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Chapter 6

MR imaging of atypical cartilaginous tumour/grade I central chondrosarcoma after curettage and phenol application; recommendations for follow-up.

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Abstract

Postoperative characteristics of uncomplicated recovery after curettage for atypical cartilaginous tumour (ACT)/grade I central chondrosarcoma or the presence/development of residual or recurrence of tumour remain difficult. We reviewed 75 cases of patients, who were treated by intralesional curettage, phenol and donor bone grafting. The first postoperative Gd-enhanced MR imaging was performed within one year after surgery. With a minimum of two scans and a mean follow-up of 72 months (range 13-169 months), patients underwent a second intervention in case of suspected lesions. These were defined as fast enhancement of the lesion or nodules increasing in size in time. The low threshold to plan a second intervention in case of suspicious lesions on the postoperative MR images can be explained due to the period (from 1994) the patients were treated for the cartilaginous lesions. Either radiofrequency ablation or curettage, phenol and bone grafting were used, depending on the size of the lesion (<10 mm or ≥10 mm). In 14 patients (18.6%) a second intervention was assessed after a mean period of 59 months (range 8-114), of whom six patients had histologically proven recurrence (8%). No upgrading in tumour grade was seen at time of recurrence. Based on the experiences in this study, we could outline a classification of four patients groups, with a different follow-up intensity and treatment. This resulted in a flow diagram for a proper and safe follow-up for this specific patient group.

Introduction

Primary central chondrosarcoma accounts for about 20% of malignant bone tumours, and is the third most common primary sarcoma after myeloma and osteosarcoma. The tumour can develop in any bone that derived from enchondral ossification and most of them are diagnosed by coincidence following radiological survey for other reasons. The pelvis, femur and humerus are the most frequently affected bones, whereas the small bones of the hands and feet are rarely involved (1% of all chondrosarcomas). Patients with atypical cartilaginous tumour (ACT)/grade I central chondrosarcoma of the long bones have been treated for years in the recent past with wide resection and reconstruction. This kind of surgery is associated with proper local control, but
often impairs limb function due to the sacrifice of a significant segment of bone or joint. Nowadays, intralesional curettage in combination with at least one adjuvant (cryosurgery, phenol or polymethylmetacrylate (PMMA) and donor bone grafting (not in case of PMMA) is state of the art in the treatment of ACT/grade I central chondrosarcoma. The bone graft may contain some cartilage from the femoral head surface. This less invasive technique is associated with fewer postoperative complications and a reported local recurrence rate of 7.5%. Application of phenol after the curettage was shown to be beneficial in reaching tumour control in vitro as well as in vivo. The sensitivity for diagnosis for static contrast enhanced MRI has been established and is not controversial in literature anymore. Subsequently, the sensitivity for grading was found to be higher in a setting using dynamic contrast-enhanced imaging which is the recommended method of choice currently and is used in this study. One of the challenges is to differentiate normal postoperative changes from development of local recurrence in the area of the bone graft. However, there is limited literature on postoperative findings in patients after intralesional curettage of ACT/grade I chondrosarcoma. The published data are hard to interpret due to small patient series and different case mixes (differences in location, tumour grade and the type of adjuvant used). In addition, the optimal frequency and timing of imaging during postoperative follow-up is yet unknown.

The purpose of this retrospective study is to identify MR imaging features of local residual or recurrent disease and normal postoperative changes after intralesional treatment of ACT/grade I chondrosarcoma, and to design a flow chart for different treatment options in case of suspicious lesions on MR imaging.

