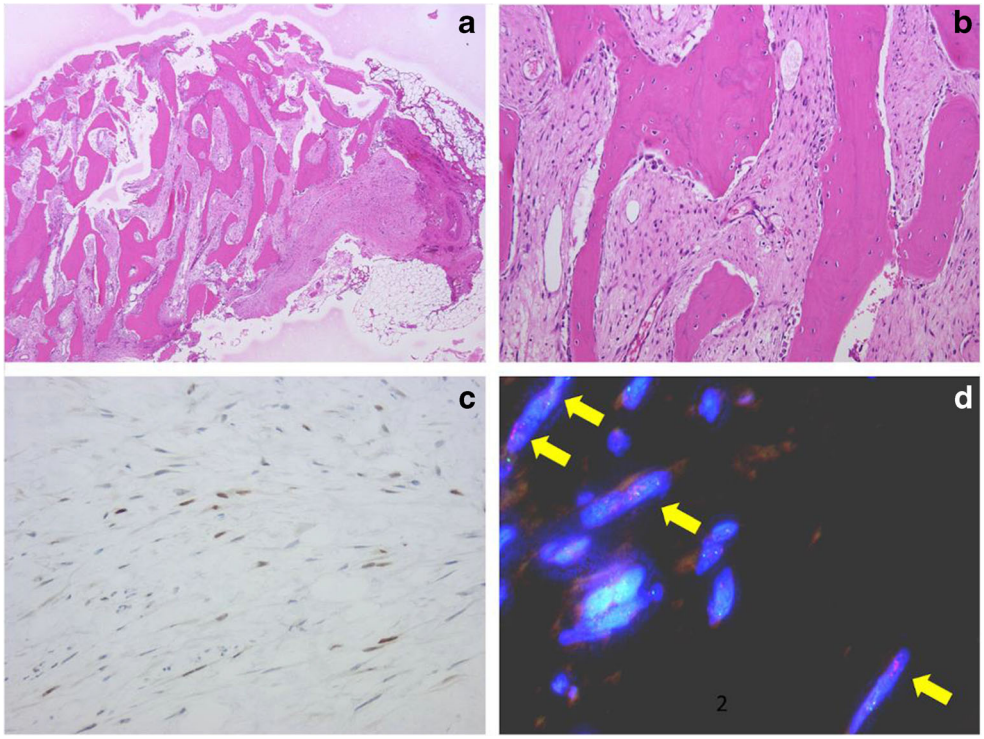
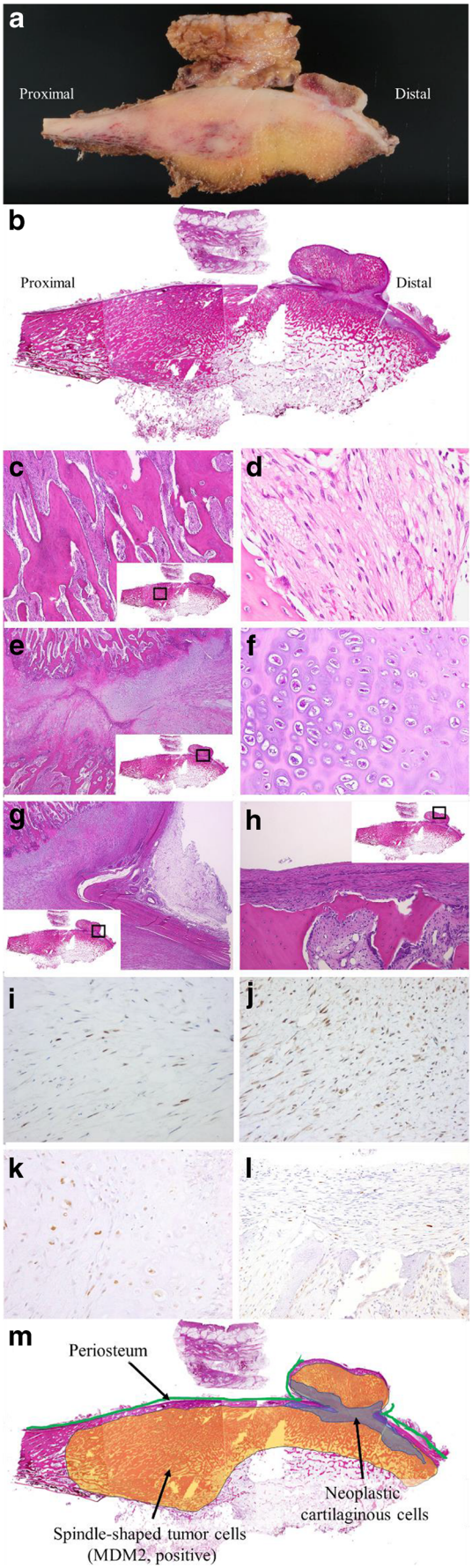


