Low grade central osteosarcoma- report of a rare entity with review of literature

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ABSTRACT

Low-grade central osteosarcoma (LGCO) is a rare variant of osteosarcoma (OS)which pose diagnostic difficulty to both clinicians and pathologists. A mimicker of benign conditions like fibrous dysplasia (FD), this sarcoma, if not treated appropriately, will recur as a higher-grade disease. LGCO has nonspecific radiologic and histologic features and so the primary diagnosis remains a challenge, especially in biopsy specimens. Accurate diagnosis of this lesion is mandatory as the treatment and prognosis is so different from a benign bone lesion. We report this case not just because of its rarity but also to emphasise on the importance of accurate and timely diagnosis of a sarcoma masquerading a benign lesion

Key words: Low grade osteosarcoma, fibrous dysplasia, distal femur, tumour.

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INTRODUCTION

LGCO or intra osseous well differentiated osteosarcoma is a rare subtype of OS, first described in 1977 by Unni etal1. It accounts for 1-2% of all OS2..This tumour has an increased propensity to occur in second and third decades of life with an equal gender distribution.3The symptoms are usually of long duration with most common sites of occurrence being long bones, mainly upper end of tibia and lower end of femur1. The patient usually complains of long standing pain in knee joint. It is unusual to occur in flat bones – in contrast to FD, its benign mimicker.4 As it is extremely difficult to differentiate LGCO from FD histologically, radiological features play an important role in preoperative diagnosis.14,9 Cortical destruction, even if focal and subtle favours a diagnosis of sarcoma over FD. Diagnosis is difficult with biopsy sample alone, especially when fibroblastic stroma predominates with minimal cellular atypia, lack of osteoid and absence of infilterative growth pattern5. As curettage alone is sufficient for FD, an erroneous diagnosis can lead to under treatment of LGCO leading to disease recurrence and in rare instances, metastasis.

CASE REPORT

A 38 year old female attended our outpatient department with complains of pain over right knee over a period of 6 months. The pain aggravated on walking and flexing knee. The patient had a history of tuberculosis for which she had completed antitubercular treatment. Clinical examination revealed no visible swelling. There was mild tenderness over lateral condyle of right femur with no features of

effusion or inflammation. No distal neurovascular deficits or lymphadenopathy was noted .A provisional clinical diagnosis of giant cell tumour of bone was made.

Plain X Ray showed an ill defined lytic lesion with narrow zone of transition involving distal metaphysis and epiphysis. Focal area of periosteal elevation and periosteal reaction, with a focus of cortical break in patello femoral joint noted, suggestive of a malignant lesion.(Fig 1,2)

J needle biopsy was attempted, histology of which showed a fibro osseous lesion with areas of haphazardly shaped bony trabeculae ("alphabet soup") with minimal cellular atypia resembling fibrous dysplasia (Fig: 4). The tissue was inadequate for further subtyping and so a repeat biopsy was advised.

MRI was done a week later in which coronal post contrast T1 weighted sequence showed a heterogenously enhancing lesion in distal metaphysis and epiphysis with minimal extraosseous soft tissue component.(Fig: 3)

Bone scan / SPECT CT showed a tracer avid lytic expansile lesion suggestive of a malignant lytic skeletal lesion involving lower end of right femur.

Open biopsy of lesion was done with a clinical and radiological suspicion of a malignant tumour. The tissue specimen consisted of multiple tan-grey fragments of 3x2 cm with bony and soft tissue components.

Microscopic examination revealed a lesion consisting of both fibrous and osseous components, in variable amounts in all sections. Cellular areas showed spindle cells with no definite features of malignancy. Trabeculae of immature bone without osteoblastic rimming and haphazardly shaped bony trabeculae were observed. No definite foci of invasion or osteoid was seen. Mitotic figures were less and IHC for Ki67 showed a low proliferative index of less than 5%.

With these morphologic and immunohistochemical features, a diagnosis of fibro osseous lesion was made. But taking into consideration, the clinicoradiological suspicion of a malignant lesion , literature search was done which showed an entity called LGCO, a rare low grade variant of OS which closely mimicks benign bone lesion.

