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Case Report

ow grade central osteosarcoma transforming to high grade sarcoma – Clinical implications and brief review of literature !

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ABSTRACT

Low grade central osteosarcoma (LGCO) are rare intramedullary bone tumours of adolescents and young adults with an excellent prognosis. They have a predilection for long bones around the knee joint, but cases have been reported in long bones of arm, tarsals and flat bones of jaw, ribs and scapula as well. Their transformation to high grade sarcomas are rarely seen. We report a case of an 16 years female who presented with complaints of progressive pain in the lower thigh 2 years back. Her x-ray suggested a simple bone cyst in distal femur, following which wide excision of the cyst was done. Histopathology however showed features of LGCO. The patient was apparently alright in the follow up period until 9 months ago when the patient had a recurrence of swelling accompanied with pain at the same site leading to difficulty in walking. This time her X-ray showed neoplastic changes after which the tumor was excised. On microscopy, areas of high grade sarcoma with soft tissue extension were seen predominantly. This case is being reported to make the clinicians and diagnosticians aware of the rare but highly significant implication of transformation of LGCO to high grade tumors as it carries a guarded prognosis and calls for a different treatment strategy compared to conventional LGCO.

Key Messages: Low grade central osteosarcoma (LGCO) are rare intramedullary bone tumors seen in adolescents and young adults. It bears an excellent prognosis. We present a case report on LGCO showing transformation to a high grade sarcoma that radically changes its prognosis as well as calls for a different treatment strategy.

1. Introduction

Low-grade central osteosarcoma (LGCO) is a rare intramedullary bone producing tumor, accounting for only 1-2% of all osteosarcomas. It has an equal gender distribution with the majority of cases occuring in the second and third decades. Any bone may be affected, but there is a strong predilection for femur and tibia.[1] Few case reports of involvement of gnathic bones, tarsal bones, fibula, long bones of arm, ribs, scapula and pelvis are also there.[2,3] It is a tumor with an excellent prognosis but its diagnosis is challenging due to the relatively nonspecific radiological and histological findings.[4] In the recent years, few case reports have highlighted the rare transformation of these LGCOs to high grade sarcomas, more commonly seen with the recurrences.[5] We present here a case of a LGCO in the distal femur of a young female that recurred with a transformation to high grade fibroblastic sarcoma emphasizing on its diagnosis, work up as well as the clinical implications.

2. Case History

A 16-year-old female presented 2 years back to our institute with chief complaints of progressively increasing pain around the left knee joint since past 8 months.

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There was no significant past/personal history. Radiograph demonstrated features of simple bone cyst in lower end of femur. (Figure 1 a) A wide margin excision was done and sent for histopathology. However, on microscopy, a solid cystic tissue was seen. In the solid part, numerous lamellated bony trabeculae were seen surrounded by mildly cellular fibroblastic stroma. It was seen permeating the bony tissues at few places.(Figure 2) Neoplastic lacy osteoid was also seen along with few multinucleated giant cells. Atypia and necrosis was not seen, though occasional mitotic figures were noted. The cystic part showed a wall lined by fibroblastic spindle cells similar to that seen in the solid part. The peripheral soft tissue was unremarkable. On the basis of these features, it was diagnosed as a Low grade central osteosarcoma. No additional therapy was given. Patient was under regular follow up. She was apparently well until 9 months back when she, (now of 18years) again presented with complaints of progressive pain at same site, that was accompanied with reappearance of the swelling, leading to difficulty in walking. Radiograph demonstrated a sclerotic lesion located in the medullary part of distal metaphyseal area of femur with periosteal elevation and soft tissue invasion suggesting a neoplasia. (Figure 1 b) A wide excision of the tumor was done. The specimen received comprised of distal part of femur bone with a central haemorrhagic necrotic area with some grayish white firm to hard nodules [tumor]. On microscopy, the areas of LGCO as seen previously were present accompanied by frequent [>50%] highly cellular areas where spindle to plump tumor cells were arranged in fascicles and interlacing bundles. These tumor cells were showing moderate nuclear atypia, pleomorphism and frequent mitoses. (Figure 3) In between these tumor cells neoplastic osteoid and numerous multinucleated giant cells were seen. (Figure 4) The tumor cells were seen infiltrating to the surrounding muscles and soft tissue as well. Accordingly, the tumor was now diagnosed as a Low grade central osteosarcoma with transformation to fibroblastic osteosarcoma. The patient was given 4 cycles of adjuvant chemotherapy post surgery. She responded well to the therapy and didn't have any evidence of recurrence / metastasis till the follow up period (5 months).

