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Reactive Mimics of Neoplastic Osseous Lesions- A Case Report

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Abstract

Fracture healing is a proliferative physiological process that follows specific regenerative patterns and altered expressions of several thousand genes.However,sometimes this biological process fails and the lesions end up showing delayed healing,infections,malunion,pseudoarthrosis or non-union.Fracture callus can simulate a bone-forming neoplasm when the bone-forming features include enlarged,highly active,immature but uniform osteoblasts that have prominent mitotic activity.These reactive lesions of the bone produce bone and cartilage matrix and are often confused with their neoplastic counterparts,posing a challenge in the appropriate diagnosis and management.We report an operated case of fracture right distal shaft of femur in a 16-year old female,who on follow-up,presented with swelling and pain over the right thigh associated with a single episode of fever.On clinical examination and radiological investigations,a suspicion for cellulitis or localized haematoma formation was kept.The haematoma was locally drained and a core biopsy was taken from the fracture site.Appropriate management was initiated.The tissue sample so obtained was sent for histopathological examination.On histopathological evaluation,it resembled exuberant callus.But in view of presence of exuberant osteoid tissue with many pleomorphic atypical cells,a suspicion of Osteogenic Sarcoma was also kept.Later immunohistochemistry was done on which it turned out to be High Grade Osteogenic Sarcoma,Osteoblastic type.Chemotherapy was initiated in a timely manner,but eventually the patient succumbed to the disease within a course of 4 months from the diagnosis.

Keywords: Osteogenic Sarcoma, Exuberant Callus, Immunohistochemistry, Chemotherapy.

Introduction

The skeletal system maybe affected by a variety of non-neoplastic lesions,which may potentially be confused with primary bone tumours on clinical,radiological and pathological grounds.These conditions include

fractures,infections,reactive and degenerative processes, as well as an array of quasineoplastic entities,such as intramedullary cystic lesions like unicameral and aneurysmal bone cysts; fibro-osseous lesions such as fibrous dysplasia and exophytic entities like osteochondromas.Systemic inflammation as observed in patients with rheumatoid arthritis,diabetes mellitus,multiple trauma or sepsis,can increase fracture healing time and the rate of complications,including non-unions[1].Reactive lesions of the bone can appear alarming on histologic examination because they are often cellular & have atypical cytological features such as distinct nucleoli, mild hyperchromasia and mitotic activity. These therefore closely resemble the osteocartilagenous malignancies. Familiarity with the clinical presentation ,radiological appearance & characteristic histological findings will prevent the unfortunate misclassification of these lesions.[2]

Osteogenic sarcoma is defined as an aggressive malignant neoplasm that arises from primitive transformed cells of mesenchymal origin and exhibits osteoblastic differentiation, producing malignant osteoid. It has a bimodal age distribution. It occurs most commonly in children and young adults between the ages of 10-30years and accounts for about 2.4% of all paediatric malignancies in the world and around 20% of all primary bone cancers.[3] Prognosis depends on numerous factors like age, gender, location of primary tumour, size, extent of necrosis and levels of alkaline phosphatase and lactate dehydrogenase[4].

Case Report

A 16-year old female came to the Orthopaedics Out-Patient Department for follow-up of operated fracture of right distal shaft of femur(operated 2months ago,with no post-operative complications).She complained of pain and swelling over the right thigh since 2months,associated with a single episode of fever.On clinical examination,there was a generalized swelling over the medial aspect of the right thigh measuring 15x10x6cm.The local temperature over the swelling was raised and a healing scar from the previous surgery was seen.Peripheral pulses were elicited over the lower limbs bilaterally.

CT scan Right thigh and knee revealed a large homogenous collection of size 15.8x11x10cm with a volume of approximately 60cc noted in the intramuscular plane over the medial aspect of right thigh.It showed multiple areas of calcification within.Imaging features were in favour of Chronic haematoma formation[Figure 1].

