CASE REPORT

Low-Grade Central Osteosarcoma: Report of Two Unusual Morphologic Variants

Neha Chopra Narang¹ · Preeti Diwaker¹ · Salil Narang¹ · Vasantha Kumar Venugopal²

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Abstract Low-grade central osteosarcoma (LGCO) is a rare subtype of osteosarcoma, constituting < 2% of all osteosarcomas. If not treated appropriately, the tumor can recur with higher-grade disease. We report two cases of low-grade central osteosarcoma with unusual morphologic features and belonging to different age groups. Both presented with pain and swelling in the lower end of femur. Radiologically, both the lesions revealed a large mass with irregular borders and soft tissue invasion.

One patient underwent above-knee amputation and wide local excision of tumor was done in the other patient. Histologically, both the tumors showed spindle cell proliferation displaying mild atypia. In synopsis with radiology, diagnosis of low-grade central osteosarcoma was made in both cases. These cases highlight the varied morphological spectrum of low-grade central osteosarcoma and underscore the diagnostic difficulties faced. Recognition of the variants of low-grade central osteosarcoma is based on aggressive radiological appearance and on adequate tumor sampling for histologic examination.

Keywords Low-grade central osteosarcoma · Morphologic variants · Young adults · Rare subtype

Introduction

Low-grade central osteosarcoma (LGCO) constitutes 1–2% of all skeletal osteosarcomas [1, 2]. This uncommon subtype is less aggressive than the other more frequent types, and has

low metastatic potential with fairly good prognosis [2]. It was first described by Unni et al. [2]; they reported 27 patients with an “intraosseous well-differentiated osteosarcoma.” LGCO usually presents in the third decade of life, with an almost equal male to female ratio [2–4]. Metaphyseal region of the long bones is usually affected, distal femur and proximal tibia being most commonly involved [2–4]. Its well differentiation and minimal cytologic atypia contributes to high rate of initial misdiagnoses [5]. The key feature to distinguish LGCO from benign mimics is to identify permeative growth pattern [6, 7]. LGCO can be confused radiologically with fibrous dysplasia, desmoplastic fibroma, nonossifying fibroma, osteoblastoma, and aneurysmal bone cysts [4, 6, 7]. Therefore, combination of radiological and histological features is essential to diagnose LGCO [7]. These tumors are adequately treated with wide excision, chemotherapy, or radiotherapy are not indicated. Incomplete resection is often followed by local recurrence, with possible dedifferentiation to high-grade sarcoma, followed by distant dissemination. With appropriate treatment, LGCO shows a good prognosis with 5- and 10-year survival rates of 90 and 85%. In this report, we describe the clinicoradiological and unusual pathologic findings in two cases of central low-grade osteosarcoma.

Case Reports

Case No. 1

History

A 12-year-old girl presented with pain and swelling involving lower end of right femur since 1 year. Clinical examination revealed a palpable circumferential, mildly tender swelling of distal femur. The patient had no relevant past medical history.

✉ Preeti Diwaker
diwaker_preeti@yahoo.in

¹ University College of Medical Sciences, New Delhi, India

² IBS Hospital, New Delhi, India

MRI showed T2W hyperintense destructive lesion in lower end of femur involving medial and lateral condyle measuring 11.8(AP) × 11.0(TR) × 15.4(CC) cm. The lesion shows sun ray branching into surrounding soft tissue and muscle and encases the right popliteal artery and vein. The lower epiphysis of femur shows STIR hyperintensity infiltration (Fig. 1). Clinicoradiological diagnosis of osteosarcoma was made. Soft tissue biopsy from right distal femur revealed osteoid producing spindle cell neoplasm, suggestive of osteosarcoma. The patient received three cycles of chemotherapy and subsequently underwent an above-knee amputation.

Histopathological Findings

Gross examination revealed 12 × 7 cm tan white hard mass involving medullary cavity of femur (metaphyseal end) with extension into adjacent soft tissue; however, knee joint was free of tumor (Fig. 1).

Microscopic examination of tumor revealed fibrous and osseous components in variable amounts. There were large areas of hyalinization along with scant fibrous stroma composed of spindle-shaped cells with minimal cytologic atypia. Trabeculae of immature bone without osteoblastic rimming and focal osteoid production were noted. In correlation with the clinicoradiological findings, a final diagnosis of low-grade central osteosarcoma was given.

Case No. 2

History

A 29-year-old male presented with chief complaints of swelling and pain in the left knee and lower end of left femur since 8 months. MRI showed a heterogenous signal intensity lesion in distal femur measuring 10(CC) × 9(AP) × 8.3 (TR) cm. The lesion predominantly involved the lateral condyle and intercondylar region and extended up to distal metaphysis with cortical breach of lateral and posterior margins and bulky soft tissue component extending laterally, posteriorly and into popliteal fossa. No evidence of intraarticular extension was seen. Mass appeared heterogeneously hyperintense in T2/STIR images with few confluent cystic areas, hypointense on T1W images and showed foci of sclerosis (Fig. 2). Clinicoradiological diagnosis of giant cell tumor was made. A prior incisional biopsy from the lesion in left femur was reported as giant cell tumor. Wide excision of the lesion was done and constrained type of knee prosthesis was placed in situ.

