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Case study

High-grade squamous cell carcinoma arising in a tibial adamantinoma ☆

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Summary Adamantinoma of the long bones is a rare, typically low-grade malignant tumor that frequently involves the tibia. Radiographically, adamantinoma is characteristically a lytic, intracortical, and expansile lesion with variable margins. Histologically, adamantinoma is a bimorphic neoplasm, composed of epithelial and osteofibrous elements. Herein, we describe a 72-year-old man with a long-standing tibial mass that, on imaging, rapidly developed cortical destruction with soft tissue extension. Imaging revealed no evidence of a distant site of origin. Needle core biopsy demonstrated high-grade squamous cell carcinoma, and metastasis was initially favored. However, the combined clinicoradiologic and pathologic features were most compatible with a high-grade squamous cell carcinoma arising in adamantinoma. The diagnosis was confirmed in the resection specimen. Both the age at presentation and histologic features make this case unusual and highlight a potential for misdiagnosis in the evaluation of squamous cell carcinoma–containing lesions of the tibia, reinforcing the importance of clinicoradiologic correlation in bone pathology.

1. Introduction

Adamantinoma of the long bones is a rare neoplasm, comprising less than 1% of primary bone tumors [1-3]. Patients typically present within the second and third decades of life with pain and swelling; there is a slight male predominance, and the symptoms can be of several years' duration. Most cases arise in the tibia, a subset of which has synchronous fibular involvement. Overlap exists in the radiographic appearance of osteofibrous dysplasia, osteofibrous dysplasia-like adamantinoma, and adamantinoma. Typically, adamantinoma will demonstrate more aggressive imaging features with greater longitudinal and medullary involvement, and irregular moth-eaten margins, although the appearance can vary [4]. Histologically, adamantinoma is a bimorphic tumor composed of both epithelial and osteofibrous components. Often, the cytokeratin (CK)-expressing epithelial component forms solid nests of basaloid cells or tubular formations; however, spindle cell and squamous variants have also been described, and multiple patterns can coexist [5,6]. Typically, the epithelial and stromal components show only mild to moderate cytologic atypia, but isolated reports of "dedifferentiation" to high-grade spindle cell tumors exist in the literature [7-9]. Herein, we present an unusual case of a 72-year-old man with a high-grade squamous cell carcinoma arising in a tibial adamantinoma.

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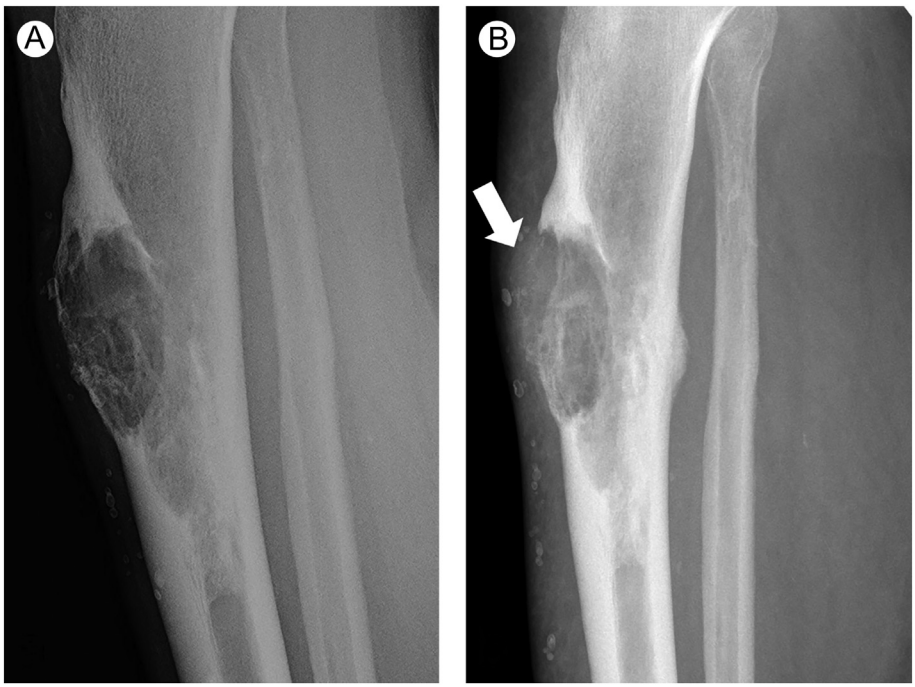

Fig. 1 Lateral radiograph of the left tibia demonstrates a lytic lesion centered in the proximal tibial diaphysis. A, The lesion demonstrates cortical expansion and peripheral areas of sclerosis. B, A 3-month follow-up lateral tibial radiograph demonstrates progression of anterior cortical destruction, arrow.

