

Original Article

Low grade central osteosarcoma dedifferentiating into a high grade leiomyosarcoma in a young adult

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Summary

An 18 –year-old male patient presented with left knee joint pain of seven month duration. The initial MRI scan was suggestive of an infective process, while the subsequent scan revealed radiological features suggestive of an osteosarcoma in the left distal femur. The biopsy was reported as an osteosarcoma in a different institution. Following neoadjuvant chemotherapy wide local excision of the tumour was performed. On histologic evaluation, a low grade central osteosarcoma was diagnosed with progression to high grade leiomyosarcoma. Low grade central osteosarcoma is an uncommon bone forming tumour which occasionally dedifferentiate into a highgrade sarcoma, most commonly to conventional osteosarcoma. The young age of the patient and dedifferentiation into a leiomyosarcoma are unusual features encountered in this case. Furthermore, we discuss the challenges encountered in diagnosing a low grade central osteosarcoma which has deceptively benign features radiologically and histologically.

Keywords: Low grade central osteosarcoma, Dedifferentiated sarcoma, osteosarcoma

Introduction

Low grade central osteosarcoma is a rare low grade malignant bone forming neoplasm, accounting for less than 1-2% of all osteosarcomas¹. It arises within the medullary cavity and 80% are located in long bones with the predominant site being the distal femur². The majority of them occur in second and third decade of life, a slightly older age group in comparison to that of conventional osteosarcoma. Significantly it shows a better prognosis with slow growth, low metastatic potential and longer survival. However, 10 -

leading to poor prognosis with recurrence, rapid growth and metastasis³. Radiologically and histologically low grade osteosarcoma commonly mimic benign lesions, making the diagnosis challenging especially in biopsy samples^{1,4}.

We report here a case of low grade central osteosarcoma with dedifferentiation into high grade leiomyosarcoma at the time of surgical resection in a young adult.

Case report

An 18- year-old male presented with a long standing left knee joint pain of seven

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Figure1 -MRI scan of left femur showing an intramedullary bone forming neoplasm involving the meta-diaphyseal region.

month duration following an initial episode of trauma. The initial MRI scan performed reported features suggestive of an infective process with abscess formation, while the subsequent MRI scan revealed radiological features suggestive of an osteosarcoma of left femur involving the meta-diaphysis with soft tissue extension (Figure 1). A biopsy had been performed in the private sector and diagnosis of bone forming neoplasm more in favour of an osteosarcoma had been made. CT scan of the chest revealed multiple lung lesions. Patient was treated with neoadjuvant chemotherapy followed by wide local excision of the tumour and prosthesis insertion.

Pathology

The wide local excision specimen comprised a part of the distal femur (16cm in length), including the epiphysis, with surrounding skeletal muscle and the skin. The cutsections showed a tan white solid tumour, measuring 6 x 6 x 7cm, involving both the medullary cavity and the cortex of the distal metaphysis of the bone. The tumour was seen



Figure 2 The gross appearance of the wide local excision of the femur. The tumour involves the medullary cavity at the metaphyseal region (orange arrow). The outer part of the bone cortex is intact at this plane. The blue arrow indicates the soft issue

extending into the adjacent soft tissue and skeletal muscle tissue with an irregular mass formation. It did not extend into the epiphysis (Figure 2).

Microscopically, the tumour in the medullary cavity was composed of abundant long parallel and curved anastomosing lamellar like bone trabeculae, surrounded by a moderately cellular spindle cell stroma which contained moderate amount of collagen (Figure 3a). The cells had minimal atypia and mitotic figures were sparse. The spindle cells permeated the pre-existing cortical bone at some foci. Cartilaginous differentiation was not evident.

In the rest of the tumour, predominantly in the soft tissue extension, the histomorphology was different (Figures 3b to 3E). There were interlacing fascicles of spindle cells with pleomorphic nuclei and eosinophilic and elongated cytoplasm. Mitotic activity was high with occasional atypical mitoses. The stroma was scanty and haemangiopericytoma like vascular pattern was also evident focally. Osteoid was not identified.

