Reviewer's report

Title: Treatment strategy to reduce the risk of rituximab-induced cytokine release syndrome in patients with intravascular large B-cell lymphoma: a case report and literature review

Version: 2 Date: 22 June 2013

Reviewer: Pashtoon Murtaza Kasi

Which of the following following best describes what type of case report this is? Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

I would like to congratulate the authors on the write up and review of literature for a side effect that is very rare and have put forth some important and useful recommendations.

In the introduction part, would recommend outlining the fact that overall the risk of serious adverse events (SAEs) associated with the use of Rituximab are in general very rare. It is due to the increased frequency of usage for a myriad of conditions that adverse events are now more commonly reported (copy of our review attached for your reference).
When mentioning the efficacy of various regimens, it would be useful to mention the actual rates in terms of remission and the improvement with the addition of rituximab to these regimens.

With respect to the random biopsies, were there any lesions or suspected areas that were biopsied and why that was chosen as the approach would be helpful.

With respect to the mentioning of the R-CHOP regimen, please mention what it comprises.

The conclusions are very interesting and clinically useful. However, since the recommendations are still based on different cases/series and the numbers though considerable, are still small. Therefore, it should be mentioned in the conclusions that this would need to be verified by prospective randomized controlled trials.

Also in this study, the pt had received some steroids earlier and thus the prednisone/prednisolone was not given as part of the chemotherapeutic regimen. However, we do know that some of the severe allergic reactions are markedly reduced with premedication with IV steroids right before the chemotherapeutic regimens; which somewhat are on the same clinical spectrum as CRS. As to how this would change the incidence of these reactions from Rituximab would also be worth mentioning in the discussion.

The only other thing that should be added to the case report before publication is to explicitly outline the search strategy for the literature review in more detail; as to how many papers were retrieved and how many studies were selected. A table of the studies selected and their patient characteristics in more detail would indeed be very useful and would add to the value of the case report since this adverse event is very rare.

**Quality of written English:** Acceptable

**Declaration of competing interests:**

'I declare that I have no competing interests'