Author's response to reviews

Title: Left ventricular thrombus in a patient with cutaneous T-cell lymphoma, hypereosinophilia and Mycoplasma pneumoniae infection - a challenging diagnosis: a case report

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Author's response to reviews: see over
Dear Editor,

We very much appreciate the reviewers’ comments and have revised our manuscript accordingly.
Please find enclosed the revised version of our manuscript. Changes are marked with yellow highlighting.
Additionally, we submit two echocardiographic cine-loops:
Echocardiographic cine-loop 1 (transthoracic) shows the apical third of the left ventricle completely filled with the thrombus and akinesia of the subjacent myocardium.
Echocardiographic cine-loop 2 (transthoracic) shows the thrombus considerably smaller in size, free-floating and pedunculated, arising from the lateral wall of the left ventricle without regional akinesia.
Please find a point-by-point response to the concerns of the reviewers below.

Yours sincerely,
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Response to reviewer Mr. Robert J. Siegel, MD

Thank you for reviewing our paper and your comments.

1. The case report and commentary are too long- they should both be more concise and focused.
   The sections “Background”, “Case presentation” and “Conclusions” have been shortened as suggested. More precisely, we shortened the paragraph about secondary neoplasms, the patient’s medical history, and the paragraph about thrombosis incidence in adult lymphoma patients.

2. The LV apical hypokinesis described was very unlikely to be due to the CLOT.
   If there was normal wall motion- 1) a clot would be unlikely to form 2) The force of LV contraction is unlikely to be impaired by clot- it is more likely that the patient had an apical wall motion due to a stress cardiomyopathy - this concept is supported by the fact the the segmental wall motion resolved.
   Prompted by the reviewers’ suggestions, we questioned the causes of the thrombus formation again and contacted the hospital in Australia, where the patient was first treated during her trip. When asked whether a more detailed explanation of the investigation results from the TTE was available than was given in the summarising letter from the doctor, the hospital sent us the original echocardiography report, in which wall motion abnormalities were described. In view of this additional information, we agree with the reviewers’ considerations - namely, that the wall motion abnormalities were causally associated with the formation of the thrombus, and that the thrombus did not cause the wall motion abnormalities.

3. On generally wants to avoid taking patients with apical thrombi to the for removal.
   The standard treatment would be intravenous heparin. Were there any clues in retrospect that the mass was a clot and not a tumor? These clues could serve as good teaching points to aid the reader from avoiding the pitfalls in this case that led to surgical intervention. Differentiation of tumor & clot should be feasible by MRI and PET scanning - this should be discussed. This was a difficult case and raises issues that the clinician can learn from - the authors should highlight how the thrombus diagnosis could have been made absent surgical intervention.
Based on the course with shape change and size reduction of the intracardiac mass, we finally assumed that this intracardiac mass was most likely a thrombus. Owing to the detection of two small lesions in the cranial MRI that are consistent with a recent embolic/ischemic event and the consequently estimated very high risk for further embolization, the conscious decision for urgent surgery was made in this patient. According to the literature, surgical intervention might be considered in high-risk patients and may be beneficial for the patient’s outcome. Risk-benefit assessment in our patient prompted us to surgically remove the intracardiac mass, respectively thrombus, as described.

As we discussed in our report, MRI was the first modality to correctly identify the cardiac mass as a thrombus, but the suggested infiltrative process of lymphoma was not confirmed in the histopathological examination. We therefore highlighted the remaining difficulties in diagnostic MRI scans of cardiac masses.
Response to reviewer Mr. Richard W. Asinger, MD

Thank you for reviewing our paper and your comments.

1. Include congestive heart failure as the cause of the initial hospitalization to explain the symptoms, signs and radiographic findings. Most important here would be the ejection fraction on the initial echocardiogram.

   We included congestive heart failure as the cause of the initial hospitalization and as the explanation of the patient’s symptoms and diagnostic findings. Unfortunately, the ejection fraction wasn’t measured echocardiographically at the time of the initial hospitalization in Australia.

2. The trend in troponin I levels and serial ST-T changes from the initial hospitalization. These could support infarction or stress cardiomyopathy

   The troponin I level stayed on the same level (around 0.23µg/l) for the first 24 hours after the first hospitalization in Australia. The following day, the troponin level was falling (0.177µg/l). When the patient was admitted to our hospital, troponin levels were within the normal range. Serial ECG evaluation showed continuous existence of sinus rhythm with ST-segment depression and T-wave inversion in precordial leads.

3. Between the last two imaging procedures was the patient continued on anticoagulant? If so the decrease in size of the mass would have been the clue that this was thrombus rather than tumor.

