

# Solid Tumour Section

## Mini Review

## Bone: Adamantinoma

Hans Marten Hazelbag, Pancras CW Hogendoorn

Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands (HMH, PCWH)

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### Identity

#### Note

Adamantinoma of long bones is a low-grade, malignant biphasic tumor, characterized by a variety of morphological patterns, most commonly epithelial cells, surrounded by a relatively bland spindle-cell osteo-fibrous component.

### Clinics and pathology

#### Etiology

Cumulating evidence indicates that classic adamantinomas derive from their osteofibrous dysplasia (OFD)-like counterparts. OFD and adamantinoma show common cytogenetic abnormalities (see below), and by immunohistochemistry, it has been shown that the epithelial component of adamantinoma is directly derived from the fibrous tissue. However, clinical aggressiveness among OFD, OFD-like adamantinoma and classic adamantinoma varies considerably, and many OFD-like lesions may never progress to classic adamantinoma.

#### Epidemiology

Adamantinomas are rare, they comprise 0.1-0.5% of primary bone tumors. The peak incidence is in the second and third decade. The youngest age group (up to 15 years) mainly includes patients with osteofibrous dysplasia (OFD)-like adamantinoma, whereas in older patients classic adamantinomas are predominant.

#### Clinics

At conventional radiography, typically a well-circumscribed, central or eccentric, (multi-) lobulated

osteolytic lesion is seen. Multifocality in the tibia as well as ipsilateral fibula is regularly observed. MRI is essential for pre-operative staging of the tumor and planning surgical margins. The treatment for most cases wide en-bloc resection.

Adamantinomas may display a protracted clinical behavior. Some tumors have radiologically proven to be present 30 years prior to histological diagnosis, whereas metastases may occur decades after local treatment. Recurrence rate after irradiation surgery may be as high as 90%, whereas up to 25% of these patients may develop metastases.

#### Pathology

Two main subtypes of adamantinoma are recognized: OFD-like adamantinomas lack a clear histological epithelial component, and mainly consist of osteofibrous tissue, in which woven bone trabeculae are rimmed by osteoblasts. Keratin immunohistochemistry highlights individual or small aggregates of positive cells. Classic adamantinomas have abundant epithelium, which may be arranged in basaloid, tubular, squamoid, spindle-cell, or mixed differentiation. Recently, sarcomatous dedifferentiation of the epithelial component has been described.

### Cytogenetics

#### Cytogenetics Morphological

With DNA flow and image cytometry it was shown that about 40% (6 of 15) of adamantinomas were aneuploid, all of them classic adamantinomas, and most of them near diploid. The aneuploid population was always restricted to the epithelial component.

