Cancer Association of South Africa (CANSA)

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Fact Sheet on Adamantinoma

Introduction

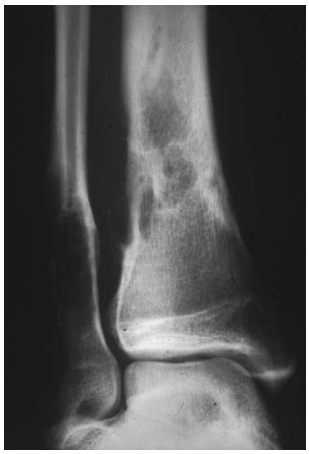
Bone cancer develops in the skeletal system and destroys tissue. It can spread to distant organs, such as the lungs. The usual treatment for bone cancer is surgery, and it has a good outlook following early diagnosis and management.

The two main types are primary and secondary bone cancer. In primary bone cancer, cancer develops in the cells of the bone. Secondary bone cancer occurs when cancers that develop elsewhere spread, or metastasize, to the bones.

Adamantinoma

Adamantinoma

Adamantinoma is a rare bone cancer. It makes up less than 1% of bone cancers. Most of the time, adamantinoma grows in the lower leg. It often starts as a lump in the middle of the shinbone (tibia) or the calf bone (fibula). Adamantinoma can also occur in the jaw bone (mandible) or, sometimes, the forearm, hands, or feet. An adamantinoma lump can be painful, swollen and red, and can cause movement problems.



[Picture Credit: Adamantinoma]

Adamantinoma mostly occurs in the second to fifth decade. The median patient age is 25 to 35 years, with a range from 2 years to 86 years. It is slightly more common in men than women, with a ratio of 5:4. It rarely occurs in children. Adamantinoma is a serious condition. Treatment is important for survival but it is possible to make a full recovery.

Limaiem, F. & Malik, A. 2019.

"Adamantinoma is a rare low-grade malignant bone tumor of uncertain histogenesis which occurs commonly in the diaphyses and metaphyses of the tibia. The term adamantinoma has been given to this tumor due to its histological resemblance to ameloblastoma of the jaws. Its histopathology shows biphasic patterns of epithelial cells and osteofibrous components. There are two types of adamantinoma: the classical and the

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differentiated type, which resembles osteofibrous dysplasia. Despite advances in imaging techniques, the definitive diagnosis of adamantinoma is mainly established by histopathological examination."

Snapshot of Adamantinoma

- An adamantinoma is a rare tumour that occurs most often in boys and young men
- An adamantinoma is a serious condition requiring aggressive treatment
- The cause of this bone tumour is unknown
- An adamantinoma does not respond to some traditional cancer treatments, such as chemotherapy or radiation
- Surgery is usually recommended to remove the tumour
- This kind of cancer spreads to other parts of the body about 20 percent of the time
- The best treatment is surgical removal of the tumour
- Amputation is rare, but it can be necessary in some cases
- Ongoing follow-up care is very important for keeping a child healthy and checking to see if the tumour has grown back
- For most children with adamantinoma, the long-term outlook is very positive

Incidence of Adamantinoma

The outdated South African National Cancer Registry (2016) does not provide any information regarding Adamantinoma.

Causes and Risk Factors for Adamantinoma

The cause of this bone tumour is unknown. Its origin remains controversial.

Ali, N.M., Niada, S., Morris, M.R., Brini, A.T., Huen, D., Sumathi, V. & Latif, F. 2019.

"Adamantinoma and osteofibrous dysplasia (OFD)-like adamantinoma are rare primary bone tumors that are predominantly confined to the tibia. These 2 entities show similarities in location, histology, and radiologic appearance; however, adamantinoma is malignant and therefore differentiating between these bone tumors is essential for optimal patient care. To elucidate their genomic and transcriptomic alteration profiles and expand their etiological mechanisms, whole exome sequencing (WES) and RNA sequencing (RNA-Seq) were conducted on adamantinoma and OFD-like adamantinoma tumors. Copy number variation analysis using WES data revealed distinct chromosomal alteration profiles for adamantinoma tumors compared with OFD-like adamantinomas, allowing molecular differentiation between the 2 tumor subtypes. Combining WES and copy number variation analyses, the chromatin remodelling-related gene KMT2D was recurrently altered in 3/8 adamantinoma tumors (38%), highlighting the potential involvement of deregulated chromatin structure and integrity in adamantinoma tumorigenesis. RNA-Seq analysis revealed a novel somatic gene fusion (EPHB4-MARCH10) in an adamantinoma, the gene fusion was fully characterized. Hierarchical clustering analysis of RNA-Seq data distinctly clustered adamantinoma tumors from OFD-like adamantinomas, allowing to molecularly distinguish between the 2 entities. David Gene Ontology analysis of

differentially expressed genes identified distinct altered pathways in adamantinoma and OFD-like adamantinoma tumors, highlighting the different histopathologic characteristics of these bone tumor subtypes. Moreover, RNA-Seq expression profiling analysis identified elevated expression of DLK1 gene in adamantinomas, serving as a potential molecular biomarker. The present study revealed novel genetic and transcriptomic insights for adamantinoma and OFD-like adamantinoma tumors, allowing to differentiate genetically and transcriptomically between the 2 lesions and identifying a potential diagnostic marker for adamantinomas."

