

Responses to the comments from reviewer #46325

1. Case presentation: in the discussion there is further information on treatment given, in that the patient was said to have had 8 months of platinum based chemotherapy. This seems bizarre, if he had no lymph node or distant metastases, and treatment is aligned to normal lung adenocarcinoma treatment, where this would not normally be done. In addition the conclusion contains detail on the histology of the tumour. It would be better to move all clinical details, such as histology, staining, staging, post operative management and outcome (ie alive after 8 months) to the case discussion section. This would aid flow, and also allow justification of treatment choices made for this particular individual. There may well have been a reason for using chemo, but this was not clear at present.

Response: Because there is a time lag between the completion of the manuscript and now, we followed up again. Chemotherapy was given once in the first month after operation with paclitaxel and carboplatin. Because of a serious adverse reaction to chemotherapy, the patient did not continue with chemotherapy and other treatment and he died 15 month after surgery in December 2018.

(page 9)

2. Discussion: whilst this was comprehensive it was also difficult to follow as a result. I would favour the use of some subheadings to divide it up. The initial introductory paragraph is ok pretty much as is (see language comments later) but then sections might be considered on (1) Clinical features of HAL - this would include the table of past cases and discussion of features relative to this case, as well as paragraphs on biochemical features (eg the parts on AFP) and clinical imaging. The lung adenoca pathway would also go here; I noticed that whole body radiotherapy was mentioned as part of routine lung cancer care in the absence of metastasis, which is not the case in my country. I suggest justifying this by citing guidelines, or reviewing accuracy for China. I note that most past cases have been in China; is there a known or speculated genetic or environmental factor that

might explain this? There are some other malignancies more common in the Far East (eg nasopharyngeal) and I wondered about shared aetiology (2) Mechanistic aspects of HAL -this would include the histological and embryonic elements of the discussion

Response: HAL is essentially a special type of lung adenocarcinoma and guidelines for diagnosis and treatment of lung cancer should be followed. The general principle is that if there is distant metastasis, systemic chemotherapy and local radiotherapy should be performed after a clear diagnosis. If there is no distant metastasis, surgical treatment or local radiotherapy should be performed. Chemotherapy should be considered according to the postoperative stage of HAL. We strongly recommend that patients undergo genetic and immunological tests. (page 9) I'm so sorry that whole body radiotherapy is a translation error. We had asked the professional English medical translation company to revise the articles again. At present, the relevant literature in China is only case report, and there is no relevant research on the mechanism.

3. Language - there are several instances where the sentence construction is odd, appearing like it is a list instead of full text. For example, in the opening paragraph of the discussion "Aggressive tumor that most commonly arises from the gastrointestinal tract" might be better stated 'HAL is an aggressive tumor...'. Short sentence structure is also apparent in several places, for instance in the second paragraph of the discussion "The prognosis is closely related to the pathological stage. The clinical manifestations are non-specific." Using many short sentences gives the impression of a list again, which does not aid flow when reading. These aspects should be carefully reviewed throughout the manuscript.

Response: I'm so sorry for the shortcomings and problems in the translation of articles. We had made a thorough revision to the articles and asked the professional English medical translation company to revise the articles again.

4. I would favor a conclusion which summarises the literature around HAL and what this case adds, perhaps with some recommendations for future research

rather than simply restating the case. For example 'In conclusion, HAL is a rare cancer, most commonly reported in [authors should describe patients], similar to the case presented here. Since pathophysiology is poorly understood case registries in countries where cases have been reported previously might be considered in order to aid research into the condition. This might include [describe types of research authors think is needed]'

Response: Thank you very much for your suggestion. We have also improved the clinical information and follow-up information of patients in the revised articles.(page 5)