The case:

A 73-year-old woman with no significant past medical history presents with a palpable lump in the midshaft of the left tibia and intermittent mild discomfort for the past 8 months.

Figure: Frontal radiograph of the left tibia and fibula.

Your diagnosis?

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Diagnosis:
Adamantinoma

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Answer to Radiologic Case Study
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A 73-year-old woman with no major medical problems and no history of trauma to the leg presented with a palpable lump and mild leg discomfort for the past 8 months. On physical examination, there was a firm, nontender, small bulge along the anteromedial midshaft of the left tibia without an associated soft tissue mass. There was no lymphadenopathy in the inguinal region or elsewhere.

A frontal radiograph of the left tibia and fibula (Figure 1) revealed a mildly expansile osteolytic lesion in the midshaft of the tibia with endosteal scalloping and a small amount of focal smooth periostitis laterally. Distally, there was some sclerosis and mild cortical thickening.

Coronal T1-weighted (Figure 2A) and sagittal fatsaturated T2-weighted (Figure 2B) magnetic resonance images demonstrated a low T1, heterogeneous high T2 signal marrow infiltrating neoplasm involving the mid tibial shaft with involvement of the anterior and lateral cortex. There was no associated soft tissue mass. No additional lesions were identified in the tibia or fibula.

For a patient with no history of primary neoplasm and a solitary bone lesion below the knee in this location and with these imaging features, the differential diagnosis is adamantinoma or fibrous dysplasia. Isolated metastases rarely occur below the knee.

Prior to consultation, this patient had a mammogram that had negative findings and a positron emission tomography scan that showed no solid organ neoplasm. Routine laboratory studies had unremarkable results. An open biopsy was performed with histological findings of an epithelioid neoplasm with squamous and basaloid differentiation in a densely fibrous stroma. An immunohistochemical evaluation showed that the neoplasm was strongly positive for cytokeratins AE1/3, CK7, and CAM5.2.

Pathology findings were consistent with primary adamantinoma of bone. The patient went on to en bloc resection of the midshaft tibia with wide margins and reconstruction with tibial allograft Musculoskeletal Transplant Foundation with tibial rodding, bone grafting at...
the junctional sites, as well as stabilization with a lateral plate and screws.

**Discussion**

Adamantinoma is a rare low-grade primary neoplasm of the bone that accounts for less than 1% of all primary bone tumors. The lesion was first described by Maier in 1900; in 1913, Fischer named the tumor “primary adamantinoma of the tibia” because of its histologic resemblance to ameloblastoma, a lesion most commonly seen in the jaw that was initially called adamantinoma. Despite the similarities, these tumors have not been proven to have the same genetic origin.

Most cases of adamantinoma are seen in the tibia, usually involving the anterior cortex of the midshaft. Adamantinoma is usually solitary, but a synchronous lesion may occasionally be present in the ipsilateral fibula. Involvement of other bones of the appendicular and axial skeleton is rare. A few cases isolated to the pretibial soft tissue without bony involvement have been reported. There is a slight male predominance, and although cases have had a range of ages, the typical age at presentation is in the 2nd through 4th decades.

Presenting symptoms are nonspecific, usually consisting of localized dull pain or swelling of gradual onset. Symptoms last for months to several years. There may or may not be a history of prior trauma to the affected area. In one large review, Moon and Mori found that just more than 60% of 133 cases had a significant traumatic incident prior to tumor diagnosis. The history of preceding trauma is of interest because the pathogenesis of this slow-growing primary epithelial tumor is thought by some to be posttraumatic. This theory was proposed in 1932 by Ryrie, a pathologist who described one of the earliest cases of adamantinoma. He postulated that because of the tibia’s superficial location and sharp anterior edge, injury leads to subperiosteal epithelial cell implants with hematoma and subsequent ossification and it is the aberrant repair of this injury that leads to tumor formation. An earlier hypothesis proposed by Fischer is that of a cell rest originating during the intrauterine period rather than posttraumatic implantation. Synovial cell as well as angioblastic origins have also been proposed; however, electron microscopy and immunohistochemical studies have confirmed the epithelial origin of the neoplasm.

