Author’s response to reviews

Title: Subcutaneous emphysema of the leg after hardware removal and bone allografting for infected non-union of the distal femur

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Author’s response to reviews:

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“Leg emphysema after hardware removal and bone allografting for infected non-union of the distal femur: a case report.”

Dear Editor,

Many thanks for the opportunity to revise the above manuscript. Please find attached the revised version of the above manuscript. The comments of reviewers have been carefully considered, and implemented as follows:
Reviewer: 1

Comments to the Author

This manuscript reported on a male who developed leg emphysema after hardware removal and bone allografting for an infected non-union of the distal femur. The patient was managed by debridement of the surgical wound, antibiotic therapy, multiple fasciotomies, and application of a VAC (vacuum-assisted closure) system. This work is of valuable and a great experience for surgeon. However, certain revisions are necessary for more details. Please consider the following revisions for improvements of this manuscript.

1) The imageology data are quite important for orthopedics surgery. Can the authors show the X-ray or other imageological examinations of the distal femur pre-operative of hardware removal?

ANSWER: We thank the reviewer for his/her suggestion. We added pre-operative x-ray in the manuscript, Figure 3.


ANSWER: We thank the reviewer for his/her suggestion. The infected non-union was classified in type A1 according to Jain AK et al. We added the clinical stage of the patient.

Jain AK et al. classification: . Type A is infected nonunion of long bones with nondraining (quiescent) infection, with or without implant in situ; Type B is infected nonunion of long bones with draining (active) infection. Both are classified further into two subtypes: 1) nonunion with a bone gap smaller than 4 cm or 2) nonunion with a bone gap larger than 4 cm. Single-stage
debridement and bone grafting with fracture stabilization are the methods of choice for Type A1 infected nonunions. Adequate debridement, fracture stabilization, and second-stage bone grafting gives desirable results in Type B1 infected nonunions. Distraction histiogenesis is the preferred procedure for Type A2 and B2. The autogenous on vascularized fibular graft, posterolateral bone grafting for the tibia, and centralization of the ulna over distal radial remnant (single bone forearm) may be good treatment options in selected cases.

3) For suspicion of infected non-union, full spectrum of microbiological tests of samples are recommend. In my opinion, deep tissue samples including primarily non-union fibrous tissue, curetted bone and/or canal reamings, marrow cavity and secondarily sinus tract material should all be tested. What samples did you take? Would you please clarify those in the article?

ANSWER: We thank the reviewer for his/her suggestion. We analysed samples from surgical wound, non-union fibrous tissue, curetted bone and canal marrow cavity during hardware removal and bone allograft implantation and from surgical wound and soft tissues during the debridement of the surgical wound and fasciotomies. Now we state: “The patient underwent hardware removal and bone allograft implantation. Samples for microorganism cultures were obtained at surgery from surgical wound, non-union fibrous tissue, curetted bone and canal marrow cavity, but no pathogens were identified.”  at line 65 and “The patient underwent exploration and debridement of the surgical wound, and multiple fasciotomies. Samples from surgical wound and soft tissues for microorganism cultures were obtained at surgery, but no pathogens were identified.”

4) It is mentioned in the report that the patient was allowed for weight bearing 14 days postoperatively the VAC system being removed. There were few information about the surgery process. Could you please provide some images of the non-union management during the surgery or non-union sites? Did you use any fixation alternatives after surgery?

ANSWER: We thank the reviewer for his/her suggestion. Unfortunately no images of the non-union management during the surgery are available. The reason for not applying the external fixator was that the patient denied his consent for the application of an external fixator. Additional surgeries and correction of axis were planned as second step.
5) In my opinion, this article needs some language corrections before being published

ANSWER: We thank the reviewer for his/her suggestion. English language was improved.

Reviewer 2:

The authors have presented a case report of a Leg emphysema after hardware removal and bone allografting for infected non-union of the distal femur.

They have not provided any proof for the source of infection, type of the bacteria or even any relation to the specific situation of the patient. They have mentioned non clostridial crepitant infections as an infection we have to be cautious about, but they do not present any results of bacteriology or culture.

I cannot accept a case report based upon extrapolations.

Answer: We do not agree with this reviewer comment. We report on a male who developed subcutaneous emphysema of the leg after hardware removal and bone allografting for an infected non-union of the distal femur. Clinically he had crepitant infection and the gas is clearly visible in the CT scan, arriving to compromise the foot. This was a very difficult case to manage.

We performed several biopsies to identify pathogens, but no pathogens were identified. The question is: how should we manage a patient with a similar history?

Our experience can be beneficial for physician dealing with the same emergency situation.