Fig. 4 **a**, **b** The tumor showed a proliferation of spindle-shaped cells with bone trabeculae arranged in parallel. **c** The spindle-shaped tumor cells were positive for MDM2. **d** MDM2 gene amplification was detected by fluorescence in situ hybridization

base and central portions rather than in the peripheral portions. Parosteal osteosarcoma is not accompanied by a periosteal reaction, so it is postulated to arise from the outer layer of the periosteum [1]. Periosteal osteosarcoma is a low-to-intermediate-grade bone-forming neoplasm with predominantly chondroblastic differentiation that develops on the surface of long bones. Its incidence peaks from ages 10 to 35. Histopathologically, periosteal osteosarcoma predominantly exhibits features of cartilage differentiation. In this tumor, immature bone production can be found. Spicules of reactive bone that have prominent osteoblastic rimming are also seen. MDM2 and CDK4 gene amplification is not observed in periosteal osteosarcoma [6]. On plain radiography, periosteal osteosarcoma shows a radiolucent fusiform lesion on the surface of a long bone and prominent periosteal new bone formation in the form of perpendicular striae and Codman's triangles. Because periosteal osteosarcoma is accompanied by a periosteal reaction, it is thought to originate in the deep layer of the periosteum or in the outer layer of the cortex [1]. In the current case, the histopathological findings, the existence of MDM2 amplification, and the unique radiographic findings indicated that this tumor was parosteal osteosarcoma, not periosteal osteosarcoma. The histological feature of covering the periosteum suggested that the tumor originated deep in the periosteum or on the bone surface.

A case report has been published of parosteal osteosarcoma presenting a morphological growth feature very similar to that in our case [7]. The interpreting radiologist suspected that our case was osteomyelitis in the radiology report, although a differential diagnosis of neoplasm was also suggested. We also identified a case report showing photographic findings similar to those in the current case. Specifically, this case report was of an 8-year-old boy showing a mineralized mass with a smooth outline, gradual and significant thickening of the cortical bone, and no periosteal reaction [7]. In both the previous case and our current case, there was a unique appearance in that the edges were smooth and the tumor thickened as it approached the center. The smoothness of edge would reflect dense mineralization of the subperiosteal lesion. Both the previously reported case and the current case occurred in childhood, at which stage vigorous bone formation is maintained. Therefore, the radiological features of these two cases are suggestive of an association with vigorous bone growth before closure of the epiphyseal line. It may be preferable to perform histological analysis by biopsy for lesions presenting these peculiar imaging findings in children. In summary, we have presented a case report of parosteal osteosarcoma with a manifestation of subperiosteal low-grade central osteosarcoma. When plain radiography shows uniformly dense mineralized and gradually thickened mass having a smooth outline in the bone cortex of children, biopsy and histological analysis are desirable.



◀ **Fig. 5** **a** Cut surface of the resected specimen. The polypoid mass was continuous with the bone cortex. The bone cortex was gradually thickened. **b** Reconstructed image of HE staining. **c** Well-formed parallel bone formation. **d** Spindle tumor cells with minimal atypia. **e**. Cartilaginous cells were found in the stalk of the polypoid mass. **f** High-power field of cartilaginous cells. **g** The periosteum was inverted along the polypoid mass. **h** The periosteum was not seen at the top of the polypoid mass. **i** Immunohistochemical positivity for MDM2 in spindle cells. **j** Immunohistochemical positivity for CDK4 in spindle cells. **k** Cartilaginous cells were also positive for MDM2. **l** The cells at the top of the polypoid mass were positive for MDM2, indicating that the top of the polypoid mass was not covered by the periosteum. **m** An overview of histological feature mapping showed that tumor cells proliferated more on the proximal side (left) than on the distal side (right). The periosteum covered the surface of the polypoid mass, apart from its top. Neoplastic cartilaginous cells were found around the polyp stalk

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Declarations

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Ethics Committee of our University (nos. 29-429, 29-625).

Informed consent Informed consent was obtained from the participant included in the study.

Conflict of interest The authors declare no competing interests.

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