#### PICTORIAL REVIEW

# Radiological appearances of appendicular osteosarcoma: a comprehensive pictorial review

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Osteosarcoma is the most common primary malignant tumour of bone in adolescents and young adults. Hence, a comprehensive knowledge of the common and unusual imaging appearance of this tumour is essential. Correct diagnosis of the various varieties of osteosarcoma is important for optimal clinical management including staging, biopsy, treatment and follow-up of patients. This review article provides a comprehensive approach to the radiological diagnosis of the different types of appendicular osteosarcoma and illustrates the role of CT and MRI in further characterisation. © 2006 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.

# Introduction

Osteosarcoma (OS) is the most common primary malignant tumour of bone in adolescents and young adults, representing approximately 15% of all primary bone tumours.<sup>1,2</sup> The tumour is characterised by the production of malignant osteoid matrix and immature bone. The components of the tumour matrix are highly variable and include chondroblastic and fibroblastic, as well as osteoblastic tissue. Plain radiography is the primary imaging technique for the assessment of bone tumours and is the keystone to the radiological diagnosis of OS, followed by magnetic resonance imaging (MRI) for accurate local staging prior to surgical management. Therefore, a comprehensive knowledge of the common and unusual imaging appearance of this tumour on radiography is

essential. The classification of primary OS is presented in Table 1.

This pictorial review illustrates the various patterns of radiographic presentation of primary osseous appendicular OS, with relevant CT and MRI correlation. The role of MRI in local staging has recently been reviewed and will not be covered.<sup>3</sup>

## Intramedullary osteosarcoma

#### High-grade intramedullary OS

The classic high-grade tumour, also referred to as the conventional central OS is the commonest type, accounting for approximately 75% of all cases.<sup>1,2,4</sup> This highly aggressive lesion typically presents in the second decade of life, usually in the long bone metaphyses (90%) with the femur being the commonest site (45%), followed by the tibia and humerus. Extension of the metaphyseal lesion into the epiphysis occurs in 75-88% of cases, despite an open growth plate.<sup>1,2,4–6</sup> Radiographs demonstrate three classical patterns. The commonest is the mixed form of combined osteolysis

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Table 1 Classification of primary osteosarcoma	
Intramedullary OS High-grade OS or Conventional central OS	Surface OS Parosteal OS
Telangiectatic OS	Periosteal OS
Small cell OS	High-grade surface OS
Epiphyseal OS	Intracortical OS
Pseudocystic OS	<u>Multicentric OS or</u>
Low-grade central OS	Osteosarcomatosis
Osteoblastoma-like OS	Multifocal OS

and osteosclerosis, seen in approximately 50% of cases.

Radiographs show fluffy, cloud-like areas of increased bone density, representing immature bone production and permeative lytic areas representing bone destruction (Fig. 1a).<sup>1,2,4</sup> If mineralized osteoid tissue predominates, then the lesions are osteoblastic, as is seen in approximately 25% of cases (Fig. 1b) and if fibrous tissue and/or unmineralized cartilage predominate, then the lesions are osteolytic (Fig. 1c). The aggressive nature of the lesion is demonstrated by violation of the cortex without bone expansion. Various types of periosteal reaction are seen, the most classical being the 'sunburst spiculation' appearance (Fig. 2a,b). It is almost pathognomonic of an aggressive OS but can rarely be seen with

osteoblastic metastases. A Codman's triangle is common in OS (Fig. 1c) but is not specific, also being seen in other neoplasms (eg. aneurysmal bone cyst, Ewing sarcoma) and non-neoplastic conditions such as acute osteomyelitis. Associated soft tissue masses are seen in up to 90% of the cases (Fig. 1a),<sup>1,2,4</sup> and these may show variable matrix mineralisation. CT plays an important role in the detection of even small areas of mineralized matrix, especially in the radiographically lytic lesion (Fig. 3), thus helping to differentiate OS from other aggressive tumours such as Ewing sarcoma.

MRI is the technique of choice for pre-operative staging of OS,<sup>3</sup> but plays a limited role in the further characterisation of the lesion beyond radiography. MRI typically demonstrates extensive intramedullary infiltration, with intermediate T1W signal intensity (SI) and heterogeneous intermediate/high T2W SI.<sup>7–9</sup> Fluid levels and vertical periosteal reactions are also occasionally demonstrated.

A rare variant of central high-grade OS, called pseudocystic OS has been described by Sundaram et al.<sup>10</sup> These lesions are purely osteolytic, intracompartmental and tend to expand the bone without any associated periosteal reaction or soft tissue mass (Fig. 4a,b). Simple bone cyst (SBC) and aneurysmal bone cyst (ABC) were the primary radiological diagnoses in all of their cases.



