Peer Review File

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Reviewer A Comments

Thanks for the manuscript. Find appended in track changes with a few suggestions.

Comment 1: quoted data is from an italian urban and should be quoted as such.

Reply 1: We have modified this sentence as requested to provide further context regarding the setting of the cited study.

Changes in the text: Pericarditis is the most common disease of the pericardium with one study from an Italian urban area suggesting an incidence of 27.7 cases per 100,000 people (1) (lines 87-88).

Comment 2: It may be good to cite TB as a common cause of pericarditis and a differential to neoplastic effusive TB both in the context of HIV and non HIV cohorts especially in Africa. see Noubiap JJ, Agbor VN, Ndoadoumgue AL, et alEpidemiology of pericardial diseases in Africa: a systematic scoping reviewHeart 2019;105:180-188.

Reply 2: As requested, we have cited tuberculosis as an additional cause of pericarditis, especially in Africa. We have also added and cited the suggested reference.

Changes in text: Other etiologies include viral infection, neoplasm, autoimmune, bacterial infection, and cardiac injury; tuberculosis is another common cause of effusive pericarditis, especially in Africa (1,2, 3). (lines 90-91).

Comment 3: Would have better read “previous cases have linked MM with pericardial effusions but reports of pericarditis without effusion in this context remains rare”.

Acute pericarditis can occur with or without effusions as seen in 2015 ESC Guidelines for the diagnosis and management of pericardial diseases (your first reference).

Reply 3: We have changed this sentence as requested.

Changes in text: Previous cases have linked MM with pericardial effusions (4), but reports of pericarditis without effusion in this context remain rare (5). (lines 99-100).

Comment 4: Also, instead of reference 4,5, a better and updated reference that reports over 27 cases of MM and pericardial effusion from extensive literature search may be better. see Skipina TM, Sane DC, Cui C, Song S, Phillips SG, Jarrett RW. Cardiovasc Pathol. 2019 May-Jun;40:41-46. doi: 10.1016/j.carpath.2019.02.002.

Reply 4: We have replaced references 4 and 5 with the suggested reference.

Changes in text: Previous cases have linked MM with pericardial effusions (4), but reports of pericarditis without effusion in this context remain rare (5). (lines 99-100).

Comment 5: regimen

Reply 5: We have fixed this typo.

Changes in text: One prior case report describes acute pericarditis attributed to DCF chemotherapy regiment, which includes docetaxel, cisplatin, and 5-flourouracil (7). (lines 104).

Comment 6: There are reported cases with this association

1. Simão Raimundo D, Cordeiro AI, Parente Freixo J, Valente Pinto M, Neves C, Farela Neves J. Case Report: Patient with deficiency of ADA2 presenting leukocytoclastic vasculitis and pericarditis during infliximab treatment. Front Pediatr. 2023 Jun 14;11:1200401.

2. Clozapine is known to cause both neutropaenia and pericarditis

Reply 6: We have modified this sentence to reflect that although pericarditis in the setting of neutropenia has not been well-documented, there are still a few rare reports that detail this association. We have added and cited the suggested reference. We also have added a sentence discussing the association between clozapine, neutropenia, and pericarditis.

Changes in text: Pericarditis in the setting of neutropenia is not well-documented. There are few reported cases of this association on literature review (9), although clozapine is a known cause of both pericarditis and neutropenia. (lines 156-158).

Reviewer B Comments

Interesting and rare case. A few points worth noting, in order as presented in the paper:

Comment 1: Viral pericarditis does not exclusively result in low volume pericardial effusions.

Reply 1: We have modified this sentence to highlight that viral pericarditis usually causes low volume pericardial effusions but that this is not always observed.

Changes in text: Viral pericarditis usually, but not always, results in a low volume serous pericardial effusion. (lines 91).

Comment 2: I am unclear as to what the statement "neoplasm is a known etiology for pericarditis" means, and I imagine other readers will be as well.