**Materials and methods**

**Study population**

Between 1994 and 2005, 75 consecutive patients with a histologically proven ACT/grade I central chondrosarcoma of long bones were treated at the Leiden University Medical Center. Diagnosis was established by histological biopsy (45% one-stage, 55% two-stage). Histological criteria were the ones applied according to the 2013 WHO classifications and all histological diagnosis were reviewed. Diagnostic work-up was according to the ESMO guidelines. Pre-operatively, a Gd-MRI scan
was performed. All patients underwent intralesional curettage followed by the use of phenol 85% and ethanol 96% to destroy any tumour cells remaining after curettage. Subsequently, the bone cavity was filled with donor bone chips obtained from donor femoral heads (Dutch Bone Bank Foundation, Leiden, The Netherlands). The study population consisted of 27 male and 48 female patients; mean age at surgery was 47.1 years (range 15-70 years). Lesions were located in the femur 37 (49%), humerus 24 (32%), tibia 6 (8%), fibula 5 (7%), ulna 2 (3%) and radius 1 (1%). All patients underwent conventional radiography (Table I) and at least two postoperative MR scans. Two independent observers retrospectively reviewed all conventional radiographs and MR imaging studies. In case of discrepancy the two observers re-evaluated the case in concert to see if they could reach a consensus view on the case. A second treatment was performed when local recurrence was suspected on MR imaging during follow-up. Local recurrences were treated by radiofrequency ablation (lesion size <10mm) or with repeated intralesional curettage, phenol and bone grafting (lesion size ≥10 mm).

<table>
<thead>
<tr>
<th>Table 1. Overview of Imaging follow-up protocol</th>
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<tbody>
<tr>
<td>time, post-operative</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>before discharge</td>
</tr>
<tr>
<td>6 weeks</td>
</tr>
<tr>
<td>12 weeks</td>
</tr>
<tr>
<td>6-12 months*</td>
</tr>
<tr>
<td>2 years#</td>
</tr>
</tbody>
</table>

* Introduced since 2003 as baseline MRI
# After 2 years, follow-up continues annually or every two years.

Conventional radiography

Conventional radiographs were obtained in two directions. The images were reviewed in order to evaluate the consolidation of the bone window, the incorporation of the bone graft and signs suggestive for local recurrence or residual disease (e.g. increasing focal radiolucent areas or chondroid matrix mineralization).
MR imaging

The MR studies consisted of standard T1- and T2-weighted fat-suppressed MR images, dynamic contrast-enhanced imaging as well as static late contrast-enhanced T1-weighted MR images with fat suppression. All MR images were acquired on a Philips 0.5 (T5-II; Philips Medical Systems) or 1.5T (NT; Philips Medical Systems) MR system using a surface coil.

We assessed the appearance of any enhancement areas in the treated region within the medullary cavity and the consolidation of the bone window. In time, increasing, decreasing of the enhancement and decreasing of postoperative edema, or the occurrence of new lesions suspicious for recurrence of chondrosarcoma were scored.

Results

Patients group

All patients received at least two MR studies during follow-up (range 2-8) with a mean follow-up time of 70 months (range 8-169 months). A second treatment was performed due to radiological suspicion of residual or recurrent tumour in 14 patients. Eight out of 14 patients underwent curettage and five out of 14 patients underwent RF ablation. In one case, ten years after curettage of an ACT of the distal femur, this patient underwent surgery for total knee replacement. During surgery, a biopsy was taken. Histology of the tissue was not conclusive (Table 2, patient 2). Histological examination was performed on small needle biopsy taken during the RF ablation session or on curettage tissue material. Unfortunately, no histological biopsy was performed in two patients during RF ablation (Table 2, patient 4 and 7). Histological examination proved six recurrences and was negative for histological of recurrence in five patients.

Conventional radiography

Complete consolidation of the bone window was observed in all patients. Two patients suffered from a femoral fracture through the bone window, within six weeks after curettage. Gradual incorporation of the bone graft used for filling the medul-
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at first surgery:</th>
<th>Group</th>
<th>Location of the ACT:</th>
<th>Volume of primary tumour cm³</th>
<th>Months till second intervention:</th>
<th>Type of intervention:</th>
<th>Histology:</th>
<th>Recurrence after second OR:</th>
<th>Disease-free period after second intervention (months):</th>
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<tr>
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<td>F, 28 yrs</td>
<td>II</td>
<td>femur, diaphyse</td>
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<td>2</td>
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<td>114</td>
<td>TKA</td>
<td>nc*</td>
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<td>rfa</td>
<td>nbt**</td>
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<td>nbt**</td>
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<td>45</td>
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<td>64</td>
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<td>neg</td>
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<td>unknown</td>
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<td>32</td>
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<td>neg</td>
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<tr>
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<td>neg</td>
<td>no</td>
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<tr>
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<td>humerus, prox</td>
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<td>34</td>
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<td>pos</td>
<td>yes</td>
<td>****</td>
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<td>tibia, prox</td>
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<td>69</td>
<td>curettage</td>
<td>pos</td>
<td>no</td>
<td>116</td>
</tr>
</tbody>
</table>