**Figure 1** The varied radiographic appearances of conventional central OS. (a) AP radiograph of the distal femur showing a permeative, lytic and sclerotic lesion with a large soft tissue mass containing immature bone matrix. (b) AP radiograph of the proximal tibia showing a predominantly osteoblastic OS, appearing as an area of poorly defined medullary sclerosis with subtle periosteal reaction. (c) AP radiograph of the proximal tibia showing a lytic OS (black arrow) with a Codman's triangle (white arrowhead) demarcating the distal extent of extraosseous tumour.





**Figure 2** Periosteal reaction. (a) Lateral radiograph of the distal femur demonstrates the classical 'sunburst spiculation' type of periosteal reaction in a distal femoral OS. (b) Axial T2W FSE MR image in the same patient demonstrating the 'sunburst spiculation' as multiple radiating hypointense lines arising from the posterolateral cortex.

# **Telangiectatic OS**

Telangiectatic OS was first described by Paget in  $1854^{11}$  and accounts for 2.5%-12.5% of OS cases.<sup>12-16</sup> It usually arises in the metaphysis of long bones, most frequently around the knee (62%) and presents in the second and third decades of life.<sup>14-16</sup> The prognosis was initially thought to be worse than conventional central OS, but recent studies indicate a survival similar to or mildly better than conventional OS.<sup>14,17,18</sup>

Radiographically, the most common pattern is a moth-eaten, lytic lesion with a wide zone of transition (Fig. 5). Lack of significant sclerosis,



**Figure 3** Axial CT showing small areas of subtle soft tissue matrix mineralization (arrows), which were radiographically occult.

aggressive periosteal reaction, associated soft tissue mass and pathological fractures are the other common findings.<sup>19</sup> Vanel<sup>20</sup> has described an early radiographic sign, in the form of oblique parallel striations in the shaft (Fig. 5), which are thought to be secondary to hypertrophy of normal intraosseous veins and can also be seen in other highly vascular bone lesions.<sup>21</sup> This sign is not seen in advanced cases due to destruction of the bone. Telangiectatic OS may appear pseudocystic or multilocular and can mimic benign lesions such as ABC, simple bone cyst or giant cell tumour (GCT).<sup>21</sup> The cross sectional imaging finding of multiple fluid-fluid levels secondary to haemorrhage simulates ABC. However, Murphy et al.<sup>21</sup> found three features on CT and/or MRI that can help distinguish telangiectatic OS from ABC. The first was the detection of thick, peripheral, enhancing nodular tissue on post-contrast images. Pathologically, this peripheral tissue corresponds to the viable high-grade sarcomatous areas surrounding the hemorrhagic and necrotic spaces. The second feature was the detection of mineralization in the lesion best appreciated on CT, reflecting the osteoid producing nature of the tumour. The third feature was cortical destruction with an infiltrative and non-encapsulated margin protruding into a soft tissue mass. This was seen in 89% of cases on MRI and 96% on CT. Conversely, ABC showed a well defined, encapsulated rim or margin and lack of a soft tissue mass.

## Low-grade central OS (LGCOS)

LGCOS is very rare variant of intramedullary OS, first described by Unni et al. in  $1977^{22}$  and





**Figure 4** Pseudocystic OS. (a) AP radiograph of the right hip showing a poorly-defined lytic lesion in the femoral neck. Note the lack of periosteal reaction and extraosseous extension. (b) Axial CT in the same patient demonstrating an intra-compartmental lesion with no soft tissue component, typical of pseudocystic OS.

accounting for less than 1% of cases. Its distribution is similar to classical conventional central OS, although it affects patients in the third and fourth decade, grows very slowly and has a far better prognosis. Histologically, it is a low-grade



**Figure 5** Telangiectatic OS. AP radiograph of the proximal humerus showing a moth eaten, lytic lesion with a wide zone of transition. Note the presence of lytic vertical striations in the cortex.

neoplasm similar to parosteal OS, which is treated with primary surgical resection, as there is a risk of transformation into high-grade tumour if treated with curettage.<sup>22</sup>

Four radiographic patterns have been described by Andersen et al<sup>23</sup>; lytic with coarse trabeculation, predominantly lytic, densely sclerotic and mixed lytic and sclerotic. The most common of these is the lytic lesion with coarse trabeculation. Histologically and radiographically it is similar to fibrous dysplasia and differential diagnosis includes an ossifying or nonossifying fibroma and fibroxanthoma. In the series by Anderson et al.,<sup>23</sup> cross-sectional imaging showed a soft tissue mass or cortical effacement in all cases, hence CT or



**Figure 6** Parosteal OS. (a) Lateral radiograph showing a dense, sclerotic, lobulated mass with irregular margins arising from the posterior surface of the distal femur. (b) Axial CT in the same patient showing the unmineralised thickened periosteum at the site of the attachment of the lesion. (c) Sagittal T1W SE MRI in the same patient showing medullary extension of tumour (black arrow), low-grade tissue (white arrowhead) and dedifferentiated high-grade tissue (double white arrowheads).

