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Title: Disseminated osteomyelitis after urinary tract infection in immunocompetent adult: a case report

Name of Journal: World Journal of Clinical Cases

Response to Reviewers' comments

Dear Editor,

We thank you for your careful consideration of our manuscript. We appreciate your response and overall positive initial feedback, and suggested modifications to improve the manuscript. After carefully reviewing the comments made by the reviewers, we have modified the manuscript to improve the presentation of our case presentation and discussion, therefore, providing a complete context for the research that may be of interest to your readers.

We hope you find the revised paper suitable for publication, and we look forward to contributing to your journal. Please do not hesitate to contact us in case of other questions or concerns regarding the manuscript.

Best regards, Jae-Hoon Lee

Reviewer #1

*There is an error in "History of present illness": The (she) had been hospitalized.....
I find it useful to let people know and / or remember that urinary tract infections can cause
osteomyelitis*

Reviewer #2

*The authors present an interesting case, with good quality images of radiological
exams. There is, however, a necessity to improve the writing in the english language.*

Response: We apologize for the oversight and appreciate your indication of the mistake. Accordingly, the manuscript has been repeatedly reviewed in detail and revised. We are non-native speakers of English; therefore, we have consulted a professional editing company for English language editing as a better alternative to the highlighted.

Reviewer #2

The authors thoroughly summarized a rare case of disseminated osteomyelitis in the long bones after upper urinary tract infection. This case report might remind physicians about hematogenous osteomyelitis after the treatment of any infectious disease. The language quality is acceptable; however, it is still needed correction. Nonetheless, there are a few questions about this case report required to be aware; - After UTI treatment (2 months), what is your follow-up protocol? Did you follow-up on CRP during that time? (which is essential in the surveillance of infectious disease, or might help early awareness of relapse infection). If so, could you provide the results before mentioned that CRP rose from 3 to 112.82 mg/L. - How did you define this patient as an immunocompetent host? According to Cierny-Mader classification (which was also mentioned in this report), this patient is extremely aged and supposed to be classified in type Bs (systemically compromised). - Even only 1/3 of patients with hematogenous osteomyelitis have positive blood culture, what are the results of this patient (including the first episode of UTI) - According to your physical examination and MRI, what is the reason for arthrocentesis and laboratory examination? (no joint swelling, no limit motion, no sign of joint fluid from MRI) - According to MRI result, could you explain how did you debride this lesion for both femur? And how did you manage such a large bone defect? Do you use any antibiotic-augmented cement beads? Any pictures demonstrated intra-operative findings could make this report more remarkable. - E. coli was a causative organism in this case. Why did you use broad-spectrum antibiotics like meropenem? Was it a drug-resistant E.coli? - What are the results during one year of follow-up? Pictures of bone scan indicated clear of disease? CRP or MRI during that time?

Response: We appreciate your review and recommendation. According to your advice, the manuscript has been additionally revised and proofread for English.

1) We usually do not follow up after the completion of treatment for urinary tract infection. The patient visited the hospital due to leg pain. On first admission for urinary tract infection, the CRP improved to normal, and she was discharged. CRP 3 (normal 0-5) is at the time of first discharge. Similarly, this content has been added to the text, accordingly.

2) We agree with your comment. According to the Cierny-Mader classification, extreme ages are classified under type Bs (systemically compromised). However, this system of classification helps to determine treatment and prognosis in long bone osteomyelitis rather than the site of infection. Although elderly have less immunity than young people, they are generally not considered “immunocompromised patients”. In addition, even in the elderly, few cases involving long bone or widespread to both sides barring factors, such as the use of immunosuppressants, have been reported.

3) On the first visit, symptoms of urinary tract infection, such as flank pain and urinary frequency, were apparent. In addition, *E.coli* was observed in cultures of the urine and blood; therefore, she was diagnosed with bacteremic UTI. At that time, she complained of leg

pain, which resolved shortly after. Thus, she was placed on a 2-week antibiotic therapy for UTI, which was insufficient for osteomyelitis. Possibly due to the short duration of treatment, osteomyelitis was not properly treated and seemingly recurred after the discontinuation of the antibiotic.

4) Physical examination revealed no prominent local inflammation; however, the pain did not resolve continuously. Imaging test was performed and osseous infection was suspected; therefore, further evaluation, including laboratory examination and joint aspiration, was performed.

5) As illustrated by the images, the lesions were extremely wide, and if all the lesions were removed, the patient would be disabled. Hence, we reamed the medulla and drained through a hole, and antibiotics bead was subsequently inserted. I apologize for not presenting the picture of the surgery. The surgical team didn't take photo during surgery.

6) The pathogen was ESBL-producing *E.coli*; hence, we treated with meropenem.

7) We did not routinely follow up for one year. Additionally, response was not evaluated by imaging test, rather based on clinical symptoms and inflammation levels. During discharge, improvements were observed in both symptoms and inflammation levels. A year later, the visit was made for other reasons, and the patient requested for imaging and laboratory examination. The bone scan showed an improvement in the previous findings, and the patient's medical history showed no recurrence.