Author's response to reviews

Title: Malignant fibrous histiocytoma of the distal femur after an arthroscopic anterior cruciate ligament reconstruction: A case report and a review of the literature

Authors:

Turgay Efe (efet@med.uni-marburg.de)
Susanne Fuchs-Winkelmann (ortopae@med.uni-marburg.de)
Peter Rexin (rexinp@med.uni-marburg.de)
Thomas Heyse (heyse@med.uni-marburg.de)
Jan Schmitt (schmitt@med.uni-marburg.de)

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Author's response to reviews: see over
Dear Editor-in-Chief,

Thank you very much for the revision of the manuscript. We have read the comments with great interest. They helped to substantially improve the manuscript. As suggested we revised the manuscript. Our changes are shown in **bold type**. We have changed the title as it appears to be very hypothetical. The new title is: **Malignant fibrous histiocytoma of the distal femur after an arthroscopic anterior cruciate ligament reconstruction: A case report and a review of the literature**

Response to reviewers' comments:

**Reviewer #1:**

The title is very hypothetical and connects directly the arthroscopic ACL reconstruction with the appearance of MFH. This was not proven in this article and the two facts may not be related. Thus, it should be changed into a title more descriptive, like i.e. “Malignant fibrous histiocytoma of the distal femur at the site of an arthroscopic ACL reconstruction”

The authors agree with reviewers point of view hat the title seems to be very hypothetical and that the connection of the ACL reconstruction with the appearance of the MFH is not proven in this case report. We changed the title to: **Malignant fibrous histiocytoma of the distal femur after an arthroscopic anterior cruciate ligament reconstruction: A case report and a review of the literature**

The authors try to make a connection of the tumor appearance with the fixation materials. However, the Endobutton fixation seems from the X-Ray to be rather far from the lesion. Also the Endobutton is not invasive material like a screw. They should comment on this, as it does not appear to be connected.

We are very thankful for this comment and agree with your point of view. We have rewritten the discussion and have emphasized that in this present case a causal relationship between the Endobutton and the development of the MFH is most unlikely.

They should present also a figure of the initial pre-operative MRI for comparison with the tumor-one, so that the reader won’t have any suspicion about a pre-operative small lesion existence that the authors didn’t notice.

**As you suggested we added MRI sequence (Figure 7) preoperatively**

How did the tumor infiltrate the femoral graft tunnel? As it seems from the X-ray position of the Endobutton (Figure 1), the femoral tunnel is situated at the 11 o’clock position at the lateral femoral condyle (LFC) and from the MRI (Figure 2) the lesion seem to occupy the
medial condyle and does not cross the notch. The authors need to present an MRI image demonstrating the tunnel along with the infiltration lesion.

The authors do fully agree with the above statement, retrospectively. Unfortunately we are unable to present the required MRI sequence. After reviewing all MRI sequences there are no images demonstrating the tunnel along with the infiltration lesion. The information that the MFH infiltrates the femoral drill tunnel was made by a consultant of radiology at our university hospital. Therefore we modified the text and Figure 2.

Were there any histiocytes and giant cells in the histopathologic evaluation? The authors should clarify the type of cells encountered in the biopsy.

It was composed of spindle cells mainly. Areas of necrosis, increased vascularity and CD68 positive histocytes (Fig. 3a) were seen. New Figure 3a added.

The sentence in the Discussion about the connection of surgical implants with cancer, as demonstrated in animals “However, animal….cancerogenic effects” should be eliminated, as it is a study from 1964 and concerns the cadmium. There is no study connecting the titanium (used in this study) with cancerogenic effects.

As you suggested we eliminated the above mentioned sentence. We agree there is no study which shows a causal relationship between titanium and cancerogenic effects.

In other similar case report by Caron et al (leiomyosarcoma at the distal femur after ACL reconstruction, where the sarcoma was located close to the interference screw), the authors considered it to be very unlikely that there is a connection between the malignant degeneration and material fixation, although their anatomic connection. The authors should comment on this.

