

Dear Editors:

We would like to thank you and the reviewers for the valuable comments and suggestions. We have reviewed our work again and have carefully revised the manuscript accordingly. We have provided our point-by-point responses below. We hope the revisions and responses meet the requirements of the *World Journal of Clinical Cases* and satisfactorily answer the questions and concerns of the reviewers.

Reviewer #1

Comment 1: It is difficult to understand the exact timing of the events the patient had, such as blood purification, ECMO, IABP and cardiac ultrasound, etc. I heavily recommend rewriting the case presentation section entirely taking into consideration the journal's guidelines.

Response: We would like to thank Reviewer 1 for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

We have rewritten the case presentation section entirely taking into consideration the journal's guidelines and your suggestion. We added exact timings of the events the patient experienced, such as blood purification (i.e., Daily blood purification therapy was administered to the patient from days 1 to 4 of admission), ECMO (i.e., adjuvant support therapy with venoarterial ECMO (VA-ECMO) was performed within 60 min of arrival at the hospital after obtaining consent from the patient's family), IABP (i.e., An IABP was used for cardiac assistance on day 1 of admission), and cardiac ultrasound (i.e., Multiple cardiac ultrasound indicated left ventricular enlargement with severe diffuse hypokinesis of the left ventricular wall. On day 18 of admission, cardiac ultrasound revealed ejection fraction (EF) of 19.5% (Figure 3)).

Comment 2: Conclusion section is missing in the abstract and the body of the

manuscript. Please make a separate conclusion section.

Response: As per your comment, we have added the Conclusion section to the Abstract as follows: "This is the first case wherein in vivo cardiac pathology was obtained, confirming that aconitine caused acute myocardial necrosis." and in the body of the manuscript as follows: "Aconitine poisoning can cause acute myocardial necrosis. VA-ECMO played an important role in maintaining the patients' condition until heart transplantation."

Comment 3: Please provide outcome and follow-up.

Response: We have added the outcome and follow-up in the manuscript as follows: "The patient was cured and discharged 3 weeks after heart transplantation. The patient has been followed up for 1 year after discharge and has been in good living condition, with no obvious abnormalities on cardiac ultrasound or electrocardiogram."

Comment 4: "However, the patient's cardiac function did not improve. Cardiac ultrasound indicated left ventricular enlargement with diffuse hypokinesis of the left ventricular wall and an ejection fraction of 20 %. Hence, the patient underwent heart transplantation 21 days later." When was the cardiac ultrasound done and could you provide the image of the cardiac ultrasound? Are other measures taken to improve the patient's cardiac function? Could you provide other proofs of poor and irreversible cardiac function of this patient? Why heart transplantation was performed "21 days later"?

Response: According to your comment, we have added some content in the manuscript as follows: "Multiple cardiac ultrasound indicated left ventricular enlargement with severe diffuse hypokinesis of the left ventricular wall. On day 18 of admission, cardiac ultrasound revealed ejection fraction (EF) of 19.5% (Figure 3). The patient had difficulty in removing the ECMO and IABP. Hence, he underwent heart transplantation 21 days later."

Other measures were taken to improve the patient's cardiac function as follows: "An

IABP was used for cardiac assistance on day 1 of admission, and a conventional dose of levosimendan therapy was initiated on day 5 and day 12.”

