Surgical outcome and oncological survival of osteofibrous dysplasia-like and classic adamantinomas an international multicenter study of 318 cases

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Surgical Outcome and Oncological Survival of Osteofibrous Dysplasia-Like and Classic Adamantinomas

An International Multicenter Study of 318 Cases

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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.

Osteofibrous dysplasia-like adamantinoma (OFD-AD) and classic adamantinoma (AD) are rare bone tumors that occur usually in the anterior aspect of the tibial diaphysis before the age of 30. Together, they account for approximately 0.2% to 0.4% of all primary bone tumors[1-4]. They are recognized as distinct histopathological entities on a

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spectrum[5]. The World Health Organization (WHO) definition of AD is a malignant biphasic tumor characterized by clusters of epithelial cells surrounded by a relatively bland spindle-cell osteofibrous component[4]. Histologically, OFD-AD differs from osteofibrous dysplasia OFD by the inclusion of abundant isolated or small clusters of epithelial cells spread throughout the lesion whereas AD tumors have easily identifiable islands of epithelial tissue. AD is regarded as a malignant lesion with metastatic potential whereas OFD-AD is seen as a variant of AD with a less obvious epithelial component. There is an ongoing discussion about whether OFD-AD should still be considered a subtype of AD[6]. There is controversy regarding the potential for OFD-AD to transform into AD[7]. Proof of this potential would possibly result in different treatment strategies. Currently, it is important to clearly distinguish OFD-AD and AD histologically as treatment and follow-up strategies may differ[7].

Adamantinomas are usually found in the anterior tibial cortex with occasional involvement of the ipsilateral fibula (Fig. 1). The origin of adamantinoma remains disputed; however, the most favored hypotheses are epithelial cell transfer during embryological development or direct trauma to the anterior cortex of the tibia where it is closest to the skin[8,9].

Current treatment strategies for OFD-AD include observation, curettage, and resection[10]. AD is usually treated according to oncological principles for a malignant tumor. Yet, despite wide surgery, the reported prevalence of local recurrence is reported to range from 20% to 30%[1,7]. It is not clear which factors contribute to this high recurrence rate or if there are factors that predict the likelihood of local recurrence.

The goals of this multicenter retrospective cohort study were to (1) describe the treatment and outcomes in the largest cohort of OFD-AD and AD cases of which we are aware, with a minimum of 2 years of follow-up; (2) determine which factors contribute to local recurrence and the development of metastatic disease; and (3) provide insights regarding the hypothesized progression of OFD-AD to AD based on the data set.

Materials and Methods

A multicenter retrospective database analysis was set up. Surgeons and histopathologists from orthopaedic oncological centers around Europe, North America, and Asia were asked to provide data on histologically proven cases of OFD-AD and AD. Centers were invited to participate at European Musculo-Skeletal Oncology Society (EMSOS) and International Society of Limb Salvage (ISOLS) meetings. For each identified case, information was entered into a database (Table I). All consecutive cases that had been histopathologically proven and treated between 1985 and 2015 were included.

OFD-AD was defined as the presence of solitary epithelial cells staining positive on immunohistochemical analysis for keratin within osteofibrous stroma[11]. AD was diagnosed when clusters of epithelial cells were present[12]. The final diagnosis established by analysis of the surgical resection specimen was used as the diagnosis entered into the database. The criteria for inclusion of cases were an unequivocal histological diagnosis of OFD-AD or AD and 2 years of follow-up after the first surgical treatment.

Twenty-two specialized tertiary bone tumor centers provided a total of 322 cases for inclusion into the EMSOS+ adamantinoma database.

Statistical Analysis

Univariable and multivariate Cox regression analyses were performed to investigate the relationship between risk factors and

