

Peer Review File

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Round 1:

Reviewer A

1. anticoagulation was certainly advised in this case. How was it administered, prophylactic or therapeutic dose? How was the pre and post-surgical anticoagulation managed?

Reply 1: Anticoagulants were not administered before surgery, but edoxaban (60mg/day) was initiated postoperatively to prevent artificial vessel occlusion.

Changes in the text: We have clarified this point in the Case presentation section (see page 6, line 2-3, yellow highlights).

2. How was the improvement of the face swelling after surgery was performed?

Reply 2: The facial swelling improved soon after surgery.

Changes in the text: We have clarified this point in Case presentation section (see Page 5, line 18-, yellow highlights).

3. As I understand the manuscript, initial diagnosis was from a lymph node Level 7. Was a histopathological diagnosis performed on the resected lymph node, and if so, did it show distinctive differences in biological features possibly explaining the oligoprogression?

Reply 3: Unfortunately, we had erroneously referred to the #7 lymph node, when we mean to refer to the #4R lymph node. We apologize for this mistake. Furthermore, there were no differences in pathological findings and PD-L1 TPS between the EBUS-TBNA sample and the surgically resected sample.

Changes in the text: We have addressed this issue in the Case presentation section (see Page 5, line 17-18, yellow highlights).

4. even though I understand the decision to perform surgery (and it does show a good response as was pointed out), from my point of view, radiotherapy would have been a viable option as lung toxicity would be minimal in mediastinal radiotherapy. Maybe it would be a good idea to evaluate this option a bit more.

Reply 4: As you point out, radiotherapy would also have been an option for local therapy for SVC obstruction. However, the safety of intrathoracic radiotherapy in the patients receiving immunotherapy remains unknown, despite the fact that the effect on the lung may be minimal because irradiation area was mainly in the mediastinum. Furthermore, a previous study had reported the poor effectiveness and high recurrence rates with radiotherapy. Therefore, surgical resection may be a more reliable treatment for SVC obstruction, and we duly selected it. Whether surgery, stent insertion, or radiotherapy is selected, it is important to discuss the appropriate treatment strategy with oncologists, surgeons, radiotherapists and interventional radiologists.

Changes in the text: We have addressed these points in the Discussion section (see Page 8, line 1-5, yellow highlights).

Reviewer B

1. Anesthesia technique for the induction of anesthesia? Did the surgical resection require bypass?

Reply 1: We used propofol for sedation, remifentanyl for analgesia, and rocuronium for muscle relaxation. The surgery was performed using cardiopulmonary bypass.

Changes in the text: We have clarified this point in the Case presentation section (see Page 5, line 15-17, blue highlights).

2. What were the pros and cons of surgery vs SVC stent? Did the benefit of the surgical option outweigh the risk of such a procedure?

Reply 2: Stent insertion is a less invasive procedure than surgery, but carries the risk of re-obstruction. Therefore, surgery may be the more reliable option. In this specific situation, since the tumor invading the SVC increased in size despite of the chemotherapy, we believed that surgical resection would be more likely to achieve long-term relieve of SVC obstruction. We believe that both surgical resection and stent insertion should be considered as management options for malignant SVC obstruction resistant to chemotherapy.

Changes in the text: We have clarified these points in the Discussion section (see Page 7, line 13-17, blue highlight).

Round 2:

Reviewer A

1. Dear Authors, thank you very much for the adjustments and explanations after the first review. I am rather satisfied with your explanations. However, I do not think that the sentence “Furthermore, poor effectiveness and a high recurrence rate are disadvantages to the use of radiotherapy (7,8).” (page 8, line 4-5) is correct. The cited literature does show a response rate of radiotherapy of about 70%, (which was recently reported again, PMID: 35552767 DOI: 10.1007/s00066-022-01952-z). I believe ~70% cannot be described as “poor”. I suggest to adjust this sentence. Otherwise, I have no more concerns.

Reply: Thank you for your important suggestion. We agree with you, and have changed the sentence to “Furthermore, inadequate response or recurrence occur with radiotherapy in some cases”.