On USG local region(right thigh),there was a loculated collection with surrounding inflammatory changes,suggestive of Haematoma formation.

Radiogram of right knee(Anteroposterior and Lateral),features were of comminuted displaced fracture of lower 1/3rd of right femur with the proximal part displaced anteriorly[Figure 2A and 2B].

Right lower limb Arterio-Venous Doppler study showed multiple pockets of collection over the anteromedial and posterior aspect of right thigh,largest measuring 6.2x5.6x3.7cm(volume 68cc).Few pockets show thick echoes and multiple septations within.Features were suggestive of a chronic collection.

Histopathology

Grossly a single greyish brown,soft to firm tissue bit measuring approximately 2.3 x 2 x 0.8cm was received.

On microscopic examination, Sections revealed irregular fragments composed of sheets & clusters of round to oval pleomorphic cells with round hyperchromatic nuclei showing mild anisonucleosis.

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Many areas showed lace-like osteoid tissue with disorganized, broad coalescing trabeculae. Osteoclastic giant cells were seen.There was increased mitosis.However atypical mitosis was not seen.Areas of haemorrhage & few congested blood vessels were seen.

On histopathological examination,exuberant osteoid tissue was seen.But in view of presence of many sheets and clusters of pleomorphic cells showing mild anisonucleosis,a suspicion of Osteogenic Sarcoma was also kept.

Immunohistochemistry and radiological correlation were advised.

Immunohistochemistry revealed tumour cells to be positive for Osteocalcin and Osteopontin and negative for antibodies to CD31 and CD45, leading to the final diagnosis of High Grade Osteosarcoma, Osteoblastic type.

Discussion

The skeleton is affected by many non-neoplastic processes that maybe interpreted clinically and radiographically as either benign or malignant primary bone tumours.Even if a benign or nonneoplastic process is suspected,it can sometimes present with histology containing unusual or unexpected elements,such as pathological fractures,which could go unrecognized and risk misdiagnosis,without an awareness of the accompanying clinical and imaging findings. A study was carried out by Mark R Wick et al[5] in which they analysed the various proliferative, reparative and reactive benign bony lesions which can be mistaken for true neoplasms and therefore lead to interpretative problems. In another study done by Fariba Binesh et. Al[6], areas of exuberant callus formation after avulsion fracture of tibia in a 3 year old girl which were misdiagnosed as osteosarcoma were reviewed.

Conventional osteosarcoma is a primary intramedullary high grade malignant tumour in which the neoplastic cells produce osteoid, even if only in small amounts. It is largely a disease of the young and most frequently occurs in the 2nd decade of life with some 60% of patients under the age of 25years. Osteosarcoma shows a propensity for involvement of the long bones of the appendicular skeleton, in particular, the distal femur, proximal tibia and proximal humerus. Findings on physical examination maybe limited to a painful, tender mass.

A sudden dramatic increase in tumour size is generally attributable to secondary changes such as intra-lesional haemorrhage. Pathological fractures occur in 5-10% of patients.

Microscopically, osteogenic sarcoma tends to be a highly anaplastic, pleomorphic tumour in which the tumour cells may be epitheloid, plasmacytoid, fusiform, ovoid, small round cells, clear cells, mono- or multinucleate giant cells.Most cases are complex mixtures of 2 or more of these cell types. The diagnosis of osteosarcoma is predicated on the accurate identification of osteoid. Conventional osteosarcoma is further subclassified based on the predominant matrix into osteoblastic (50%), chondroblastic(25) and fibroblastic (25%) osteosarcoma. Untreated, conventional osteosarcoma is universally fatal[7] .The identification of prognostic factors has been an additive process in which factors have been investigated, identified and incorporated into the overall therapeutic strategy, stage and results of various laboratory tests have been used to predict prognosis.

