

Answering reviewer's comments

Name of Journal: World Journal of Clinical Oncology

Manuscript NO: 59217

Title: Anthracycline-induced cardiotoxicity: A case report of unexpected course and review of literatures

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Reviewer #1:

Specific Comments to Authors: There is a high incidence of cardiotoxicity caused by anthracyclines. For patients without risk factors, have you considered observing changes in heart function during treatment? For patients with risk factors, please show the changes of cardiac function properly. In addition to LVEF, are there any other meaningful echocardiographic parameters in Comparison of two echocardiography? In addition, whether other cardiac biomarkers mentioned below were detected during the treatment, such as troponin and BNP? Are drugs used to prevent cardiotoxicity during treatment and what is the effect? Do you consider adding the content of how to detect cardiotoxicity early? It is noteworthy that the early detection and treatment of cardiotoxicity, even when asymptomatic, seems to be critical for cardiac function recovery and for the reduction of associated adverse cardiac events. Most importantly, the innovation of the article needs to be strengthened. At present, the understanding of AIC is more common, the author should put forward the unusual place of this patient, and make a specific exposition.

Our responses to reviewer's comments:

We want to thank reviewer's critical comments to improve our manuscript. Our responses are as followed. We have highlighted revision text in yellow in the manuscript.

1. For patients without risk factors, have you considered observing changes in heart function during treatment

We have added the following text in pages 8 and 9 to describe this patient's cardiac function and biomarker changes during treatment.

She had a follow-up echocardiogram after 2 cycles of chemotherapy which again showed normal cardiac function with LVEF 70%. Additionally she had serial blood tests done for troponin and brain natriuretic peptide (BNP) during hospitalization for neutropenic infection with respiratory

symptoms after cycle 2 chemotherapy, and dehydration with hypokalemia after cycle 3 chemotherapy; all the troponin levels were within normal limit except transient increase in BNP with subsequent normalization was noted after cycle 3 chemotherapy.

We have added the following text in page 18.

. Most cardiotoxicity after anthracycline-containing therapy occurs within the first year and is associated with anthracycline dose and LVEF at the end of treatment. Early detection and prompt therapy of cardiotoxicity appear crucial for substantial recovery of cardiac function. When symptoms of heart failure are identified early, discontinuation of anthracycline followed by frequent monitoring of cardiac function can help to alleviate further decline. Yet, when a patient is asymptomatic, it is difficult to predict how often cardiac testing should be done.

2. In addition to LVEF, are there any other meaningful echocardiographic parameters in Comparison of two echocardiography?

We have added the following text in page 9 showing changes in both left ventricular and right ventricular function compared to prior echocardiogram results as well as elevated troponin levels.

Echocardiogram showed LVEF 5-10% with severe decrease in right ventricular systolic function. Her serial serum troponin levels were significantly and persistently elevated

3. In addition, whether other cardiac biomarkers mentioned below were detected during the treatment, such as troponin and BNP?

We have added the following text in pages 8 and 9 to describe biomarker changes during treatment.

Additionally she had serial blood tests done for troponin and brain natriuretic peptide (BNP) during hospitalization for neutropenic infection with respiratory symptoms after cycle 2 chemotherapy, and dehydration with hypokalemia after cycle 3 chemotherapy; all the troponin levels were within normal

limit except transient increase in BNP with subsequent normalization was noted after cycle 3 chemotherapy.

4. Do you consider adding the content of how to detect cardiotoxicity early?

We have added the following text in the conclusion section for discussion early cardiotoxicity detection.

Most cardiotoxicity after anthracycline-containing therapy occurs within the first year and is associated with anthracycline dose and LVEF at the end of treatment. Early detection and prompt therapy of cardiotoxicity appear crucial for substantial recovery of cardiac function. When symptoms of heart failure are identified early, discontinuation of anthracycline followed by frequent monitoring of cardiac function can help to alleviate further decline. Yet, when a patient is asymptomatic, it is difficult to predict how often cardiac testing should be done.