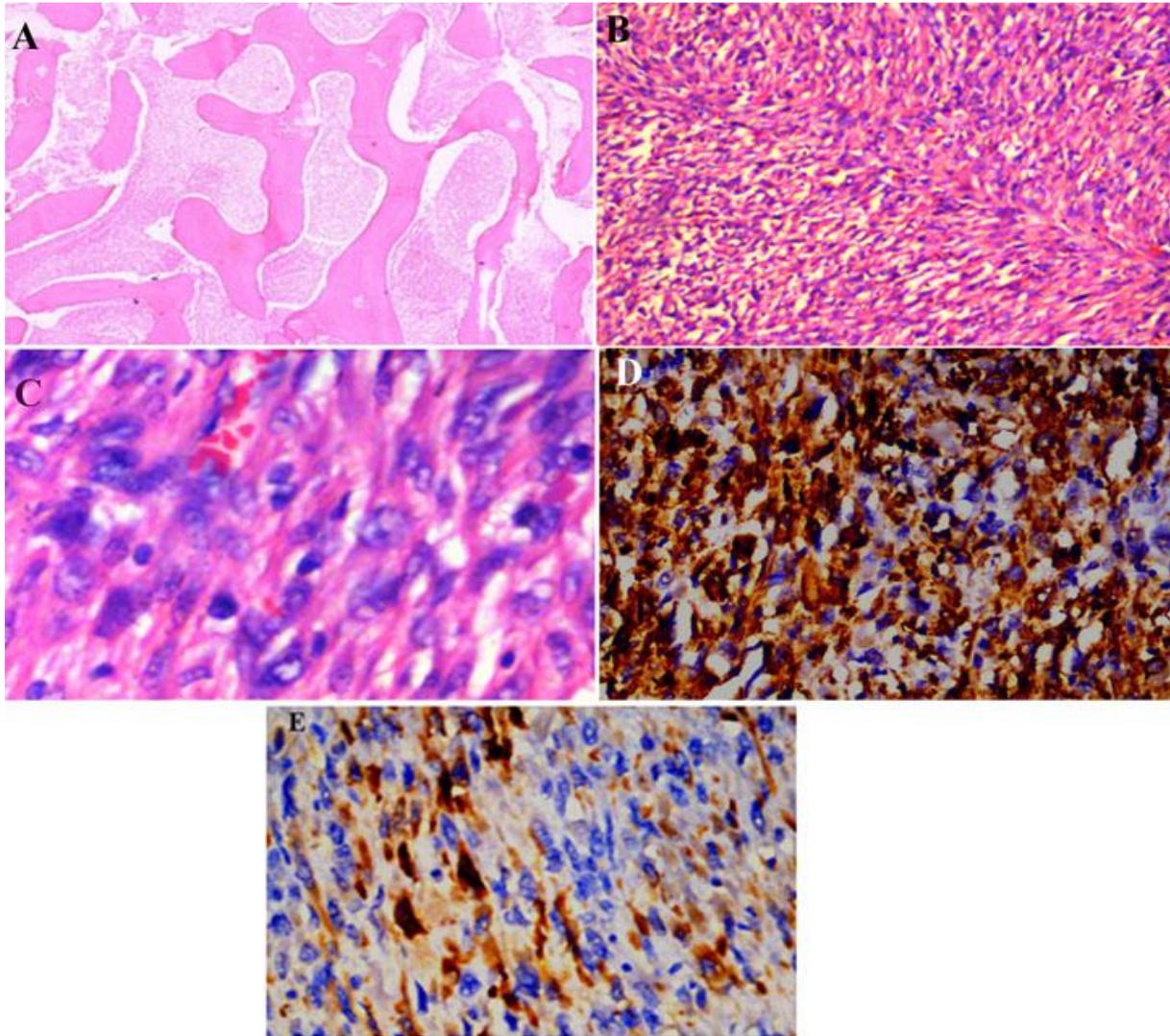


Figure 3 Microscopy of the bone tumour. A) Anastomosing bone trabeculae in a background of neoplastic stroma in low grade central osteosarcoma. B to E are from the dedifferentiated tumour B) cellular intersecting bundles of spindle cells. C) The high power view to show cellular pleomorphism D) Strong cytoplasmic positivity with smooth muscle actin E) cytoplasmic positivity with Desmin.

Immunohistochemistry revealed the spindle cells to be strongly positive for smooth muscle actin and moderate positivity for Desmin (Figures 3D and 3E). Pabcytokeratin, CD 34 and S-100 were negative.

