

Dear Reviewer,

We appreciate the opportunity to revise and resubmit our manuscript titled: Radiotherapy for Hyoid Bone Metastasis from Lung Adenocarcinoma: A Case Report. Below, we have listed how we addressed each point of concern and have updated the manuscript to reflect the answers we provided below. Thank you for your time and consideration as these comments helped add a new dimension to our paper.

Comments:

1. There was no tumor marker detection in the entire diagnosis and treatment process of the patient, so why did the author not use tumor markers for detection?

Tumor markers were used during the diagnostic process. We have added a table of biomarkers that were screened. Here are the biomarker results for the lung cancer:

Findings are consistent with lung adenocarcinoma of invasive mucinous type.

Cancer-Type Relevant Biomarkers and Genes of the Lung Tumor

Biomarker/Gene	Method	Analyte	Result
ERBB2	Seq	DNA-Tumor	Mutation Not Detected
FGFR3	Seq	RNA-Tumor	Fusion Not Detected
MET	Seq	RNA-Tumor	Variant Transcript Not Detected
NRG1	Seq	RNA-Tumor	Fusion Not Detected
PD-L1(22c3)	IHC	Protein	Negative TPS: 0%
PD-L1(28-8)	IHC	Protein	Negative: 0%
PD-L1(SP142)	IHC	Protein	Negative IC: 0%, Negative TC: 0%
RET	Seq	DNA-Tumor	Mutation Not Detected
STK11	Seq	DNA-Tumor	Mutation Not Detected
TP53	Seq	DNA-Tumor	Mutation Not Detected
ALK	IHC	Protein	Negative
PTEN	IHC	Protein	Positive
Keap1	Seq	DNA-Tumor	Pathogenic Variant
MLH1	IHC	Protein	Positive
MSH2	IHC	Protein	Positive
MSH6	IHC	Protein	Positive
PMS2	IHC	Protein	Positive
CK7	IHC	Protein	Positive
TTF-1	IHC	Protein	Positive
CK20	IHC	Protein	Negative
Napsin	IHC	Protein	Negative

2. Is the patient's lung a single lesion? Why is it not resected?

The patient had a single 2.8cm lung lesion with metastasis to an ipsilateral hilar lymph node and the hyoid bone. The tumor board did not recommend surgery as the node was in the aortopulmonary zone. While a left sided lobectomy was possible, chances of recurrence is higher with stage III.

3. Did the patient undergo PET/CT examination after radiotherapy? How to confirm hyoid lesion clearance?

The patient did undergo PET/CT after radiotherapy. The procedure was done for palliative measures, so the purpose was not to eradicate tumor. The short course of radiotherapy was effective in decreasing the SUV max in the hyoid region from 16.6 before treatment to 5.4 after radiation.

4. Why not combine radiotherapy with chemotherapy?

Given not targetable alterations, and no PDL1 expression, patient was treated with carboplatin + pemetrexed + pembrolizumab based on the Keynote 189 study:

<https://www.nejm.org/doi/full/10.1056/nejmoa1801005>.

Lung cancer did not respond to this treatment, so the patient opted in for palliative radiotherapy to abate the throat pain.

5. How long was the patient followed up? What is the survival period? Did symptoms recur after treatment?

The patient was followed up with until she passed away. Post palliative radiotherapy treatment, the patient remained asymptomatic for a year until succumbing to the advancing lung cancer. Patient's work up started at age 72 and passed away at 75.

6. No specific value was given for the blood test indicators in this case

We added a numeral value to the associated lymphocytosis: absolute lymphocyte count (ALC) of 4,336 in February 2020. ALC of 5,645 the following year.