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Original article

Long-term outcome following treatment of Adamantinoma and Osteofibrous dysplasia of long bones

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ABSTRACT

Introduction: Adamantinoma (AD) is an ultimately rare, low-grade malignant bone tumor. In most cases it occurs in the tibia of young adults. Osteofibrous dysplasia (OFD) is a rare, benign, lesion that is typically seen in children. Histopathology, ultrastructure, and cytogenetics indicate that these lesions are closely related. Yet, etiology remains a matter of debate. Local recurrence rates are high for both entities as published in literature and long-term outcomes are scarce, due to the rarity of the disease.
Hypothesis: AD should be treated by En-Bloc resection while ODF can be treated by curettage or by observation. Consequently, the aim of the present study was to answer following questions: Were local recurrence rates of both entities different based on a retrospective review within a tertiary referral center for orthopedic oncology?
Material and methods: In a retrospective cohort study, 10 patients with AD and 5 patients with OFD (including 1 patient with OFD-like-AD) were reviewed. Primary surgeries for patients with AD were: En-bloc resection in 7, curettage in 2 and amputation in 1. In the OFD group, only 2 patients underwent surgery by curettage. Mean follow-up was 16 years (range: 2–47 years). Nine patients had a minimum follow-up of 10 years (mean: 23 years; range: 10–47 years).
Results: Four patients with AD (40%) and 2 patients with OFD (40%) – all of them following surgical removal – suffered from local recurrence. In the "En bloc" resection group of AD, there were 2 LR (29%). All patients of both groups treated with curettage showed LR. One patient with AD had metastasis at time of diagnosis and died of disease. Another patient with AD was diagnosed with metastasis 67 months after surgery and was still alive with disease at latest follow-up (77 month).
Discussion: The overall prognosis of AD and OFD is good, yet local recurrence rates are high, irrespective of surgical strategy. While an internationally standardized treatment regime is still missing, a more radical surgical approach should be considered, especially when treating AD.
Level of evidence: Retrospective study; Level IV.

1. Introduction

Adamantinoma (AD) of long bones is an ultimately rare, primary low-grade and slow-growing primary malignant bone tumor. It represents less than 1% of all primary bone tumors and in most cases occurs in the midshaft of the tibia of adolescents and young adults. In addition, some other cases of AD arising in other long bones across a wide range of age were reported [1–6]. More recently an intermediate lesion named "differentiated adamantinoma" or Osteofibrous dysplasia-like-Adamantinoma (OFD-like-AD) has been described [4,7–9].

Osteofibrous dysplasia (OFD) is a rare, benign, self-limited fibro-osseous lesion that is typically seen in children. It most exclusively involves the midshaft of the tibia with or without involvement of the ipsilateral fibula [1,2,4]. Initial symptoms are often indolent and unspecific and depend on location and extend of the disease. Pain and swelling are the most common initial symptoms. Additionally, 23% of patients present with pathological fractures [2].

Etiology remains on debate. Based on histopathology, similarities in location, patients age, and radiographic appearance, it was hypothetized that AD and OFD were closely related [1,2,4,7,10–14]. Literature is limited to case reports and small series. Thus, recommendations for treatment are scarce. As AD may produce

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metastases, many authors advise wide resection [1–3,15–17]. Throughout literature local recurrence rates are ranging between 16% and 55% while metastasis occurred in 9% to 29% [5,13,18–24].

We reviewed our clinical, radiological and pathological data of all patients treated for AD and OFD in our institution between 1967 and 2009 and investigated the long-term outcome.

Our hypothesis was that AD should be treated by En-Bloc resection while ODF would require a less aggressive treatment either by curettage or simple observation. Consequently, we tried answering the following question: Were local recurrence rates of both entities different based on a retrospective review within a tertiary referral center for orthopedic oncology?

2. Patients and methods

In a retrospective cohort study, we reviewed ten patients with AD, five patients with OFD (including one patient with OFD-like-AD) of long bones (Tables 1 and 2). All medical data and patient files of the prospective Vienna Bone and Soft Tissue Tumor Registry were reviewed. Approval of the respective institutional review board was obtained prior to this investigation.

The mean age was 28 years (range: 5–62 years) and the mean follow-up was 16 years (range: 2–47 years). Nine patients had more than 10 years follow-up (mean: 23 years; range: 10–46 years). Patients with AD had a mean age of 35 years (range: 12–62 years) and a mean follow-up of 20 years (range: 4–47 years). Patients with OFD had a mean age of 15 years (range: 5–62 years) and a mean follow-up of 9 years (range: 2–18 years).