Accordingly, the tumour was diagnosed as a low grade central osteosarcoma with areas of dedifferentiation into high grade leiomyosarcoma.

Discussion

This 18-year-old boy has presented with a history of gradually worsening pain in left knee joint over an approximately seven month duration. Considering the patient's age and duration of symptoms chronic osteomyelitis as well as a primary bone neoplasm were to be considered in the differential diagnosis. At this age the most common primary bone tumour is conventional osteosarcoma. As the initial MRI

scan was suggestive of an infective process with intramedullary fluid collection, clinical diagnosis of osteomyelitis with abscess formation was made initially. Osteomyelitis is relatively common in this age group and they usually present with fever and tenderness in the affected area⁵. Some patients may have non-healing ulcers or sinus tracts overlying the affected bone. Laboratory investigations such as neutrophil leucocytosis and elevated erythrocyte sedimentation rate are useful in the correct clinical settings⁷. Since the patient did not show a satisfactory response for conservative management MRI was repeated and the results were more in favour of an osteosarcoma. Subsequent bone biopsy had been reported as an osteosarcoma NOS. Since it has been reported in the private sector it was not possible to retrieve the slides. The history demonstrates the variable clinical and radiological features of low grade central osteosarcoma which can mimic a benign lesion. The cortical destruction and the soft tissue extension of the lesion were radiological features in favour of a malignancy.

Histologically, because of the deceptively bland cytological features and the bony trabeculae, which appeared benign in contrast to malignant osteoid of osteosarcoma, low grade central osteosarcoma can be easily overlooked as a benign intramedullary spindle cell lesion such as fibrous dysplasia and non-ossifying fibroma^{1,2}. Conventional osteosarcoma-fibroblastic type and paraosteal osteosarcoma are the main malignant differential diagnoses^{1,2}.

In the presence of bland spindle cells admixed with bony trabeculae diagnosis of fibrous dysplasia is to be considered. However, the characteristic irregular Chinese letter-like trabeculae of woven bone was not identified. Furthermore, as seen in the present case, the presence of bone permeation is a useful histological feature in diagnosing low grade malignant bone tumours with bland cytological features.

Fibroblastic osteosarcoma typically has minimal amount of osseous matrix and spindle cells with significant atypia, whereas, in the present case there was dense osseous matrix and spindle cells with minimal atypia. Well-formed bony trabeculae in a hypocellular bland spindle cell matrix are also features of a paraosteal osteosarcoma⁶. However, on radiology, paraosteal osteosarcoma is typically seen on the surface of bone, with only focal invasion into cortex and medullary cavity. Furthermore, about 50% of tumours show cartilaginous differentiation. Radiological features of tumour location was the most useful feature in excluding paraosteal osteosarcoma in the present case.

Considering the above features the intraosseous component was diagnosed as a low grade central osteosarcoma. The extraosseous component, which was continuous with the low grade central osteosarcoma, showed intersecting fascicles of spindle cells with high grade nuclear features, high mitotic activity without osteoid formation. Furthermore, the cells were strongly positive for actin and desmin. Hence, the appearance was consistent with a dedifferentiation of the tumour into a high grade leiomyosarcoma.

Dedifferentiation into high grade areas in a low grade central osteosarcoma is a rare event, which can occur in the primary tumour or more commonly with recurrences³. Most commonly transformation occurs to a high grade osteosarcoma and the other forms are extremely rare³. In the present case transformation to a leiomyosarcoma was evident by immunohistochemistry and absence of malignant osteoid even focally excluded the possibility of high grade osteosarcoma. In the present case, presence of dedifferentiation in the primary tumour was not common and transformation into a leiomyosarcoma was extremely rare. On further evaluation with CT scan of the chest, patient has had multiple lung metastases. The metastases tend to be from the high grade component.

Conclusions: Low grade central osteosarcoma poses a diagnostic challenge since it can mimic benign features histologically and radiologically. High degree of suspicion based on clinical features and adequate sampling and clinico-radiological correlation are helpful in arriving at a diagnosis. Close macroscopic inspection and adequate sampling are vital for detection of areas of dedifferentiation which significantly alter the prognosis of the disease and the therapy.

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