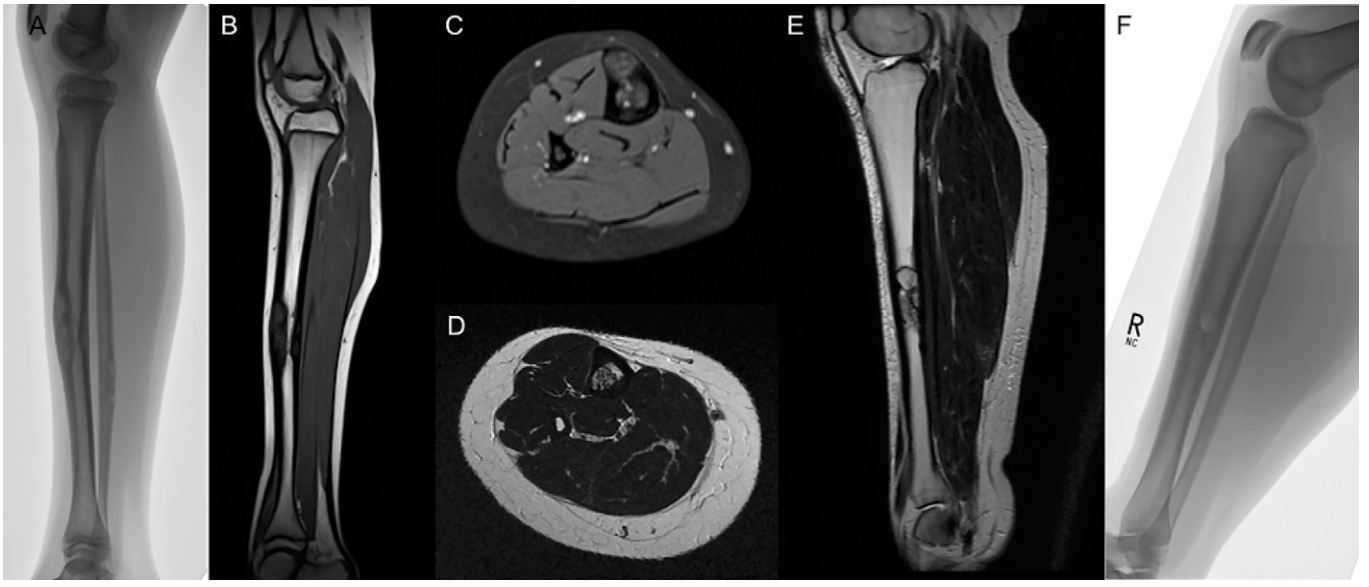

Fig. 1

Lateral radiograph (**Fig. 1-A**), sagittal T2-weighted MRI (**Fig. 1-B**), and axial T1-weighted MRI (**Fig. 1-C**) of a 9-year-old girl with OFD-AD and axial and sagittal T2-weighted MRIs (**Figs. 1-D and 1-E**) and lateral radiograph (**Fig. 1-F**) of a 42-year-old woman with AD.

TABLE I Patient Characteristics Collected

Characteristic	Collected Data
Patient	• Sex (m/f) • Relevant medical history (any) • Date of diagnosis (dd/mm/yyyy) • Age at diagnosis (months) • Trauma history (y/n) • History of pain (y/n) • Duration of pain (months) • Pathological fracture (y/n) • History of biopsy (y/n)
Radiographic	• Imaging modality used for reporting radiographic characteristics (radiograph, CT, MRI) • Gadolinium-enhanced scanning (y/n) • Positive on gadolinium-enhanced scanning (y/n) • Size of lesion (widest diameter in cm) • Number of lesions • Medulla involvement (none, partial, complete) • Extracortical expansion (y/n) • Periosteal involvement (y/n) • Soft-tissue expansion (y/n)
Treatment	• Planned treatment type (intralesional, narrow, wide resection) • Reconstructive treatment (e.g., allograft) • Perioperative exposure of lesion (y/n) • Uncontaminated resection margins at surgery (y/n) • Periosteal resection (none, partial, complete) • Biopsy track resection (y/n)
Macroscopic	• Left/right • Location of lesion (e.g., tibia) • Region within bone (e.g., diaphysis) • Location within region (e.g., proximal) • Location on clock (e.g., 12 o'clock on axial image) • Number of lesions • Size of lesion (widest diameter in cm) • Lesion type (singular, multiple) • Periosteal involvement (none, partial, complete) • Soft-tissue expansion (y/n)
Histological	• Histological diagnosis (OFD-AD, AD) • Keratin-positive cell arrangement (e.g., clusters) • Uncontaminated resection margins (y/n) • Extracortical expansion (y/n) • Periosteal involvement (y/n) • Soft-tissue expansion (y/n)
Outcome	• Local recurrence (y/n) • Recurrence histologically confirmed (y/n) • Time to recurrence (months) • Metastatic disease • Location and amount of metastases • Time to metastasis (months) • Fatal disease • Time to fatal disease (months)

local recurrence. Risk factors of interest were sex (female versus male); tumor size (≤5 versus >5 cm); pathological fracture (yes versus no); age (<18 versus ≥18 years); AD (yes versus no); perioperative spillage (yes versus no); uncontaminated resection margin (yes versus no); and high-volume center, arbitrarily defined as a center contributing ≥20 cases (yes versus no).

All risk factors were studied using univariable Cox regression analyses. Death was not considered a competing event since only 3 patients died without local recurrence.

Based on clinical expertise and the findings of the univariable analyses, a multivariate Cox regression analysis was conducted using sex, tumor size, pathological fracture,

uncontaminated margins, and AD (versus OFD-AD) as covariates.