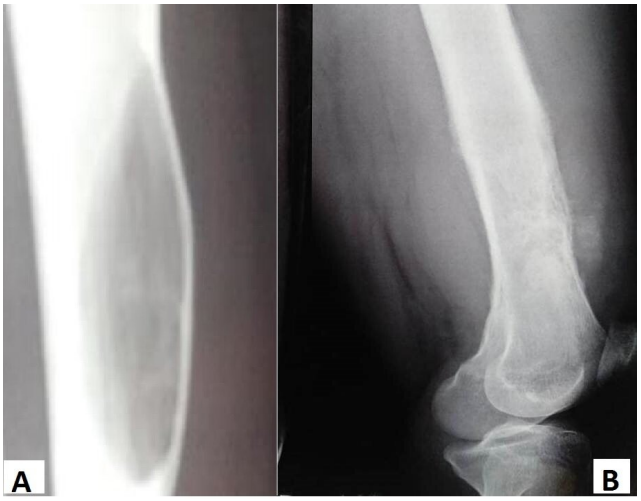

Fig. 1: A: Radiograph demonstrated features of simple bone cyst at the initial presentation; **B:** Radiograph demonstrated a sclerotic lesion located in the medullary part of distal metaphyseal area of femur along with periosteal elevation and soft tissue invasion during recurrence

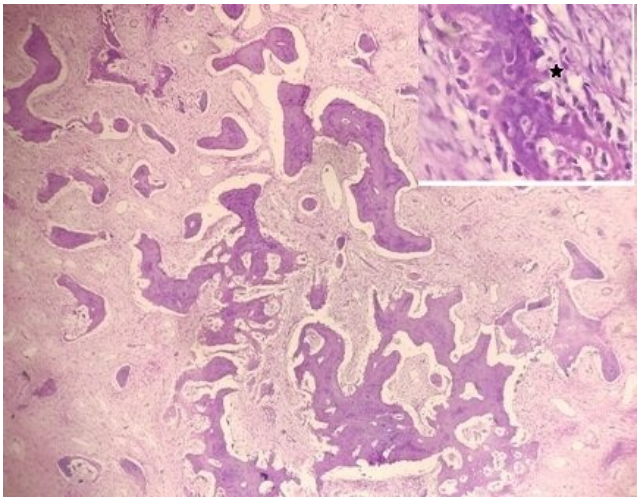

Fig. 2: Numerous lamellated bony trabeculae seen surrounded by mildly cellular fibroblastic stroma favouring Low grade central osteosarcoma (H and E X 4x); Inset- Permeation of the bony tissue was seen at few places (star). (H and E X 40x)

3. Discussion

Low grade central osteosarcoma (LGCO) are indolent tumors with the patients frequently having a relatively long history of nonspecific symptoms, most commonly pain and/or swelling which was seen in our case too.[1,3] LGCOs show nonspecific radiological and histopatholgical findings which may be mimicked by some benign conditions – bone cyst [simple / aneurysmal], fibrous dysplasia, non-ossyfying fibroma, desmoplastic fibroma and osteoblastoma. Andersen et al. have described four radiographic patterns of LGCOs: lytic with varying amounts of thick and coarse trabeculations; predominantly lytic with few thin incomplete trabeculae; densely sclerotic and mixed lytic and sclerotic.[6] In this case, the tumor was initially misdiagnosed as a Simple bone cyst on X-ray. Similar to our case, Toya et al. have also documented a case of dedifferentiated LGCO with extensive cystic changes that was initially treated as a simple bone cyst.[7]

On histopathology, LGCO is composed of a hypocellular to moderately cellular fibroblastic stroma with variable amounts of osteoid production comprising of collagen producing spindle cells arranged in interlacing bundles

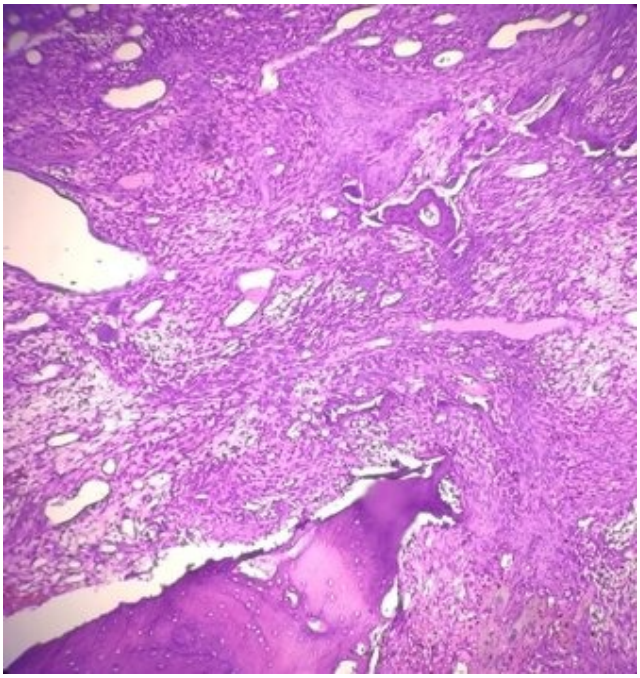

Fig. 3: Tumor cells were showing moderate nuclear atypia, pleomorphism and frequent mitoses favouring high grade sarcoma. (H and E X 10x)

