Clinicopathological Features, Diagnosis, and Treatment of Adamantinoma of the Long Bones

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Educational Objectives

As a result of reading this article, physicians should be able to:
1. Describe the radiographic characteristics of adamantinoma of the long bones.
2. List the histological patterns and radiographic characteristics commonly associated with adamantinoma.
3. Discuss treatment options for adamantinoma of the long bones.
4. Discuss the prognosis of patients with adamantinoma.

Adamantinoma of the long bones is a low-grade, slow-growing, primary malignant bone tumor composed of epithelial cells in a fibrous or osteofibrous stroma.1,2 It has a wide range of histological patterns.3-18 Despite the considerable range of each histologic pattern, most current studies have shown that long bone adamantinoma appears to be of an epithelial nature. The tibial lesion’s name comes from its somewhat similar histologic appearance to the more common odontogenic adamantinoma of the jaw bones.18,19 Despite the histological similarities there is no proof that these tumors have a similar histogenetic origin.19

Long bone adamantinomas can be divided in two main groups with distinct histological and radiographic features. The first—classic adamantinoma—is characterized by an abundance of tumor cells and a destructive growth pattern. The second, differentiated adamantinoma, is characterized histologically by a predominance of an osteofibrous dysplasia-like pattern with a small, inconspicuous component of epithelial tumor elements.12,18,19 Radiographically, classic adamantinomas are either intracortical or associated with complete cortical disruption, intramedullary involvement, and expansion beyond the periosteum into adjacent soft tissues, while differentiated adamantinomas are intracortical and often multicentric lesions.12,19,20

This article discusses the epidemiology, clinicopathological and imaging features, diagnosis, treatment, and prognosis of adamantinoma of the long bones.
malignant bone tumors.4-9,21 In 1986, Moon and Mori2 performed a meta-analysis of 200 cases. In 1996, Unni18 reported 36 cases in an analysis of 5641 primary malignant bone tumors from a single institution.

The literature suggests a slight male predominance.1,2,4-9,21 Adamantinomas usually are diagnosed after skeletal maturity. Although 75% of the cases occur between the second and third decades of life,18 adamantinomas have also been reported in older patients, as well as in children aged <14 years.18,22,23 Differentiated adamantinomas tend to occur in younger patients.18,19

More than 90% of adamantinomas appear in the tibia, with fibular involvement coexisting in 50% of the cases.12,18,19 The tumor usually is located in the diaphysis and, less frequently, the tibial metaphysis. Rare cases of adamantinomas of the olecranon, the ribs, the radius, the spine, the metatarsus, and the humerus also have been reported.24-31

CLINICAL MANIFESTATIONS
A history of previous trauma or fracture occurring months or years prior to the onset of symptoms is reported in approximately 60% of patients. The most common presentation is of a gradually evolving mass associated with dull, insidious, aching pain. Bowing deformity of the tibia and pathologic fractures may occur. Advanced or recurrent lesions may be associated with soft-tissue involvement.12,18,21 Severe paraneoplastic, hormonally mediated hypercalcaemia, hypercalcaemic coma, and pancreatitis have been reported.32-35

IMAGING FEATURES
Radiographically, adamantinoma usually appears as a mixed lytic and sclerotic central lesion or multiple, sharply circumscribed luencies with sclerosis of the intervening bone (Figure 1). This slowly growing, expansile tumor eventually causes endosteal scalloping and thinning, interruption, or destruction of the cortex without periosteal reaction. Moderate to severe anterior bowing deformity is common.10,20 Classical adamantinoma usually is intracortical with evidence of complete cortical disruption and intramedullary and soft-tissue involvement. Involvement of the anterolateral cortex of the tibia with multiple lucencies and sclerotic foci characterizes differentiated adamantinoma. These imaging features may be similar to those observed in osteofibrous dysplasia.12,18,20

Technetium pyrophosphate bone scan shows intense increased uptake tracer accumulation, corresponding closely to the extent of the lesion.18,21,36 In addition, bone scan may show a coexisting fibular involvement.