* nc: non conclusive  
** nbt: no biopsy taken  
*** new small lesion on Gd-MRI 2 years after curettage. New rfa performed 3.5 years later  
**** one year and three years after rfa new lesions, resp re-curettage and rfa. Histology suspected for new ACT
lary bone cavity after curettage was seen in time in most patients (Figure 1). However, in some patients small radiolucent defects in the bone graft remained on serial follow-up radiographs, although not increasing in size. In our series, no patients showed any suspicion for local recurrence on conventional radiographs.

Fig 1. Postoperative conventional radiographs.

A. Lobulated lesion in the proximal humerus meta-diaphysis of the left arm. The lesion is predominantly lytic with some chondroid mineralisation in the distal part. The cortex seems intact. Histological examination after curettage demonstrated ACT/grade I central chondrosarcoma.
B. Two months after curettage shows the bone graft. No postoperative complications.
C. Six months after curettage shows early incorporation of the bone graft.
D. 24 months after curettage shows further incorporation of the bone graft.

MR imaging

The recognition of a number of characteristics on the postoperative images leading to false positive predictors of recurrence resulted in the formulation of 4 different imaging patterns (Table 3).

I. A small enhancing rim of granulation tissue surrounding the area of the bone graft. This area becomes smaller in time and the surrounding bone marrow edema diminishes in time. No residual or recurrent enhancing nodules suspicious for ACT/chondrosarcoma grade I. II. Nodules are seen in or surrounding the bone graft. The granulation zone is not well defined. These nodules are diminishing in size during follow-up MR imaging. III. Nodules are seen in or surrounding the bone graft. These nodules are stable or increase in size during follow-up MR imaging. IV. A small enhancing rim of granulation tissue surrounding the area of the bone graft is seen on the first post-operative MR images consistent with the normal aspects of the bone graft. Development however of new enhancing nodules in the treated region, which are suspicious for local recurrence during follow-up MR imaging.

Dovetailing these groups resulted into the proposed flow chart for follow-up and
treatment in Figure 6. Soft tissue edema around the bone window was frequently-seen on the first postoperative MR images, which however diminished in time on follow-up MR images (Figure 2). 40 of all patients (54%) demonstrated an imaging pattern consistent with group I (normal postoperative appearances)(Figure 3). 18 Patients (24%) demonstrated an imaging pattern consistent with group II. In this group one patient was treated with a second curettage that showed no signs of recurrence on histological examination. 13 Patients (17%) demonstrated an imaging pattern consistent with group III (Figure 4) and four patients (5%) demonstrated an imaging pattern consistent with group IV (Figure 5).

<table>
<thead>
<tr>
<th>Table 3. MR imaging patterns</th>
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<tr>
<td><strong>group I</strong></td>
</tr>
<tr>
<td><strong>group II</strong></td>
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<tr>
<td><strong>group III</strong></td>
</tr>
<tr>
<td><strong>group IV</strong></td>
</tr>
</tbody>
</table>

*no signs of new tumour
**not conclusive, or no biopsy performed (n=2)

Figure 2. Axial MR images of early postoperative changes. 31 year old male with an ACT/grade I central chondrosarcoma in the left distal femur. Axial T1-weighted MR images after intravenous contrast administration with fat-suppression through the same position on different time-points.