It is correct that the interference screw is located close to the leiomyosarcoma. Nevertheless, the case report by Caron shows in the coronal T1-weighted MRI scan (Figure 3) that the interference screw is not in the midpoint of the leiomyosarcoma. Therefore the appearance of the tumor and the ACL reconstruction is most likely coincidental.

“It seems theoretically possible… was increased”: the osteonecrosis and consequent malignant degeneration theory is very hypothetical and seems rather unfeasible, due also to location of the lesion at the MFC and not at the LFC. If this was the underlying mechanism, one should expect that the lesion would occupy the lateral femoral condyle and not the medial. The hypothesis that the former trauma situation can trigger the appearance of the MFH seems more rational and is also described in the literature.

After reviewing the MRI images the authors do fully agree with the reviewer that the MFH is located in the medial femoral condyle. Furthermore, we fully agree that the osteonecrosis and the consequent malignant degeneration are very hypothetical. We deleted this sentence. Indeed, the influence of a former trauma on tumor development is described in the literature (Bader et al.; Joss et al.). We mentioned and discussed these publications in the present case report.
Figure 4 (the dissected specimen) do not show clearly that the ACL tunnel has been infiltrated from the tumor. The authors should provide a photo that demonstrates this better, macroscopically.

Unfortunately we have no more macroscopically pictures. We deleted the sentence that the femoral drill tunnel has been infiltrated from the tumor. Figure 4 changed to Figure 5. We consider Figure 5 to be important as it shows the consistence and the dimension of the tumor very well.

The authors should provide the duration of their patients’ follow-up

Latest follow-up was 6 months after the implantation of the tumor-prosthesis.

Reviewer #2:

“Possible induction of malignant fibrous histiocytoma at the distal femur by arthroscopic anterior cruciate ligament reconstruction: a case report and review of the literature”

Change to: Possible induction of malignant fibrous histiocytoma at the distal femur by arthroscopic anterior cruciate ligament reconstruction: A case report and a review of the literature

We have changed the title as it appears to be very hypothetical. The new title is: Malignant fibrous histiocytoma of the distal after an arthroscopic anterior cruciate ligament reconstruction: A case report and a review of the literature

“We report about a 29-year-old male Turkish patient who presented with severe pain in the operated knee joint 40 months after arthroscopic anterior cruciate ligament reconstruction”

Change to: We report a 29-year-old male Turkish patient who presented with severe pain in the operated knee joint 40 months after arthroscopic anterior cruciate ligament reconstruction”

Changed

“X-ray and MR imaging showed a large destructive tumor at the medial femoral condyle”

Change to: X-ray and MR imaging showed a large destructive tumor in the medial femoral condyle

Changed

“The continuous increase in recreational sports leads to a continuously increasing number of capsule and ligament injuries of the knee joint as well. About 20% of the knee injuries are accompanied by anterior cruciate ligament ruptures. Reconstruction of the anterior cruciate ligament belongs to the therapies of choice for the sportively active patient and is one of the most common surgical interventions for knee ligament reconstruction”.

3
Add references

References added


Changed

“In the case history presented below we report about the manifestation of an osseous MFH at the distal femur 40 months after arthroscopic anterior cruciate ligament reconstruction using autologous semitendinosus tendon”

Change to: In the case history presented below we report the manifestation of an osseous MFH at the distal femur 40 months after arthroscopic anterior cruciate ligament reconstruction using autologous semitendinosus tendon

Changed

“This was diagnosed by a stability investigation with a positive Lachman and Jerk test and was confirmed by MRI”

Change to: This was diagnosed by a stability investigation with a positive Lachman and Pivot shift test and was confirmed by MRI.

Changed

“The knee joint was without signs of irritation, with full extension ability and a flexion of 140°”

Change to: The knee joint was without signs of irritation. ROM was 0°-140°.

