Histologic variants of chondrosarcoma

Ivan Chebib
Francis J Hornicek
Miriam A Bredella
Vikram Deshpande
G Petur Nielsen

Abstract

The histologic subtypes of chondrosarcoma are uncommon. Despite their rarity, they present with characteristic clinical and histopathologic features distinguishing them from conventional type of chondrosarcoma. The histologic variants, clear cell and mesenchymal chondrosarcoma, are reviewed herein. Dedifferentiated chondrosarcoma, although typically arising from conventional chondrosarcoma, is also reviewed due to its distinct histomorphology. Finally, so-called extraskeletal myxoid chondrosarcoma, which may rarely arise primary in bone, is also discussed despite its uncertain histogenesis.

Keywords chondrosarcoma; clear; dedifferentiated; mesenchymal; variant

Introduction

The histologic variants of chondrosarcoma, including clear cell, mesenchymal and dedifferentiated subtypes are exceptionally rare compared to conventional chondrosarcoma, making up little more than 6% of all chondrosarcomas.[1] Despite their rarity, knowledge of these entities is not only required for accurate diagnosis but also for their varied clinical presentation and prognosis.

Ivan Chebib *MD FRCPC Instructor in Pathology, James Homer Wright Pathology Laboratories, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. Conflicts of interest: none.*

Francis J Hornicek *MD PhD Associate Professor of Orthopaedic Surgery, Chief of Orthopaedic Oncology Service, Co-director of Center for Sarcoma and Connective Tissue Oncology, Department of Orthopaedic Surgery and Center for Sarcoma and Connective Tissue Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. Conflicts of interest: none.*

Miriam A Bredella *MD Associate Professor of Radiology, Musculoskeletal Imaging and Intervention, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. Conflicts of interest: none.*

Vikram Deshpande *MBBS Associate Professor of Pathology, Director Tumor Repository, James Homer Wright Pathology Laboratories, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. Conflicts of interest: none.*

G Petur Nielsen *MD Associate Professor of Pathology, Director of Bone and Soft Tissue Pathology, Directory of Electron Microscopy Unit, James Homer Wright Pathology Laboratories, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. Conflicts of interest: none.*

Clear cell chondrosarcoma

Clinical characteristics

Characterized in 1976 by Unni et al.,[2] clear cell chondrosarcoma (CCC) make up approximately 0.4–2.5% of all chondrosarcomas.[1,3] They occur over a wide age range with the peak incidence between the third and fifth decade.[3–5] There is a slight male predominance reported, 1.3–3.5:1 male-to-female ratio.[3–5]

The majority of CCC occurs in characteristic locations: epiphysis of proximal femur and humerus.[3–6] Rarely, they occur in other long bones such as the distal femur, proximal tibia and other atypical sites including the ilium/ischium, vertebrae, ribs, sternum, scapula, skull and phalanx.[3–6] Interestingly, some patients show elevated or normal alkaline phosphatase that decreases following treatment and may be a useful tumour marker.[5,7] However, this is not being universally used in the clinical setting.

Radiology

On plain radiographs, CCC typically presents as a well-defined osteolytic lesion with sclerotic margins involving the epiphysis or epimetaphyseal region with or without bone expansion (Figure 1a).[3,4,6] Some cases show mineralization, more characteristic of conventional chondrosarcoma[5,6] or in a pattern similar to chondroblastoma.[2,4,8] Extension into the diaphysis, cortical destruction or periosteal reaction is rare.[4,6] On magnetic resonance imaging (MRI), most tumours demonstrate low signal on T1 and high-intensity on T2-weighted images (Figure 1b and c).[6]

Pathology

Grossly, the tumours show a well-delineated fleshy mass with foci of cartilage formation and may demonstrate cystic hemorrhagic areas (aneurysmal bone cyst-like component) (Figure 2).[4] Microscopically, CCC is composed of sheets of large cells with abundant clear cytoplasm and distinct cell borders (Figure 3).[2,4,6] Metaplastic bone with osteoblastic rimming is present and in some tumours aneurysmal bone cyst-like changes are identified (Figure 4). Occasionally, the bone deposition can be so extensive as to impart an osteoblastoma-like appearance to the tumour.[4] Osteoclast-type giant cells are a common component, often present at the periphery. Foci of conventional hyaline-type cartilage (resembling low-grade conventional chondrosarcoma) can also be identified. Exceptionally rarely, CCC can undergo dedifferentiation.[9]

Immunohistochemistry

The immunohistochemical profile is relatively non-specific and the diagnosis is based on the morphological appearance. CCC typically expresses S100 protein.[10–12] They also express Sox9 and Runx2, osteochondrogenic markers that are also expressed in chondroblastoma.[13,14] Expression of type II and type X collagen has also been shown,[10,11] leading some to argue that morphologically and genetically, CCC resemble chondrocytes in the hypertrophic zone of the normal growth plate.[10] CCC have been shown to focally express keratins (AE1:AE3, CK7, CK8, CK18, rarely CK20).[13] Bcl-2 expression is generally high.[14]

