

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Chondrosarcoma of the toe: report of a case and review of the literature" (ID: 77086). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: I would suggest changing it to Chondrosarcoma of the toe: a case report and a literature review.

Response: Line 5, the statements of " Chondrosarcoma of the toe: report of a case and review of the literature "were corrected as " Chondrosarcoma of the toe: a case report and a literature review ".

2. Response to comment: I have just a minor revision: " A search of the relevant databases resulted in five previously reported cases of chondrosarcoma of the phalanx": When a literature review is performed, it is mandatory to include: -which databases were used. PUBMED? EMBASE? - the keywords used for the review: chondrosarcoma? toe? -from which year to which year were the articles considered -inclusion and exclusion criteria for the review English revision is required.

Response: Line 338-356, We will searched the following 8 databases: four English medical databases [MEDLINE (PubMed), EMBASE, The Cochrane Central Register of Controlled Trials (Cochrane Library)], Web of Science Database, and four Chinese medical databases [the China National Knowledge Database (CNKI), Journal Integration Platform (VIP), WanFang Database and SinoMed(CBM)]. We

also manually searched the additional relevant studies using the references of the systematic reviews that were published previously. All of the searches were performed from inception to April 2022 and did not impose restrictions on language, population or country. The following search strategy was used for PubMed and was modified to suit other databases.

#1 (chondrosarcoma[Title/Abstract])

#2 (Toe [Title/Abstract])

#1 AND #2

Literature inclusion and exclusion criteria were as follows: (1). The site of the disease was in the toe; (2). Pathologically diagnosed as chondrosarcoma; (3). Chondrosarcoma was the main lesion; (4). Not combined with other malignant diseases.

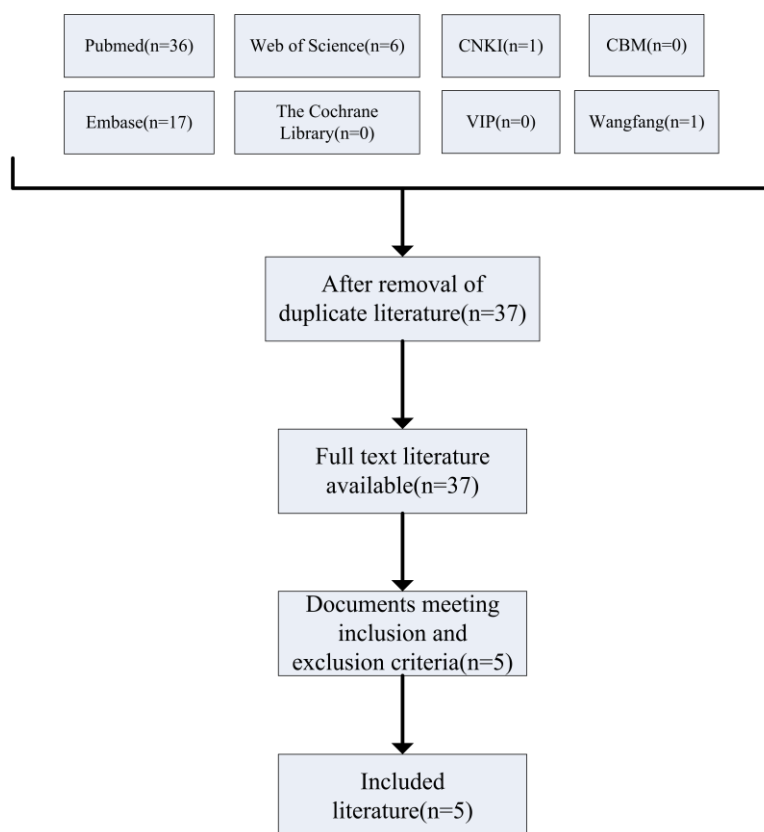


Figure 5 Flow diagram of the search process.

Special thanks to you for your good comments.

Reviewer #2:

1. Response to comment: Is there a picture of the tumor and the operation site?

Response: We performed the direct pathological examination of the tumor tissue removed intraoperatively without collecting intraoperative data, and later concluded that cases of soft sarcoma in the toe are very rare, so we also participated in the report, but we guarantee that this case is authentic and reliable. In addition, we added a postoperative photograph of the patient to the original imaging data.

