

Response to Reviewers:

Reviewer 1:

Your case is interesting and informative. I have some suggestions for your manuscript.

1 Title - The phrase “treated with antibiotics” seems unnecessary. The uniqueness of this case is that myocarditis occurred in a non-acute phase of Q fever which is very rare. Thus, it would be better if the authors add this uniqueness to the title. - As my comment in the final diagnosis part, if this case is chronic myocarditis, it is worth to be shown in the title.

Thank you for suggestion. We have removed treated with antibiotics from title. The modified title is “Rare Case of Chronic Q Fever Myocarditis in End Stage Heart Failure Patient: A Case Report”.

2 Abstract - In the case summary part, “volume overload” is not a symptom, please specify what is(are) the volume overload symptoms in this patient.

The volume overload word is removed, and line is modified as follows in abstract: A 69-year-old male was admitted with heart failure symptoms including dyspnea on exertion, and bilateral lower extremity edema.

3 Keywords – **case report word is removed from keywords**

4 Core tip - In my opinion, core tip should describe the major findings and lessons learned from the case. For example, when to suspected Q fever myocarditis, myocarditis should be differentiated even in non-acute Q fever especially concomitant with fever, how to make a diagnosis, and how to treat it. The present core tip looks like another abstract.

Thanks for the suggestion. The core tip is modified as follows:

Q fever myocarditis is a rare disease (<1% of cases) caused by infection with *Coxiella burnetii* (gram-negative proteobacteria). Q fever normally has a pleomorphic and non-specific clinical presentation which leads to delayed diagnosis and treatment, which can lead to worse outcomes. Q fever myocarditis should be kept in differentials in patients with recurrent fevers and animal contact, not only in patients with acute Q fever but also with chronic Q

fever infection, like in our case. Q fever serologies help in making diagnosis of acute and chronic Q fever. Cardiac PET and MRI can be utilized to diagnose myocarditis in setting of Q fever. Hydroxychloroquine and doxycycline in combination are used for treatment of Q fever myocarditis.

5 Introduction - *Coxiella burnetii* is a scientific name, so it ought to type in italic style throughout the manuscript.

Agreed. Thank you. Change made throughout the manuscript.

6 Case presentation

- Shortness of breath was mentioned in the abstract, but not in the case presentation.

Shortness of breath added to the case presentation.

- Previous valvular pathologies and time of surgery (for MV) should be described, especially in the second procedure on MV. Because if it was recent endocarditis, it may associate with Q fever.

Following details regarding valve procedure is added to the case report: bicuspid aortic valve s/p aortic valve replacement with 25 mm Carpentier-Edwards bioprosthetic prosthesis in October 2012 followed by transcatheter aortic bioprosthetic valve in valve (26 mm Sapien S3) in April 2019, mitral valve repair with 32 mm seguin ring repair in 10/2012 and subsequent transcatheter bioprosthetic mitral valve replacement with 29 mm Sapien 3 bioprosthetic valve for mitral regurgitation in 6/2019

- Given an absence of sinus node dysfunction described in the patient's past medical history, it should be explained why this patient needed dual-chamber ICD and why the rhythm was atrial pacing on admission. If he had SSS or other indications, please specify.

He underwent dual chamber ICD implant in 2018 due to his history of ischemic cardiomyopathy for primary prevention. No documentation of sick sinus syndrome noted in the chart. Most likely reason for atrial paced rhythm on admission, may be due to underlying inflammation/infection. The next ECG three days post admission did not show atrial pacing.

- The previous ventricular and valvular functions are worth mentioning. It is important to tell whether the present findings are resulting from a new event or just his baseline pathologies.

This information is added to case report as follows: Transthoracic echocardiogram (TTE) on admission showed LVEF of 20-25% with global hypokinesis, mild to moderate aortic regurgitation, mitral valve mean gradient of 10 mmHg (@ HR of 72 bpm) with normal right ventricle size and function and no vegetation. His most recent TTE prior to admission was done at outside facility on 7/2019 showed LVEF of 30%, no aortic valve or mitral prosthetic valve regurgitation, mean mitral valve gradient of 7 mmHg (@ HR of 67 bpm) normal RV function.

- Chest examination should be reported. From the present data, it is obvious that the patient had right-sided heart failure; however, I am uncertain whether the patient had left-sided heart failure or not.

Thank you for asking. Patient had bilateral bibasilar crackles on lung examination. This is added to the case report.

- Due to the above reason, CXR findings should be provided.

Chest X ray findings added to the manuscript: The chest X ray on admission showed moderate cardiomegaly with central venous congestion and interstitial edema.

- Echocardiogram and right heart catheterization findings indicated that the left-sided heart was the major cause of heart failure. This is the reason why symptoms and signs of left-sided heart failure should be described.

Agreed. The symptoms and signs of left sided heart failure are added to manuscript as described above.

- Authors should explain why right heart catheterization was necessary for this patient.

Following lines are added to explain this: “To determine his cardiac hemodynamics, shock profile, and whether escalation to temporary mechanical support device is needed, an urgent right heart catheterization was done”

- Why troponin-I was negative in active myocarditis should be discussed in the discussion part.

Thank you for suggestion. We have discussed this in discussion part. Negative troponin-I had been noted in prior studies with biopsy proven myocarditis. The lack of troponin-I release does not rule out myocarditis.