A. The lesion demonstrates typical peripheral guirlande-like enhancement.
B. The patient has been treated by curettage through a lateral approach. There is marked enhancement surrounding the bone window six months after treatment. The bone window is partial consolidated and demonstrates reactive periosteal and soft tissue edema.
C. Complete consolidation and incorporation of the bone graft 24 months after surgery.
Figure 3. Illustration of group I: residual nodules, which diminish in time. Female, 46 years, with ACT/grade I central chondrosarcoma of left proximal humerus.

A. Coronal T1-weighted MR imaging after Gadolinium with fat suppression after diagnosis; ring-and-arc enhancement of a cartilage tumour.
B. Six months after curettage shows the bone graft surrounded by an enhancing zone of granulation tissue with some soft tissue edema at the bone window. Still areas of hyper-intensity remain.
C. Incorporation of the bone graft, decreasing in size. No separate cartilaginous nodules suspicious for local recurrence. Areas still enhance using Gd, but decrease in size.

Figure 4. Illustration of group III. 15 years-old female with ACT/grade I central chondrosarcoma in the proximal femur. Sagittal T1-weighted MR images after intravenous contrast administration with fat-suppression.

A. First post-operative MR examination is performed 7 months after curettage. The marrow cavity in the proximal femur demonstrates marked and inhomogeneous enhancement which could represent extensive granulation tissue, however small residual nodules cannot be excluded.
B. Six month after previous MR examination demonstrates a well-circumscribed lesion with a typical guirlande-like enhancement pattern consistent with a recurrence. The enhancing granulation zone/tissue is markedly reduced. Repeated curettage was performed and histological examination showed ACT/grade I central chondrosarcoma.
Figure 5. MR imaging pattern of group IV with a local recurrence 61 months after initial surgery. 39 year old female with ACT/grade I central chondrosarcoma in the right proximal humerus. Oblique T1-weighted MR images after intravenous contrast administration with fat-suppression.

A. Preoperative MR image demonstrates the typical enhancement pattern consistent with a cartilage tumour.
B. Postoperative MR image, 12 months after treatment demonstrates inhomogeneous enhancement of the marrow cavity.
C. Postoperative MR image, 3 years after treatment demonstrates further resorption or incorporation of the bone graft mimicking small cartilage nodules.
D. Postoperative MR image, 5 years after treatment demonstrates a well-circumscribed lesion with a typical guirlande-like enhancement pattern consistent with a local recurrence. Histological examination confirmed ACT/grade I central chondrosarcoma.

Discussion

Follow-up of patients undergoing intralesional surgery for a low-grade or locally aggressive tumour like ACT/grade I central chondrosarcoma is important. The chance the lesion will develop in grade II or III chondrosarcoma, and the small risk for dedifferentiation of the tumour justifies the follow-up on these patients group. We defined four groups of imaging features and designed a flow-chart for recommendation of postoperative follow-up imaging.

Despite the fact that recently the underlying molecular genetic defects responsible for the genesis of central cartilaginous tumours were untangled, systematic treatment targeting this pathway is still lacking, leaving surgery the only treatment option.16-18 Intralesional curettage followed by local adjuvant is currently the accepted treatment for ACT/grade I central chondrosarcoma of long bones. However, long-term follow-up data on imaging characteristics and recurrence data are lacking in the current literature. In our retrospective study, we included a large number of patients all treated with intralesional curettage with regular MR imaging follow-up. Since our first patients have been treated in 1994, the threshold for a second treatment has been low because of limited knowledge about recurrence frequency
and clinical behaviour in that time period. With our current knowledge, we would-not have treated the patient in imaging pattern group II (Table 2, patient 1). MR imaging showed an ill-defined granulation zone containing some nodules. These nodules decreased slightly in size on follow-up MR imaging but under the suspicion of local residual disease, patient underwent repeated curettage with no signs of malignancy on histological examination.

Conventional radiographs in the post-operative period have proved to be important to detect early complications linked to the surgery such as fissures, fractures or large residual calcifications.

However, in our study group we didn’t detect any of the local recurrences on conventional radiographs.

