

Dear Editor and Reviewers,

Thank you for your questions and advice. We have revised our manuscript according to your comments. And the answers to the reviewers are listed below.

1. How can the authors make sure the primary lesions were gastrointestinal tract? Was it possible that epithelioid angiosarcomas originate from lymphnodes or bones and metastasize to gastrointestinal tract?

Answer: Dear reviewers, thank you for your question. Based on literatures, most cases of angiosarcomas are presented with distant metastasis at the time of diagnosis. Generally, liver, lung, lymph nodes and bone are common places of metastasis. Primary or metastatic angiosarcomas in the digestive tract are rare. In a case series of primary and metastatic angiosarcomas involving the gastrointestinal tract, the author concluded that gastrointestinal angiosarcomas can be primary to the gastrointestinal tract, secondary to direct extension of a retroperitoneal tumor, or metastatic. Primary cases and secondary involvement from retroperitoneal primaries are more common. Metastatic gastrointestinal angiosarcomas can originate from breast, liver, and spleen, but they have never been reported to originate from lymph nodes or bones. (Kimberly H Allison, Brian J. Yoder, Mary P. Bronner, John R. Goldblum, and Brian P. Rubin. Angiosarcoma Involving the Gastrointestinal Tract: A Series of Primary and Metastatic Cases. *Am J Surg Pathol*, Volume 28, Number 3, March 2004.) From the perspective of the incidence and pathogenesis of disease, it seemed more reasonable that the primary lesions happened in the gastrointestinal tract, afterwards, metastasis to lymph nodes and bones occurred.

2. Is it a colon lesion biopsy? How to make sure of the pathology result of lesion of gastric body?

Answer: Dear reviewers, thank you for your question. Neither a colon lesion biopsy or a gastroscopy biopsy could identify the nature of the lesions. Instead, an en bloc endoscopic mucosal resection of the suspected lesions made the diagnosis of epithelioid angiosarcomas. This highlighted the importance of endoscopic mucosal resection for a definite diagnosis.

In this case, because the diagnosis of malignant angiosarcomas was confirmed, the patient refused to have another large-scale biopsy of the stomach. However, the endoscopic performance of the gastric lesion is typical according to literature, we speculated that the gastric lesion was also epithelioid angiosarcomas.

3. ANA and anti-SSA of this patient was positive. Did it have any significance?

Answer: Dear reviewers, thank you for your question. In the reported case, the antinuclear antibody (ANA) titre of the patient was 1:1000, while the anti-SSA (Ro60) antibodies were weakly positive. The patient had no related symptoms like arthralgia, rash, thirst or dryness of eye. Rheumatologists considered that she had no autoimmune disease. Maybe the autoimmune

antibody was related to tumor. However, until now, there is no evidence that positivity of ANA and anti-SSA has association with epithelioid angiosarcomas. Further studies are needed to collect the information of autoimmune antibodies in patients with epithelioid angiosarcomas.

4. Is there any data about the morbidity of gastrointestinal epithelioid angiosarcomas indicating it's really rare? Where are the predilection site of epithelioid angiosarcomas?

Answer: Dear reviewers, thank you for your question. It has been reported that about 2% of soft tissue sarcomas and 5.4% of cutaneous soft tissue sarcomas are angiosarcomas (Robin J Young, Nicola J Brown, Malcolm W Reed, David Hughes, Penella J Woll. Angiosarcoma. *Lancet Oncol* 2010; 11: 983–91). About 60% of angiosarcomas occur in the skin and superficial soft tissues in the head and neck. As for gastrointestinal epithelioid angiosarcomas, only individual case reports and case series have been reported, with a lack of demographic morbidity data. Vascular tumors of the stomach represent only 0.9–3.3% of all gastric neoplasms. Colorectal angiosarcomas constitute less than 0.001% of all colorectal cancers. Angiosarcomas may arise in any part of the body, but commonly occur in skin and superficial soft tissues, with its predilection sites in the head and neck. The answers to this question have been supplemented in the discussion part.

5. It is suggested to list manifestation of each picture in Figure 4.

Answer: Dear reviewers, thank you for your question. We have supplemented the figure legends of Figure 4 as follows: Whole-body maximum intensity projection 18F-FDG PET image (a) showed increased radiopharmaceutical uptake in the colon and mediastinal lymph nodes, as well as the right humerus. PET (b), CT (c), and hybrid PET/CT images (d) in axial projection showed multiple tubular hypermetabolic lesions in the colon.

6. It is suggested to point out the significance to help clinicians from this case.

Answer: Dear reviewers, thank you for your question. Epithelioid angiosarcoma has a low incidence and is extremely rare clinically. This case report can increase the understanding of the disease for clinicians. Moreover, it proposes the endoscopic characteristics of this tumour that are related to its highly vascular nature and its tendency to cause gastrointestinal bleeding. Due to the limitations of biopsy tissue specimens, if a simple biopsy cannot make a definite diagnosis, endoscopic mucosal resection can be considered to confirm the diagnosis. The significance of this report has been illustrated in the discussion and conclusion part.