

Peer Review File

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Reviewer A

Chordoma intradural meta from CSF dissemination are rare. The potential interest of this paper is to discuss the putative physiopathology of the CSF seeding in this specific case. Modifications are needed before considering this paper for publication.

1. Line 47: correct with “slow growing”

Reply 1: It was corrected in the revised manuscript.

Changes in the text: Line 47

2. Line 65-66: avoid multiple repetition of “inner layer of the dura”

Reply 2: It was revised as “After the inner layer of the dura was opened, a part of the tumor was resected (Figure 2 C)” in the new manuscript.

Changes in the text: Line 65-66

3. Line 95: “en-bloc” resection is unfortunately not possible for clival chordoma and very difficult to obtain for spine chordomas. Sacral chordoma instead are those chordoma amenable for en bloc resection. Please clarify this and cite pertinent Literature

Reply 3: “En-bloc resection is the recommended treatment which is unfortunately very difficult for clival and spine chordomas, while sacral chordoma instead are those chordoma amenable for en bloc resection.” was added in the revised manuscript.

Changes in the text: Line 96-98

4. Line 97: post-operative radiation is now the gold standard after chordoma resection.

Please cite pertinent Literature.

Reply 4: It was revised as “Currently, the gold standard for chordoma care is complete resection, combined with radiation administered after surgery [6].”

Changes in the text: Line 98-99

5. Please add in the Discussion section different hypothetic causes of the seeding: intradural invasion, no RT/PBT after first surgery, arachnoidal invasion etc

Reply 5: It was added in the revised manuscript.

Changes in the text: 100-105

6. Did you perform directly surgery or did you observe the patient with a second MRI before deciding to do surgery? Recent paper described the innovative role of TGR for chordomas (Passeri et al, Neurosurgery 2021),

Reply 6: the errors in the figures. All the figures 1-5 and their captions were added revised in the new manuscript which provided more details of the treatment course. MRI of 16 months

after surgery showed a new lesion in the spinal canal at C1 to C2 level in the MR, and a metastatic chordoma with intradural spinal seeding was highly suspected, leading to the second operation. And the TGR for chordomas was cited and discussed in the revised manuscript.

Changes in the text: Line 73-78 and 106-109.

Reviewer B

1. The authors present an impressive case of a large, invasive skull base chordoma treated with surgical resection and Gamma Knife radiosurgery. They argue that this case is evidence of the potential for chordomas to spread via seeding of the CSF. While the case and surgical treatment are interesting and operatively impressive, the claim regarding CSF seeding does not appear sufficiently supported by the evidence. In addition, critical details are missing regarding the patient's clinical status, as well as operative details. In addition, there are errors with figure referencing that make the manuscript difficult to follow. The addition of the missing details proper supporting of qualification of claims would substantially improve this interesting case report. Comments in detail are below.

Reply: We are very grateful to your comments and suggestions for the manuscript and sorry for the errors in the figures. All the figures 1-5 and their captions were added and revised in the new manuscript which provided more details of the treatment course.

2. The initial lesion was a large chordoma of the skull base extending from the top of the clivus to at least C1 if not C2 as can be best seen on Figure 1F. It also severely encroached upon the brainstem. Post-operative images are shown and described as gross total resection. I do not doubt the authors claim of imaging consistent with gross total resection, but I cannot evaluate it from a single T1 post-contrast images in each of the axial, coronal, and sagittal planes. Additional views would be helpful to back up this claim. Specifically, there appears to be T1 slightly hyperintense material anterior to the brain stem. I assume that this is fat-packing and not residual tumor but T1 non-contrast images would demonstrate this. At the very least it should be commented on by the authors.

Reply: We are very grateful to your comments and suggestions for the manuscript and sorry for the errors in the figures. As shown in fig.1, G-I: Postoperative enhanced MRI showed total resection of the lesion. J-L: Postoperative non-enhanced MRI showed fat-packing anterior to the brain stem (Arrow).

3. There is heterogeneously enhancing material at C1-2 in the post-op imaging appearing to extend to the lateral mass of C1 (Figure 1I). Is this tumor, fat-packing, or something else? The lesion in the spinal canal that the authors claim is a CSF-seeded metastasis is at the top of C2 adjacent to where the original tumor was, especially this heterogeneous material at C1 in the post-op scan. This appears to just be local recurrence from some combination of the original

tumor or direct seeding from the surgery. I do not see why an uncommon, previously undescribed method of spread, such as CSF, needs to be invoked for this lesion.

Reply: In the present case, the patient refused to take radiotherapy or proton beam therapy after surgery for some insurance reasons. So, gamma-knife radiosurgery was given when the recurrent tumor was found in situ 10 months after the first operation. However, the recurrent tumor still grew quickly 6 months after the gamma-knife radiosurgery. As the new lesion was found in the spinal canal at C1 to C2 level which was far away from the initial chordoma, intradural spinal seeding metastasis is more likely than intradural or arachnoidal invasion of the clival chordoma.

4. What are the arrows in Figure 1A-F meant to show? This should be described in the caption and possibly the main text. The figures are completely mis-referenced. Some examples: Figures 2H-M do not exist. Figure 4 in the text appears to refer to Figure 5. The caption of Figure 4 appears to apply to Figure 5 which itself does not have a caption. The arrows in figures 1, 3, and 4 are unreferenced.

Reply: All the figures 1-5 and their captions were added revised in the new manuscript which provided more details of the treatment course.

5. Please provide annotations in Figure 2 to orient the reader. I suspect that the top of the images is actually the caudal direction as the vertebral arteries are at the top of the images and the basilar artery below them. Also “basal artery” should be “basilar artery.”

Reply: We are very grateful to your comments and suggestions for the manuscript and sorry for the errors in the figures. All the figures 1-5 and their captions were revised in the new manuscript. And “basal artery” was revised as “basilar artery.”

6. What was the approach for the resection of the C2 lesion? It seems odd to call this a craniotomy since the lesion is in the spine. Is it a modified version of a far lateral approach or something else? Please orient the reader in Figure 4E-F. Which way is up? What is being retracted?

Reply: Actually, it was midline suboccipital approach and orientation was added in figure 4E-F. The spinal cord was retracted to show the lesion.

7. More details are needed regarding the clinical status of the patient. It is stated that she presented with imbalance and had relatively intact visual fields. What is the meaning of relatively intact? Did she have any cranial neuropathy or motor weakness? How was CSF leak managed after surgery? Did she have any new deficits or complications after surgery? Please discuss the stability of the spine. Was occipito-cervical fusion considered given the invasion to C1-2.

Reply: visual fields test showed a few some blind spots which was not related to the clival chordoma. The patient had no cranial neuropathy or motor weakness before first surgery. The skull based was reconstructed successfully using thigh fascia and nasal flap. And there was no new deficits or complications after surgery. As the atlanto-odontoid joint was intact through midline suboccipital approach, the stability of the spine was not destroyed and occipito-cervical fusion was not needed.

8. The authors state that the secondary lesion was removed. Please demonstrate this with post-operative imaging. What was the treatment for the pontine lesion that did not respond to Gamma Knife? What is the treatment or follow up plan?

Reply: As shown in figure 4 E-F, the secondary lesion was removed and the 6 months follow-up MR were added in figure 4 G-I. For the pontine lesion that did not respond to Gamma Knife, the patient refused to have operation and chose to have an MRI scan every 6 months.