- It should be “Infectious disease specialist was consulted”.

This is modified in case report. Thank you.

- It should be “It showed a moderate paravalvular aortic regurgitation”.

This is modified in case report. Thank you.

- Since the mitral valve was replaced, the sentence “the repaired mitral valve was functioning normally with no stenosis or regurgitation” should be corrected.

This is modified in case report. Thank you.

- If available, previously treated antibiotic regimens should be mentioned.

Sorry, we don’t have this information as patient went to outside local clinic and does not remember the name of the antibiotic he was prescribed.

- Radiotracer used in PET scan should be named.

18-Flourine fluorodeoxyglucose (FDG) was used as radiotracer and it is now incorporated in case report.

- It should be “heterogenous areas of increase 18F-FDG uptake” (if 18F-FDG was used).

This is modified in case report. Thank you.

7 Final diagnosis - It should be specified and given the reason that this patient had (i) acute myocarditis in acute Q fever, (ii) chronic myocarditis in acute Q fever, (iii) chronic myocarditis in acute Q fever or (iv) chronic myocarditis in chronic Q fever. If it was chronic myocarditis in chronic Q fever, this would be the novelty and highlight of this case. Since all of the previous reports were mostly acute myocarditis in acute Q fever. To the best of my knowledge, this should be the first case of chronic myocarditis in chronic Q fever.

Thank you for sharing this very useful information. Our patient indeed meets criteria for chronic myocarditis in chronic Q fever patient. On our literature search, we also could not find any case of chronic myocarditis in chronic Q fever patient. We have modified the case report accordingly to incorporate this important change.

8 Treatment - The dosage of Doxycycline and Hydroxychloroquine should be reported.

The dosage is now mentioned in case report: “treatment with doxycycline 100 mg twice daily and hydroxychloroquine 200 mg three times daily was initiated for an 18-month course.”

9 Outcome and follow-up - It was very astonishing that paravalvular AR was resolved.

Paravalvular regurgitation almost always results from mechanical causes, thus it was unlikely to be resolved after myocarditis subsides (though the severity may be varied from hemodynamics). This was very interesting and should be discussed further.

Yes, indeed we were astonished to see that too. One of the plausible reasons for it could be valvulitis in patients with Q fever. This could have led to mild to moderate aortic regurgitation which got better with the treatment. Following changes made to discussion: “There had been few cases in past showing that Q fever infection can cause valvulitis (*Deyell MW, Chiu B, Ross DB, Alvarez N. Q fever endocarditis: a case report and review of the literature. Can J Cardiol. 2006 Jul;22(9):781-5. doi: 10.1016/s0828-282x(06)70295-1. PMID: 16835673*) and this can be the reason for aortic regurgitation in our patient which got better with treatment of Q fever.

10 Discussion - As mentioned above, “why troponin-I was negative in active myocarditis” and “why paravalvular AR disappeared” should be discussed. - Since this case is related to non-acute Q fever, the publications about myocarditis in non-acute Q fever should be reviewed and mentioned in the discussion part. - Please look for the publication about chronic myocarditis in Q fever, to the best of my knowledge, I have never seen it before. If there is no previous publication and the authors conclude that this case was chronic myocarditis, the authors can mention that this is the first published case and emphasized that chronic myocarditis can be the presentation of Q fever.

Thank you for your valuable insight on this. We could not find any case of chronic myocarditis in chronic Q fever patient. The negative troponin in patient with myocarditis is discussed in case report.

11 Conclusion - Not only cardiac PET is important for the diagnosis of myocarditis, but also other imaging modalities. Thus, it would be better to summarize that multimodalities imaging e.g., echocardiography, cardiac MRI, and cardiac PET can be utilized in diagnosing myocarditis in patients with Q fever.

Agreed. The conclusion is modified to include this.

12 Abbreviations - Please check the abbreviations again, some of them look strange e.g., 18F-fluorodeoxyglucose positron emission tomography, Center for Disease Control and Prevention (CDC).

Thanks for pointing it out. Corrections made to the abbreviations

13 Figure - Before and after treatment PET scans should be demonstrated in the same views. In my opinion, the multi-plane image in figure 1A is better to show all myocardial segments.

Agreed. We really wanted to show the same views. But, first PET study was dedicated cardiac PET scan, hence we had multiplanar images. The second study was whole body PET study to

look for any residual Q fever infection, hence we do not have multiplanar images for figure 1b.

Reviewer 2:

Specific Comments to Authors: Overall this is an interesting case about a 69-year-old male patient with a history of multiple comorbidities who was initially thought to be a regular case of acute on chronic heart failure but later diagnosed with Q fever myocarditis. This case report still has a lot of room for further refinement. This case report is potentially useful but needs more detail. Some novelty and newly published information should be included.

Thank you for the suggestion. The case report had been extensively revised. We have also highlighted the point that this is the first case of chronic myocarditis in patient with chronic Q fever. This will act as the novelty of our case. The English and grammar throughout the manuscript has also been edited.

In this case report, authors concluded that Q fever myocarditis should be kept in differentials, especially in cardiomyopathy patients with recurrent fevers and contact with farm animals. In conclusion part the author should add some other perspectives to make this part informative.

We have reworded the abstract conclusion as follows: "Chronic Q fever myocarditis if left untreated carries poor prognosis. It should be kept in differentials, especially in patients with recurrent fevers and contact with farm animals."