Answer To Test Yourself Question: A 19-year-old male presents with progressive distal lower limb pain

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Test yourself answer

High-grade osteoblastic osteosarcoma arising from a pre-existing low-grade central osteosarcoma

Discussion

The radiograph (Fig. 1) shows a mixed lytic-sclerotic lesion in the distal tibial metadiaphysis expanding the lateral cortex. MRI (Fig. 2) demonstrates an irregular intramedullary lesion with cortical breach and a small posteromedial extraosseous mass. CT (Fig. 3-below) shows heterogeneous sclerosis laterally with a lytic component medially, suggesting a bi-phasic tumour morphology. CT-guided biopsy of both the lytic and sclerotic components revealed a high-grade osteoblastic osteosarcoma (HG-OS) with murine double minute type 2 (MDM2) gene amplification, likely arising from a pre-existing low-grade central osteosarcoma (LG-COS) (Fig. 4).

LG-COS comprises ~2% of all osteosarcoma sub-types, usually presenting in the 3rd decade of life with an equal male to female ratio and a strong predilection for long tubular bones [1]. Several imaging appearances have been

attributed to LG-COS, in order of decreasing frequency: lytic with coarse incomplete trabeculation, mainly lytic, mainly sclerotic, and a mixed lytic-sclerotic picture [2]. In our case, the low-grade component was seen laterally manifest by heterogeneous medullary sclerosis. The juxtaposition of sclerosis and lysis in LG-COS can mimic fibrous dysplasia (FD), leading to misdiagnosis [3]. An extraosseous mass, cortical breach, and progressive marrow invasion do not however occur in FD. Three distinct histopathological patterns of LG-COS have been reported with some overlap with FD [3]. Crucially, cortical and Haversian system permeation as well as host bone entrapment at the lesion periphery are not seen in FD and MDM2 protein expression can now safely help diagnose LG-COS [3]. Wide local excision is the accepted treatment, but involved surgical margins are associated with a high rate of local recurrence which typically exhibit a higher histological grade with dedifferentiation and potential for metastases [4]. Radiotherapy and chemotherapy are not typically utilised, the latter only in the setting of a recurrent high-grade lesion or possibly a de-differentiated component at presentation.

We presume that the history of previous fracture is of no relevance, since isolated case reports of OS developing several years after trauma drew no definitive link between the trauma and tumour [5]. Dedifferentiation of LG-COS is rare, estimated at 10–36% [6] and tends to exhibit a higher histological grade [7]. Some authors regard the high-grade component of a LG-COS as a separate entity, considering it as de-differentiated warranting systemic adjuvant therapy. However, this distinction and treatment approach is not universally accepted, and it is not known whether areas of HG-OS within a LG-COS actually differ from conventional HG-OS regarding local recurrence, metastasis, and overall survival rates.

The demarcation between the bland LG-COS and high-grade component on imaging is consistent with de-differentiation and should warrant further MDM 2 testing. The possibility of a low-grade component due to the aggressive

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Fig. 3 Coronal CT MPR of the right distal tibia showing a heterogeneous sclerotic lesion (thick arrows) in the lateral aspect of the distal tibia with expansion but no destruction of the cortex representing the low-grade central osteosarcoma, and a lytic area (thin arrows) in the centre of the medullary cavity which has permeated the medial tibial cortex representing the dedifferentiated high-grade osteosarcoma

overall appearances can be easily overlooked, and it may have just represented a sclerotic area within conventional osteosarcoma. The current case illustrates why such lesions should be biopsied in a dedicated sarcoma centre. Accurate diagnosis relies on careful pathological and radiological correlation to highlight the bi-phasic nature of the tumour and avoid a potential misdiagnosis of fibrous dysplasia, often leading to multiple repeat biopsies [8].

Declarations

Conflict of interest The authors declare no competing interests.

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