Peer Review File

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Reviewer A

The work does not seem to provide significant contributions compared to other similar cases already published; however, it is always interesting to learn about another experience with this type of tumor.
I think the authors should correct some aspects:

Comment 1

• P.2, l.38, l.67: Liposarcomas are low-grade malignancy neoplasms; talking about aggressive behavior can be misleading. Authors should specify that they are locally aggressive, as specified in P.3, l.82.
Reply: Thank you for this comment. It was in the text corrected accordingly.
Changes in the text: P.2, l.39, P.3 l.67

Comment 2

• P.2, l.66-73: The authors should highlight some novel aspect of their work, compared to what has already been published.
Reply: Thank you for this comment. With our work, we would like to draw attention to the fact that extensive resections and broncho-vascular reconstructions (which are very rare presented in the recent literature) can become (when needed) the standard in the treatment of locally advanced primary mediastinal liposarcoma in high-volume centers with the aim of improving the control of local recurrence and overall survival. It was added in the text accordingly. Changes in the text: P.2, l.76 - l.78

Comment 3

• P.3, l.88-89: The expression "venous output" seems incorrect. It really is about "venous return".
Reply: Thank you for this comment. It was in the text corrected accordingly.
Changes in the text: P.3, l.91

Comment 4

• P.3, l.90: Bibliographic references 7-10 are redundant and irrelevant to the subject of the work; the authors should have included the one they considered most significant.
Reply: Thank you for this comment. It was in the text corrected accordingly.
Changes in the text: P.3, l.90: Bibliographic references

Comment 5

• P.3, l.122: Authors must write the meaning of an acronym when it is used for the first time (POD in this case).
Reply: Thank you for this comment. It was in the text corrected accordingly.
Changes in the text: P.3, l.125

Comment 6

• Was a preoperative PET-CT study performed?. The authors do not mention it, but I think they should have included a review of its possible role in the Discussion

section (as they do with MRI).
Reply: Thank you for this comment. The use of PET/CT in the diagnosis of primary mediastinal lesions is considered as an additional examination with relatively low specificity. Highly PET-avid tumors are generally considered to be tumors with a lower degree of differentiation. On the contrary, well-differentiated tumors can show false negativity and therefore histological verification of the lesion (with other imaging methods mentioned in the text) is a "condition sine qua non". In our case, PET-CT was not performed due to the relative long waiting time for examination and the necessity of surgical resection in case of high suspicion of liposarcoma. It was added in the text accordingly. Changes in the text: P.4, l.152 - l.154

Comment 7
• The text contains some minor errata.
Reply: Thank you for this comment. The text corrected accordingly.

Reviewer B
I am very interested in your report of an unusual case. I would like to list a few points for improvement.

Case presentation

Comment 1
1. I think the measured tumor markers should be described in detail.
In the CT scan, lesions should be indicated by arrows and annotated in the description (e.g., arrow).
Reply: Thank you for this comment. It was in the text and in the CT scan corrected accordingly.
Changes in the text: P.3, l.105

Comment 2
2. In the CT scan, the lesion should be indicated by arrows and annotated in the description (e.g., arrow). If not, please explain why not.
Reply: Thank you for this comment. It was in in the CT scan corrected accordingly.

Comment 3
3. In this case, an ultrasound-guided biopsy was performed, but did you consider the possibility of needle tract seeding in the case of malignancy? I think this point is worth mentioning in the discussion.
Reply: Thank you for this comment. In the case of large tumor with an unclear possibility of radical surgical resection, fine-needle biopsy is the option of choice (also to rule out hemato-oncological disease). According to the available literature, the risk of needle tract seeding is very low and negligible. Although en bloc-excision of the needle tract with the primary tumor can be performed the evidence for improved oncologic outcomes is lacking.
Changes in the text: P.4, l 168-171

Comment 4
4. Since this is a surgical case, I think you should describe the details of the surgery.

Reply: Thank you for this comment. We have improved the details of the surgical procedure in the text.
Changes in the text: P.3, l 117-l122

Discussion

Comment 5
5. I think it is important to consider that postoperative radiotherapy has a high possibility of causing adverse events because of the proximity of the heart and lungs in this case. I think it would be better to add this point to the discussion.
Thank you for this comment. It was in the text corrected accordingly.
Changes in the text: P.4, l.182

Comment 6
6. In addition, I think that we should provide specific information on postoperative anticancer drug therapy.
Reply: Thank you for this comment. Because surgical treatment represents the only option for radical treatment and the ineffectiveness of conventional chemotherapy, we briefly mentioned the possibilities of using immune-checkpoint inhibitors and angiogenesis inhibitors, the practical use of which must be verified in clinical trials in the future. Within the scope of the report, we do not think that more extensive descriptions of chemotherapeutic agents, which were not used in our patient, will improve the quality of the presented work.

Comment 7
7. I think you should present the literature and discuss what kind of cases have been treated.
Thank you for this comment. As part of the discussion and extensive processing of literary references (27 references), we tried to cover all aspects of diagnosis and treatment of primary mediastinal liposarcoma within the scope of the report. After analyzing the individual case reports, we have not found anything that deviates from the standard therapy recently, except for the few case reports associated with vascular resections, which we want to draw attention to with our case.

