Author's response to reviews

Title: Intrathoracic splenosis presenting as persistent chest pain

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Author's response to reviews: see over
Dear Drs. Zamvar and Taggart,

I wish to submit the revised manuscript titled “Intrathoracic Splenosis Presenting as Persistent Chest Pain” to the Journal of Cardiothoracic Surgery.

We are very grateful for the reviewers’ helpful comments. We have addressed all their concerns.

The revised portions were highlighted in yellow in the manuscript.

The revision and comments are as follows.

Referee #1

Comment 1: The finding of the CT angiogram is missing. The authors should have known the vessels supplying "the intra-thoracic mass".

Response: The feeding vessels of the splenosis were not clearly visualized on the CT scan even though it
was with intravenous contrast study. There were no identifiable blood vessels. It is obvious that it derives from the pleura based on the location as described in the previously published reports (reference 7: Nathan T. Connell, Andrew M. Brunner, Christine A. Kerr and Fred J. Schiffman. Splenosis and sepsis: The born-again spleen provides poor protection. Virulence 2011; 2: 4–11).

Comment 2: The degree of the diaphragmatic injury is missing. Was it repaired primarily or repaired with mesh. The author should have this information from intraoperative findings.

Response: The patient underwent surgery 30 years ago at outside hospital and we were unable to obtain the surgical report at that time. Neither how they repaired the injury, nor the usage of prosthesis material was known preoperatively. Based on the intraoperative findings from our surgery, we found that the diaphragm was primarily repaired at that time.

Comment 3: How did author speculate the relocation of the spleen?

Response: As we mentioned in the manuscript, it is known that splenosis is caused by autotransplantation of splenic tissue into the pleural cavity after splenectomy for traumatic or iatrogenic injury. In addition, Tc-99m labeled colloid scintigraphy has high sensitivity and specificity for the diagnosis of ectopic splenic tissue. Clinical presentation and positive scintigraphy result were enough for the diagnosis.

Comment 4: Scintigram finding is not clear and author should have submitted figures.

Response: The image of the Tc-99m labeled colloid scintigraphy was added as Figure 2.
Comment 5: The pathological review may help the reader to understand the tissue the author resected was the splenic tissue as a conformation.

Response: Regarding the pathological report, we did not appreciate any findings suggestive of the growth. We discussed with pathologists at our institution. The reason we did not describe any more details of pathology findings was that it did not reveal anything characteristic other than the patterns of normal splenic tissue.

Comment 6: Quality of written English is not good as publication.

Response: As for the quality of written English, this manuscript was revised by three native American physicians followed by a professional English editing service “Edanz” that Journal of Cardiothoracic Surgery is recommending (Track number: J1202-42082-Fukuhara, Edanz Group Japan, +81-92-715-7208). After your review, we had another American physician to check the quality of written English aggressively and some changes were added.

Referee #2

Comment 1: The paragraph is too long throughout the entire manuscript, especially Case presentation and Discussion.

Response: We would agree that the case presentation and discussion may be too long. However, it also contains important pertinent positive, negative findings and relevant information. We made an effort to make
it more concise.

Comment 2: It would be better to add the Tc-99m sulfur colloid scintigram.

Response: The image of the Tc-99m labeled colloid scintigraphy was added as Figure 2 in the manuscript.

Comment 3: P4 line3 ‘Tc-99m sulfur colloid scanning’ The authors should write ‘scintigraphy’, not scanning.

Comment 4: The sentence ‘To our knowledge…’ should be moved to discussion.

Comment 5: Please mention the size of ectopic splenic tissue of previous reports.

Response: Comments 3-5 were all addressed in the manuscript.

Comment 6: Please describe the size of intrathoracic splenic tissue not only in the figure legends but also in manuscript.

Response: We think it would be redundant if we mention it in the body of the manuscript. It is clearly mentioned in the figure legends. In order to make it concise, we would not duplicate same description.

Comment 7: Please arrange about need for surgical removal.