MRI can be very useful to differentiate LGCOS from benign lesions.

# Small cell OS

Small cell OS was first described in  $1979^{24}$  and is a distinct type of OS composed of small round blue cells, accounting for 1-4% of cases.<sup>25-28</sup> Its age of presentation and skeletal distribution is similar to classical OS, with the distal femur being the commonest site. Its prognosis is extremely poor. Radiographically, it is indistinguishable from conventional central OS. The osteoid matrix is very subtle and is best detected on CT.

# Osteoblastoma-like OS (Ob-like OS)

Ob-like OS is a recently recognised, low-grade variant of OS that resembles osteoblastoma clinically, radiologically and pathologically and accounts for 1.1% of appendicular OS.<sup>29,30</sup> The tumour is characterized by a longer clinical history and less aggressive radiographic features than conventional OS. In the series from the Rizzoli Institute,<sup>31</sup> 9 out of 11 cases had an initial diagnosis of a benign lesion. Radiographic features varied from a lytic lesion, lesions with a variable degree of mineralization to a densely sclerotic lesion. A benign lamellar and uninterrupted periosteal reaction may be seen,<sup>32</sup> but subtle cortical destruction and permeative borders to the lesion are the key to the diagnosis of a more aggressive lesion. $^{29-31}$ Due to its metastatic potential and high recurrence

rate, it is very important to distinguish this from a benign osteoblastoma and the treatment of choice is wide surgical excision.<sup>29</sup>

# **Epiphyseal OS**

OS confined to the epiphysis is extremely rare with less than 10 cases reported in the literature. Unni<sup>33</sup> reported a case in the proximal tibial epiphysis and a retrospective analysis of more than 1000 cases in his institute identified only one other case. Another review of 900 cases of OS<sup>34</sup> revealed 4 cases in the epiphysis with only one of them occurring in the presence of an open physis. Radiographs show a non-specific lesion with mixed areas of sclerosis and lysis, disruption of the cortex and a soft tissue mass.<sup>35</sup> The unusual location for this tumour may result in the true diagnosis going unsuspected and any interventional diagnostic procedure, such as open biopsy may lead to gross contamination of the surrounding soft tissues. Where any doubt regarding the potential aggressive nature of an epiphyseal lesion exists, the route for image guided needle biopsy should be discussed with the surgeon who will perform the definitive surgery, so that the biopsy tract can be readily excised.

# Surface osteosarcoma

Osteosarcomas arising from the surface of a long bone account for 4-10% of all  $OS^{36-40}$  and include



**Figure 7** Periosteal OS. (a) Lateral radiograph demonstrating a thickened irregular cortex with vertical spiculated periosteal reaction (arrows) adjacent to the proximal anterior tibia. (b) Coronal T2W FSE fat suppressed MRI in the same patient showing high SI chondroid tissue adjacent to the cortex and reactive marrow changes (arrowheads) deep to an intact tibial cortex.

parosteal, periosteal, high-grade surface and intracortical lesions.

## Paraosteal OS

Parosteal OS is the commonest surface OS accounting for 65% of surface lesions.<sup>36–41</sup> It is typically a low-grade lesion with a better prognosis than conventional central OS and occurs in an older age group, typically in the 3rd-4th decades. However, higher-grade parosteal OS may also occur and the tumour can undergo dedifferentiation, typically to high grade OS. In the latter case, the prognosis and management becomes similar to conventional OS. The commonest site is the metaphysis of the posterior surface of the distal femur (70% of cases),<sup>36,42</sup> followed by the proximal humerus and proximal tibia. Radiographically, it presents as a large, densely sclerotic, lobulated mass with irregular margins and a sessile attachment to the underlying cortex (Fig. 6a). At the site of attachment there is a radiolucent line, which represents the uncalcified thickened periosteum<sup>43,44</sup> (Fig. 6b). Extension into the medulla is not uncommon and is optimally demonstrated with CT or MRI (Fig. 6c).<sup>19</sup> Cross sectional imaging studies are also invaluable for demonstrating areas of high-grade tumour or dedifferentiation,<sup>45</sup> which appear as poorly defined regions of unmineralised soft tissue attenuation on CT and regions of intermediate T1W SI or increased T2W SI on MRI (Fig. 6c).

The differential diagnosis includes myositis ossification and osteochondroma.<sup>46</sup> In myositis ossification the ossification is more marked at the periphery than at the centre (the zoning

phenomenon), and vice versa in paraosteal OS. In osteochondroma, there is direct continuity of the marrow spaces between the lesion and the underlying bone and a cartilage cap of variable thickness, which is best appreciated on axial T2W MRI.