Statistical analysis was carried out using SPSS version 22 (IBM) and R version 3.5.1 (R Foundation for Statistical Computing).

Ethical Consideration

This study was conducted according to the Declaration of Helsinki (October 2013) and approved by the institutional review board of the Leiden University Medical Center (March 10, 2016; G16.012).

Results

Four cases in which the histopathological diagnosis remained doubtful were excluded from further analysis, leaving 318 cases for the study. The overall study group demographics are presented in Table II. A higher percentage (59.7%) of the included patients had AD. The mean age at diagnosis was 17 years (median, 14.5 years; range, 1 to 65 years) in the OFD-AD group compared with 32 years (median, 28 years; range, 1 to 81 years) in the AD group. The average tumor size, as measured macroscopically, was 7.8 cm (median, 7 cm; range, 0.5 to 26 cm) in the 2 groups combined, 7.2 cm (median, 6 cm; range, 0.6 to 22 cm) in the OFD-AD group, and 8.4 cm (median, 7 cm; range, 0.5 to 26 cm) in the AD group. There was local recurrence of 28 (21.9%) of the OFD-AD tumors and 46 (24.2%) of the AD tumors.

Data Included in Regression Analysis

Of the 318 patients, 60 with missing information regarding local recurrence were excluded, leaving 258 patients for further statistical analyses. The biopsy-based diagnosis matched the diagnosis based on the resection specimen in all cases in this subset. The characteristics of this data set are presented in Table III. In this subset, 40% of the patients were <18 years of age at the time of inclusion and 17% of the patients had a pathological fracture. The mean tumor size was 7.8 cm in the OFD-AD and AD groups combined. Histopathologically demonstrated tumor-free resection margins were reported in 67% of the cases, whereas this information was missing or the data were inconclusive in 10%. The median follow-up was 83 months (95% confidence interval [CI]: 75 to 103 months). Of the 258 patients included in the risk analysis, 18 died of AD (with 15 of the 18 having local recurrence), 73 developed a local recurrence, and 24 developed distant metastases (usually in the lungs) (Table III).

Data on risk factors were incomplete for multiple variables (see Appendix 1). All available information was used for the univariable Cox analysis, whereas a subset of patients with complete information on all covariates (n = 210) was used for the multivariate Cox regression analysis.

Clinical Presentation

Patients often presented to an orthopaedic clinic with deformity, pain, and a palpable lesion of the anterolateral aspect of the tibia. There was a history of pain in the majority of cases

TABLE II Patient Demographics for All Cases Submitted to the EMSOS+ Database with a Known Diagnosis of Adamantinoma

Diagnosis	Total	OFD-AD	Classic AD
No. (%)	318 (100)	128 (40.3)	190 (59.7)
Patient demographics			
Mean age* *(yr)*	26 ± 17.8	17 ± 11.6	32 ± 18.8
Sex: male/female *(%)*	47/53	39/61	53/47
Tumor characteristics			
Lesion size* *(cm)*	7.8 ± 5.0	7.2 ± 4.6	8.4 ± 5.2
Lesions *(no. [%])*			
Single	185 (58.2)	92 (71.9)	93 (49.0)
Multiple	63 (19.8)	30 (23.4)	33 (17.4)
Missing	70 (22.0)	6 (4.7)	64 (33.7)
Radiographic findings *(no. [%])*			
Tibial location	305 (95.9)	125 (97.7)	180 (94.7)
Diaphyseal location	230 (72.3)	101 (78.9)	129 (67.9)
Microscopic periosteal involvement	106 (33.3)	39 (30.5)	67 (35.3)
Reported pathological fracture	51 (16.0)	23 (18.0)	28 (14.7)
Outcome *(no. [%])*			
Local recurrence	74 (23.3)	28 (21.9)	46 (24.2)
Metastatic disease	35 (11.0)	0	35 (18.4)
Fatal disease	20 (6.3)	0	20 (10.5)

*The values are given as the mean and standard deviation.

