Adamantinoma is a rare, malignant biphasic tumor with varied morphological patterns. It is of unknown histogenesis and accounts for approximately 0.5-1% of all primary bone tumors [1, 2]. This lesion was first described by Maier in 1900, and later Fischer [3] in 1913 suggested congenital implantation of epithelial cells to be its origin and named the lesion “adamantinoma of tibia” because of its characteristic resemblance to ameloblastoma, a lesion most commonly seen in jaws. However, recent opinion seems to suggest that adamantinoma is a tumor of epithelial origin, based on ultrastructural and immunohistochemical studies [4].

Adamantinoma and osteofibrous dysplasia

Adamantinoma and osteofibrous dysplasia has been postulated as a potential precursor of adamantinoma. Similarities in the anatomic location, age distribution, and radiological features of osteofibrous dysplasia also add some deal of evidence to this theory which also suggests the evolution of an underlying adamantinoma [5]. The presence of an identifiable epithelial component in osteofibrous dysplasia lesions helps differentiate it from adamantinoma. The existence of a spectrum with adamantinoma at one end and fibro-osseous lesions like osteofibrous dysplasia at the other end has been supported by Czerniak et al. [5].

Etiopathogenesis

Fischer’s congenital implantation of epithelial cells hypothesized the origin to be a cell rest originating during the intrauterine period rather than post-traumatic implantation [5]. Post-traumatic implantation theory supported by Ryrie, Dockerty, and Meyerding 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 irregular repair of this injury which leads to neoplasm formation. Synovial origin theory was supported by Lederer, Sinclair, and Naji. The most widely adopted theory is basal epithelium displacement during embryological development and is supported by the predominant involvement of anterior tibia, where enchondrally formed bone is closest to the skin surface. Based on ultrastructural and immunohistochemical studies, the tumor cells show strong positive staining with pancytokeratin antibody immunohistochemically. This suggests the epithelial origin of adamantinoma [6, 7].

Epidemiology and Clinical Features

Epidemiology and Clinical Features Adamantinoma mostly occurs in the second to fifth decade. It is slightly more common in men than women. The tumor has a predilection for the long bones, specifically, the tibia. The initial symptoms of adamantinoma are often non-specific and depend on location and extent of the disease. The onset is insidious, and its course shows a slow, progressive character. Around 60% of 200 cases reviewed by Moon and Mori had a history of trauma [8].

Abstract

Adamantinoma is a rare, malignant biphasic tumor with varied morphological patterns. Adamantinoma mostly occurs in the second to fifth decade and is slightly more common in men than women. The onset is insidious, and its course shows a slow, progressive character. Radiography is the initial and most reliable imaging modality for adamantinoma of bones because of the tumor’s classic location and appearance on a plain radiograph. Present management modalities which include en bloc resection (mostly intercalary resection) with limb salvage and limb reconstruction. Chemotherapy and radiotherapy have no established role. Amputation does not improve survival but may be advisable in cases with local recurrence and in cases with few large, recurrent lesions where en bloc resection is not possible.

Keywords: Adamantinoma, malignant biphasic tumor, management.
Most of the patients present with swelling with or without pain. The patient may present with bowing deformity of the tibia due to the involvement of anterior tibial surface.

**Radiological Features**

Radiography is the initial and most reliable imaging modality for adamantinoma of bones because of the tumor’s classic location and appearance on a plain radiograph, a typical adamantinoma of the tibia will present as an eccentrically or centrally placed multilocular because of the sclerotic margins of overlapping radioluencies, expansile, well-defined osteolytic lesion (Figure 1) with marginal sclerosis, and variable degree of intralesional septation and opacities. The characteristic “soap bubble” appearance is produced by the multifocal radioluencies surrounded by ring-shaped densities [9]. Even though adamantinoma is commonly found in the diaphyseal region of the long bones, metaphyseal involvement in the form of extensions from the diaphysis or isolated lesions is not uncommon. The lesion is usually intracortical, but the destruction of the cortex and subsequent involvement of the extracortical soft tissues is seen in few cases [4].