Response: We had mentioned the necessity of surgical removal in the manuscript. His symptoms were
refractory to non-operative therapy and other possible etiologies that might cause the nagging pain had been ruled out on the imaging study. Again, splenosis does not require surgical removal unless it is causing symptoms and symptomatic splenosis is exceedingly rare. The indication for surgical removal is one of the most important points of this paper.

Comment 8: The authors need to describe the conclusion specifically.

Response: Conclusion was revised.

Referee #3

Comment 1: Description of the pain is inconsistent between in the abstract and in the case presentation. Is it vague chest pain or sharp pain?

Response: The pain was vague. The main body of manuscript was corrected.

Comment 2: The pathological result was simply described as splenic tissue. Is there any suggestive finding to explain the progressive growth?

Response: Regarding the pathological report, we did not appreciate any findings suggestive of the growth. We discussed with pathologists at our institution. The reason we did not describe any more details of pathology findings was that it did not reveal anything characteristic other than the patterns of splenic tissue.
**Comment 3:** Regarding the legends of Fig. 2, sizes of the small fragments could be omitted.

**Response:** The pictures of other fragments were unfortunately not saved. Figure 3 (formerly Figure 2) was the representative one we have.

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**Referee #4**

**Comment 1:** The authors chose an open surgery instead of thoracoscopic approach. Do you still recommend open approach for the disease? What exactly was “careful preoperative planning”? It would be helpful if you can provide your suggestions regarding surgical approach after having actually done your surgery.

**Response:** We again retrospectively reviewed the case and the description in the manuscript was not completely accurate. VATS was initially set up when we started the case and was actually attempted. Severe adhesions, friable tissues and active bloody oozing, secondary to the previous trauma and large splenosis, were encountered shortly after we entered into the thoracic cavity. The working space for VATS was limited and visualization was poor under thoracoscopy. The decision was made to convert to open thoracotomy (still not formal big thoracotomy incision) fairly earlier during the case because of the initial difficulty of visualization. As we described in the manuscript, this disease entity does not require surgical intervention. Surgical removal is currently considered to be contraindication. However, our case was extremely unusual case and surgical removal was justifiable. Symptomatic splenosis has not been previously reported in the literature except for 3 cases with chest pain and hemoptysis (references 3, 4, 5 in the manuscript).
Comment 2: The authors described that the mass was spread along the phrenic nerve. The affinity for nerve tissue is of particular interest and needs further discussion.

Response: As you pointed out, the phrenic nerve involvement is an important point of discussion. As we mentioned in the manuscript, we postulated that the pain in our patient was referred pain due to a mass effect and irritation of the pericardium, parietal pleura, and diaphragm mediated by the phrenic nerve. Other than mass effect, there was no good explanation for the pain. There was no literature supporting that direct invasion of a benign thoracic lesion can cause symptoms related to phrenic nerve. In addition, there was no diaphragmatic elevation on the preoperative chest radiograph.

Comment 3: The mass has grown rapidly in one year, even though the disease is benign. The patient has important medical background including HCV infection and heavy smoking habit. The information on the current status or recent change in liver function/cirrhosis and chronic lung inflammation such as COPD is crucial and should be provided.

Response: As we mentioned in the manuscript, his laboratory results including liver function enzymes were within normal limits. There was no evidence of liver cirrhosis or COPD on the preoperative workups.

Comment 4: The presence or absence of diaphragm laceration should be clarified.

Response: The patient underwent surgery 30 years ago at outside hospital and we were unable to obtain the surgical report at that time. Neither how they repaired the injury, nor the usage of prosthesis material was
known preoperatively. Based on the intraoperative findings from our surgery, we found that the diaphragm was primarily repaired at that time. The previous repair was contributing the severe adhesion as well. We did not think this intraoperative finding of the diaphragm was relevant for the discussion because; 1) it is obvious that he had a diaphragmatic injury and repair in order to have an intrathoracic splenosis and; 2) there was no more particular interesting findings we were able to provide other than the presence of severe adhesion around the left lung base. These were the reasons that we did not describe it specifically in the body of the manuscript.

We hope that the revised version of our paper is now suitable for publication in the Journal of Cardiothoracic Surgery and we look forward to hearing from you at your earliest convenience.

Yours sincerely,

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