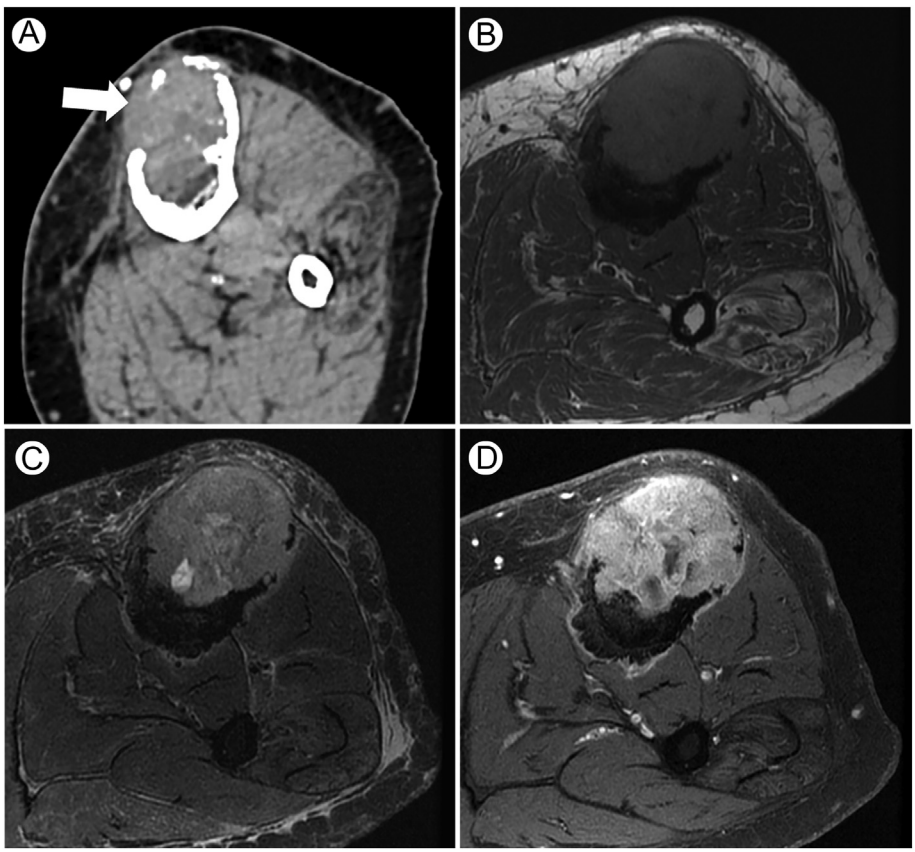

Fig. 2 A, Axial CT without contrast confirms an area of cortical destruction and a small soft tissue mass (arrow). Axial T1-weighted (B), T2-weighted fat-saturated (C), and postgadolinium fat-saturated (D) images show the intramedullary involvement.

The combination of the patient age at presentation and histologic features of the tumor underscores the potential for misdiagnosis in the evaluation of squamous cell carcinoma–containing lesions of the tibia, particularly in older adults.

2. Case history

A 72-year-old white man presented with a painful left lower leg mass. He reported that the mass had been present since age 10 years but noted increasing pain after a recent fall. Imaging studies performed in his mid-30s (not available for review) were interpreted as a benign process, and he was told that no additional clinical or radiologic follow-up was necessary. His medical history was otherwise noncontributory. Physical examination revealed a palpable mass overlying the proximal left anterior tibia with no neurologic or vascular compromise in the distal limb.

Radiographs demonstrated a lytic lesion centered in the anterior cortex of the midtibial diaphysis. The lesion expanded the tibial cortex with adjacent sclerosis suggesting an indolent lesion (Fig. 1A); however, there were indistinct areas of the anterior cortex suggesting cortical destruction that had increased in a 3-month period (Fig. 1B). Computed tomography (CT) and magnetic resonance imaging demonstrated extensive medullary involvement in addition to cortical destruction and a soft tissue mass (Fig. 2). The imaging differential diagnosis included adamantinoma and metastatic disease. Adamantinoma was the favored imaging diagnosis based on areas of peripheral sclerosis, cortical expansion, and long-standing history of a tibial mass.