   The patient received anticoagulation therapy between the imaging procedures showing reduction in size of the intracardiac mass. Based on the course with shape change and size reduction of the intracardiac mass, we finally assumed that the intracardiac mass was most likely a thrombus.

4. Surgical findings: a. Was the ‘fibrin rich collagen scar’ part of the thrombus or ventricular wall? b. Did the surgeons biopsy the left ventricular lateral wall to evaluate for malignancy?

   The fibrin rich collagen scar was part of the thrombus. Biopsies were also taken from the apical region. Malignant cells weren’t detected at histological evaluation.
5. Were follow-up images of the left ventricle performed and if so, did the left ventricular lateral wall and apex look and move normally? Postoperatively performed echocardiography showed normal left ventricular systolic function and normal wall movement in absent of akinetic areas one day and two and a half month after the operation.

6. The authors feel the left ventricular thrombus caused the wall motion abnormality rather than the other way around but they present no mechanism to explain this and the literature would not support this contention. They should propose a mechanism for their opinion.

Prompted by the reviewers’ suggestions, we questioned the causes of the thrombus formation again and contacted the hospital in Australia, where the patient was first treated during her trip. When asked whether a more detailed explanation of the investigation results from the TTE was available than was given in the summarising letter from the doctor, the hospital sent us the original echocardiography report, in which wall motion abnormalities were described. In view of this additional information, we agree with the reviewers’ considerations - namely, that the wall motion abnormalities were causally associated with the formation of the thrombus, and that the thrombus did not cause the wall motion abnormalities.
Response to reviewer Mr. Bruno Pinamonti, MD

Thank you for reviewing our paper and your comments.

1. Case presentation, third paragraph. No echo image showing the thrombus, nor its characteristics have been provided.
   
   Unfortunately, our attempts to organize cine-loops of the initially performed echocardiography in Australia were unsuccessful.
   
   However, we submit two cine-loops of the echocardiographic investigations performed at our hospital. These two cine-loops show the thrombus and provide evidence of the described transient akinesia:
   
   The first cine-loop shows the apical third of the left ventricle completely filled with the thrombus and akinesia of the subjacent myocardium.
   
   The second cine-loop shows the thrombus considerably smaller in size, free-floating and pedunculated, arising from the lateral wall of the left ventricle without regional akinesia.

2. Case presentation. Fifth paragraph. No documentation on transient (?) akinesia has been provided.
   
   Please see comment on point number 1.

3. Same paragraph. F-18 FDG PET/CT findings consistent with an infiltrative process must be explained.
   
   The myocardium was thickened and there was a discoloration of the tissue.

4. Same paragraph. TTE findings that seemed consistent with EMF must be explained.
   
   Echocardiographic findings leading to the picture of endomyocardial fibrosis included the combination of myocardial thickening, a thrombus adherent to the endocardial surface, and enlargement of the left atrium.

5. Case presentation. Last paragraph. Suspicious incisional margin ?? Explain please. No information was provided about surgical findings of the myocardium of apex surrounding the thrombus.
   
   After incision of the aorta, a suspicious incisional margin involving the apical region up to the middle of the left ventricle was identified. The margin to the surrounding
tissue was not defined and it therefore was suspicious for being a malignant infiltration. The margin was removed as far as possible, and a biopsy of the apical region was taken. In the histopathological analysis no malignant cells were detected.

6. Conclusions. Fourth paragraph. Intraventricular thrombus usually is associated with local blood stasis due to akinesis. In my knowledge the only disease in which a thrombus can be present with normal kinetics is loeffler eosynophilic endomyocarditis. Does the patient may have a similar pathology? The authors could discuss about this diagnostic possibility

Endomyocarditis is not supported by histopathologic analyses.

7. Conclusions, last paragraph. The interpretation of the authors about the transient wall motion akinesis as the result of thrombus filling the apex is not supported from the current Literature. The alternative hypothesis of thrombus consequence of an endomyocarditis and apical akinesis cannot be excluded without showing appropriate images or cineloops.

Prompted by the reviewers’ suggestions, we questioned the causes of the thrombus formation again and contacted the hospital in Australia, where the patient was first treated during her trip. When asked whether a more detailed explanation of the investigation results from the TTE was available than was given in the summarising letter from the doctor, the hospital sent us the original echocardiography report, in which wall motion abnormalities were described. In view of this additional information, we agree with the reviewers’ considerations - namely, that the wall motion abnormalities were causally associated with the formation of the thrombus, and that the thrombus did not cause the wall motion abnormalities.