Peer Review File

Article information: https://dx.doi.org/10.21037/acr-23-50

Reviewer A

Management of a patient with LVAD associated infection remains common and the infection may progress or recur despite antibiotic treatment. The case report may reserve as a reference for the management of LVAD associated infection complicated with cerebral septic emboli. However, I would like to suggest quite a number of issues in the manuscript.

I would like to know if there is any discussion with neurologist, cardiologist, and cardiac surgeon about the management plan and anticoagulation concerning the presence of both intracardiac clot and cerebral hemorrhage. I believe that it is a very difficult situation, and it should be highlighted in the case report. Otherwise, the current manuscript lacks novelty. And your team must have done a great job so that the patient could have full neurological recovery!

Title page: The author information does not match the superscripts. There should be 2 lines of matching author information without the need for individual e-mail addresses.
Corrected in the revised version, with changes highlighted in appropriate lines

Abstract
background: I believe it is inappropriate to conclude that neurological complication is common despite the use of anticoagulant because it can be a hemorrhagic event due to anticoagulation.
Corrected in the revised version, with changes highlighted in appropriate lines

Line 48: “in the wait of” should be ” or “awaiting”
Line 48: “which meanwhile had” should be “and meanwhile having”
Line 50: cross out “due to”
Line 54: Staphylococcus epidermidis should italicized.
Line 55: cross out “with” before supportive therapy
Line 56: change “with” to “resulting in” before full recovery.
Corrected in the revised version, with changes highlighted in appropriate lines

Introduction
Line 75: “and” instead of “or”

Case presentation
Line 81: “hypertension” instead of “high blood pressure”
Line 83: what is the exact LVAD device use in this patient? Heartmate 3 LVAD carries a lower risk of thromboembolism, so there might not be an urgency to resume anticoagulant in this patient suffering from cerebral hemorrhage.
Line 84: “heart failure medications” instead of “anti-congestive medications”
Line 87: it should be called “driveline exit site” instead of “percutaneous exiting lead”
Line 87: hemodynamic vital signs should be reported together with mean arterial pressure. Given the figure provided, the mean arterial pressure should be 70mmHg which is normal for patient with LVAD.
All suggestions have been accepted and due corrections made.

Line 88: what is the exact heart rhythm?
Line 89: what is the definition of fever?
Line 90: what is the proper unit for WBC.
Line 92: Please confirm the Hemoglobin value (?10/70)
Line 94: raised the suspicious of sepsis
Line 98: slurred instead of slurry
Line 103: there is no need to report the prothrombin time when INR is available.
All suggestions have been accepted and due corrections made.

Line 106: what was the choice and dosage of antibiotics? It is because the reader will be interested to learn about the use of antibiotics in this patient.
Line 108: cross out “of” before intravenous
Line 108: what is the dosage interval
Corrected in the revised version, with changes highlighted in appropriate lines

Figure 1A legend: I believed the lesion is in the left occipital lobe instead of temporal lobe. Would you please obtain the opinion from a radiologist/neurologist?
Corrected in the revised version

Line 116: Was there any finding related to the LVAD, such as collection or soft tissue stranding surrounding the LVAD that might indicate LVAD associated infection?
Line 118: regardless of
Line 124: “complaint of “ instead of “referred”
Line 131: could you please elaborate “acute inflammation of left auricula” in

echocardiogram?
All suggestions have been accepted and due corrections made.

Figure 2B legend: I believed the finding should be infected pump pocket instead of "intraluminal infection".
Figure 2C: I believe there is also evidence of drive line infection which is actually the source of infection of a skin flora organism because it provides the conduit for entry of bacteria into the pump pocket and hence bloodstream.
Corrected in the revised version, with new comments in the legend of the figure

Line 141: what was the exact dosage of Enoxaparin
Corrected in the revised version, with changes highlighted in appropriate lines

Line 144-145: it is less meaningful if only a single value of ESR and fibrinogen without previous value or trend provided.
I have omitted unnecessary data

Line 145: what do you mean by prothrombin time 65%?
I have omitted unnecessary data

Discussion
Line 156: a new sentence should start after "for survival",
Line 157: cross out "noticed" after shortage
Line 160: played instead of paid
Line 162: cross out "out" after carry
Line 176: Please clarify the sentence. I believe "septic or" does not belong to the sentence.
Line 178: Please elaborate the sentence. According to both ESC and ACC guideline, cardiac surgery should be delayed by 4weeks after cerebral hemorrhage in infective endocarditis.
Corrections and re-phrasing done appropriately (highlighted)

Line 180: I believe prothrombin complex concentrate is an option and should be the first line medication in treating over-warfarinization and it should be included in the discussion.
Line 180-182: Please explain the problem of vitamin K in a grammatically correct sentence.
Line 185 Reference 11: I do not agree with this citation given there is more updated and accepted guideline such as "European Stroke Organisation

Guideline on Reversal of Oral Anticoagulants in Acute Intracerebral Haemorrhage. Eur Stroke J. 2019 Dec;4(4):294-306."
All suggestions have been accepted and due corrections made.