TABLE III Demographics of 258 Patients Included in Statistical Analysis

Diagnosis	Total	OFD-AD	Classic AD
No. (%)	258 (100)	117 (45.3)	141 (54.7)
Patient demographics			
Mean age* *(yr)*	25.6 ± 17.8	16.7 ± 11.4	33.0 ± 18.8
Sex: male/female *(%)*	47/53	38/62	54/46
Tumor characteristics			
Lesion size* *(cm)*	7.6 ± 4.8	6.6 ± 4.1	8.5 ± 5.1
Pathological fracture *(no. [%])*			
No	183 (70.9)	90 (76.9)	93 (66.0)
Yes	45 (17.4)	22 (18.8)	23 (16.3)
Missing data	30 (11.6)	5 (4.3)	25 (17.7)
Uncontaminated margins at index treatment (R0) *(no. [%])*			
No	59 (22.9)	34 (29.1)	25 (17.7)
Yes	174 (67.4)	76 (65.0)	98 (69.5)
Inconclusive/missing data	25 (9.7)	7 (6.0)	18 (12.8)
Primary surgical treatment type (intention) *(no. [%])*			
Amputation (R0)	12 (4.7)	0 (0.0)	12 (8.6)
Intralesional resection (R2) (intentional) incl. curettage	43 (16.7)	27 (22.7)	16 (11.5)
Marginal surgical resection (R0)	58 (22.5)	37 (31.1)	21 (15.1)
Wide surgical margins (R0)	145 (56.2)	53 (45.3)	92 (65.2)
Oncological outcome *(no. [%])*			
Local recurrence	73 (28.3)	28 (23.9)	45 (31.9)
Metastasis	24 (9.3)	0 (0.0)	24 (17.0)
Fatal disease	18 (7.0)	0 (0.0)	18 (12.8)

(OFD-AD: 60%, AD: 72%), often for >1 year (mean, 16 months), and 16% presented with a pathological fracture. A history of trauma to the site of tumor was reported in only 33% of the OFD-AD cases and 25% of the AD cases.

Tumor Location

In the entire data set of 318 cases, 99% of the OFD-AD tumors were located in the tibia, the fibula, or both osseous sites. One case was located in the ulna. Ninety-eight percent of the AD tumors were found in the tibia, the fibula, or both locations. There were 3 cases in the femur, 2 cases in the humerus, and 1 case in the foot. No tumors in the spine were reported. Most tibial tumors were in the anterolateral aspect of the diaphysis. Very few cases were found in the metaphysis, and even fewer were in the epiphysis (Fig. 2).

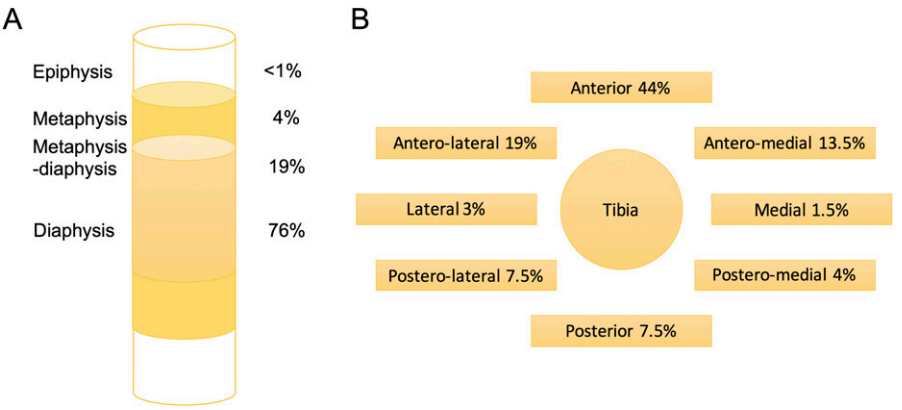

Fig. 2

Proportionate locations within the long bones for OFD-AD and AD cases (**Fig. 2-A**) and axial locations where the tumors were located within the tibia (**Fig. 2-B**).

TABLE IV Multivariate Cox Regression Model Outcomes for Local Recurrence

Variable	HR	95% CI	P Value
Sex: female vs. male	0.535	0.300-0.952	0.033*
Size: >5 vs. ≤5 cm	1.384	0.734-2.608	0.315
Pathological fracture: yes vs. no	1.968	1.076-3.600	0.028*
Uncontaminated resection margins (R0): yes vs. no	0.164	0.092-0.290	<0.001*
AD vs. OFD-AD	1.549	0.849-2.828	0.154

*Significant.

Local Recurrence

The results of the univariable analysis are available in Appendix Table E1. Those of the multivariate Cox regression (Table IV) demonstrated a significant hazard ratio (HR) of 0.164 (CI = 0.092 to 0.290, $p < 0.001$) for uncontaminated resection margins.

The unadjusted cumulative incidence of local recurrence significantly differed between AD and OFD-AD (Fig. 3). At every time point, the unadjusted cumulative incidence of local recurrence was higher if a pathological fracture was reported (Fig. 4-A). The unadjusted cumulative incidence of local recurrence was also higher if resection margins were contaminated (Fig. 4-B), much higher when perioperative spill was reported (Fig. 4-C), and higher for male patients at all ages (Fig. 4-D). The unadjusted cumulative incidence of local recurrence did not significantly differ in patients under the age of 18 years, and no difference was seen between centers where ≥20 and <20 patients were treated (see Appendices 2 and 3).