The diagnosis of the tumors was based on clinical and imaging findings and was always confirmed by biopsy and histological analysis. Indication of the respective surgical procedure was based on histology, local extension and anatomical features of the tumor: (i) Lesions that included neurovascular structures were treated by ablative procedures. (ii) In cases of tumor effusion into the joint space or into the epi-metaphyseal area of the bone—thus prohibiting conservation of the affected joint-, segmental resection with endoprosthetic reconstruction was achieved. (iii) When the tumor resection allowed obtaining clear bony margins against the residual joint surface, En-Bloc resections with reconstruction were performed for patients with AD (iv), while small AD lesions or OFDs were eligible for less extensive curettage or biopsy only.

In the AD group, En-bloc resection was performed in seven patients. Reconstruction was performed in five cases (Case 3, 6, 9–12) by transposition of the vascularized ipsilateral fibula (fibula pro tibia), and in another patient, by homologous bone graft (Case 4). In the last patient, En-Bloc resection was followed by implantation of a custom-made modular prosthesis of the proximal femur. Four patients (Case 6, 9, 10, 12) suffered from complications, which led to revision surgery in three patients (Case 9, 10, 12). The patient with the custom made prosthesis suffered of an infection 51 months after surgery, which was successfully treated by one-stage revision. Subsequently this patient sustained a hip dislocation 53 months after surgery, which was successfully treated by open reduction. Curettage was performed in two patients with small lesions. One patient was reconstructed with homologous cancellous bone chips (Case 2) and one with autologous iliac crest (Case 5). One patient (Case 2) suffered of a fracture eight years after surgery followed by pseudarthrosis, which finally had to be treated by osteosynthesis and stabilization with an external fixator. Amputation had to be carried out in one patient (Case 1) due to local extend of the tumor.

In the OFD group, curettage was performed in two patients (Case 8 & 14) followed by reconstruction with cancellous bone chips. One of these 2 patient (Case 8) suffered from osteomyelitis, which was treated by intravenous antibiotics.

Our follow-up protocol included clinical and radiographic examination of the tumor site as well as four monthly chest X-rays during 3 years, six monthly from 3 to 6 years and yearly thereafter. With increasing availability, thoracic/abdominal CT scans and yearly bone scans became systematically incorporated into this algorithm and now represent our standard of care. Advanced local imaging was only applied when there was the suspect of recurrent tumor on standard radiographs. Local recurrence was defined as re-occurrence of a tumor at least 4 months after surgery, whenever microscopically confirmed complete tumor removal has been confirmed by histology for both AD and OFD. All other cases have been defined as residual tumor. Screening for distant metastasis was performed by chest X-rays or chest CT scans.

Function was evaluated at the latest follow-up according to the Musculoskeletal Tumor Society (MSTS) functional scoring system [25].

Histological investigations were all performed by experienced and specialized mucolo-skeletal pathologists. Immunohistochemistry for all patients providing the main differentiation as follows: AD [4,5,8,15,26–28] versus OFD [2,10,19,27,29] and OFD-like-AD [2,7,29,30].

2.1. Statistical methods

Data analysis focused on oncological outcomes of treatment of AD and OFD: Therapeutic (type of surgery) pathological (type of tumor) and demographic (age, sex, and follow-up) variables were examined. Investigated endpoints were death of disease (i.e. death related to the tumor) and local recurrence. Descriptive summary statistics included means and frequencies. Follow-up was calculated from the time of diagnosis to death or last follow-up visit. Local-recurrence-free-survival (LRFS) was calculated from the date of surgery to the date of first local recurrence. All statistical calculations and graphical visualization were made with Excel® for Mac 2011 (Microsoft®).

3. Results

None of the patients died of their underlying disease, except one patient with AD (Case 3) and primary metastasis at time of diagnosis (DOD). Two patients (Case 1 & 2) died of other causes (DOC). Another patient (Case 12) with AD developed lung metastasis 62 months after surgery and is still alive with disease (AWD) after resection of the metastasis at latest follow-up (77 month).

Overall, four patients with AD (40%) and 2 patients with OFD (40%) – all of them following surgical removal – suffered from local recurrence. In the AD group, two out of seven (29%) patients who underwent En-bloc resection experienced LR (Case 6 and 9). One was treated by amputation and one by *en-bloc* resection. In contrast, all patients who underwent curettage finally had a recurrence after an average of 106 months after initial surgery. One (Case 2) underwent iterative curettage with no further local recurrence to date, while the other patient (Case 5) was secondarily treated by *En-bloc* resection and reconstruction with allograft and osteosynthesis at 366 months from the initial surgery (Figs. 1–4). The patient treated by amputation had a residual tumor one month after surgery, which required further resection of the stump.

In the OFD group, two patients (100%) treated with curettage (Case 8 & 14) sustained a local recurrence after a median time of 10 months (range: 6–14 month). One of them (Case 8) presented another recurrence for another three consecutive times and was treated by iterative curettage. In two other patients, who had no surgery (Case 7 & 13), there was no tumor progression until their last follow-up. Also the patient with OFD-like-AD (Case 15) had no surgery and no further progression of disease.