Reviewer’s report

Title: A pediatric cancer patient with suspected chemical coping following high-dose opioid therapy: A case report

Version: 0 Date: 09 Aug 2019

Reviewer: Teodora Alexa - Stratulat

Reviewer's report:

1. Do you believe the case report is authentic?
   Yes

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.
   Comments: I have no ethical concerns

3. Does the Introduction explain the relevance of the case to the medical literature?
   Yes

4. Does the article report the following information? Where information is missing, please specify.
   a. The relevant patient information, including:
      - De-identified demographic information (age, gender, ethnicity) - PARTIALLY
      - Main symptoms of the patient - YES
      - Medical, family and psychosocial history - NO
      - Relevant past interventions and their outcomes - NO

   b. The relevant physical examination findings
      YES

   c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month.
      I think the authors should devise a timeline via a table/figure

   d. Diagnostic assessments, including:
      - Diagnostic methods
      - Challenges (e.g., financial, language/cultural)
      - Reasoning and prognostic characteristics (e.g., staging), where applicable
      YES

   e. Types and mechanism of intervention
      YES

   f. A summary of the clinical course of all follow-up visits
      PARTIALLY
5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented? 
YES

6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.
Yes

7. Is the Abstract representative of the case presented?
YES

8. Does the case represent a useful contribution to the medical literature?
YES

9. Additional comments for the author(s)?
The article "A pediatric cancer patient with suspected chemical coping following high-dose opioid therapy: A case report" by Miura et al. presents the case of a pediatric ALL patient suspected of chemical coping. The case is interesting and worth publishing; however, I think some changes are required prior to publishing.

1. I think the case report section should be better structured. Your description of the oncology part of the case is very brief. Also, you mention some things about the patient's pain treatment, but I am unclear as to what time period had passed between fentanyl dose escalations and oxycodone switch, how many times did you have to increase the fentanyl dose, if you treated this patient for pain with fentanyl only in the hospital or if he also went home with fentanyl, and so on and so forth. Perhaps a timeline of the case would help.

2. Page 7, rows 47-54 - "Considering the possibility of opioid overdose in response to complaints of nausea and fatigue, dose reduction was planned; however, he exhibited strong resistance." If I understood correctly, the patient exhibited significant nausea and fatigue, which is why you decided to reduce the dose. However, you do not explain that prior to this sentence. Also, I think the onset and the severity of these two symptoms should be included in the case presentation as they are important.

3. At the beginning of page 8, you say that "Physically, his pain was considered to have alleviated;" - How did you assess that? Did you repeat the CT? Did you use any other assessment tools to diagnose chemical coping other than the team's opinion?

4. You mention that you tried giving Duloxetine to your patient, together with some other non-pharmacological measures. How long did you give the drug for? What was his analgesic need at that point?

5. In the abstract, you mention that "opioid education was provided" for this patient. However, in the case presentation I did not read anything about that - please reconcile.

6. In the Discussions section, you state that "When chemical coping is suspected, it is important to
differentiate pseudo-addiction, opioid tolerance, and opioid-induced hyperpathia" and then proceed to talk about the possibility of pseudo-addiction in your patient. I think you should add one-two paragraphs discussing the possibility that your patient could have also had opioid tolerance or opioid-induced hyperpathia at some point in his disease.

7. The importance of this case report should be emphasized more - how many other such cases have been reported in the literature?

Minor observations:
- page 5, rows 22-23 - "and limited coping mechanisms are" instead of "and limited coping mechanism are"
- page 5, rows 29-30 - "opioids exhibited signs of chemical" instead of "opioids were determined to exhibit chemical"
- page 7 rows 23-25 - "and the number of rescuing did not decrease in association with the increased amount of continuous dosing" - please rephrase

Level of interest
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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Please complete a declaration of competing interests, considering the following questions:

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Were you mentored through this peer review?

No