Metastatic Potential

Metastatic disease was restricted to the AD group, in which 24 patients developed metastatic disease (with the majority presenting in the lungs), representing 9.3% of the analyzed subset data subset and 17.0% of all AD cases (Table III). Only 4 of these 24 patients had no prior local recurrence. The time to diagnosis of metastatic disease is demonstrated in Figure 5. Most of the patients with metastatic disease were adults (mean age, 39 years; median, 33 years; range, 20 to 68 years), with only 2 patients under the age of 18 (9 and 12 years old).

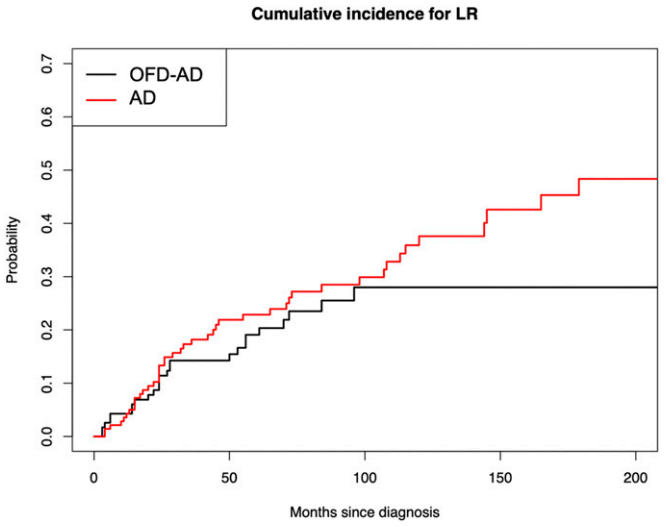

Fig. 3

Unadjusted cumulative incidence of local recurrence (LR) of OFD-AD versus AD in the months following treatment.

Fatal Disease

Eighteen patients died of the disease, representing 7.0% of the analyzed data subset and 12.7% of the AD cases. Of the 24 patients with metastasis, 16 died of the disease and 8 patients were alive with metastases at the time of submission of the data set. All of the patients who died in the series had metastatic AD.

Progression of OFD-AD to AD

One patient who showed progression of an untreated OFD-AD to AD was identified. This case was initially diagnosed as OFD in 1987 and was followed using radiographs for several years, after which the patient was lost to follow-up. In 2016, the patient returned to the clinic with a painful new swelling in the tibia that was diagnosed as AD in a larger area of OFD-AD (Fig. 6). Additional imaging and histological findings are presented in Appendix 4. Hatori et al. described a very similar case, in a patient treated at a young age for OFD-AD who presented more than a decade later with painful progression in the same area that was diagnosed as AD after resection[13].

Discussion

These results offer interesting insights into the outcomes of treatment of OFD-AD and AD. The greatest strength of this data set is that it represents the largest collection of adamantinoma cases in the scientific literature, to our knowledge, with a median follow-up of 83 months (95% CI = 75 to 103 months) and inclusion of a subgroup (n = 87) with long-term follow-up (>10 years).

Several other adamantinoma series have been published in the literature (see Appendix Table E2), with the majority focusing on AD. In those series, the rates of metastatic disease ranged from 0% to 43% and the rates of fatal disease, from 0% to 33%. Before 1989, no distinction was made between OFD-AD and AD in the literature. Only 36 cases of OFD-AD are reported on in all of the published series combined. Our study strongly surpasses this number.

