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Reviewer A

Comment 1: All pedicle and lateral body cervical spine ABCs surround the vertebral artery, neural foramina, and often impinge upon the cord.

Reply 1: You are absolutely correct. We also believe that a good description of the lesion is important.

Comment 2: The angiography is always like that so can be omitted from the care plan unless the vert is being embolized prior to surgical debulking.

Reply 2: We presented the angiography because in our case it was an essential step in patient care. As of our knowledge, irrigation of cervical spine ABCs is not limited to the vertebral artery. For example, angiography can demonstrate tumor arterial supply anastomosing with the left and right vertebral artery stemming from the ascending and deep cervical artery branches (*Landon D. Ehlers, Joe McMordie, Pasha Lookian, Daniel Surdell, Mark Puccioni, Cervical Spine Aneurysmal Bone Cyst in a Pediatric Patient: Embolization Considerations and Potential Pitfalls, World Neurosurgery, Volume 139, 2020, Pages 163-168*). We think that a diagnostic angiography is essential in order to choose the best available treatment in this case (had it not be the vertebral artery, we would probably opt for arterial embolization).

Comment 3: The cryo did not work to treat the ABC but it did entirely destroy the vertebral body (see Fig 3b). I think you need to speak to the COMPLETE destruction of the vertebral body which would not have happened with just using doxy. Cryo destroys not only the tumor, but also normal bone, and most importantly the periosteum which prevents the bone from healing back to a normal shape.

Comment 4: What you showed was that cryo or surgery can debulk these things, with huge cost to the patient in outcome (due to loss of vertebral body in your case, and fusion in surgical case), but sclerotherapy with a liquid agent, like doxycycline is needed to percolate to all the small spaces is needed to actually treat the lesion and allow it to heal. I think the case would be publishable if you explained the data this way. Cryo was a debulking step, much like surgery, but doxy is needed to treat the walls of the locations. In my opinion, you should skip the cryo and surgery and just do the doxy.

Reply 3-4: Your comments are very interesting and insightful for us. With your permission, we would like to address Comments 3 and 4 in this single reply. Sclerotherapy is indeed a safe and effective treatment option for ABCs and we like to apply it as much as possible. However, in our limited experience, it is harder to perform correctly than cryoablation, which results in more rounds of treatment and ultimately a higher rate of recurrence. This is partially confirmed by Arleo et al (*Arleo TL, Hawkins CM, Fabregas JA, Gill AE. Percutaneous image-guided treatment of aneurysmal bone cysts: is there a superior treatment option? Pediatr Radiol. 2022;52:1539–49*). This is why we prefer to use cryoablation or a combination of both in sensitive cases like this one. Regarding the destruction of bone by cryoablation, we would like to point that there are studies showing frozen and necrosed bone induces new bone formation through the release of growth factors, albeit in rabbits (Xu G, Yamamoto N, Nojima T et al (2020) The process of bone regeneration from devitalization to revitalization after pedicle freezing with immunohistochemical and histological examination in rabbits. *Cryobiology* 92:130–137). In any case, it is a very

interesting, but hard debate because of the limited evidence comparing both types of treatments.

Comment 5: You show 10-month follow-up images that show residual or recurrent disease that you say is inconsequential. But you show no further imaging. This is woefully inadequate, not only for patient care, but also for publication. ABC recurrence risk in the cervical spine is at least 50% after one surgery or one sclerotherapy session and recurrences can occur up to 5 years after treatment while most are within 2 years. You need to show a follow-up imaging study AT LEAST 2 years after treatment (better would be 3-5 years later) to claim this treatment was permanently successful and not just tolerated

Reply 5: Thank you for your comment. We agree that a 10 month follow up is far from ideal. We are including the most recent imaging technique dating December 2023, which was done approximately 21 months after the last treatment. We would like to explain why no other diagnostic imaging techniques were done in this timespan, and that was because the patient became claustrophobic and tolerated poorly both MRI and CT scans. There was a debate between performing an MRI under sedation or following with conventional X-ray, and after talking with the parents the latter option was decided because the patient was feeling good and had no pain nor other symptoms.

Changes in the text: we added a new figure demonstrating recent conventional X-ray (Figure 3A). Change in legend of Figure 3 was made also.

Reviewer B

Comment 1: An interesting case report, well structured. Figures appropriate for the text.

In "case presentation" one thing should be described more clearly: After DS, the procedure of second CYOA was done immediately, or after several minutes? Please describe it.

Reply 1: Thank you for the feedback. DS and CYOA were performed during the same procedure, after verifying correct sclerosis of the edge of the lesion contacting with the spinal cord. It did not take more than an hour between procedures.

Changes in the text: we added "which was carried out during the same procedure" in lines 7-8, page 9 to avoid confusion.

Comment 2: The second problem is with the written consent: it was not obtained, but why? there was no contact with parents or they did not agree?

Reply 2: We can confirm that we have obtained consent from the patient's parents for publication of the case report.

Changes in the text: text changed to confirm informed consent (line 14, page 9).

Reviewer C

Comment 1: Was there any preoperative biopsy of this lesion with pathologic confirmation? If so, I would recommend a figure describing histology. As you are aware, secondary ABC changes can radiographically mimic a primary ABC. So histology might be helpful in this regard.

Reply 1: Thank you for the suggestion. We confirmed our suspicion of a primary ABC with an intraoperative histological analysis that was done right before the first round of cryoablation. We will modify the text accordingly.

Changes in the text: we added "Intraoperative analysis of the sample confirmed a primary ABC" (line 20, page 8).

Reviewer D

Comment 1: During my assessment, I have identified several intriguing aspects. However, I must also address certain shortcomings that demand specific attention and improvements. The discussion appears to be lacking. It would be beneficial to see references to other techniques employed, such as those utilizing concentrated bone marrow.

Reply 1: We agree with the reviewer that the administration of concentrated autologous bone marrow injections is a promising treatment for ABCs, so we have added a sentence in the discussion about it, supported by the following reference: *Barbanti-Brodano G, Girolami M, Ghermandi R, Terzi S, Gasbarrini A, Bandiera S, et al. Aneurysmal bone cyst of the spine treated by concentrated bone marrow: clinical cases and review of the literature. Eur Spine J. 2017;26:158-66.*

Changes in the text: we added the following: “An alternative investigational treatment involves the administration of concentrated autologous bone marrow injections, which have shown promising outcomes for these lesions” (page 10, line 4-6). We also added a reference (*Barbanti-Brodano G, Girolami M, Ghermandi R, Terzi S, Gasbarrini A, Bandiera S, et al. Aneurysmal bone cyst of the spine treated by concentrated bone marrow: clinical cases and review of the literature. Eur Spine J. 2017;26:158-66*).

Comment 2: “DS proved useful as a complementary and protective agent to CYOA during the 176 treatments of a cervical ABC located next to critical neurovascular structures”: It is not accurate to claim the demonstration of treatment efficacy in this case report, as its nature is limited to a case study. The statement should be rephrased accordingly.

Reply 2: thank you for the kind words and the suggestions. We will rephrase the conclusion accordingly.

Changes in the text: we added “might” to line 2, page 12 and “Nevertheless, this experience is limited to our case and further evidence is needed.” to lines 4-5, page 12.

Comment 3: Nevertheless, the work remains highly intriguing, and I strongly encourage further revision and enhancement. Your efforts in this research are commendable, and I appreciate the opportunity to review this study. Thank you for your dedication and contribution to the field.

Reply 3: Thanks to the reviewer for their comment.