When pathogens spread into the surrounding tissues, as in our patient, then fulminant gas gangrene is the result. The infection spreads rapidly from diseased to healthy tissues, and an entire limb may become gangrenous within the space of a few hours. At this stage amputation of the infected limb or removal of all of the infected tissues is the only effective management. Without this, the toxins produced by the bacteria rapidly kill the patient. We were ready to the possibility to amputate the limb of the patient.
Unfortunately, despite of our efforts, we were not able to determine the nature of the gangrene (clostridial or non clostridial). Multiple samples were performed both at surgery for hardware removal and during fasciotomies, as well as hemoculture and culture of the allograft, but no pathogens were isolated. The results of the cultures were of course a false negative. Otherwise, we have not a scientific explanation to the emphysema (all the way down to the toes of the foot) and for the increased uptake at the bone scan. In clinical practice, sometimes, despite clinical diagnosis of infection, hemoculture and culture are negative and it is not possible to isolate pathogens responsible of the disease. In these cases, it is important to apply general principal and utilise large spectrum antibiotics. This strategy allowed us to save the limb in this patient.

We point that it would have been much more simple to manage the patient if a pathogen was identified. However, in the real life, often pathogens are not identified.

We think that our therapeutic strategy can be helpful for other physicians who will have to deal with a similar condition. In our case the patient saved his lower extremity and his life.

Reviewer 3:

The authors present an interesting case report dealing with a life-threatening soft tissue infection after hardware removal and bone allografting at the femur. The described interventions saved not only the patient’s lower extremity, but also his life.

However, several questions must be addressed in addition to minor and descretionary revisions:

Major revisions:

• p3, line 42-44 and 56/57: .... teicoplanin 800 mg/die.... 800 mg/day, but more importantly: Administration per os? Bioavailability of teicoplanin per os is zero. Was it administered i.v.? If not, what was the rational of oral administration (i.e. additionally suspected pseudomembranous colitis?)

ANSWER: We thank the reviewer for his/her suggestion. Teicoplanin was administered i.v.
• Why was a bone allograft used which has no osteoinductive properties? Did you consider autologous bone craft (i.e. iliac crest?)

ANSWER: We thank the reviewer for his/her observation. We used a bone allograft because of patient requests. The patient denied his consent for autologous bone graft.

• Non-unions (septic/aseptic) usually require stability to heal. Was an external fixator applied? If not, why? Malalignment might have been addressed with additional corrective osteotomy and external fixator? Or was correction of axis planned in second Intervention after consolidation?

ANSWER: We thank the reviewer for his/her observation. The patient denied his consent for the application of external fixator. Additional surgeries and correction of axis were planned as second step.

Minor revisions:

I would avoid the term "leg emphysema". I think it is more accurate to describe it as subcutaneous emphysema of the leg or gas gangrene

ANSWER: We thank the reviewer for his/her suggestion. Now we state “subcutaneous emphysema of the leg” in the whole manuscript.

p3, line 5/6: ...fixation of the fracture (the patient associated) with irrigation...

ANSWER: We thank the reviewer for his/her suggestion. We changed it.
p3, line 14/15 and 23/24, p4, line 7: Range of motion was 0-40°. What does it mean? Total range of Motion? I advise a more precise description: i.e. extension/flexion 0/0/40°

ANSWER: We thank the reviewer for his/her suggestion. We have provided a more precise description of range of motion in the manuscript.

p 3, line 18/19: ...adhesions (instead of adherences) ...

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “adhesions”

p3, line 54/55: use maximum instead of "massive" dosage

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “maximum”

p3, line 56/57: ... i.v...., dosage /day

ANSWER: We thank the reviewer for his/her suggestion. We changed it.

p4, line 9: rifampicin?

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “rifampicin”
Discretionary revisions:

p2, line 2: Infected non-unions....

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “Infected non-unions

p2, line 7: ... originate...

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “originate”

p2, line 16: ... further orthopaedic ??? (interventions?)

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “orthopaedic interventions”

p2, line 27: The patient saved the limb. (?) I guess, it was you who saved the leg. The patient’s limb was saved. Apart from that, I think this sentence may be better in the case Report section.

ANSWER: We thank the reviewer for his/her suggestion. We changed it.

p3, line 9 and line 21/22: Weight bearing...
We thank the reviewer for his/her suggestion. Now we state: “Weight bearing was allowed three months after surgery.”

p3, line 42/43: ...osteomyelitis...

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “osteomyelitis”

p5, line 12/13: life-threatening

ANSWER: We thank the reviewer for his/her suggestion. Now we state: “life-threatening”

We thank the Editorial Board for having given us the opportunity to revise our manuscript. We appreciate yours and the reviewer’s comments. We hope that the additions have now improved the manuscript, and that it has now reached the standard necessary to be formally accepted for publication in the BMCMusculoskeletal Disorders.