An image-guided needle core biopsy of the mass was entirely composed of moderately differentiated squamous cell carcinoma, characterized by nests and islands of large epithelioid cells with conspicuous nucleoli, cell-cell bridging, and central necrosis (Fig. 3A and B). The neoplastic cells were strongly positive with multiple wide-spectrum cytokeratin (CK) antibodies (CK OSCAR and CK AE1/AE3). Although a diagnosis of metastatic squamous cell carcinoma was considered, extensive imaging, including CT of the chest, CT of the abdomen, CT of the pelvis, positron emission tomography–CT, and whole-body bone scan, showed no additional sites of disease. Moreover, the tibial imaging showed features more compatible with adamantinoma than metastasis. As such, the tumor was favored to represent high-grade squamous cell carcinoma arising in an adamantinoma, and the patient subsequently underwent wide excision of the mass.

Grossly, the resected tumor formed an 8 × 5 × 3.2-cm lobulated, tan solid mass centered in the anterior tibial cortex with extension into the medullary canal and surrounding soft

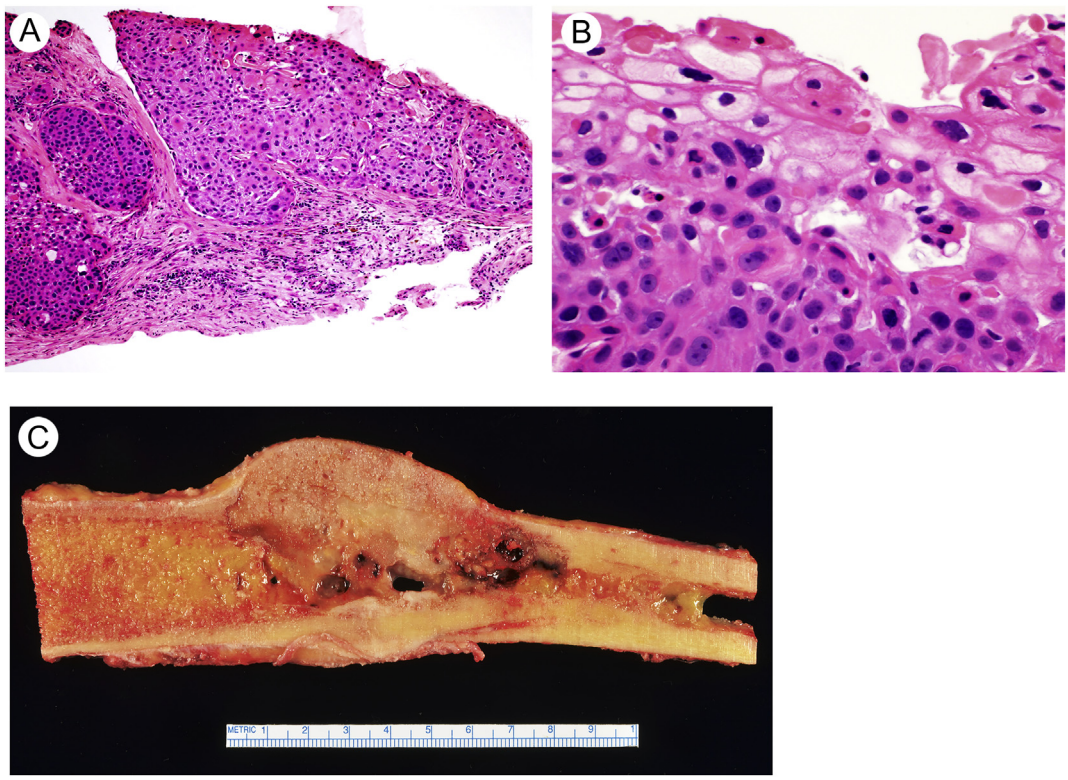

Fig. 3 Image-guided needle core biopsy of the left tibia mass revealed high-grade squamous cell carcinoma. Gross pathology of en bloc resection specimen showed a solid, lobulated, tan, homogeneous mass destroying the anterior tibial cortex with medullary and soft tissue extension. Original magnifications ×100 (A), ×200 (B), and ×400 (C),