Computed tomography reveals an osteolytic lesion with expansion and destruction of the cortex (Figure 2), and probable extension to the surrounding soft tissues.21,37 Magnetic resonance imaging (MRI) is useful in providing information concerning the intramedullary and soft-tissue extent of the tumor.9,20,36-38 On T1-weighted MRI, the lesion has a low intensity signal, whereas on T2-weighted MRI the signal is much brighter and does not diminish with the fat suppression technique.

Two morphologic patterns were distinguished in MRI: a solitary, lobulated focus versus a pattern of multiple small modules in one or more foci.

HISTOLOGIC FEATURES
Histologically, adamantinoma is composed of epithelial islands in a spindle cell stroma. The relative amounts of the two components can vary considerably (Figure 3). Several histologic variants have been
Adamantinoma generally is painful, is observed during adulthood, has different radiographic features, is progressive during adult age, and may expand into the soft tissues. However, osteofibrous dysplasia seldom progresses during childhood, and any progression of the lesion stops after puberty. Exceptional cases have been reported of adamantinoma that began during childhood and have radiographic features similar to osteofibrous dysplasia.25-27

Adamantinoma must be suspected if a tibial lesion becomes painful or if it grows after puberty. In such cases, extensive biopsy from the most radiolucent areas is recommended. However, given the heterogeneity of the histology within different areas of adamantinomas, sampling errors are possible with limited biopsy specimens. These errors have led to reclassification of these tumors from osteofibrous dysplasia to adamantinoma after repeat biopsy with adequate tissue.25-27

TREATMENT AND PROGNOSIS

Owing to the rarity of adamantinomas, data is insufficient concerning the safest and most effective treatment modality. These tumors are of low-grade malignancy and highly radioresistant.48,49 Thus surgery is the treatment of choice. Although limited experience with them has been reported, chemotherapy and radiation therapy have not been shown to be effective.5

Operative treatment includes either surgical resection with wide margins and reconstruction of the segmental defect,5,8,9,12,18,21,50-52 or amputation.1,2,59 Limb reconstruction options include the use of allografts (intercalary, osteocutaneous, or morselized), vascularized and nonvascularized fibular autografts, metallic segmental implants, and distraction osteogenesis.5,9,21,51,53 Intercalary reconstruction appears to be the most successful method (Figure 4). Qureshi et al9 reported a limb salvage rate of 84%. They used allografts in 61% of the reconstructions after resection of adamantinomas of long bones. The majority were intercalary reconstructions. No differences in the efficacy of different fixation techniques were noted. Complications related to the reconstruction were unacceptably high (48% of patients), including nonunion (24%) and fracture of the allograft (23%). Vascularized fibular grafts have been considered the best type of graft for large segmental bone defects after bone tumor resections.54,55

Local recurrence is common in inadequately treated patients.12,21,56,57 Wide operative margins are associated with a lower rate of local recurrence than marginal or intralesional margins.5,8,24 However, a 18.6% rate of local recurrence at

Figure 3: Histological appearance of adamantinoma. Low-power view (A) shows islands of epithelial cells surrounded by fibrous tissue and high-power view (B) of the cluster of epithelial cells within the fibrous stroma.

Figure 4: AP (A) and lateral (B) plain radiographs after wide resection of the tumor and reconstruction using a 13 cm intercalary tibial allograft fixed using a DCP plate and screws and autologous iliac bone grafting at the host bone allograft junction.
10 years has been reported after wide-margin surgical excision of adamantinomas. Local recurrences usually occur 5 to 15 years after primary excision of the tumor. Late local recurrences have been reported at 24 and 36 years after diagnosis. No statistically significant difference between local recurrence rate and tumor stage, duration of symptoms, patient gender and age, type of biopsy, and type of grafting has been documented. Wide resection is also indicated for recurrent tumors.

The near-benign biology and slow-growing nature of adamantinoma are reflected in the good survival rates even after local recurrences and lung or regional lymph node metastases. Late metastases may occur in 10%-30% of patients with adamantinomas, most frequently in the lungs, the regional lymph nodes, or the bones. After wide margin surgical excision of the tumor or amputation, overall 10-year survival rates vary from 82% to 87%.

