

Peer Review File

Article information: <https://dx.doi.org/10.21037/apm-21-341>

**Reviewer A**

The author describe an interesting case of a patient with SLE who developed TEN.

Suggestions:

**Comment 1:** Abstract and discussion: the authors need to report if the TEN was induced by SLE or by other trigger.

**Reply:** I think it is important to mention trigger in the abstract. The TEN was induced by a drug not SLE.

**Changes in the text:** Page 1, line 8

**Comment 2:** Page 2, line 4: rewrite and included the phrase altered mental status

**Reply:** The manuscript has been revised accordingly.

**Changes in the text:** Page 2, line 10-11

**Comment 3:** Discussion references session: please include and discuss about the findings of a study that investigated patients with autoimmune diseases, including SLE, who were admitted in a burn center. Parperis K, Bhattarai B, Hadi M, Malla S, Barlingay G, Ramakuri M, Foster K. Burn center admissions of patients with autoimmune rheumatic diseases: clinical characteristics and outcomes. Rheumatol Int. 2020 Oct;40(10):1649-1656.

"SJS/TEN related to the underlying autoimmune disease was observed in two patients with SLE, and the etiology was unknown in one patient"

**Reply:** It would make our article more persuasive to present some concrete data for discussion. We have added the content to the manuscript.

**Changes in the text:** Page 4, line 16-20

**Comment 1:** more discussion about TEN as an SLE manifestation

**Reply:** The above content has been added to the article.

**Changes in the text:** Page 2, line 2-5

**Reviewer B**

Interesting case combination of SJS/TEN in an SLE patient. I have some comments and suggestions for improving the presentation case.

**Comment 1:** The self administration of astaxanthin relevant. This should be explored in the discussion (circa page 3 line 22). This is a carotenoid that gives the pink color in salmon, trout, lobster and other seafood. It has been proposed that in susceptible individuals, Carotenoids might release toxic retinoid compounds into the circulation result in a resultant endogenous hypervitaminosis A leading to granulysin mediated cytotoxicity recognized to be an underlying pathological feature in SJS/TEN.

**Reply:** Adding the above content makes our manuscript more convincing and we have added it.

**Changes in the text:** Page 6, line 16-19

**Comment 2:** What was the total body surface area involvement at presentation and as the disease progressed?

**Reply:** The above content has been added to the article.

**Changes in the text:** Page 2, line 12-13

**Comment 3:** The patient had a scorten of 3. It would be useful to qualify how this was scored i.e. which parameters were positive at the point of evaluation within the case history section from which the 3 was derived plus associated mortality (ie 35%), as the general reader may not be familiar with SJS/TEN and may not understand the significance of this.

**Reply:** I have added the scoring rules of scorten and the scoring items of this patient in the article.

**Changes in the text:** Page 3, line 8-10

**Comment 4:** The patient was intubated and NG feeding initiated: this needs to be brought out in the history.

**Reply:** I have made a supplementary explanation in the article.

**Changes in the text:** Page 3, line 14-18

**Comment 5:** The patient photographs are identifiable: has permission been sought from the patient and if so, this should be declared.

**Reply:** We have obtained the consent of the patient herself and her family, and have signed the informed document and uploaded it to the submission system.

**Changes in the text:** Page 3, line 22

**Comment 6:** If Fig 1A and 2A are on admission, and those marked 'B' on transfer to the rheumatology ward, please specify the time after presentation this occurred. Form the text this might be 3 weeks but it is unclear.

**Reply:** We have added a timeline to the image annotation.

**Comment 7:** The authors state SJS/TEN is a rare disease and those with SLE is even rarer. Incidence and prevalence values of SJS/TEN would be useful to put this statement into context.

**Reply:** We have added the incidence of SJS/TEN.

**Changes in the text:** Page 1, line 15-16

**Comment 8:** I do not know in which country this patient was treated: there are published national patient pathway guidelines in the UK on how best to treat acute SJS/TEN disease both in adults and children:

- a. <https://pubmed.ncbi.nlm.nih.gov/27287213/>
- b. <https://pubmed.ncbi.nlm.nih.gov/30829411/>

**Reply:** We are in line with the UK guidelines for the management of Stevens–Johnson syndrome/toxic epidermal necrolysis in adults 2016 .

**Changes in the text:** Page 6, line 21-22

**Comment 9:** Whilst the patient first presented with eye symptoms and the authors indicate that 55% of patients have 'pain at the level of the eyes' how was this treated? Were there any specific surgical measures required such as amniotic membrane?

**Reply:** The original article mentions only clinical features and risk factors and does not mention treatment. But we found it in other articles.

**Changes in the text:** Page 5, line 21-22 ; Page 6, line 1-2

**Comment 10:** Table 1 would benefit from a column detailing triggering event/ underlying cause for acute reaction, duration of SLE, national origin of the patient, prodromal symptoms for which cold medicines (paracetamol or NSAIDS) may have been used, or immunosuppressive agents (used at the time of developing SJS TEN) for the SLE. There is evidence that genetic predisposition to certain drugs and

national origin might predict the severity of chronic disease course experienced by some patients.

**Reply:** Thank you very much for your comments. We have completed the table.

### Reviewer C

**Comment 1:** Authors reported a case of TEN who also had concomitant SLE and reviewed previously reported cases. However, I cannot find many characteristics from the present case. I would expect more test results or mechanism discussion from this case and literatures to let us know whether SLE is a risk factor to severe drug eruptions and some advanced findings in positive antibodies that were shown in SJS/TEN.

**Reply:** We will add the above to the manuscript.

**Changes in the text:** Page 4, line 20-22; Page 5, line 1-3

### Reviewer D

**Comment 1:** There are multiple grammatical and formatting errors in the article which have been identified in the attached file.

**Reply:** We reviewed the manuscript and corrected grammatical and formatting errors.

**Comment 2:** Because this report discusses concomitant SJS/TEN with SLE, both conditions should be appropriately defined in the introduction.

**Reply:** Since there is no clear definition of SJS/TEN with SLE at present, we will include the definitions of the two separately in this paper.

**Changes in the text:** Page 1, line 21-22

**Comment 3:** Because both conditions of interest of MSK manifestations, any patient features of that systems should be presented in great detail. The patient's history of SLE should also be further defined, other than just chronic medication.

**Reply:** The patients presented in Table 1 are all TEN/SJS patients with SLE, which has been described in the title.

**Comment 4:** Given the additionally "review" nature of this article, the review should either be separate from the discussion or very heavily integrated. As it stands, the discussion currently reviews the literature without offering clinical insight and discussion based on current findings and past literature.

**Reply:** We have added some basic research in the manuscript.

**Changes in the text:** Page 5, line 4-9

**Comment 5:** The discussion currently condenses review, discussion, and conclusion. None of these sections are sufficiently addressed. They should be expanded and more information about how the authors' case and clinical journey contributes to the current available literature. The future implications and conclusion must further be discussed.

**Reply:** The discussion on this aspect is insufficient, and we have added it in the manuscript.

**Changes in the text:** Page 5, line 1-3 ; Page 6, line 21-22 ; Page 7, line 1-5