# **Periosteal OS**

Periosteal OS is rare, accounting for 25% of all surface lesions and 2% of all OS.<sup>1,2,4,19</sup> It arises from the deep surface of the periosteum. Although the clinical presentation, age and gender distribution are similar to classical OS, it commonly occurs along the diaphysis of a long bone and has a better prognosis. However, the prognosis is worse than that of parosteal OS and metastatic disease causes death in up to 16% of cases.<sup>36,47</sup> Pathologically, periosteal OS is an intermediate or high-grade chondroblastic lesion.

Radiographically, the most common presentation is of a broad based soft tissue mass attached to the cortex without any medullary cavity involvement.<sup>48</sup> In a study by Murphey et al.,<sup>49</sup> the cortex was thickened and irregular with associated vertical spiculated periosteal reaction seen in 95% of cases (Fig. 7a). Soft tissue mineralization is varied in appearance, with chondral type of calcification also seen. CT and MRI findings include a soft tissue mass with predominantly chondroid matrix showing relatively low attenuation on CT, intermediate SI on T1W MR images and high SI on T2W MR images (Fig. 7b). MRI may demonstrate abnormal SI in the medullary cavity, which may be either reactive in nature or due to tumour extension. Reactive marrow change appears as marrow oedema (low SI on T1W and high SI on T2W and STIR) adjacent to but not contiguous with the surface mass and associated with an intact cortex (Fig. 7b), whereas microscopic tumour infiltration has similar signal characteristics, but is contiguous with the surface lesion through a destroyed cortex.<sup>49</sup>

## High-grade surface OS (HGSOS)

HGSOS is extremely rare, accounting for approximately 1% of all OS.<sup>50</sup> It typically presents in the third decade in the diaphysis of long bones, most commonly the femur. Pathologically, the lesion is identical to conventional central OS and has the same prognosis.

Radiologically, it has similar features to a periosteal OS,<sup>50</sup> although appearing more aggressive (Fig. 8). It is characterized by a broad based mass arising from the outer surface of the cortex.



**Figure 8** High-grade surface OS. AP radiograph demonstrating a large, broad based mass arising from the outer surface of the medial femoral cortex with an aggressive periosteal reaction.

Unlike periosteal OS, HGSOS often involves the entire circumference of the bone and frequently invades the medullary cavity.<sup>19</sup>

#### Intracortical OS

Intracortical OS is the least common of all osteosarcomas, accounting for less than 1% of cases.<sup>51</sup> It usually presents in the second decade and commonly arises in the diaphysis of the femur or tibia. It is characterized as a sclerotic variant of OS that



**Figure 9** Osteosarcomatosis. Bone scan showing a dominant lesion in left distal femur, with multiple bone and lung metastases.

may contain foci of cartilaginous or fibrous differentiation.  $^{51-53}\,$ 

Radiographically, the typical lesion shows an intracortical, geographical area of bone lysis with small areas of mineralization, measuring less than 4 cm in size.<sup>51,54</sup> The margin is well defined with thickening of the surrounding cortex. Medullary invasion is very rare.<sup>51,54</sup>

#### Multicentric or multifocal OS

In these conditions, there is involvement of more than one bone. They account for approximately 3-4% of all OS.<sup>55-57</sup> The definition of these lesions is still controversial.

Multicentric OS is also termed osteosarcomatosis and is characterised by the simultaneous appearance of multiple symmetrical bone lesions, particularly in the metaphyses of long bones. It is a very aggressive form of OS, predominantly presenting in the first decade of life.<sup>58</sup> More recently, osteosarcomatosis has been thought to represent rapidly progressive metastatic disease<sup>56,57</sup> (Fig. 9). This concept has been endorsed by Murphey et al.,<sup>19</sup> as they could identify a radiographically dominant lesion with ill defined margins, aggressive periosteal reaction, cortical disruption and adjacent soft—tissue extension, with otherwise symmetrical lesions, which were well defined, sclerotic and lacked a periosteal reaction. They also found multiple pulmonary metastases on chest CT in the majority of patients. Due to the aggressive nature of the lesion the prognosis is very poor with mean survival of only 12 months.

Multifocal OS is characterized by one or more lesions appearing over time after the treatment of a primary OS. These lesions are generally asymmetrical, of different sizes and may not always be osteosclerotic.<sup>59</sup> Multifocal OS affects adolescents and young adults and also has a poor prognosis.

## Conclusion

OS is the most common primary malignant bone tumour in children and young adults and the second most common malignant bone tumour after multiple myeloma. As discussed above it has a varied spectrum of radiological appearances depending on the type. We have discussed the salient features of the various types of OS on radiography and highlighted the importance of MRI in identifying dedifferentiation. It is important for a radiologist to recognise these imaging features to guide clinicians to the correct diagnosis, prompting earlier referral and hopefully improvement in the clinical outcome.

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