Author's response to reviews

Title: Takotsubo cardiomyopathy in an adolescent affected by pancreatic adenocarcinoma

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Author's response to reviews: see over
Dear Reviewer 1,

We would like to thank you for your suggestions.

Changes have been made in the manuscript, according to comments. All changes have been bolded in the text

1 - This case reports a teenager who developed transient global left ventricular dysfunction and shock following 5-Fluorouracil administration. This association has been reported previously in older subjects but there is little data on this in younger subjects. This makes this report somewhat novel. The case report is well written. I find the chemotherapy protocol is explained in too much detail and could be shortened without altering the main message of this report

Answer: chemotherapy protocol description has been shortened, according to reviewers’ suggestion (page 3, lines 57-60);

2 - The discussion is unfocused. The author start describing what Takotsubo cardiomyopathy is; they then go on to explain mechanisms involved in its development and finally try to describe mechanisms of action and why 5-Fluorouracil may cause ventricular dysfunction. The main issue with the current report is that the authors fail to prove the point that this patient developed Takotsubo cardiomyopathy. This patient developed transient global left ventricular dysfunction and shock but did not develop several of the typical findings associated with Takotsubo cardiomyopathy. This type of cardiomyopathy is characterized by development of chest pain, ECG changes, a troponin rise and wall motion abnormalities involving the apical left ventricular segments. How do the authors explain the fact that there was no rise in troponin levels? Did they measure this serially?

Answer: discussion has been edited, focusing on typical findings of TC. Details about those findings, which were consistent for TC, have been added to the Discussion section (page 5, 110-115);

3 - The authors could add videos of echocardiograms at presentation and at follow-up to demonstrate findings and improvement.

Answer: videos of echocardiograms will be uploaded as separate files, for the online version of the manuscript.

English has been reviewed and corrected by a mother-tongue native English speaker.
Dear Reviewer 2,

We would like to thank you for your suggestions.

Changes have been made in the manuscript, according to comments. All changes have been bolded in the text

Major compulsory revisions:

1) The authors did not mention if this was the first infusion of 5-FU or if 5-FU was given again in this patient. This is important to assess how specific the effect of 5-FU is.

Answer: we agree with reviewer request and we added a line stating that the event followed the first infusion of 5-FU (page 3, line 60-61); we also specified that 5-FU was omitted after this event (page 3, line 80-81);

2) Although I agree that this is the first report of an adolescent with TC after using 5-FU, there have been at least 5 reports on TC occurrence after 5-FU administration in adults. These should be discussed!

Answer: discussion have been modified, including a short statement about 5-FU induced TC in adults, as well as references on this subject (page 4, lines 103-106).

3) The authors presented echo data, but showed no data. A figure of the echo data during TC and after recovery would be illustrative.

Answer: videos of echocardiograms will be uploaded as separate files, for the online version of the manuscript.

4) It would be helpful is the authors included a reference (if available) on how often 5-FU is used in children/adolescents.

Answer: a specific reference about the use of 5-FU in children and adolescents is still not available in medical literature. However in the Discussion section we report incidence of carcinomas in pediatric population, whose treatment is based on protocols with 5-FU (page 5, lines 121-123).

Minor essential revisions:

In lines 87-88 the authors state that the mean age ranged from 59-73. I assume that they mean that the age of the patients ranged from 59-73 (not the mean).

Answer: the sentence has been corrected, according to reviewers’suggestion.