Cancer Association of South Africa (CANSA)

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Fact Sheet on Adamantinoma

Introduction

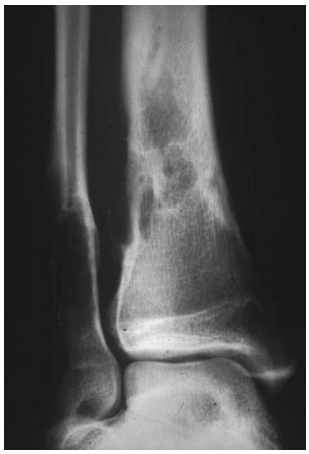
Bone cancer develops in the skeletal system and destroys tissue. It can spread to distant organs, such as the lungs. The usual treatment for bone cancer is surgery, and it has a good outlook following early diagnosis and management.

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., Tafti, D. & Malik, A. 2020.

"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 mandible. 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

Aytekin, M.N., Öztürk, R. & Amer, K. 2020.
Objective: Adamantinomas are rare low-grade malignant bone tumors. This study aims to describe the demographic characteristics and survival rates of patients suffering from adamantinomas.
Methods: The National Institute of Cancer Surveillance, Epidemiology, and Recent Results (SEER) database was used, and patients diagnosed with adamantinoma between 1973 and 2016 were screened. Patients were classified according to sex, age, race/ethnicity, and marital status, and also tumors were classified according to year of diagnosis, laterality, type of treatment, and follow-up.
Results: The mean age of patients was 30.8 ± 16.7 (range: 4-75). A total of 92 patients were identified; of these, 43 were females and 49 were males. The mean follow-up period was 138.1 ± 90.3 (range: 1-156) months. Mean survival duration was 287.8 ± 15.4 (95% CI: 257.7-317.9) months. Five- and ten-year survival rates were 98.8% and 91.5%, respectively. Besides, survival time was also observed to be independent of gender, age groups, race, marital status, tumor location, and year of diagnosis.
Conclusion: Adamantinoma is a very rare bone tumor that affects the long bones in lower extremities and is more common in men. Five- and 10-year survival prognoses are reasonably satisfactory. Also, survival time is independent of variables such as gender, age, and tumor location.

Incidence of Adamantinoma

The outdated South African National Cancer Registry (2017) 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."

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.
"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."

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

Schwarzkopf, E., Tavarez, Y., Healey, J.H., Hameed, M. & Prince, D.E. 2020.
Background and objectives: Adamantinomas are primary, low-grade malignant tumors of the bone that have metastatic potential to the lungs, lymph nodes, and other regions. The rarity of this disease and its nonspecific symptoms complicate diagnosis.
Materials and methods: Records for 20 patients who underwent treatment for adamantinoma from 1975 to 2018 were reviewed for demographic, clinical, and pathological data, treatment details, postoperative complications, and outcomes.

Results: Patients presented at a median age of 22 years (1-79 years): 14 patients had a localized primary tumor, three presented with local recurrence, and three with metastatic disease. Median tumor size was 5.7 cm (0.5-15.5 cm). Wide excision was performed primarily in 15 cases; the remaining five patients underwent intralesional curettage. At a median follow-up of 7.3 years, 14 patients had no evidence of disease; two patients were alive with disease, and four patients died from the disease. Local recurrence and distant metastasis occurred at a median of 11.4 years (6 month-19 years) and 15.8 years (4 month-23 years) after diagnosis.
Conclusions: Adequate histopathological diagnosis is crucial to avoid misdiagnosis of this rare tumor. Local and distant recuAbs_Para_meprrence can occur more than 20 years after the initial diagnosis. Life-long follow-up with clinical examination and imaging is required.

Schutgens, E.M., Picci, P., Baumhoer, D., Pollock, R., Bovée, J.V.M.G., Hogendoorn, P.C.W., Dijkstra, P.D.S., Rueten-Budde, A.J., Jutte, P.C., Traub, F., Leithner, A., Tunn, P.U., Funovics, P., Sys, G., San-Julian, M., Schaap, G.R., Dürr, H.R., Hardes, J., Healey, J., Capanna, R., Biau, D., Gomez-Brouchet, A., Wunder, J., Cosker, T.D.A., Laitinen, M.K., Niu, X., Kostiuk, V., van de Sande, M.A.J.; Adamantinoma Research Group. 2020.
Background: Osteofibrous dysplasia-like adamantinoma (OFD-AD) and classic adamantinoma (AD) are rare, neoplastic diseases with only limited data supporting current treatment protocols. We believe that our retrospective multicenter cohort study is the largest analysis of patients with adamantinoma to date. The primary purpose of this study was to describe the disease characteristics and evaluate the oncological outcomes. The secondary purpose was to identify risk factors for local recurrence after surgical treatment and propose treatment guidelines.
Methods: Three hundred and eighteen confirmed cases of OFD-AD and AD for which primary treatment was carried out between 1985 and 2015 were submitted by 22 tertiary bone tumor centers. Proposed clinical risk factors for local recurrence such as size, type, and margins were analyzed using univariable and multivariate Cox regression analysis.
Results: Of the 318 cases, 128 were OFD-AD and 190 were AD. The mean age at diagnosis was 17 years (median, 14.5 years) for OFD-AD and 32 years (median, 28 years) for AD; 53% of the patients were female. The mean tumor size in the OFD-AD and AD groups combined was 7.8 cm, measured histologically. Sixteen percent of the patients sustained a pathological fracture prior to treatment. Local recurrence was recorded in 22% of the OFD-AD cases and 24% of the AD cases. None of the recurrences in the OFD-AD group progressed to AD. Metastatic disease was found in 18% of the AD cases and fatal disease, in 11% of the AD cases. No metastatic or fatal disease was reported in the OFD-AD group. Multivariate Cox regression analysis demonstrated that uncontaminated resection margins (hazard ratio [HR] = 0.164, 95% confidence interval [CI] = 0.092 to 0.290, $p < 0.001$), pathological fracture (HR = 1.968, 95% CI = 1.076 to 3.600, $p = 0.028$), and sex (female versus male: HR = 0.535, 95% CI = 0.300 to 0.952, $p = 0.033$) impacted the risk of local recurrence.
Conclusions: OFD-AD and AD are parts of a disease spectrum but should be regarded as different entities. Our results support reclassification of OFD-AD into the intermediate locally aggressive category, based on the local recurrence rate of 22% and absence of metastases. In our study, metastatic disease was restricted to the AD group (an 18% rate). We advocate wide resection with uncontaminated margins including bone and involved periosteum for both OFD-AD and AD.
Level of evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

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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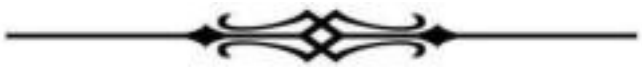

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Adamantinoma Picture
http://www.tumorlibrary.com/case/image.jsp?title=Adamantinoma+-+Tibia+and+fibula+-+X-ray&uri=/case/images/5361.jpg

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