Pathologists should be familiar with the clinical,radiological as well as histological features of the most commonly biopsied non-neoplastic and neoplastic lesions of the bone,along with the sex,age

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groups,anatomical sites those lesions favour,all crucial data that must be considered when generating the differential diagnosis. Thus an interdisciplinary approach is quintessential for the accurate diagnosis of primary bone tumours.

Conclusion

Osteogenic sarcoma is the most common osteoarticular malignancy of nonhematopoetic origin. The burden of the disease at large is immense considering the young age of patients, residual disability consequent to radical surgeries and long periods of rehabilitation.Osteogenic sarcoma is a great histologic mimicker and poses the diagnostic challenge especially in small tissue biopsies.Therefore a triple diagnostic approach, i.e., clinical, radiological and histopathological is essential in all cases Any case which fails to show concurrence between triple diagnostic approaches should be viewed with suspicion. Demonstration of osteoid is essential to diagnosis of Osteogenic sarcoma, however, the amount varies widely between tumors. Reactive lesions of bone and periosteum also produce bone and cartilage matrix, resulting in confusion with osteosarcoma or chondrosarcoma.Thus the markers of osteoblastic differentiation such as osteocalcin, osteonectin, SATB2 have been proposed to be potentially useful. Prognosis of conventional High Grade Osteogenic Sarcoma remains grim, especially in those who present with metastases. Most often it spreads to the lungs, but it can also spread to other bones, the brain, or other organs. The 5-year survival rate for people with localized osteosarcoma is in the range of 60% to 80%. These tumours are more likely to be cured if they are resectable. For high-grade osteosarcomas that can be resected completely, chemotherapy is still an essential part of treatment.Without it,there is a high chance of recurrence of the tumour.