2. Has abnormality genetics been checked for IDH1 and IDH2 genes?

Response: We read the literature on the treatment of chondrosarcoma of the foot, and in the reports, no IDH1 and IDH2 genetic tests were performed on the patients^[1-3]. Therefore, we similarly did not perform IDH1 and IDH2 gene tests during the treatment of our patients.

3. Why whole-body pet scan was not performed for the metastasis workshop?

Response: We read the literature on chondrosarcoma of the foot, and pet scans were not performed in the reports^[1-3]. For determining the presence of metastases in other parts of the body, patients also underwent a CT scan of the chest or a whole-body scan. In addition, we recommended that the patient undergo a pet scan, but due to the high cost of the test and the patient's lack of financial means, the patient and family decided not to undergo a pet scan after discussion.

[1] Özmanevra R, Calikoglu E, Mocan G, Erler K. Grade 2 Chondrosarcoma of the Great Toe: An Unusual Location. J Am Podiatr Med Assoc. 2019;109(5):393-396. doi:10.7547/18-097.

[2] Masuda T, Otuka T, Yonezawa M, et al. Chondrosarcoma of the distal phalanx of the second toe: a case report. J Foot Ankle Surg. 2004;43(2):110-112. doi:10.1053/j.jfas.2004.01.002.

[3] Rafi M, Abbas S, Intakhab B, et al. Chondrosarcoma of right big toe with metastases to left orbital and left infra temporal region. J Pak Med Assoc. 2019;69(6):896-898.

Special thanks to you for your good comments.

Other changes:

1. Line 131, the statements of “ Computed tomography (CT) ” were abbreviations as “ CT ”.
2. Line 131, the statements of “ magnetic resonance imaging (MRI) ” were abbreviations as “ MRI ”.
3. Line 138, the statements of “ T1-weighted (T1W) ” were corrected as “ T1 Weighted Image (T1WI) ”.
4. Line 201, the statements of “ T2WI ” were corrected as “ T2 Weighted Image ”.
5. Line 201-202, the statements of “ MRI DWI ” were corrected as “ MRI diffusion-weighted imaging ”.
6. Line 240-241, the statements of “ isocitrate dehydrogenase (IDH1 or IDH2) ” were corrected as “ isocitrate dehydrogenase type 1 (IDH1) or isocitrate dehydrogenase type 2 (IDH2) ”.
7. Line 251, the statements of “ hereditary multiple exostoses (HME)” were corrected as “ hereditary multiple exostoses ”.
8. Line 277, the statements of “ isocitrate dehydrogenase type 1 (IDH1) or isocitrate dehydrogenase type 2 (IDH2) ” were corrected as “ IDH1 or IDH2 ”.
9. Line 328, the statements of “radical operation (RO) ” were corrected as “ radical operation ”.
10. Line 637-638, the statements of “ T1WI ” were corrected as “ T1 Weighted Imaging ”.
11. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author’s intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure

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Response: We have made changes to the images as requested by the company's editor-in-chief.

12. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: We have revised the form as requested by the company's editor-in-chief.

13. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

Response: Line 90-94, “ One study found that the prevalence of chondrosarcoma of the foot is about 3.0%, with the highest prevalence in the metatarsal bone, and the overall survival of chondrosarcoma of the foot is better than that of chondrosarcoma of other anatomical sites^[6].” was added.

Line 385-389, “ Lesenský et al^[35] concluded that curettage is the treatment of choice for ACT/Grade I tumours; however, surgeons should be aware of the potentially high local recurrence and recurrence rates. Resection is recommended for Grade II and Grade III chondrosarcomas.” was added.

[6] Tsuda Y, Fujiwara T, Stevenson JD, Abudu A. Surgical outcomes of bone sarcoma of the foot. *Jpn J Clin Oncol.* 2021;51(10):1541-1546. doi:10.1093/jjco/hyab118.

[35] Lesenský J, Matejovsky ZJ, Vcelak J, et al. Chondrosarcomas of the small bones: analysis of 44 patients. *Eur J Orthop Surg Traumatol.* 2021;31(8):1597-1602. doi:10.1007/s00590-021-02964-8.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Best regards,
Libo Zhou