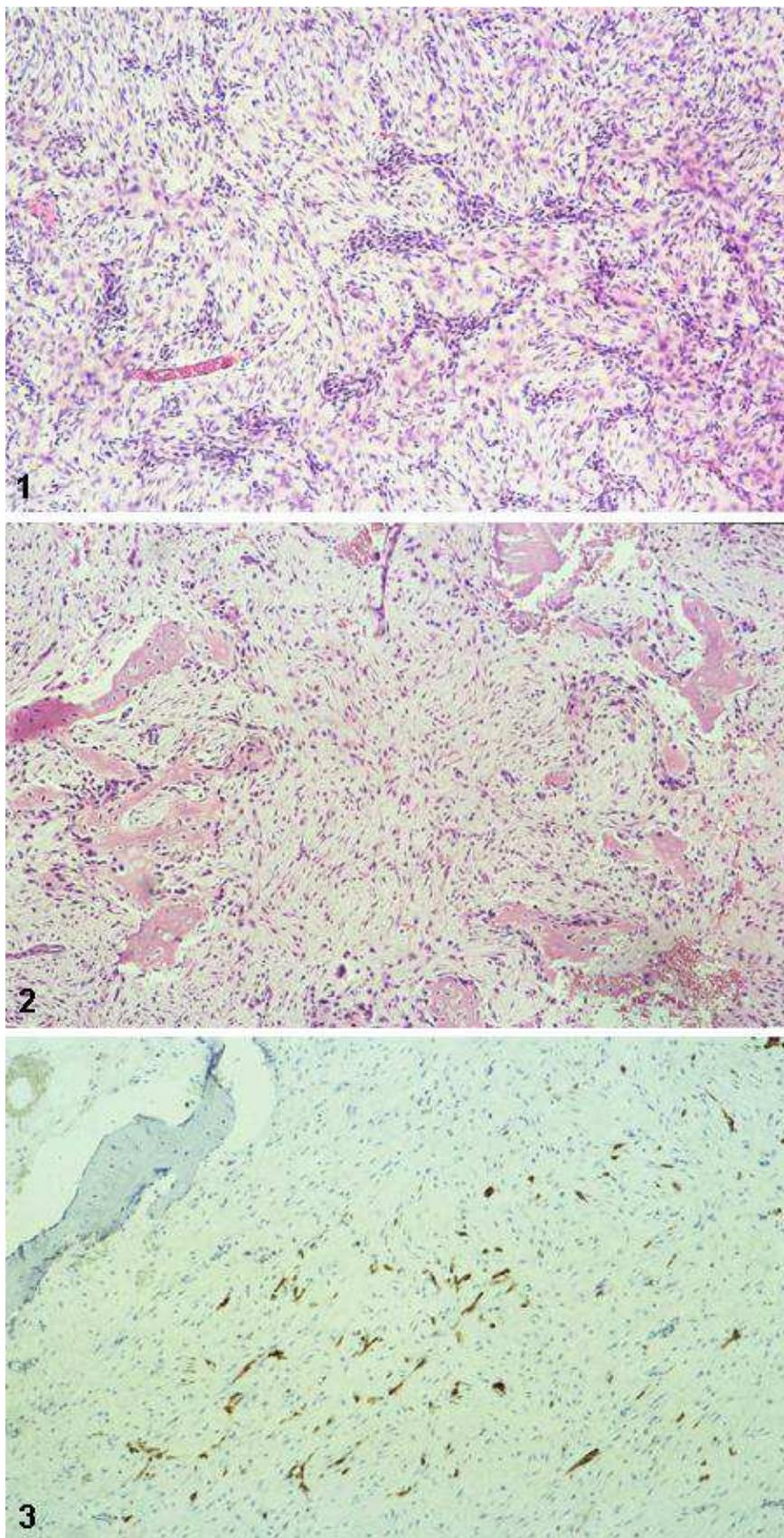


Figure 1: Classic adamantinoma, hematoxylin and eosin, x 100. Strings of epithelial cells embedded in fibrous tissue.

Figure 2: OFD-like adamantinoma, HE x 100. No epithelial cells are distinguishable in osteofibrous tissue.

Figure 3: OFD-like adamantinoma, immunohistochemistry for pankeratin, x 100. Individual keratin-positive cells (same case as figure 2).

p53-Protein accumulation was shown by immunohistochemistry (IHC) in 48% (12 of 25) adamantinomas, all classic subtype. LOH at the p53 locus was confirmed in DNA-sorted nuclei of epithelial cells in an IHC-positive tumor.

Cytogenetic analysis by GTG-banding is restricted to 15 cases of adamantinoma (n=11) and OFD (n=4) in literature. OFD and the fibrous and epithelial component of adamantinoma show comparable numerical chromosomal abnormalities, mainly involving trisomies of chromosomes 7, 8, 12, 19 and 21. These findings further substantiate the clonal origin of OFD and the common histogenesis of OFD and adamantinoma. The finding of translocations, deletions, and inversions is common but not structural, and only present in adamantinomas. This suggests that expansion of an abnormal clone to include structural changes may parallel progression from OFD to adamantinoma. One young patient with classic adamantinoma had a constitutional t(7;13)(q32;q14), also present in his father.

In literature some cases have been described with histological features of both Ewing's sarcoma and adamantinoma, sometimes called 'atypical' of 'Ewing-like' adamantinoma. Ewing's sarcoma is characterized by a t(11;22)(q24;q12). In one study on 3 archival cases with epithelial features, originally described as adamantinoma or non-typical Ewing's sarcoma (of which two were not located in the tibia), it was shown by FISH and RT-PCR that all had the typical t(11;22). They were therefore named 'adamantinoma-like' Ewing's sarcoma. Additionally, using RT-PCR on archival tissue, a t(11;22) or t(21;22) was not found in any of 12 informative adamantinomas. These data indicate that tumors showing overlapping morphological and immunohistochemical features can be readily distinguished with these techniques.

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