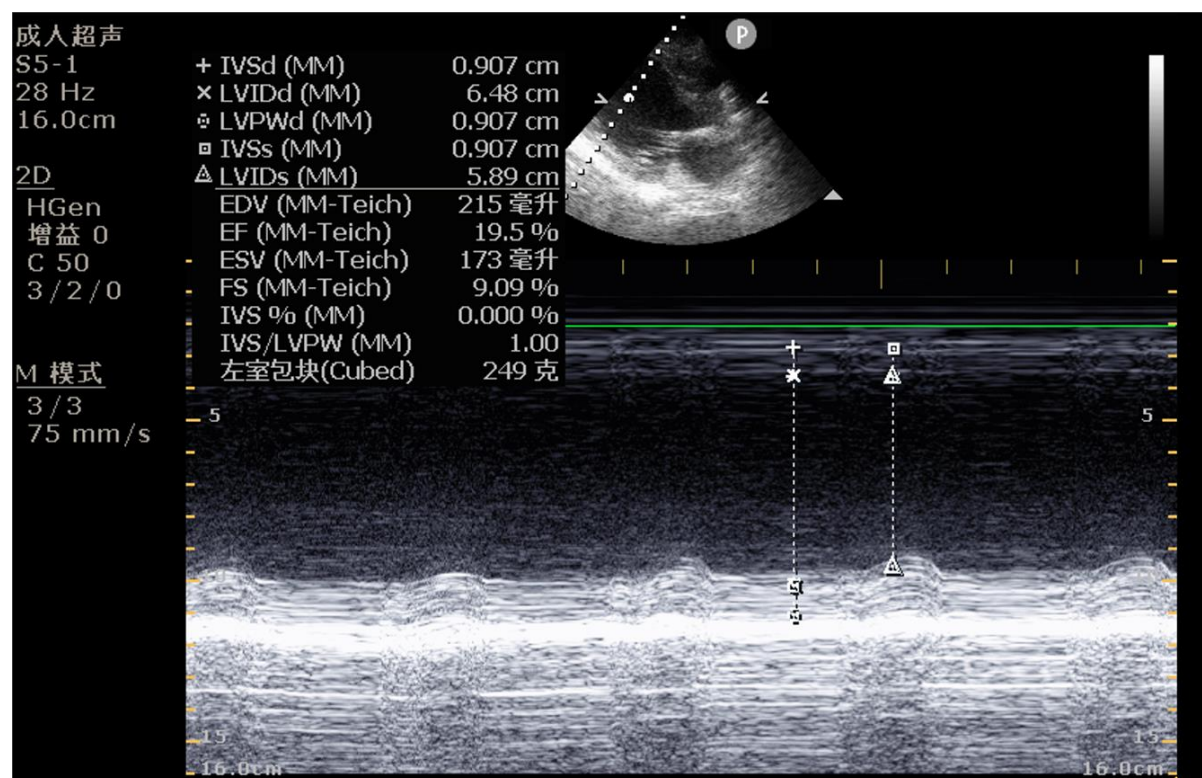


Figure 3 Cardiac ultrasound findings on day 18 of admission. The ejection fraction was 19.5%

Comment 5: It was mentioned that the patient consumed homemade Chinese herbal medicinal wine repeatedly one month prior to the visit, so whether aconitum alkaloids were accumulated in the blood to lethal concentrations? I suggest discussing it in the manuscript.

Response: We have added some discussion points in the revised manuscript according to your suggestion as follows: “To the best of our knowledge, no exact lethal dose of aconitine has been reported to date. In one case of mortality reported in the literature, the patient’s antemortem aconitine blood concentration was 39.1 ng/mL, and the postmortem urine concentration was 67.4 ng/mL^[9]. In our case, the aconitine concentration in the blood and urine was significantly higher than that reported in the aforementioned study, which is considered to be associated with the accumulation of

oral aconitine from herbal medicinal wine that was repeatedly ingested 1 month before the patient's visit."

Comment 6: It is not clear what is shown in Figure 3a-d. The description in the figure legend is also confusing. Please point to them with arrows or asterisks if they are important.

Response: We apologize for any unclear text/figure. We have now changed the description in the figure legend according to your suggestion as follows: "**Figure 4 Pathology of heart after aconitine poisoning.** A: Gross specimen of the heart. B: Necrosis of part of the left ventricular wall accompanied by hemorrhage. C: Ventricular septum partial necrosis. D: Right ventricle histiocytic infiltration. B, C, and D were observed using hematoxylin-eosin staining under a light microscope at 20x magnification".

Reviewer #2

Comment: Herbal medicines are associated with several challenges; microbial contaminants, heavy metals, antibiotic adulterants, etc. There is need to to explain why "Aconitine" was chosen as a concern of interest. - **DISCUSSION:** Explain in details, the imporatnce of your findings to; (i) Future research, (ii) Commuinty, (iii) herbalists/ethinopharmacology practices, (iv) Policy makers. - Thank you for reporting this case.

Response: We would like to thank Reviewer 2 for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments. We hope that our responses and revisions appropriately address your comments.

As per your suggestion, we have re-written the case entirely taking into consideration the journal's guidelines. Extracts from plants of the aconitine species are widely used in clinical practice to treat rheumatism, cardiac dysfunction, and pain. Aconitine overdose would induce a series of cardiotoxic effects, including polymorphous

arrhythmias and myocardium damage. Before the development of aconitine-based drugs with potential cardioprotective benefits, several issues should gain more attention in future studies.