

## Peer Review File

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### Reviewer A

It's a very well-written and interesting case which brings new treatment strategy in a scarce but challenging condition.

Could the authors precise what are for us the indications to surgically manage a thyroid cardiac metastasis? Haemodynamic criteria? Single cardiac and resectable site (which is rare)?

Reply 1: Unfortunately, no clear indication for cardiac metastasis can be determined from past reports. We believe that the feasibility of surgery should be determined on a case-by-case basis.

Minor revision: line 120 : it should be Table 2

Reply 2: We have modified our text as advised.

### Reviewer B

Well written case report of a rare occurrence. Was there a germline genetic variation tested?

Reply 1: In this case, only the RET fusion gene was detected from the cancer tissue, so we did not test germline mutations.

### Reviewer C

This is a very interesting and valuable report that drug therapy was effective for cardiac metastasis of differentiated thyroid cancer, and the report has worth of being published.

On the 90th line of case presentation section, "metastatic lesions" should be changed. At this point, it shouldn't be clear whether it was cardiac metastasis from thyroid cancer. And it should be described that the patient was diagnosed as cardiac metastasis of papillary thyroid cancer based on her medical history and the imaging finding.

Reply 1: We have modified our text as advised (see line 91. 95 and 96).

On the 92th line of case presentation section, normal values for Tg should be listed.

Reply 2: We have modified our text as advised.

When describing adverse events of drug therapy, it is better to describe grade evaluation by CTCAE.

Reply 3: We have modified our text as advised (see line 108-111).

In the Discussion section, you would be better to describe a low bleeding risk using of Selpercatinib using clinical trial results (LIBRETTO-001 Clinical Trials) listed in your report as the 5th reference. In this clinical trial, there was no adverse events due to vascular rupture.

Reply 4: We have modified our text as advised (see line 143 and 144).

### Reviewer D

The authors report a very rare case of new thyroid cancer metastasis arisen more

than 40 years from the first diagnosis and treatments. Moreover, the patient disclose a symptomatic cardiac metastasis, which is a rare event too.

The authors reported very high quality images of the cases and they performed a cutting-edge radiological, pathological and molecular work-up. Also the therapeutic strategy adopted is coherent with current discoveries.

Finally, they also included a brief literature review (with a summarizing table and figure) of the cases of cardiac metastasis originated from thyroid cancer reported in the literature till to date.

However, there are some points that need to be ameliorated:

Abstract:

- Line 36: please specify already here the site where the CNB have been performed (ndr right chest wall)

Reply 1: We have modified our text as advised (see line 37).

- Line 42-43: please specify which type of metastasis respond to the different types of drugs

Reply 2: All metastatic lesions shrunk. Details are given in Table 2. We have modified our text (see line 41 and 43).

Case presentation:

- Could the author retrieve the last Tg level measured before the clinical presentation of the new metastasis? What dose of LT-4 was she taking? and what was her TSH level?

Reply 3: We could not retrieve the Tg level before the clinical presentation of the new metastasis. She was taking 125 µg/ day of levothyroxine and her TSH level was 0.053 µIU/ml. We have modified our text (see line 83, 84 and 93).

Discussion:

-Line 114-115. please revise the grammar of this sentence "The most common case..."

Reply 4: We have modified our text as advised (see line 118 and 119).

- The authors state that surgery is the main way of management of cardiac metastasis from PTC, as reported by literature. However, they don't motivate enough why this option was excluded in favor of systemic therapy in their case. Overall, the concepts written in lines 135-150 are repetitive and confusing, so please revise accordingly.

Reply 5: We have modified our text as advised (see line 141-150).

- Generally, I would prefer to use the term of "systemic therapy" rather than "drug therapy" when referring to the administration of TKI. So please, revise accordingly in all manuscript.

Reply 6: We have modified our text as advised.

Heading of Table 2.

-Please add that the reported cases are collected from 2011.

Reply 7: We have modified our text as advised (see line 247).