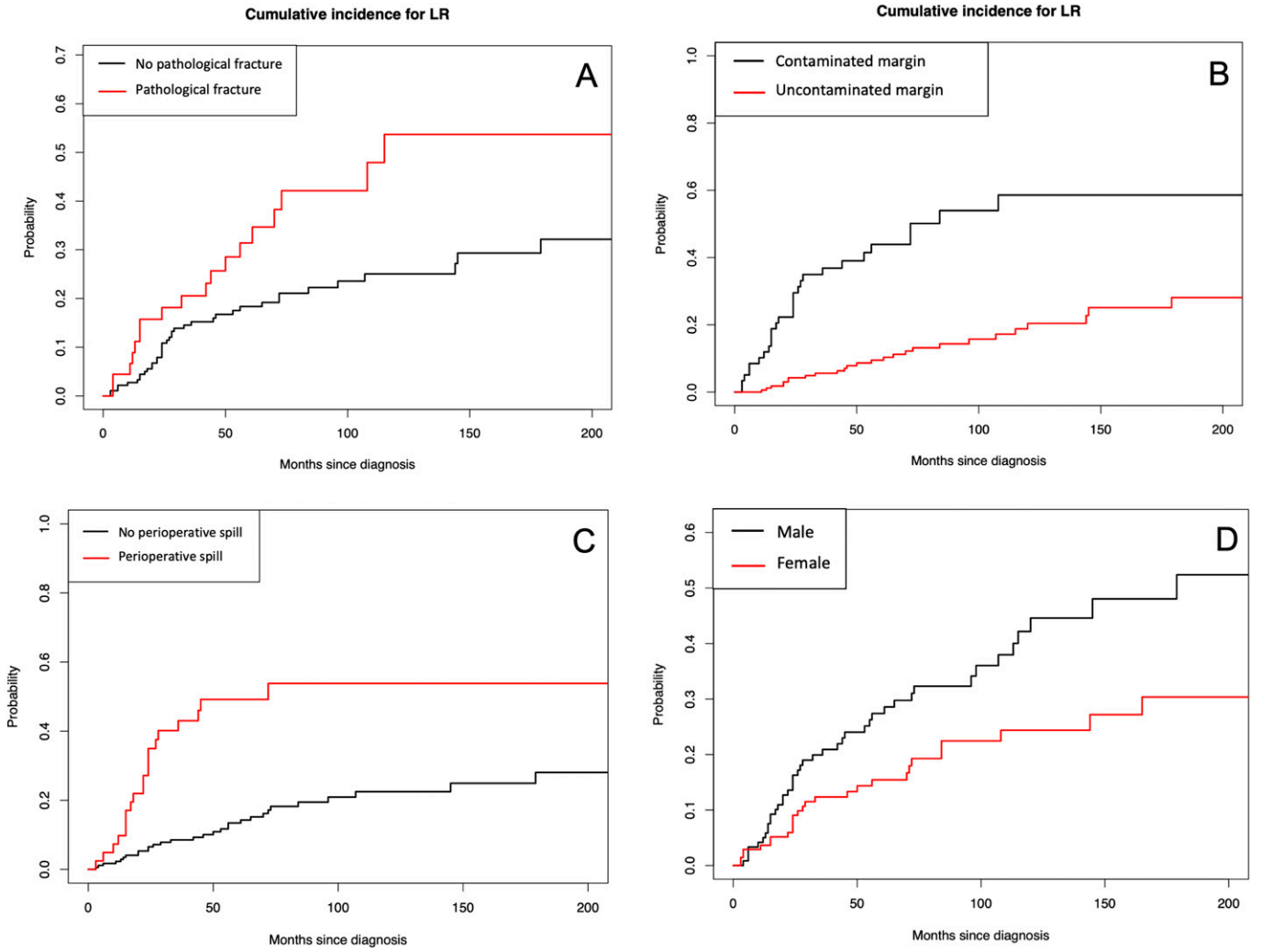

Fig. 4

Unadjusted cumulative incidence plots for local recurrence (LR) of OFD-AD and AD combined, comparing a history of pathological fracture versus no history of pathological fracture (**Fig. 4-A**), contaminated versus uncontaminated surgical margins according to the histopathology report (**Fig. 4-B**), no perioperative spill versus perioperative spill (**Fig. 4-C**), and female versus male sex (**Fig. 4-D**).

The WHO classification distinguishes among OFD, OFD-AD, and AD. It is now well established that AD is malignant, which is supported by the data from our series. The malignant potential of OFD-AD is not completely understood in the literature as it does not metastasize but is locally aggressive[14]. Results from this study clearly confirm the locally aggressive, non-metastatic behavior of OFD-AD in 128 cases. Within this data set, only 1 OFD-AD case was left untreated for a longer period of time and it showed progression to AD after 29 years (see Appendix 4).

Reduction in Local Recurrence

The observed local recurrence rate for the OFD-AD and AD cases combined was 28%. We have demonstrated that the risk of local recurrence is multifactorial. These risks can be divided into modifiable and non-modifiable. The latter include patient sex, tumor size, and disease type. With regard to modifiable factors, we suspect that the risk of local recurrence after surgery may be reduced by preventing pathological fracture after diagnosis and achieving uncontaminated margins with resection. Patients in this study were not treated with adjuvant chemotherapy or radiation therapy as there is currently little evidence to support those interventions[15].

Twenty-eight patients (OFD-AD: 9, AD: 19) who had uncontaminated margins (according to the histological report) at resection experienced local recurrence. We presume that a proportion of these recurrences were due to undetected skip lesions as well as the possible presence of disease in the periosteum. This would underline the importance of an uncontaminated resection of the involved bone including the periosteum at the time of surgery.