**CONCLUSION**

Adamantinoma of the long bones is a rare, primary, low-grade, slow-growing malignant bone tumor. It is expressed with a wide range of histological patterns. Histologically, the tumor is composed of an epithelial component surrounded by a fibrous stroma that may or may not contain spicules of woven bone. In the majority of cases, adamantinomas are located in the tibial diaphysis. Limb salvage with wide surgical resection and reconstruction or amputation is the most effective treatment. Local recurrence is associated with incomplete resection. Survival rates range from 82% to 87%. Late metastases, mainly to the lungs, may occur.

**REFERENCES**


Adamantinoma of the Long Bones

1. Which of the following is true regarding epidemiology of adamantinomas of the long bones?

A. Adamantinomas of the long bones are rare tumors accounting for 0.3%-1.0% of all malignant bone tumors.
B. Differentiated adamantinomas tend to occur in younger patients.
C. The tibial diaphysis is the most common location, with fibular involvement coexisting in 50% of the cases.
D. All of the above.

2. Clinical manifestations of adamantinomas of the long bones at presentation include:

A. A history of trauma or fracture few months or years prior to the onset of symptoms in approximately 60% of patients.
B. Dull, aching pain associated with a gradually evolving mass.
C. Regional lymph node involvement or distant metastases.
D. A and B.

3. Which of the following is false regarding imaging of adamantinomas of the long bones?

A. Classical adamantinomas usually are intracortical, with evidence of complete cortical destruction and intramedullary and soft-tissue involvement.
B. A mixed lytic and sclerotic lesion, periosteal reaction, and the Codman's triangle usually are observed.
C. Moderate to severe anterior bowing deformity is common.
D. Differentiated adamantinomas usually involve the anterolateral tibial cortex, with imaging features similar to osteofibrous dysplasia.

4. Which of the following is true regarding histopathology of adamantinomas of the long bones?

A. Adamantinomas show a wide range of morphologic patterns, with a biphasic (epithelial and mesenchymal) origin.
B. In immunohistochemical studies, epithelial cells express basal cell type cytokeratins, which are probably the malignant element of the tumor.
C. Mesenchymal component is composed of a loose stroma of immature spindle cells producing collagen, resembling osteofibrous dysplasia.
D. All of the above.

5. Differential diagnosis of adamantinomas of the long bones includes:

A. Fibrous and osteofibrous dysplasia.
B. Haemangioendothelioma and haemangiosarcoma of bones.
C. Low-grade chondrosarcoma.
D. A and B.
6. Which of the following is true regarding biopsy of suspected tibia lesions for adamantinomas of the long bones?
   A. Extensive biopsy is recommended from the most radiolucent areas.
   B. Sampling errors are rare, even with limited biopsy specimens.
   C. The lesion shows histologic homogeneity.
   D. B and C.

7. Current treatment for adamantinomas of the long bones includes:
   A. Limb salvage and neo-adjuvant chemotherapy.
   B. Limb salvage with wide surgical resection and intercalary reconstruction, or amputation.
   C. Limb salvage and adjuvant radiation.
   D. Limb salvage, chemotherapy, and radiation.

8. After surgical resection of adamantinomas of the tibial diaphysis, reconstruction of the bone defect can be achieved by:
   A. Intercalary allograft.
   B. Vascularized fibular autograft.
   C. Metallic segmental implant.
   D. All of the above.

9. Which of the following is false regarding local recurrences of adamantinomas of the long bones?
   A. Local recurrences usually occur 5-15 years after the primary excision of the tumor.
   B. Local recurrence depends on the duration of the clinical symptoms and the stage of the tumor.
   C. Very late local recurrences have been reported.
   D. Wide resection is also indicated for the recurrent tumors.

10. Which of the following is false regarding prognosis of adamantinomas of the long bones?
    A. Late metastases may occur in 10%-30% of the patients.
    B. Metastases usually are to the lungs, the regional lymph nodes, or the bones.
    C. The overall 10-year survival rates vary from 82%-87%.
    D. Poor survival rates are associated with the occurrence of local recurrences, regional lymph nodes, and lung metastases.