Surgeons then went ahead with right limb salvage surgery. The specimen measured 10x8cm. On section, an irregular grey white growth seen, measuring 9.4x6.2cm with necrosis and cortical breach (Fig: 5). Histology showed a marrow infiltrative fibroosseous neoplasm with bony trabeculae of varying sizes and intervening spindle cell stroma.(Fig: 6).Hyper and hypocellular areas seen with hypocellular areas showing spindle cells with minimal nuclear atypia, scattered amidst dense collagenous stroma. Hypercellular areas show spindle cells with moderate nuclear atypia arranged in fascicles. Areas with osteoid production and necrotic areas seen (Fig 6). Tumour invaded pericortical soft tissue. Based on the morphological features described allied to the clinical findings, the diagnosis of low-grade central osteosarcoma was confirmed.

The specimen was found to have adequate surgical margin and so was decided in the multidisciplinary board of our institute to keep the patient on follow up with no other adjuvant treatment.

Postoperatively the patient is doing well with routine follow up every 3 months.

Fig:1:plain X ray showing ill defined lytic lesion with narrow zone of transition involving distal metaphysis and epiphysis.

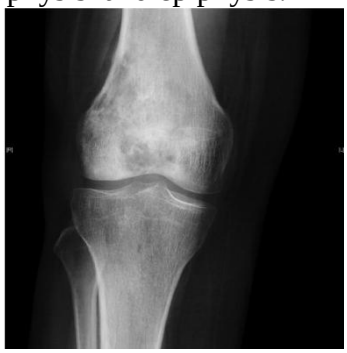


Fig: 2 plain X ray showing Focal area of periosteal elevation and periosteal reaction, with a focus of cortical break in patello femoral joint noted

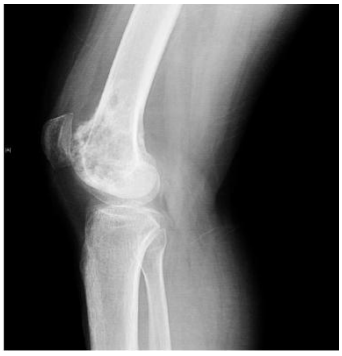


Fig:3 MRI coronal section: post contrast T1 weighted sequence showed a heterogenously enhancing lesion in distal metaphysis and epiphysis with minimal extraosseous soft tissue component.

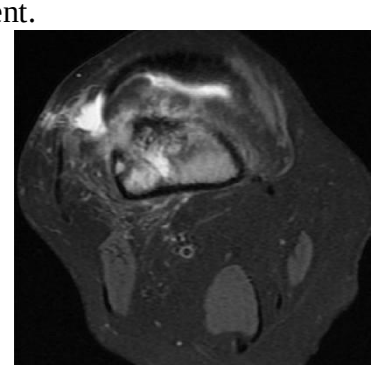


Fig: 4 (H&E 40 x) showing both fibrous and osseous components

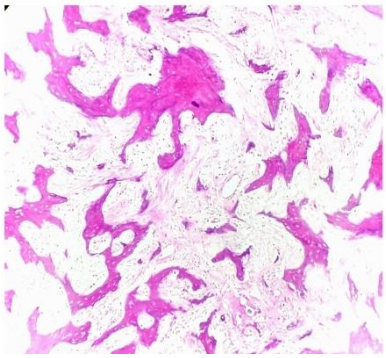


Fig: 5 Gross picture showing irregular grey white growth seen, measuring 9.4x6.2cm with necrosis and cortical breach

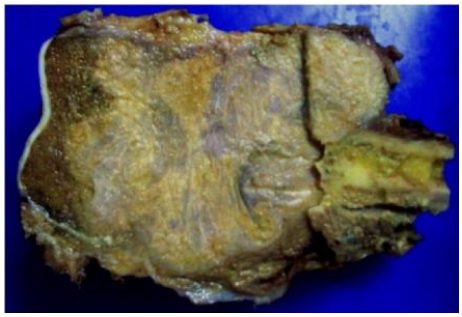
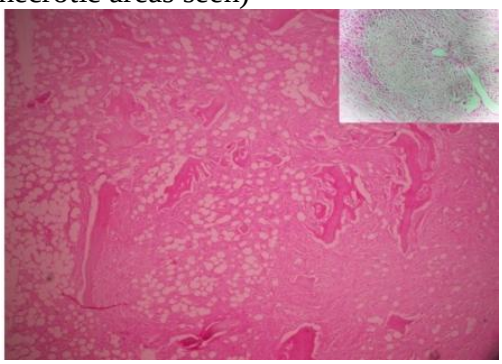