tissues (Fig. 3C). Histologic examination revealed high-grade squamous cell carcinoma, with features identical to those observed in the biopsy, comprising most of the neoplastic tissue (Fig. 4A and B). However, adjacent to this high-grade component, foci of irregular woven bone trabeculae admixed with a cytologically bland spindle cell stromal component and scattered small epithelial groups and nests were noted. These areas were consistent with classic adamantinoma. The epithelial components in these foci contained compressed cuboidal cells forming tubule-like spaces and small solid squamous nests with minimal cytologic atypia (Fig. 4C and D). CK OSCAR and AE1/AE3 immunostains highlighted both the benign-appearing epithelial nests and high-grade squamous cell carcinoma (Fig. 4E). Based on the constellation of radiologic and pathologic features, a final diagnosis of high-grade squamous cell carcinoma arising in an adamantinoma was made. Because of chronic nonhealing and hardware exposure at the surgical site, the patient underwent left knee disarticulation 19 months after the initial resection. Currently, at 21 months of follow-up, there is no clinical or radiologic evidence of recurrent or metastatic disease.

3. Discussion

Adamantinoma of the long bones is a rare, slow-growing malignant tumor. The mainstay of treatment is surgery with a wide margin, and the prognosis is generally good, with

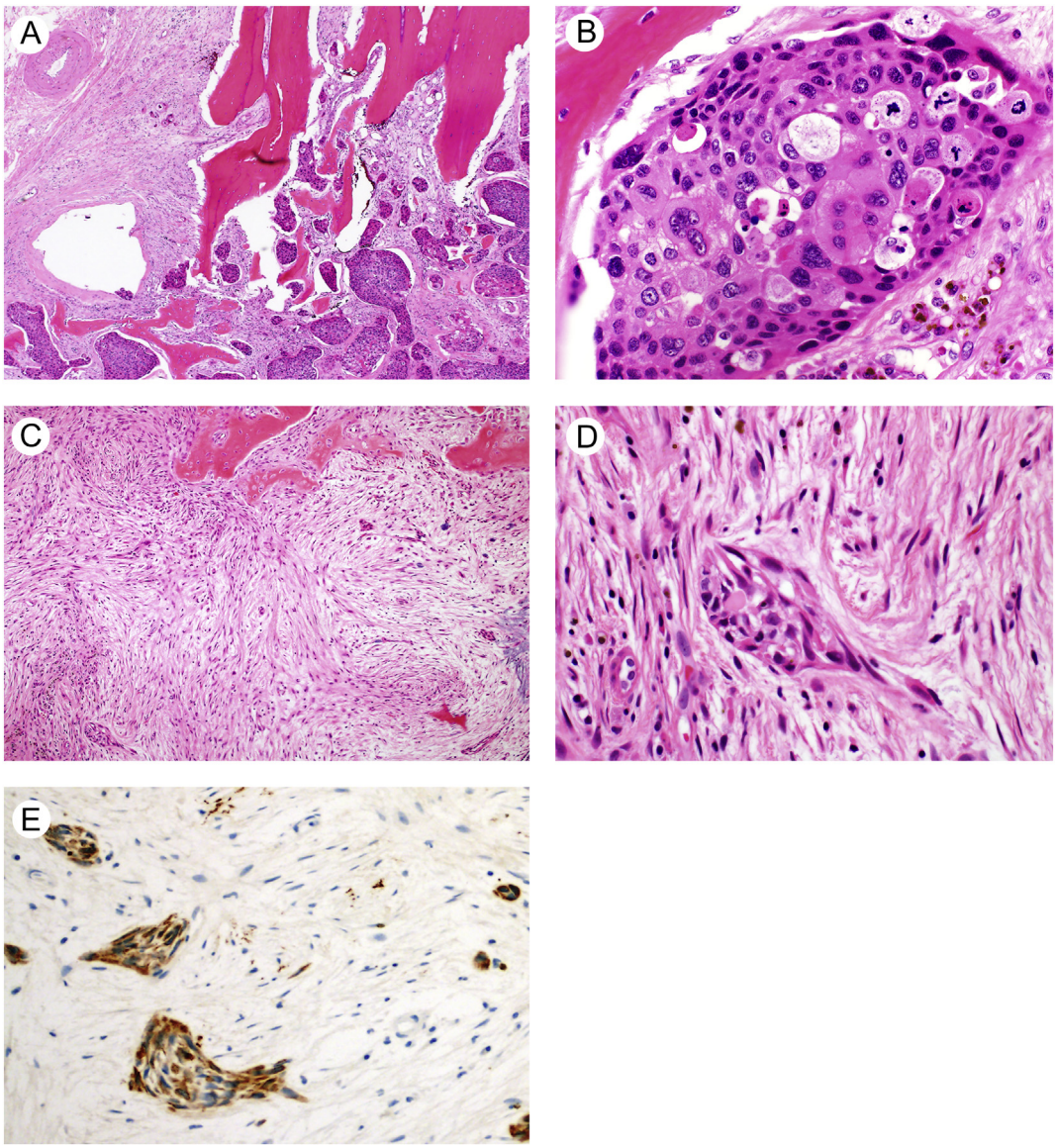

Fig. 4 The resected tumor was composed predominantly of high-grade squamous cell carcinoma (original magnification ×40 [A] and ×200 [B]), admixed with small foci of histologically classic adamantinoma, with tubular and squamoid epithelial patterns (×200 [C] and ×400 [D]) highlighted by CK-AE1/AE3 staining (E).

larger series reporting approximately 85% 10-year survival rates [5,10]. However, metastasis occurs in approximately 25% of cases, often after a significant disease-free interval, reducing the long-term survival rate to approximately 40% at 20 years [10,11]. Younger patient age at diagnosis, pain at presentation, lack of squamous differentiation, intralesional or marginal surgery, and extracompartmental growth are associated with increased likelihood of recurrence and metastasis [5,12,13].

Histologically, adamantinoma is divided into osteofibrous-like adamantinoma and classic adamantinoma. Classic adamantinoma has a readily identifiable epithelial component, which is classified into basaloid, tubular, squamous, or spindled types, whereas the epithelial elements in the osteofibrous-dysplasia subtype are more subtle. In classic adamantinoma with tubular morphology, differentiation from metastatic adenocarcinoma on biopsy material can be difficult, especially in adults when metastatic disease would be the most common bone malignancy. Although the spindle cell population of adamantinoma will show CK staining, raising the possibility of sarcomatoid carcinoma, it