Histologically, the tumor is composed of varying types and proportions of epithelial cells in a background of fibrous or osteofibrous stroma. Four histological patterns have been described for classic adamantinoma—basaloid, spindle, tubular, and squamous—with the basaloid and tubular patterns being the most common. Because of its epithelial nature and histological variability, adamantinoma can resemble lesions ranging from benign to malignant, including epithelial metastasis. The histologic finding of rare mitotic figures, patient age, and patient clinical history are important discriminating factors. The relationship of adamantinoma to osteofibrous dysplasia has been studied, with classic adamantinoma believed to be at one end of the spectrum and osteofibrous dysplasia at the other. To avoid a false-negative result, when a biopsy is performed, the lesion should be sampled widely including centrally, as an osteofibrous dysplasia-like pattern is known to occur peripherally. Also, immunohistochemistry should be used to detect cytokeratin, an epithelial marker.

Radiography is the initial and most reliable imaging modality for diagnosis. The typical lesion is located in the midshaft of the tibia anteriorly. It is an eccentric expansile cortical or intramedullary lytic lesion with a multilocular appearance and intervening areas of sclerosis. The margins can be sharp or ill defined and extension into the adjacent soft tissue can occur. Periostitis is minimal unless there is a pathologic fracture. Deformity with anterior bowing of the tibia is common. When a lesion is completely intracortical, imaging features do not permit distinction of classic adamantinoma from differentiated adamantinoma or osteofibrous dysplasia. Age is an important discriminating factor.

As with all other primary malignant tumors of bone, magnetic resonance imaging...
is the best imaging modality to evaluate the intramedullary and soft tissue extent of the lesion. Magnetic resonance imaging will show a low T1, high T2 signal-intensity lesion that can extend into the soft tissue. Magnetic resonance imaging is also used to detect possible skip lesions as well as lesions in the ipsilateral fibula, which have been reported in approximately 10% of cases. A bone scan will show increased radioisotope uptake on all 3 phases.

Adamantinoma is a slow growing tumor that has been known to locally recur and has the potential to metastasize. Local recurrence rates between 18% and 32% have been reported and more aggressive behavior has been seen with locally recurrent neoplasms. Metastases have been reported in 15% to 30% of cases and have occurred up to 27 years after initial treatment. The most common site of metastasis is to the lungs. Lymph node metastasis occurs less frequently, and skeletal metastatic disease is rare. Because imaging and histology cannot identify which patients will develop local recurrence or metastatic disease, patients must receive long-term follow-up.

**Conclusion**

Historically, primary bone tumors were treated with amputation. However, due to surgical advances and improved imaging modalities, limb salvage is now considered the standard of care. Radiation and chemotherapy have not proven useful for the treatment of adamantinoma. The current treatment of choice is en bloc resection with wide operative margins and reconstruction. Allografts and fibular autografts have been most commonly used.

In a multicenter review, Qureshi et al evaluated the outcomes of 70 cases of adamantinoma of the long bones treated surgically. Ninety-one percent had attempted limb salvage, the majority using allograft reconstruction. Mean follow-up was 7 years, and the final limb salvage rate was 84%. At 10 years, the local recurrence rate was 19% and the mortality rate was 13%. Wide operative margins at initial treatment resulted in a significantly decreased rate of local recurrence.

Compared with routine orthopedic reconstructions, reconstructions after extensive resection for tumors have an increased complication rate, with most complications occurring in the first 3 years. Qureshi et al reported a complication rate of 48% after reconstruction; nonunion and fracture were the most common complications, regardless of the type of graft. Infection was more common when nonvascularized autogenous bone graft was used and has been reported to be the main cause of failed allografts. Despite the high rate of complications, most resolve with additional treatment.

**References**