

*Dear Reviewers,*

*Attached you may find the changes in italicized fonts.*

The manuscript by Loba et al entitled 'Pericardial Effusion with Tamponade: An Uncommon Presentation Leading to the Diagnosis of Eosinophilic Granulomatosis Polyangiitis' describe

a case of cardiac tamponade complicated with EGPA, which was confirmed by pericardial and lung biopsy. Isolated cardiac tamponade is rare, and as authors emphasize by the review of other reports, this case indicates the importance of tissue biopsy to diagnose it.

This is interesting report, but some issues should be revised to make it better.

• In this case, cardiac tamponade is diagnosed by TTE, demonstrating right ventricular diastolic compression. Of course, this sign is representative for diagnosis of cardiac tamponade, however there are many other signs of cardiac tamponade including paradoxical pulse, diastolic pressure equalization by cardiac catheterization, signs of low output, low blood pressure, etc... If other signs were observed, please mention about it. Especially, the reviewer thinks vital signs (blood pressure, heartbeat) and Lab data (BNP, the value of troponin, WBC...) are needed for excluding other diseases. In addition, details of echo-cardiac findings should be described, including negative findings (i.e. left ventricular dysfunction, myocardial edema, local ventricular wall thickness) The detail of effusion (i.e. exudative or transudative) is also needed.

*Vital signs were notable for blood pressure of 124/79 mmHg, sinus tachycardia with heart rate of 119 beats per minute, hypoxia with oxygen saturation of 89%, respiratory rate of 16 breaths per minute and afebrile temperature. On examination, she demonstrated sinus tachycardia, a pericardial friction rub, and rales in her bilateral lower lung fields. She did not demonstrate pulsus paradoxus. Initial laboratory findings were notable normal white blood cell count of 11/nL, however with 45% peripheral eosinophilia. Troponin was mildly elevated at 1.1 ng/mL and NT ProBNP was elevated at 2,101 pg/mL. D-Dimer was elevated at 3.66 ug/mL.*

*Transthoracic echocardiogram demonstrated normal left ventricular cavity size, wall thickness and systolic function with estimated ejection fraction greater than 55%. No regional wall motion abnormalities were detected. Aortic and mitral valves were normal. There was trace tricuspid regurgitation. The right atrium was normal in size. The right ventricle collapsed in diastole. There was a large pericardial effusion. The diastolic compression of the right ventricle was suggestive of tamponade physiology.*

*Pericardial fluid studies were notable for a cloudy, exudative effusion with white blood cell count of 3,092 uL and 25% eosinophilia. Pericardial fluid cytology was negative for malignancy.*

*Aerobic, anaerobic, and fungal cultures were negative for any growth.*

- Authors said this case was isolated pericarditis, but troponin was elevated. As describe in above, it is better to describe exact value of troponin, and refer more detail about why other disease like myocarditis is excluded. Authors used cardiac MRI to exclude it. When cardiac MRI was performed? If it was performed at follow-up phase, it might have failed to detect active phase. Late gadolinium enhancement is useful sign to detect cardiac abnormality. The detail of cardiac MRI measurement including with contrast or not should be described, too.

- As authors mentioned, coronary artery vasculitis is one of the complications of EGPA. Mild elevated troponin and mild ST-T change in ECG were observed. How coronary artery diseases were excluded? Was cardiac catheterization including coronary angiography or coronary CT performed?

*Following the drainage of pericardial fluid, the patient demonstrated relief of her presenting symptoms. She denied any chest pain or shortness of breath. Repeat troponin levels were within normal limits. Other laboratory workup including respiratory viral panel, blood cultures, rheumatologic marker including ANA, rheumatoid factor and ANCA were negative. Hypersensitivity pneumonitis panel was also negative. Repeat echocardiogram the following day showed normal biventricular function, valvular function, and wall motion. It did not demonstrate accumulation of new pericardial effusion. As such coronary catheterization was deferred.*

*At one-month interval, cardiac MRI with and without contrast were performed to monitor disease progression. Cardiac MRI with and without contrast showed normal biventricular volume and systolic function. There were no areas of focal hyperenhancement, consistent with the absence of myocardial scarring or fibrosis. A post gadolinium LAVA sequence was acquired which demonstrated normal measurements of biventricular dimensions, volume and ejection fraction. The patient was scheduled to have a Cardiac MRI the same week she was discharged from the hospital, however she was not able to make it to the appointment until a month after initial diagnosis.*

- In this case, mepolizumab, a humanized monoclonal anti IL-5 antibody was used. The reason why mepolizumab was administrated should be described more detail. It was reported that the effect of anti-IL-5 treatment depends on the result of bone marrow findings. Was bone marrow examination done in this patient?

*Biologics such as mepolizumab, a humanized monoclonal anti-IL-5 antibody has been shown to maintain higher proportion of study participants in remission, as well as reduce glucocorticoid use in patients with EGPA (9, 10). IL-5 is a cytokine involved in eosinophil proliferation, maturation, and differentiation. IL-5 is found to be at increased*

*levels in patients with EGPA (10). Mepolizumab binds to IL-5 and prevents interaction with its receptor on the eosinophil surface, thus providing consistent reduction of peripheral eosinophilia and clinical improvement in patients with eosinophilic disorders such as severe eosinophilic asthma and EGPA (10). The decision to initiate mepolizumab was made by a rheumatologist/cardiologist/pulmonologist – unfortunately there was no consideration to perform a bone marrow biopsy prior to initiation.*

Minor

• For the reviewer, there are small ST-T change in ST-T (V2, 3,V6, III, aVF). It might be overstatement to describe 'without ST-T change', if you agree, please revise the description.

*Changed.*

*Thank you for your comments and reviewing our manuscript.*