Study Limitations

We recognize that the quality of the histopathological reports determines the quality of our data. Some reports were several

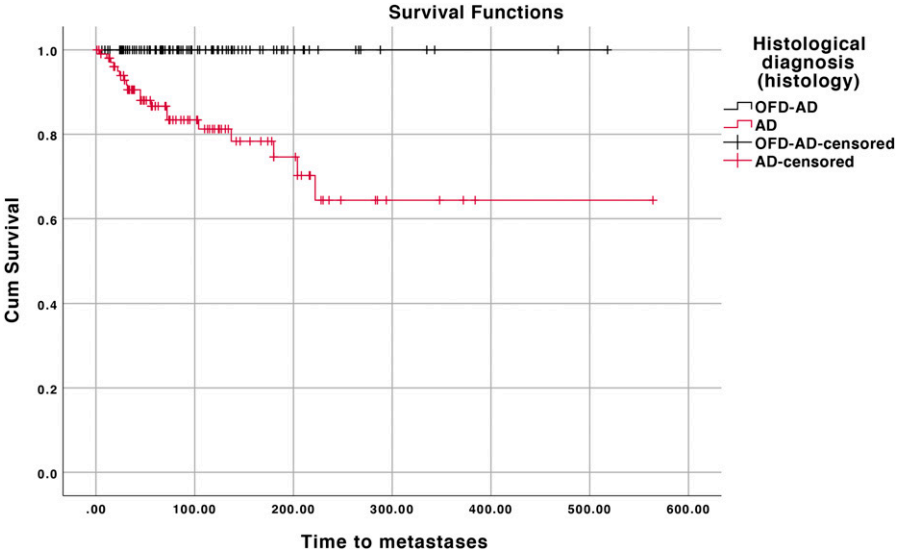

Fig. 5

Kaplan-Meier plot showing time (months) to detection of metastasis stratified by OFD-AD and AD. Cum = cumulative.

decades old. To remedy this, it would have been necessary to carry out a central histopathological review of the original specimen blocks at a single center. For this study, it was only possible to re-review a sample of 136 cases (70 OFD-ADs) provided by 4 centers, and this showed no changes compared with the submitted data. Excluding the cases that were not reconfirmed would have substantially reduced the numbers available to study.

This study was exploratory in nature. We conducted multiple univariable analyses to investigate risk factors before deciding on a multivariate model. With this approach multiple comparisons are made, and the final multivariate model may be subject to overfitting and must be interpreted with caution. The results may not be translatable to other centers; they can, however, stimulate future research.