Hua, H.J., Li, K.D., Fang, H.S., Li, H., Zhu, Y., Li, X., Song, G.X., Liu, C., Zhang, Z.H. & Fan, Q.H. 2019.
Objective: To investigate the clinicopathological features and differential diagnosis of adamantinoma of long bone.
Methods: Seven cases of adamantinoma on long bone were selected at Jiangsu Province People's Hospital from June 2012 to May 2018. Clinicopathologic details, immunohistochemical and molecular analysis were performed,and the relevant literature reviewed.
Results: There were 6 males and 1 female patients,age ranging from 21 to 60 years (mean 38 years). Six cases were on the right side and one case was on the left; in five cases the tumors arose from tibia, one from patella and one from humerus. Microscopically,tumour cells were mainly composed of spindle cells arranged in bundles or braids,with irregular epithelial island. Immunohistochemically,the epithelial island expressed high molecular weight cytokeratin but not CK8/18. Both epithelial and spindle components expressed vimentin. One case that was microscopically similar to intraosseous synovial sarcoma did not show SYT gene rearrangement. Clinical follow-up was available for five patients: one patient had axillary metastases seven months after operation, one patient had recurrence 34 months after surgery, 3 patients were uneventful with follow up duration from half a month to 32 months.
Conclusion: Adamantinoma occurring in long bones is very rare. The correct diagnosis requires adequate sample selection, careful morphologic observation, immunohistochemistry and molecular genetics.

Signs and Symptoms of Adamantinoma
The initial symptoms of adamantinoma are often indolent and include swelling with or without pain.

A history of trauma and fracture may be predated to the diagnosis.

Patients may, however, present with:

- Pain
- Swelling
- bowing deformity
- pathological fracture

Metastases especially in the lungs may be observed.

Diagnosis of Adamantinoma
Plain radiography, computed tomography (CT) scanning, and magnetic resonance imaging (MRI) may all be used to help assess suspected adamantinomous tumours. Limitations of plain-film radiography include the relatively long list of differential diagnoses for adamantinoma.

Histologic examination is key to the identification of an adamantinoma; the histologic features of these tumours have many variations.

Chen, J. & Zhang, J. 2019.
"Adamantinoma of the bone is a rare low-grade bony tumor that accounts for less than 1% of all primary bone tumors. On imaging, adamantinoma may be similar to other tumors such as osteofibrous dysplasia, for which the treatment protocol is completely different. Therefore, correct diagnosis and staging of adamantinoma ensures that the patient will undergo appropriate surgery. We present a case of atypical adamantinoma to highlight the fact that adamantinoma should be considered in the differential diagnosis of tibial tumors."

Ali, N.M., Niada, S., Morris, M.R., Brini, A.T., Huen, D., Sumathi, V. & Latif, F. 2019.
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Conclusion: Adamantinoma occurring in long bones is very rare. The correct diagnosis requires adequate sample selection, careful morphologic observation, immunohistochemistry and molecular genetics.

Treatment of Adamantinoma
The best treatment option for adamantinoma is surgery because these tumours do not generally respond to chemotherapy or radiation therapy.

Surgery may include:
- Limb-salvage surgery to help preserve the limb by removing the tumour and some healthy tissue surrounding it
- Amputation if the tumour involves major nerves or blood vessels

Houdek, M.T., Sherman, C.E., Inwards, D.Y., Wenger, D.E. Rose, P.S. & Sim, F.H. 2018.
BACKGROUND: Adamantinomas are rare bone tumors, commonly affecting the tibia. Due to the rare nature of disease, previous studies are small or from multiple centers. The purpose of this study is to investigate outcomes of patients with adamantinoma treated in a single institution.
METHODS: Forty-six histological confirmed adamantinomas of the extremities were reviewed at our institution between 1939 and 2012. Follow-up data included clinical and radiographical information focusing on complications, local recurrence, metastasis, and overall survival after the treatment. The mean follow-up was 16 years (range 2-42 years).
RESULTS: The most common location was the tibia (n = 31). Patients commonly presented with pain and swelling. The mean age was 24 years (7-79 years). Thirty-seven patients were treated with limb salvage. The 39% of patients required a reoperation. The 10-year disease specific- and recurrence free survival was 92% and 72%, with three patients having a recurrence over 15 years postoperative. Older (> 20 years) patients and males were at increased risk of local recurrence ($P < 0.05$).
CONCLUSION: Treatment of adamantinoma of the long bone consists of limb-salvage surgery. Male patients should be cautioned on their increased risk of disease recurrence, and advocate for continued surveillance of patients even greater than 15-years postoperatively due to late tumor recurrence.

Zumárraga, J.P., Cartolano, R., Kohara, M.T., Baptista, A.M., Dos Santos, F.G. & de Camargo, O.P. 2018.
OBJECTIVE: Adamantinoma accounts for less than 1% of the primary bone neoplasms. The tibia is the most affected bone and it is predominant in male patients between the second and third decades of life. The objective of this study is to obtain epidemiological and clinical information on patients with adamantinoma of the tibia treated surgically between 1989 and 2016.
METHODS: Retrospective series of seven patients diagnosed with adamantinoma of the tibia that underwent surgery at the orthopedic oncology service of our hospital. The information was obtained from the medical records and histopathological reports of our institution.
RESULTS: A total of 2870 medical records with histological reports were evaluated. Seven cases of adamantinoma of the tibia were included. The mean age was 28.5 (17-49) years. We found a predominance of females (71.4%) and the most affected side was the left one, with four cases (57.1%). The biopsy revealed bone adamantinoma in four (57.1%) patients, while the diagnosis of the other patients was confirmed after the histological examination of the surgical specimen. All the patients underwent surgery as definitive treatment. No positive margins were reported. No local recurrence (LR) was reported and two patients had distant metastasis (DM).

CONCLUSION: The prognosis of survival in cases of adamantinoma of the tibia is high. The rates of LR and DM were low. Surgical treatment with extensive tumor resection is the treatment of choice. ***Level of Evidence IV, Case Series.***

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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Adamantinoma Picture
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