Histopathological Findings

Gross examination revealed 10 × 8 × 7 cm, gray-white firm mass involving the entire distal femur (Fig. 2).

Fig. 1 **a** Gross examination. Tan white hard mass involving medullary cavity of femur (metaphyseal end) with extension into adjacent soft tissue. **b** Microscopic examination. Large areas of hyalinization (H&E × 100). **c** Bony spicules, surrounded by hypocellular spindle cell stroma (H&E × 200). **d** Fibrous stroma composed of spindle-shaped cells with minimal cytologic atypia and focal osteoid production (H&E × 200). **e** X-ray AP and lateral view shows an expansile destructive sclerotic mass lesion with wide zone of transition having irregular spiculated margins extending into surrounding soft tissue with marked periosteal reaction. **f** Magnetic resonance imaging. Sagittal T2 image showing destructive lesion in the lower end of femur with sunray branching into adjacent muscle and soft tissue. **g** PET scan reveals metabolically active mass lesion involving right femur metadiaphyseal region infiltrating into surrounding soft tissue

Microscopic examination of tumor mass showed spindle cells arranged in fascicles with mild cytologic atypia set in a collagenous matrix along with intervening fragments of woven bone. Tumor cells permeated surrounding bony structures entrapping bony trabeculae. Focal osteoid production was seen. Peculiar feature noted was the presence of variable-sized blood vessels scattered throughout the tumor. Final diagnosis of LGCO was given.

Discussion

Osteosarcomas make up 20% of primary malignant bone tumors [8]. Most (75–85%) are high-grade osteosarcomas. Low-grade osteosarcomas constitute approximately 3–5% of all osteosarcomas [9].

LGCO usually presents between 18 and 45 years; however, one of our patients was 12 years old and belonged to a minority since only 7–21% of patients in other studies were younger than 18 years [4, 10, 11]. There is only one patient described in literature younger than 12 years [4].

Central low-grade osteosarcoma is a rare variant of osteosarcoma characterized histologically by a proliferation of elongated bland spindle cells arranged in interlacing fascicles in a collagenous matrix, with bone or osteoid formation. The amount of bone or osteoid produced is highly variable. In many cases, there is scant osteoid production, and therefore, the histologic picture is dominated by the spindle cell proliferation, resulting in histologic appearance of desmoplastic fibroma or low-grade fibrosarcoma [4, 6]. More commonly, the tumor is characterized either by production of bony trabeculae similar to those seen in parosteal osteosarcoma or by thin osteoid seams having the ‘Chinese letter’ appearance seen in fibrous dysplasia [4, 6]. In rare instances, the tumor may mimic the appearance of osteoblastoma, or may have a fibrochondromyxoid appearance, or may show areas of cartilage matrix production [4]. Instead of the well-recognized patterns, the cases presented here

Fig. 2 **a** Gross examination. Gray-white firm mass involving the entire distal femur. **b** Magnetic resonance imaging. Sagittal T2 image showing lytic expansile lesion with periosteal reaction, osteoid matrix, and cortical break. **c** Microscopic examination. Spindle cells arranged in fascicles set in a collagenous matrix (H&E $\times$ 100). **d** Tumor cells show mild cytologic atypia with focal osteoid production. Variable-sized blood vessels seen scattered throughout the tumor (H&E $\times$ 200)

show varied morphologic patterns. Case no. 1 shows large areas of hyalinization with markedly low cellularity, while case no. 2 shows spindle cell proliferation with peculiar vascular pattern which has not been previously described in literature. The diagnosis is based on aggressive histologic features in central low-grade osteosarcoma, such as permeation of the bone marrow, entrapment of bony trabeculae, which are usually present at the growing edge of the tumor. However in biopsy material, these features may be missed, and therefore, it is essential to carefully evaluate the radiological details. The radiological features of LGCO are variable, as reported in the literature. Andresen et al. described four different radiographic patterns of LGCO: lytic with varying amounts of thick and coarse trabeculation, predominantly lytic with few thin, incomplete trabeculae, densely sclerotic and mixed sclerotic and lytic. MRI or CT scans essentially detect features of aggressiveness, such as cortical breach and intramedullary or soft tissue extension. Thus, MRI and CT scans become the modality of choice to differentiate between benign lesions and low-grade malignancies [3]. In both the present cases, radiological findings revealed poorly defined tumor margins, cortical invasion, and extraosseous extension which are highly suggestive of malignancy.

We describe two cases of central low-grade osteosarcoma with unusual histologic features. These cases further expand the histologic spectrum of central low-grade osteosarcoma. In

accordance with previous studies, inadequate treatment of these tumors may result in recurrence and eventually in dedifferentiation to high-grade osteosarcoma, with development of distant metastases. Recognition of this variant of central low-grade osteosarcoma is essential and diagnosis is based on the aggressive radiologic appearance and adequate tumor sampling for histologic examination.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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