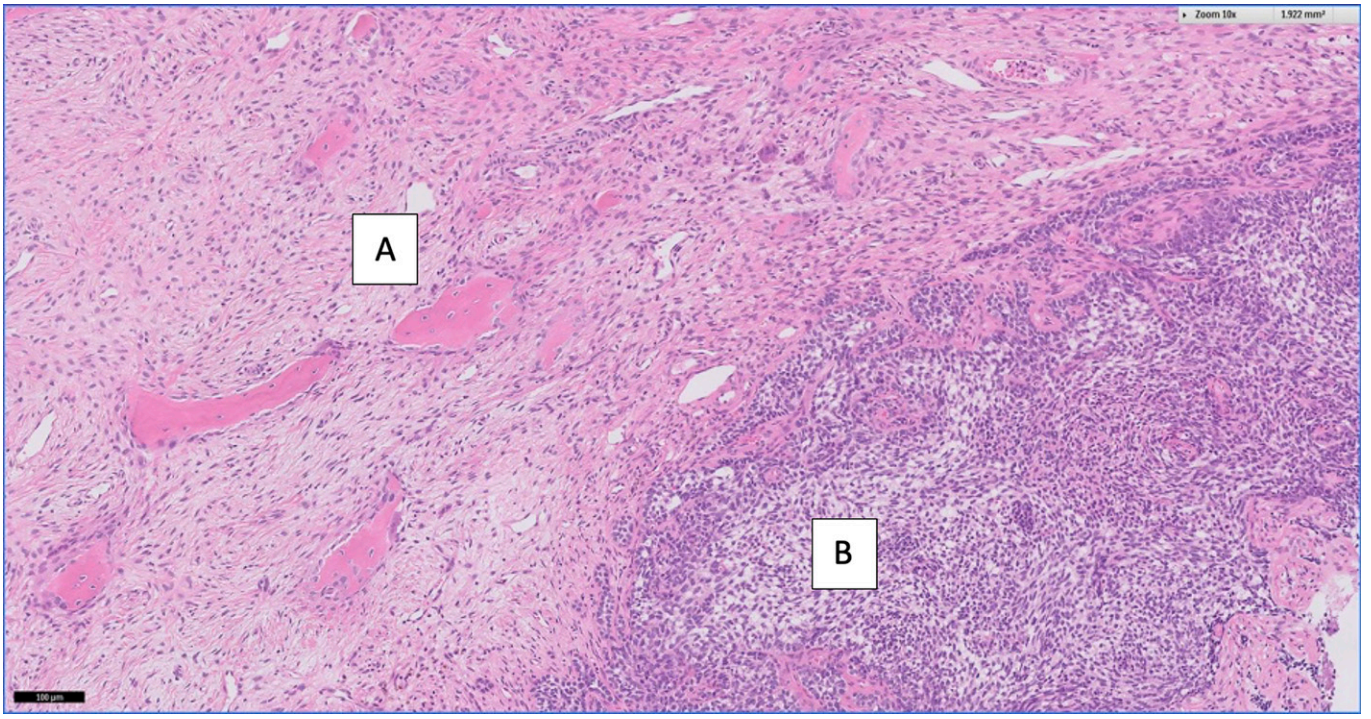

Fig. 6

Hematoxylin and eosin-stained slides of a resection specimen removed in 2016 showing an area of OFD-AD (A) surrounding an area of AD (B). The black bar in the left lower corner represents 100 μm.

Another limitation of our study is the long time period in which the data were collected. There may be differences in outcomes for patients treated at different times for which we did not account.

Treatment Guidelines

AD is a malignant entity that requires wide surgical resection including the periosteum (which was involved in 38.8% of the cases in our series), after complete preoperative analyses including radiographs, magnetic resonance imaging (MRI) of the involved bone, representative biopsy, and computed tomography (CT) of the chest in AD cases. Follow-up should be long-term with at least chest radiographs (the lungs are the most likely site for metastasis) and local radiographs or MRI of the surgical site, as 5 (11%) of the 45 local AD recurrences were diagnosed after >10 years of follow-up in this series.

We recommend that, if surgical treatment is undertaken for OFD-AD, it be personalized to the patient's requirements. We suggest marginal but R0 resection to reduce the risk of local recurrence. As OFD-AD should be regarded as a locally aggressive but benign disease, the timing of surgical resection can be tailored to the preference of the patients (and parents) and should take into account the growth potential of the involved bone but also the risk of fracture, bone deformity, and pain. When even a marginal resection might cause substantial functional deficits, especially in the growing skeleton, surgery may be postponed as the metastatic potential is extremely small and progression to AD is exceedingly rare. Delaying surgery, while performing close follow-up, may be an option. When performing a surgical resection, one should also anticipate the growth of small and possibly undiagnosed skip lesions. At some centers, intralesional resection has been associated with a significantly higher risk of local recurrence and thus of a reoperation[1,7,16,17]. For very young patients, one should consider planning the resection after the age of 6 to 8 years, before which there should be careful observation with consideration of protected weight-bearing if appropriate.

Reclassification of OFD-AD

In the current WHO classification, OFD-AD is considered a subtype of AD and both are considered malignant. Our data support considering OFD-AD to be locally aggressive instead of having full malignant potential. Evidence of this includes no reported cases, in the literature—to our knowledge—or in our series, of metastatic disease in patients with OFD-AD and a very low prevalence of progression of OFD-AD to AD. We identified 1 case of such progression and Hatori et al.[13] described another. In addition, OFD-AD presents at an earlier age than AD; therefore, our demographic data also support considering OFD-AD and AD as 2 separate entities within a single spectrum.

Conclusions

Our series from 22 different bone tumor referral centers provides evidence that AD has full malignant potential. Our exploratory study suggests that patients with AD could benefit from aggressive surgical treatment involving uncontaminated-margin resection, where possible, at the earliest possible opportunity. Our series confirmed the locally aggressive behavior of OFD-AD without metastatic potential. We therefore recommend an uncontaminated-margin resection, but the timing can be amended to optimize functional reconstruction. Waiting for further skeletal maturity may be an option in some cases, especially in metaphyseal locations, and be indicated to facilitate surgical reconstruction in very young patients. As OFD-AD should be considered locally aggressive and of low metastatic potential, the benefits of increased bone stock should be weighed against the risk of progression in size, pathological fracture, and decreased remodeling capacity after allograft/autograft reconstruction. We highlight the importance of long-term follow-up for both entities, as tumors of this type have recurred up to 20 years after primary treatment.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/G66). ■

NOTE: In addition to the authors listed in the byline, members of the Adamantinoma Research Group include Reinhard Windhager, MD, PhD; Guido Scoccianti, MD; Eric Mascard, MD; Anthony Griffin, MSc; Zhiping Deng, MD; Andreas Krieg, MD, PhD; Olivera Calukovic, MSc; Rianne Schoo, MD; and Robert van der Wal, MD.

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