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Legend Figure

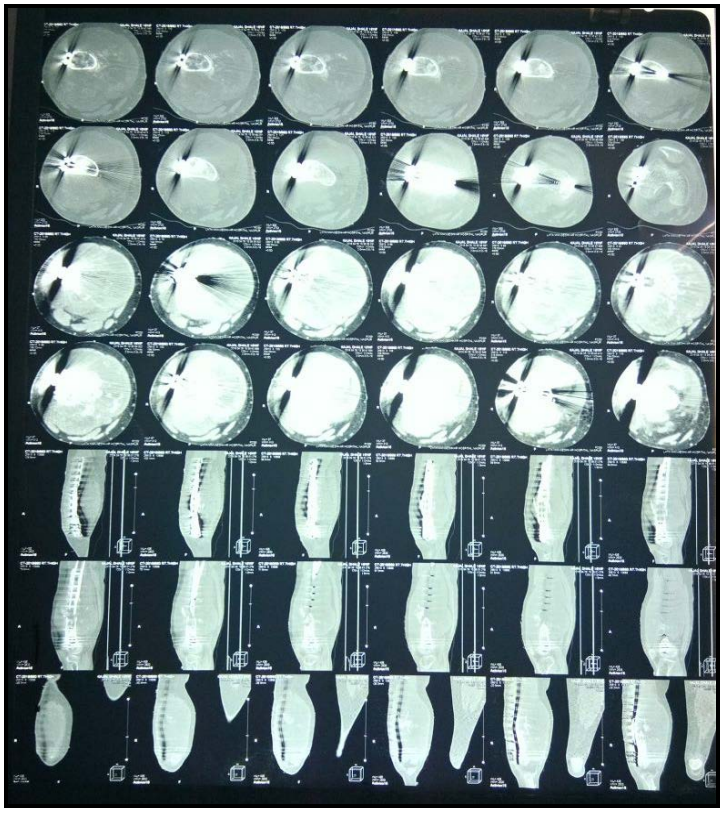

Figure 1: CT SCAN RIGHT THIGH AND KNEE

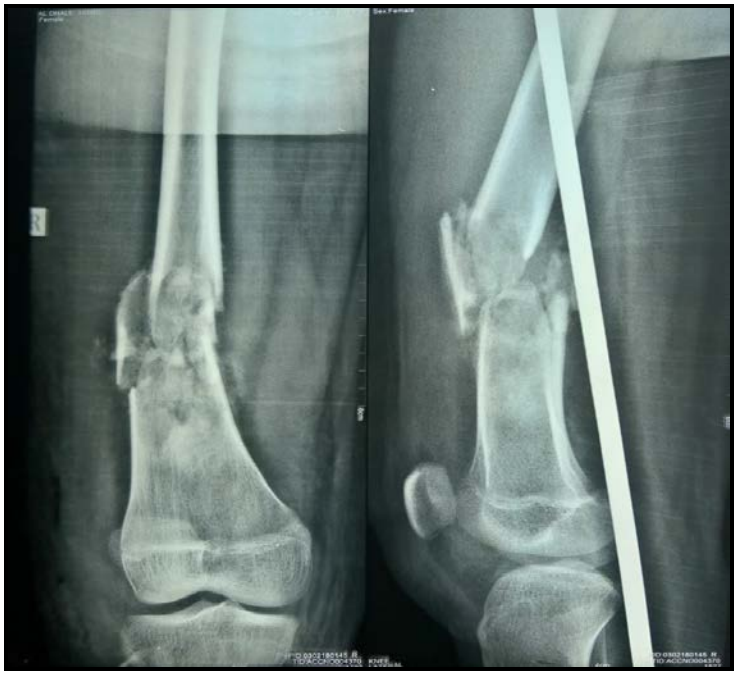

Figure 2A: XRAY RIGHT KNEE-AP VIEW

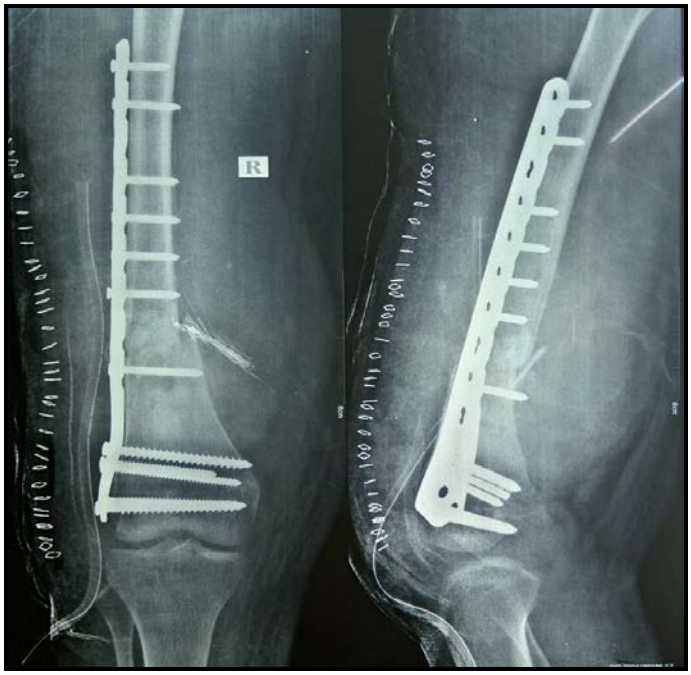

Figure 2B: XRAY RIGHT KNEE-LATERAL VIEW

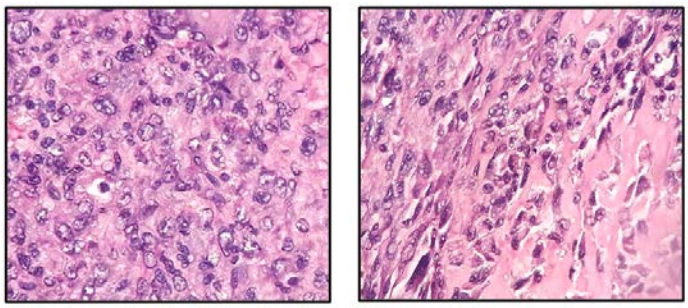

Figure 3: Sections reveal irregular fragments composed of sheets & clusters of round to oval pleomorphic cells with round hyperchromatic nuclei showing mild anisonucleosis.