is generally cytologically bland. Rarely, dedifferentiation or sarcomatoid progression of the epithelial component of adamantinoma can occur, potentially creating a greater diagnostic challenge. This phenomenon has been described in 5 tumors, including primary and recurrent tumors [7,9], and dedifferentiation or reversion to a mesenchymal (immuno)phenotype; lacking epithelial differentiation has also been described in 1 case [8]. In all of these cases, the tumors had the morphologic appearance of high-grade spindled, sarcomatoid tumors.

Distinguishing the squamous variant of adamantinoma from metastatic squamous cell carcinoma is generally not a diagnostic challenge because the former lacks significant cytologic atypia. In contrast, the challenging feature in the current case is the presence of high-grade squamous cell carcinoma within an adamantinoma. Although squamous or squamoid differentiation is an established histologic subtype of adamantinoma, the presence of high-grade squamous cell carcinoma is much less common. In this scenario, particularly in an older adult, metastatic carcinoma would be the most likely diagnostic consideration, and neither immunohistochemistry nor molecular testing is a helpful adjunct. Tibial metastasis from carcinomas of numerous distant anatomic sites has been reported, including primary squamous cell carcinomas of the lung, penis, and uterine cervix, among others [14-18]. In addition to metastasis, the histologic differential diagnosis may also include squamous cell carcinoma arising in chronic osteomyelitis [19,20]. In our case, the patient's clinical history of a long-standing tibial mass would be unusual for metastatic disease, and the imaging characteristics suggested an indolent process without evidence of a distant primary malignancy or long-standing chronic osteomyelitis. Although we speculate that this squamous cell carcinoma associated with a (presumably) long-standing adamantinoma in an older adult may represent a slow or delayed form of disease progression in a classic adamantinoma, no prior radiologic images were available for comparison and the patient had no prior biopsy to review to confirm our suspicion.

In summary, we report a case of high-grade squamous cell carcinoma arising within a tibial adamantinoma. As described, it may be challenging to differentiate squamous cell carcinoma arising in adamantinoma from metastatic squamous cell carcinoma, particularly in older adults and in biopsy specimens. However, as the clinical management of tibial metastatic squamous cell carcinoma and tibial adamantinoma may differ significantly, it is critical to differentiate between them. This case highlights the necessity of a multidisciplinary approach in the diagnosis and management of bone tumors, including careful clinical and radiologic correlation, to avoid this potential diagnostic pitfall.

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