Fig: 6 (H&E 40 x) marrow infiltrative fibroosseous neoplasm with bony trabeculae of varying sizes and intervening spindle cell stroma(insert : Areas with osteoid production and necrotic areas seen)



DISCUSSION

LGCO is a rarely encountered subtype of OS, with a favourable outcome if treated appropriately. An online literature search about LGCO shows that since its first description in 1971, only a few cases have been reported, the largest series being published so far by Kurt etal comprising of 20 cases.3.The main reason behind this might be the difficulty in diagnosing the lesion as it resembles benign lesions like FD, clinically, histologically and even radiologically. Other benign conditions resembling LGCO include ossifying fibroma, aneurismal bone cyst, giant cell tumour and chondromyxoid fibroma.7,8 Our case was initially diagnosed clinically as giant cell tumour.

The clinical presentation of LGCO varies considerably. The patient usually presents with pain or vague swelling of long duration, resulting in delayed medical consultation18.

This tumour is also notorious for its variable radiographic appearance.9,10 The lesion usually appears as a large medullary tumour often with trabeculation and sclerosis. Though a potential cortical interruption due to localized destruction and soft tissue extension are the most typical radiographic findings11,no periosteal new bone formation or frank soft tissue extension is usually seen, and is thus easily mistaken for a benign lesion12. It is emphasised that careful radiological evaluation is mandatory to identify at least a small region showing cortical perforation, soft tissue shadows or calcification and a periosteal reaction that should strengthen a suspicion of malignancy6

Grossly these tumours usually appear as well-demarcated firm whitish masses with a fibrous whorled appearance, typically centred in the medullary cavity of metaphysis or meta-diaphyseal region of long bones19. Microscopically, the tumours are hypo-cellular consisting of interlacing fascicles of spindle cells with minimal cytological atypia and low mitotic activity.14 The tumour typically has a permeative growth pattern surrounding native bony trabeculae. One should also carefully look for features of cortical destruction and soft tissue extension. 14 Osteoid production is minimal and so is difficult to identify in curettages.

On a biopsy material, LGCO can be indistinguishable from benign fibrous lesions such as desmoplastic fibroma and fibrous dysplasia. LGCO is distinguished from benign tumours by virtue of its infiltrative growth pattern , entrapment of bony trabeculae, cortical destruction, soft tissue extension, spindling fascicles and cytological atypia, though minimal.13,1

Recent years have seen that immuno histochemical stains like murine double minute type 2 (MDM2) and cyclin-dependent kinase 4 (CDK4) has opened a new door to aid the histological diagnosis of LGCO. Doubleminute type 2 (MDM2) genes (found on chromosome 12q13–15) are genetic markers with a reported sensitivity of 89–100% and a specificity of 97–100% (when either one or both genes are present) 14,15,16However an in depth understanding of histological features with an accurate clinicoradiologial correlation is still vital in raising the suspicion of LGCO in order to apply these tests.

Literature review shows that wide excision is the only accepted treatment of LGCO .Wide excision with adequate margin is almost never followed by recurrence9.A high incidence of local recurrence is encountered in local excisions with inadequate surgical margins or those lesions treated with curettage

alone. Recurrences of LGCO are often found to exhibit a higher histologic grade or dedifferentiation with an increased propensity for metastasis.17

A local recurrence with a higher clinical or histologic grade ,with or without evidence of metastasis is the only indication for adjuvant chemotherapy .Radiotherapy is used in some centres in cases with inadequate margins so as to sterilise excision borders.18

Distal metastasis are rarely seen with time of appearence ranging from months to years after diagnosis. Common sites of metastasis include lung, lympnodes and bone.18

CONCLUSION

This case is reported so as to make aware of such an entity which closely resembles a benign lesion. We also strongly recommend that any bone lesion with diagnostic difficulty or those with disparities in clinicoradiological and pathological diagnosis should be approached with caution and ideally referred to a specialist centre for evaluation without delay.

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