**Table 1: Adamantinoma- Summary**

<table>
<thead>
<tr>
<th></th>
<th>Osteofibrous dysplasia</th>
<th>Adamantinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical behavior</strong></td>
<td>Benign</td>
<td>Locoregionally aggressive</td>
</tr>
<tr>
<td><strong>Age of occurrence</strong></td>
<td>Below 20 years</td>
<td>3-86 years</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td>Long bones(tibia and fibula)</td>
<td></td>
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<tr>
<td><strong>Clinical presentation</strong></td>
<td>Pain, pathologic fracture, tibial bowing</td>
<td>With or without pain, occasionally pathologic fracture</td>
</tr>
<tr>
<td><strong>Pre-disposing factors</strong></td>
<td>Absence of trauma</td>
<td>History of trauma is present</td>
</tr>
<tr>
<td><strong>Radiology</strong></td>
<td>- Well-defined intracortical lytic lesion, with variable degree of osteolysis, and osteosclerosis</td>
<td>- Eccentrically or centrally placed, multilocular lesions</td>
</tr>
<tr>
<td></td>
<td>- “Sawtooth appearance”</td>
<td>- Expansile, well-defined osteolytic lesion</td>
</tr>
<tr>
<td></td>
<td>- Anterior tibial bowing</td>
<td>- “Soap bubble” appearance Destruction of cortex and involvement of extracortical soft tissue is not uncommon</td>
</tr>
<tr>
<td></td>
<td>- Pathological fractures</td>
<td></td>
</tr>
<tr>
<td><strong>Histopathology</strong></td>
<td>Loose fibrous background containing spicules of woven bony trabeculae lined by a layer of prominent osteoblasts</td>
<td>Presence of epithelial cells forming small nests/strands recognized in H and E</td>
</tr>
<tr>
<td><strong>Metastatic potential</strong></td>
<td>No</td>
<td>Yes, usually lung and local lymph nodes</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>- Spontaneous regression at puberty</td>
<td>- En bloc resection (mostly intercalary resection) with limb salvage and limb reconstruction</td>
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<tr>
<td></td>
<td>- Careful observation and plain radiography</td>
<td></td>
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<tr>
<td></td>
<td>- Optimizing function</td>
<td></td>
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<tr>
<td></td>
<td>- Treating pain</td>
<td></td>
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<tr>
<td></td>
<td>In cases with pathologic fractures or deformities</td>
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<tr>
<td></td>
<td>Extraperiosteal “shark-bite” excision</td>
<td></td>
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<tr>
<td></td>
<td>Curettage, bone grafting, and internal fixation after deformity correction</td>
<td></td>
</tr>
</tbody>
</table>

**Role of computed tomography (CT) imaging**

CT imaging findings in adamantinoma lesions are non-specific. Cortical involvement and the occasional soft tissue involvement are some of the findings on CT imaging. It also helps in detection of pulmonary metastasis and during routine workup [4]. Magnetic resonance imaging (MRI) is useful in determining soft tissue and intramedullary extension of the lesion and picturing distant cortical foci, thus helping in the local-regional staging of the tumor. Two distinctive morphological patterns have been described by Van der Woude based on MRI findings, namely, single lobulated and multiple small nodules (Figure 2) [10]. Nuclear medicine is a nascent diagnostic modality for adamantinomas. Few characteristic findings suggestive of adamantinoma are increased blood pooling at the site, increased
accumulation of technetium-99m methylene diphosphonate. Bone scan imaging is helpful in detecting simultaneous fibular involvement [11].

**Pathology**

Histologically, epithelial, and osteoblastic components are the two major components of adamantinoma with various other intermingling phases. It has classified into two distinct classic and differentiated types. Classic adamantinoma usually occurs after the second decade of life with an aggressive clinical course. Soft tissue or intramedullary involvement is usually seen in this type. Differentiated adamantinoma (osteofibrous dysplasia like adamantinoma) occurs usually in individuals younger than 20 years of age. It has a relatively benign clinical course.

**Gross appearance**

It presents as a well-defined, yellow-gray or grayish-white and fleshy or firm in consistency, lobulated, and firm to hard cortical lesion with peripheral sclerosis. Differentiated adamantinomas are more solid due to large osteogenic areas. Macrocystic spaces filled with straw-colored or blood-like fluid are occasionally found on gross examination.

**Microscopic appearance**

The timorous cells of the adamantinoma vary in size. Nuclear atypia and mitotic figures are not commonly seen [12]. Several patterns of growth, namely, basaloid, tubular, spindle cell, squamous, and osteoblastic dysplasia type have been described. Nests of basaloid cells are characteristic of classic adamantinoma. Spindle cells, foci of calcification have also been reported in adamantinomas [13].

**Immunohistochemistry**

The epithelial component in all histologic subtypes of adamantinoma shows co-expression of basal cell keratins (14 and 19) and vimentin-64. The immunoreactive behavior of the keratins is independent of the histologic subtypes thereby suggesting a common histogenesis for all them [14-16].

**Cytogenetics**

The presence of extra copies of one or more of chromosomes 7, 8, 12, and 19 has been reported in both classic and differentiated adamantinomas. The support for an osteofibrous dysplasia and adamantinoma relationship is supported by the presence of extra copies of chromosomes 7, 8, and 12 except 19 in cases of osteofibrous dysplasia [17].

**Differential Diagnosis**

Some of the lesions such as aneurysmal bone cyst, unicameral bone cyst, eosinophilic granuloma, osteomyelitis, chondrosarcoma, epithelial metastasis, osteofibrous dysplasia, fibrous dysplasia, non-ossifying fibroma, chondromyxoid fibroma, and hemangioendotheliomashow similar clinicopathological and radiological features and can be considered as differential diagnosis.

**Clinical Behavior**

Usually known to be slow-growing, adamantinomas are locally aggressive with metastatic potential. More often recurrence is due to incomplete resection, and the recurrent lesion has profound similarities to sarcomas. Local recurrence rates range from 18% to 32% [18]. 18-30% of the cases metastasize, lung being the most common site followed by regional lymph nodes and nearby bones [18-20].

**Treatment**

Present management modalities which include en bloc resection (mostly intercalary resection) with limb salvage and limb reconstruction (Figure 3) have shown to have lower local recurrence rates and improved overall survival rates. Vascularized fibular grafts are usually the preferred choice for reconstruction even though distraction osteogenesis, allografts, and metallic replacements are also being used [18, 19]. Chemotherapy and radiotherapy have no established role. Amputation does not improve survival but may be advisable in cases with local recurrence and in cases with few large, recurrent lesions where en bloc resection is not possible.

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