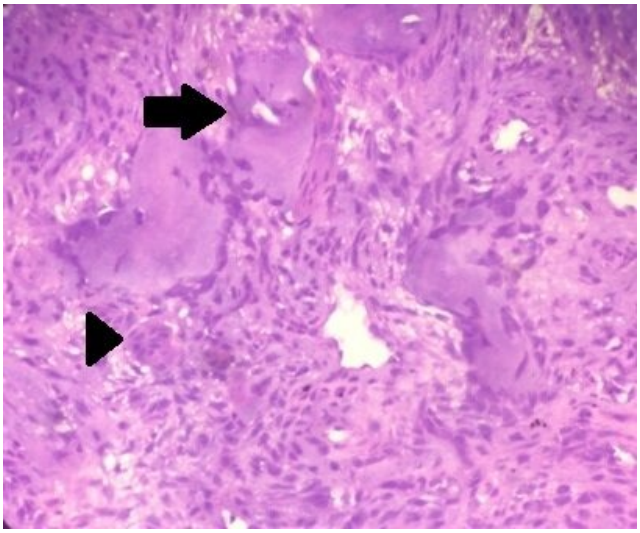

Fig. 4: Neoplastic osteoid (arrow) and numerous multinucleated giant cells (arrow head) seen. (H and E X 40x)

that permeate surrounding pre-existing bony trabeculae and marrow. The cells may show subtle degree of cytological atypia. Occasional mitotic figures and multinucleated giant cells are frequently seen.[1] In this case, at the initial presentation, all these features were seen on microscopy.

The close mimickers of LGCO on histopathology are desmoplastic fibroma, fibrous dysplasia and parosteal osteosarcoma. Desmoplastic fibroma may show bone permeation sometimes but osteoid production is practically never seen, whereas in the latter two, bone permeation is never seen.

For added confirmation, Murine Double Minute 2 (MDM 2) and Cyclin Dependent Kinase 4 (CDK4) may be done, which is positive in LGCO and Parosteal osteosarcoma and negative in all its benign mimickers and is based on the fact that LGCOs often harbor characteristic amplification of 12q13-15.[6,8]

The treatment of choice for LGCO is wide excision. Adjuvant chemotherapy or radiation therapy appears unnecessary, and with adequate initial treatment, the long-term prognosis is excellent.[2,5]

Progression to high grade sarcoma is a rare event seen in LGCO occurring in 10 to 36% of cases. The high grade component of LGCO is thought of as a form of morphologic progression (dedifferentiation) of a low-grade osteosarcoma. The transformation is much more common with recurrences rather than at the time of initial presentation with very few case reports on the latter.[9] In this case also, the tumor showed transformation to a high grade sarcoma during recurrence.

The World Health Organization [WHO] endorses the use of a two-tier system designating an osteosarcoma as low-grade or high-grade. This histologic grading has an important impact on clinical outcome especially with respect to the risk of distant metastases. Righi et al. in their study showed a correlation between the percentage of high-grade (grade 3) areas and risk of metastatic spread as those patients with high grade component less than 50% of the tumor showed good survival regardless of the use of adjuvant chemotherapy whereas the clinical behavior of tumors featuring a high-grade component greater than 50% was quite aggressive.[5] This implies that adjuvant chemotherapy must always be given to patients showing high grade transformations in LGCO.

Furthermore in their study they documented that the majority of the patients had a transformation into fibroblastic osteosarcoma, followed by osteoblastic and chondroblastic forms. Similarly in our study too transformation to a fibroblastic sarcoma was seen. In one study by De Silva et al. an LGCO transforming to Leiomyosarcoma has also been documented.[10]

MDM2/ CDK4 amplification characteristic of LGCO, seem to be well retained even after high-grade progression. In contrast, MDM2/CDK4 amplification is rare in

conventional osteosarcomas.[8]

To conclude, Low grade Central Osteosarcomas pose a diagnostic challenge. High degree of clinical suspicion combined with adequate sampling and radiological correlation are helpful. Detecting dedifferentiated foci is critical in the radiologic and histologic evaluation of low-grade osteosarcomas since if present in a considerable proportion, it carries an entirely different clinical implication and treatment strategy.

4. Source of Funding

None.

5. Conflict of Interest

The authors declare no conflict of interest.

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