Line 186-191. Please reconcile the case presentation and the discussion as the use of vitamin D is not mentioned in the case summary. And there are more specific studies concerning the use of vitamin D in LVAD patients. It would be also interesting to know if the vitamin D level was checked in the patient.
All suggestions have been accepted and due corrections made. I have omitted entirely the issue of vitamin D as irrelevant to our specific case.

Line 194-195: Please kindly rephrase the first sentence with appropriate grammar.
Rephrasing is done and the new reference has been inserted (highlighted in color)

Conclusion: the conclusion in abstract and main body do not match. It may not be wise to start a new argument in conclusion about delaying the resumption of anticoagulation in patients with LVAD complicated with cerebral hemorrhage.

"Key findings": "awaiting" instead of "queued". I suggest adding fever in the presenting symptoms.
All suggestions have been accepted and due corrections made.

"What is known and what is new?": "implantable cardiac devices" instead of "heart external devices". Again, it is inappropriate to conclude that the risk of these patients remains high despite anticoagulation because there can be both ischemic and hemorrhagic infarct. I would also advise to consult the corresponding multidisciplinary team or hospital once a LVAD associated infection is suspected apart from having a high index of suspicion for the attending medical staff.

"What is the implication, and what should change now?": Please rephrase the sentences will correct grammar.
All suggestions have been accepted and due corrections made.

According to 2019 EACTS Expert Consensus on long term mechanical circulatory support, it is recommended treatment for at least 6 weeks for deep infection instead of 4 weeks as mentioned in the case report.
Many thanks, however our patient received only four weeks of vancomycin, after

first four days or treatment under cefuroxime. Negative hemoculture and consistent improvement of clinical picture led us to this decision.

Reviewer B

Interesting case, well presented but I have got some revisions to suggest:
- the authors should clarify why the patient was supported by VAD, cardiac failure is not enough in a very young patient;
- the echocardiography imaging should be very appreciated in this case and should be added in the paper.

All suggestions have been accepted and due corrections made. Echocardiography imaging has been added as a new figure with respective legend (figure 2).

- in the discussion paragraph, it would be correct add the Duke's criteria addressed to confirm the diagnosis of endocarditis and if this is expressed in the table it will be greatly appreciated;

Duke criteria are added and mentioned in the highlight table as well.

- Pag 3 line 92: HB is expressed 10/70 maybe it was 10.70, please check and correct.

All suggestions have been accepted and due corrections made.

Reviewer C

The manuscript presents a case of LVAD infection complicated by sepsis and multiple cerebral emboli and haemorrhagic lesions. The Authors highlighted the crucial role LVAD plays in the treatment of advanced heart failure, although the high risk of serious complications. IE and the potential neurological complications are a significant cause of morbidity and mortality in LVAD carriers and their management is especially challenging as these patients require anticoagulation treatment. Clear data about the most appropriate preventive strategies and treatment of LVAD-related infections are still lacking.

I congratulate the Authors for the management of this complex scenario and I believe this case can provide helpful insights in the management of this difficult clinical setting.
Yet, there are minor points that should be addressed:
1) Driveline infections are considered the most common infection associated with LVADs. If possible, I would discuss the patient's prophylaxis and wound

dressing strategies. I would specify the type of LVAD involved too. Patient was describe as hypotensive; blood pressure was not expressed in mean arterial pressure (MAP), but it actually reveals a rather pulsatile flow (90/60 mmHg). I would clarify that as well.
All suggestions have been accepted and due corrections made.

2) In line 106 the Authors say "intravenous antibiotic therapy was started appropriately". Then, after haemocultures results, vancomycin was started. I think it could be useful to specify the initial antibiotic administered. On the other hand, the Authors explained quite clearly the reasons behind the anticoagulation therapy management.
Corrected in the revised version, with changes highlighted in appropriate lines

3) In lines 116 and 117 the Authors say "The following day the patient went through a thoraco-abdominal CT scan, which noticed two enlarged reactive paratracheal lymph nodes." . What about the cardiac findings? Did it show any vegetations, or the left atrial thrombosis mentioned in line 131? Also, I would eliminate the sentence "acute inflammation of left auricula" in lines 131-132, as echocardiography cannot clearly highlight the presence of inflammation.
All suggestions have been accepted and due corrections made.
CT was a routine thoraco-abdominal imaging, and cardiac structures could not be evaluated there.

4) It was delightful to find out the patient's conditions improved considerably. However, I believe it would be useful to the Readers to find out how the LVAD itself was managed. The patient was transferred to a cardiac surgery facility (line 57), but, if possible, I would shortly mention what happened next (LVAD replacement?).
Explained in the revised version, with changes highlighted in appropriate lines (lines 154-156).