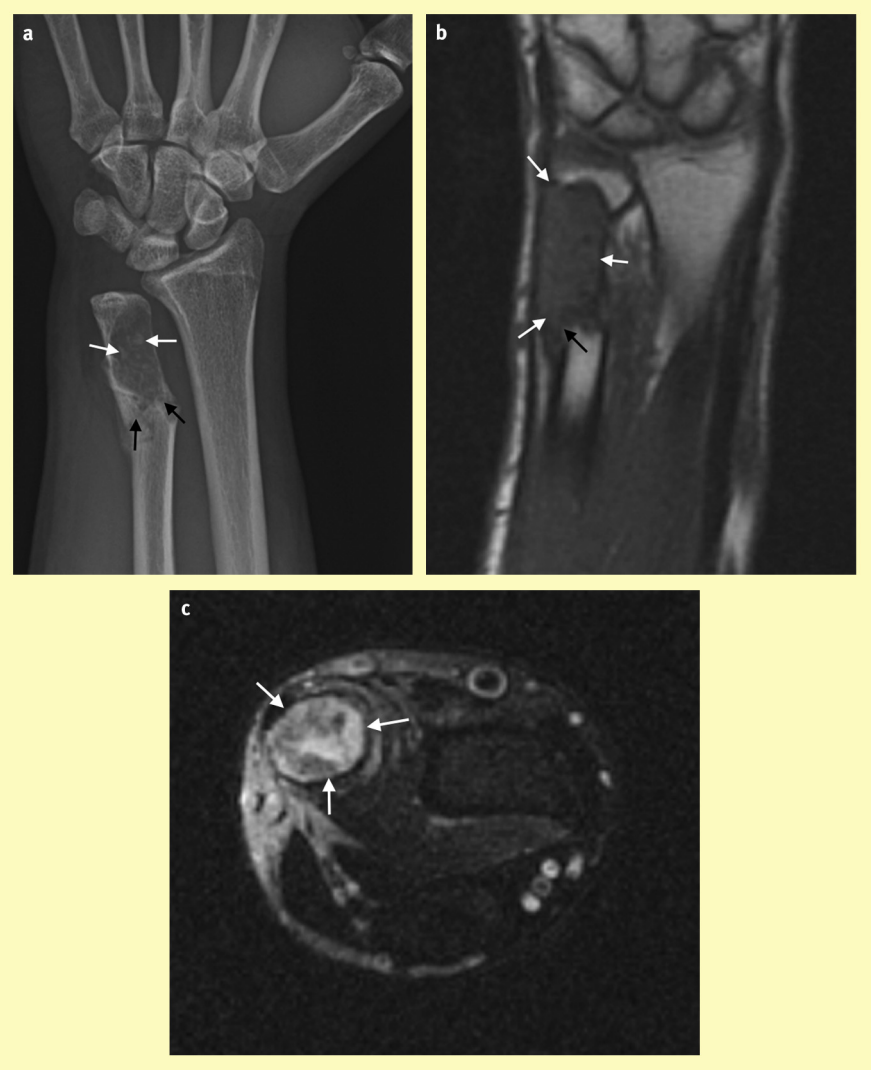

Figure 1 (**a**) Radiograph of the wrist demonstrates a mildly expansile, well-defined lytic lesion involving the distal ulna with chondroid matrix (white arrows). A pathologic fracture is present (black arrow). Coronal T1 (**b**) and axial fat-suppressed T2 (**c**) weighted MR images demonstrate low T1 and heterogeneous high T2 signal of the lesion (white arrows) with pathologic fracture (black arrow).

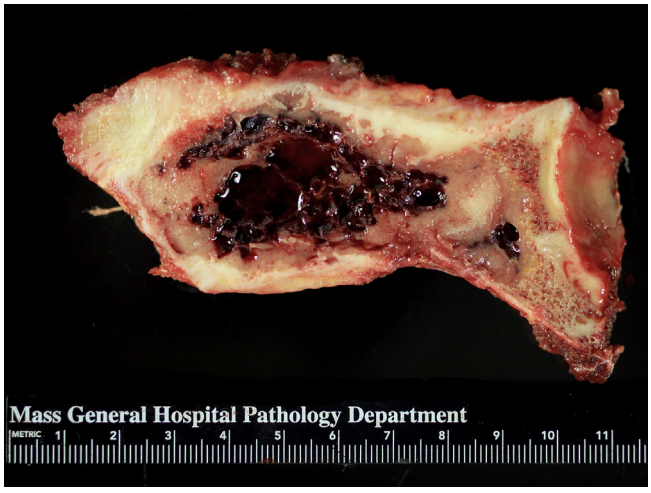

Figure 2 Clear cell chondrosarcoma of pelvis with prominent aneurysmal bone cyst-like hemorrhagic spaces.

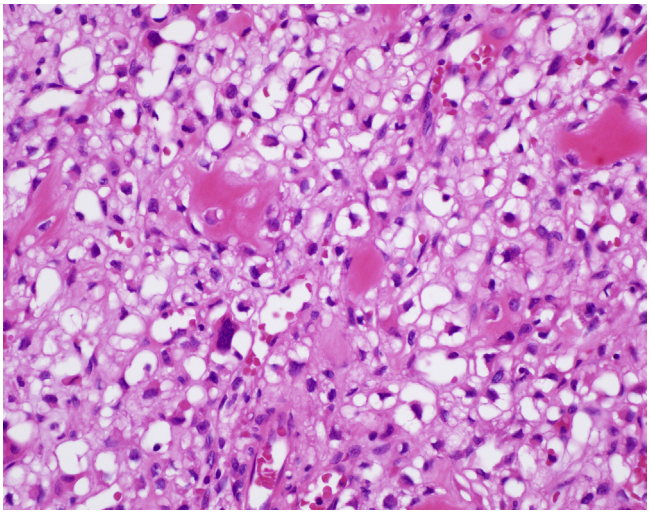

Figure 3 Clear cell chondrosarcoma with sheets of clear cells with minimal atypia, scattered multinucleated osteoclast-like giant cells and metaplastic bone lined by osteoblasts (400×).