Reply 2: We were attempting to suggest that cancers, or neoplastic phenomenon, can cause pericarditis. We have attempted to clarify this in the highlighted sentence.

Changes in text: Cancers are a known cause of pericarditis with the most common ones being breast cancer, lung cancer, Hodgkin's disease, leukemia, and lymphoma by local invasion (1). (lines 95-98).

Comment 3: Do you plan to include the components of the "CARE reporting checklist"? I have written up case reports and I am not familiar with this guideline, but it may be worth including for your readers (or at least detailing the most salient parts)

Reply 3: The CARE guidelines are one suggested standard for case reports and are required for all reports published by JECCM (see: https://jeccm.amegroups.org/announcement/view/124#). If our manuscript is accepted, our submitted checklist, which details the components of the CARE guidelines, will be published alongside our case report for readers who may be unfamiliar with this reporting standard. As requested, we have also added a sentence to our manuscript that briefly details the salient parts of this reporting guideline.

Changes in text: This reporting standard for case reports ensures that all pertinent information,

including patient demographics, diagnostic assessments, therapeutic interventions, and a discussion of relevant literature is included for readers. (lines 111-113).

Comment 4: The concept that someone cannot develop pericarditis due to neutropenia is inaccurate; while neutrophils are an integral part of the inflammatory process there are many key players to this, including NLRP3 inflammasome, IL-1a, IL-1b, etc. Moreover, in an immunocompromised patient one should expect the unexpected.
Reply 4: We completely agree with the reviewer, and this is the primary lesson that we have sought to impart to readers throughout the manuscript – neutropenia does not preclude the development of pericarditis, as seen by our patient. We have clarified this point in the discussion and highlighted the other players of the inflammatory process that were suggested by the reviewer.
Changes in text: However, importantly, neutropenia does necessarily preclude the development of pericarditis, as there are many other key molecular regulators that can drive this inflammatory process such as the NLRP3 inflammasome, IL-1a, and IL-1b. (lines 169-172).

Comment 5: Interesting that the D-dimer was low in a patient with active malignancy. Was a CRP checked? Troponin? Any noncontrast chest imaging obtained?
Reply 5: We apologize for our mistake. Our initially published D-dimer (0.3) was incorrect, given the associated units. We have modified this to the correct value (300). Based on a quick literature review, roughly 50% of patients with multiple myeloma will have a negative d-dimer. We did not check CRP as we did not deem a clinical reason for ordering one. A troponin was ordered and negative, which we have already reported in the paper (see line 129).
Changes in text: We corrected the d-dimer value (see line 139). We did not make any other modifications to the text, as we have already included the troponin value, and did not order any of these other tests.

Comment 6: Reasonable treatment approach given neutropenia. I would indicate that the risk of recurrence for pericarditis is higher in patients who are treated with steroids.
Reply 6: Thank you. We have added a sentence discussing the higher risk of pericarditis recurrence after steroid therapy.
Changes in text: However, a significant detriment of steroid therapy for pericarditis is a higher risk of post-treatment disease recurrence. (lines 180-181).

Comment 7: I think it would be useful for the reader to know that guidelines dictate 2 out of 4 criteria are necessary for diagnosis (pain, EKG changes, rub, effusion). This patient had characteristic chest pain + EKG changes, but no rub or effusion. It should be emphasized that lack of effusion does not rule out diagnosis. That being said, ruling out PE in this patient is important.
Reply 7: We have added this relevant information to our discussion of the diagnosis of pericarditis to provide more information about accepted guidelines for diagnosis and that the lack of effusion does not preclude a diagnosis of pericarditis.
Changes in text: Diagnostic guidelines for pericarditis generally require that patients exhibit two of the four following symptoms: pleuritic pain, ECG changes, pericardial friction rub, and pericardial effusion. Thus, the lack of an effusion or auscultated friction rub were not required for diagnosis, as our patient clinically demonstrated the first two symptoms. (lines 188-192).