Reviewer C
I am grateful for the opportunity to review the case report "Resection of a giant mediastinal liposarcoma by median sternotomy with vascular reconstruction - a case report".

First of all, I would like to commend the successful resection of a giant well-differentiated liposarcoma of the mediastinum, the successful vascular resection and reconstruction, which seem to be very rarely reported, and the recurrence-free survival 6 months after surgery.

As a rare case report, I believe this is an important case report that will be of interest to readers of the Mediastinum journal. On the other hand, because of the rarity of this case report, I believe that proper presentation is very important. I would appreciate your response to my comments below.

Issues:

Comment 1

1. Although there have been a large number of reports of resection of giant well-differentiated liposarcoma of the mediastinum, why are there overwhelmingly fewer reports of large vessel invasion, large vessel resection, and vessel reconstruction compared to thymoma? Does it have a compressive growth but is less invasive to the surrounding area? Your opinion would be appreciated.

Reply: Thank you for this comment. We assume that it is caused by a combination of several factors. On the one hand, the low incidence of primary mediastinal sarcomas (even compared to thymomas), on the other hand, slow expansive growth with compression of surrounding structures. Intraoperatively, it is sometimes difficult to distinguish between intimate contact of the tumor with the adjacent structure and direct infiltration, and therefore, from an oncological point of view, it is more appropriate, in the interest of preserving radicality as a key factor for long-term survival and limiting the occurrence of possible local recurrence, to perform vascular resection with subsequent replacement in case of uncertainty. Therefore, these operations should be carried out in centers with sufficient material and technical equipment and experience with the given issue, even in the case of unexpected vascular resection based on intraoperative findings.

Comment 2

On the other hand, in your case, the left brachiocephalic vein was involved and resected, how did the tumor invade the vein? Did the tumor extend into the lumen of the vessel? Since this is a rare case report, please provide a convincing presentation of the justification for the vascular resection with pathological images of the invasion of the blood vessels.

Reply: Thank you for this comment. As was mentioned in the comment above, sometimes intraoperatively it is difficult to distinguish between intimate contact of the tumor and the vessel with direct infiltration if the given structure is completely surrounded by a tumor. In the interest of achieving the radicality of the resection and the sufficient experience of our center with resections and replacements of large vessels, in case of uncertainty and the possibility of replacement with the aim of complete restoration of the anatomical arrangement, we always lean towards vascular reconstruction.

Comment 3

2. Lines 140-142, page 4: "These tumors occur mainly in the posterior mediastinum, followed by the anterior, and most rarely in the middle 142 part of the mediastinum [15]. Intrapulmonary growths has also been reported in care cases."

I think "has" should be changed to "have", or "growths" should be changed to "growth" in the above sentence. Also, should "care" be changed to "rare"? As you

can see, there are some mistakes in English. Please consider having a native English speaker check the English.
Reply: Thank you for this comment. It was in the text corrected accordingly.
Changes in the text: P.2, l 143

Comment 4
3. Staging Systems for Soft Tissue Sarcoma of the Extremity or Trunk: AJCC 8th edition, the T factor considers tumor size and localization to be important and does not take into account extension into large vessels or mediastinal structures, while upstage (Stage IIIB) in N1 is severe. Conversely, I speculated that the TNM in soft tissue sarcoma may be constructed because invasion into blood vessels is not often expected or is extremely rare. What do the authors think about this point? On the contrary, I thought it is essential to prove and present pathological evidence of the tumor's invasion into blood vessels.
Reply: Thank you for this comment. this is an interesting, but hypothetical question. According to the available data, the degree of dedifferentiation of the sarcoma increases the probability of growth into neighboring tissues and the formation of metastases. In consequence, a well-differentiated liposarcoma has a relatively low probability of infiltrative growth into the surrounding area. If the structure is embedded in the tumor mass, regardless of its infiltration, it is not possible to perform an R0 resection without breaking the tumor capsule, and the only possibility to preserve radicality is to remove the structure together with the tumor. Due to the rarity of infiltration of vascular structures by sarcoma, it is not possible to determine the potential impact on survival, and hypothetically, the classification of invasion into vessels would be meaningless and would rather copy impaired survival, clearly conditioned by the degree of tumor dedifferentiation. On the basis of the pathological reevaluation of the microscopic finding, it is not possible to provide convincing evidence of infiltration of the vein wall as a result of total compression with chronic occlusion and thrombosis, with the impossibility of differentiating the border of the fibrous remnant of the vein in the tumor and from the tumor mass itself, where the resection of such a changed vein is not only from a technical but also from an oncological point of view represents a necessary predisposition to achieve R0 resection.

Comment 5
4. In general, if the tumor invades the left brachiocephalic vein, only resection is required and there is no need for reconstruction due to the presence of collateral blood circulation. In this case, the same vessel was reconstructed rather than resected only. Please provide the reason why this reconstruction was necessary.
Reply: Thank you for this comment. We agree with the reviewer, with chronic closure of the brachiocephalic vein and developed collateral circulation, a simple resection without reconstruction is also possible. The evidence that would prefer a simple resection of the vein in comparison with reconstruction and vice versa in this situation are not convincing. However, as mentioned above, we try to restore the anatomical conditions if possible.