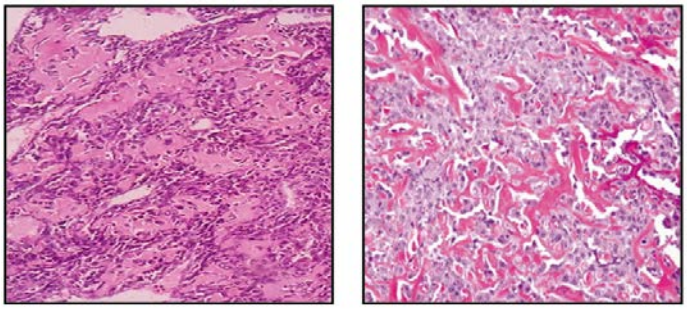

Figure 4: Many areas show lace-like osteoid tissue with disorganized, broad coalescing trabeculae.

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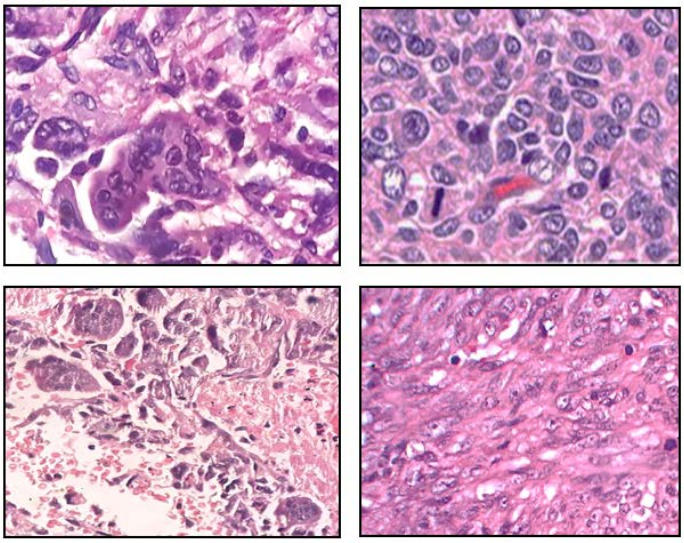

Figure 5: Osteoclastic giant cells are seen. There is increased mitosis.However atypical mitosis is not seen.

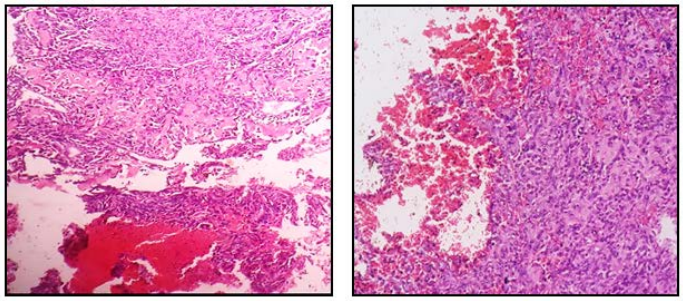

Figure 6: Areas of haemorrhage & few congested blood vessels are seen.

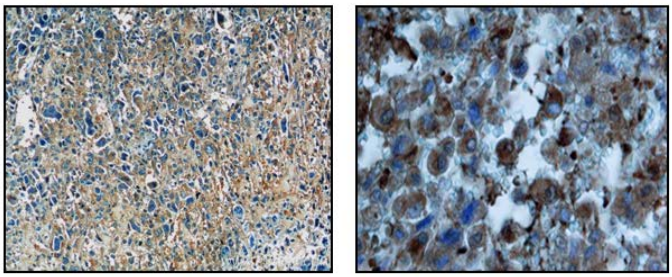

Figure 7 : Immunohistochemistry revealed tumour cells to be positive for Osteocalcin and Osteopontin.

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