Changed

“Endobutton (B. Braun, Aesculap AG, Tuttlingen, Germany)”

Changed to Endobutton (Smith & Nephew, Schenefeld, Germany)

“40 month after surgery, the patient presented again, as he had been suffering from strongly increasing pain for about 6 weeks, especially at the medial femoral condyle of the operated knee joint”

Rewrite

Changed to: 40 months after surgery, the patient presented with strongly increasing pain in the medial femoral condyle of the operated knee joint.
“mainly located at the metaphysis (Figure 1)”

Change to: mainly located in the metaphysis (Figure 1).

**Changed**

“(Figure 1)”. Any X-rays taken preoperatively or right after surgery?

**No X-rays were taken preoperatively or right after the ACL reconstruction. Preoperatively MRI images were available.**

“The strong positive immune reaction against smooth muscle actin antibodies did not support the possibility of a fibrosarcoma of bone”

Change to: The strong positive immune reaction against smooth muscle actin antibodies did not support the possibility of a fibrosarcoma of the bone.

**Changed**

“Differential diagnosis of a leiomyosarcoma of bone had to be taken into account, but this was less likely because the tumor was negative for desmin and myogenin”

Change to: Differential diagnosis of a leiomyosarcoma of the bone had to be taken into account, but this was less likely because the tumor was negative for desmin and myogenin

**Changed**

“On the medial side, covering of soft-tissue defects by means of a flap was not necessary”

Change to: On the medial side, covering of the soft-tissue defects with a flap was unnecessary

**Changed**

“For subsequent distal femur reconstruction, a silver-coated non-cemented modular knee joint prosthesis (MUTARS, Implantcast, Buxtehude, Germany) was used”

Add x-ray!

**X-rays are added (Figure 4)**

“Among the primary malignant bone tumors, MFH belongs to the rare ones with less than 5%.” Of the total?

**Less than 5% of the total malignant bone tumors are MFH**


**Changed**

“Caron et al. [16] reported about a leiomyosarcoma at the distal femur 12 years after anterior cruciate ligament reconstruction”

Change to: Caron et al. [16] reported a leiomyosarcoma at the distal femur 12 years after anterior cruciate ligament reconstruction.

**Changed**

“In this case, too, a joint adjacent fixation with a metal interference screw had been performed”

Change to: Also in this case a joint adjacent fixation with a metal interference screw had been performed

**Changed**

“These authors consider it to be very unlikely that there is a connection between the malignant degeneration and interference screw fixation”

Change to: These authors consider it to be very unlikely that there is a connection between the malignant degeneration and the interference screw fixation

**Changed to:** The authors consider it to be very unlikely that there is a connection between the malignant degeneration and the interference screw fixation, as the fixation material was not at the midpoint of the leiomyosarcoma.

“major part of the MFH was localised at the medial femoral condyle; at the femoral drill channel”

Change to: major part of the MFH was localised at the medial femoral condyle; at the femoral drill tunnel

**Changed**

…“at the femoral drill tunnel”…*is deleted*

Channel should be changed to tunnels throughout the document

**We have done this throughout**

“Bader et al. [17] reported about a 14-year-old girl who underwent plate osteosynthesis because of supracondylar femur fracture”

Change to: Bader et al. [17] reported a 14-year-old girl who underwent plate osteosynthesis due to supracondylar femur fracture

**Changed**
“Joss et al. [18] reported a 25-year-old patient”

delete about

**Deleted**

“By reanalysing the MR images taken in 2005, MFH presence prior to anterior cruciate ligament reconstruction could be excluded”

show the image

**Figure 7**

“However, until surgical removal of the tumor, the patients’ pain had completely disappeared”

Change to: The pain, however, had completely disappeared between neoadjuvant chemotherapy and surgical removal of the tumor

**Changed**

Thank you very much for your comments, editing and proofreading of the manuscript. We hope that we could answer your questions satisfactory and would be happy to receive a positive answer.

Best regards