The number of planned re-interventions in this study is 13 (17%). One patient had a second biopsy during a total knee arthroplasty (Table 2, patient 2). However, only in six patients (8%) the histological confirmation of residual or recurrent ACT/chondrosarcoma grade I could be made (three patients of MR pattern group III and three patients of group IV). Unfortunately, in two patients in the RFA-group no biopsy was taken. No upgrading or dedifferentiation of the cartilaginous tumour was seen at recurrence. In five patients, there was no sign of tumour recurrence or the volume of tissue was too small to make a definite diagnosis. Over the past years, improvements in biopsy needle design, sampling technique and expertise of radiologists have developed in concert with oncological and quality control guidelines which emphasize the need for adequate biopsy prior to percutaneous radiofrequency ablation in the same session.15

On postoperative MR imaging we carefully evaluated the treatment area. In all patients, we observed bone graft material demonstrating signal intensities more or less comparable with normal bone marrow surrounded by a zone of variable thickness. This zone showed predominantly high signal intensity on T2-weighted fat suppressed images and demonstrated enhancement on the late static contrast-enhanced MR images consisting of granulation tissue as a fibrovascular reaction of the host to the allograft bone chips in combination with the necrotizing effect of the applied phenol. On the first postoperative MR images (about six months after surgery) it can, therefore, be difficult to recognize small residual nodules or foci of remnant chondroid tumour because they demonstrate similar imaging features as granulation tissue. However, in time, the granulation tissue zone will become smaller and well-demarcated. If the enhancing nodules persist (MR imaging pattern group III) or if new enhancing nodules develop (MR imaging pattern group IV) than local recurrence of residual tumour need to be considered. Depending on the
size, the location and patient-related factors a wait-and-see policy can be considered or a second treatment can be performed (RF ablation or intralesional curettage). Moreover, the bone graft used for filling the defect in the marrow cavity after curettage may contain cartilage chips of the surface of the bone graft e.g. femoral head. This may lead to a false-positive interpretation of residual foci of chondroid tissue, however in time the foci will not increase.

The dynamic contrast-enhanced MR images may be potentially very helpful in differentiating recurrent disease from granulation tissue on follow-up MR imaging. However, in our patients, the diagnosis of recurrent disease was suggested (Group III and IV) based on the morphological criteria as described in Table 3. In our patients, the dynamic contrast-enhanced sequence was of poor quality or not performed in the correct area of interest as MR examinations performed on the 0.5 T MR systems could cover only two slices through the postoperative area.

Based on the recurrences we have seen and the MR imaging patterns we recommend a work up as detailed in Figure 6. We are convinced that curettage combined with adjuvant and bone grafting is a safe and patient friendly procedure for patients with central ACT/chondrosarcoma grade I. When follow-up is performed according to the proposed schedule eventual local recurrences are detected accurately and in a safe time window.
intralesional curettage, adjuvant* and bone grafting for ACT/grade I central chondrosarcoma of long bones

one year: baseline MRI

suspicious lesions?**

no (group I)**

repeat MRI 5 and 10 years after surgery

suspicious lesions?

no (group I)**

no longer follow-up necessary

re-intervention including histological confirmation

yes (group II and III)**

repeat MRI in two years

suspicious lesions?

no (group I)**

suspicous lesions diminished (group II)**

suspicous lesions do not reduce in size (group III)**

wait and see

yes (group IV)**

suspicous lesions increase in size or have fast enhancement (group III)**

re-intervention including histological confirmation

Figure 6: Recommendation for follow-up of patients after intralesional treatment for ACT/grade I central chondrosarcoma of the long bones.

* as adjuvant, Radio Frequent Ablation, phenol or cryotherapy can be used

** enhancement of nodules within the granulation zone

*** group I: Normal aspect of the bone graft without suspicion for residual or recurrent tumour on all postoperative MR images

group II: Nodules within the granulation zone on postoperative MR imaging, diminishing in size during follow-up

group III: Nodules within the granulation zone on postoperative MR imaging, stable or increasing in size during follow-up or fast enhancement of the nodules

group IV: Normal aspect of the bone graft on postoperative MR images. Development of a new enhancing lesion suspicious for local recurrence during follow-up
References
