

Dear Editor,

Thank you for the reviewers' comments concerning our manuscript entitled "Stevens Johnson Syndrome And Concurrent Hand Foot Syndrome During Treatment With Capecitabine: Case report"(Manuscript NO.: 62178). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our case report. We have carefully considered these comments and suggestions, and answered the questions accordingly. The revisions (in red) have been proposed in the revised version to meet the reviewers' comments. The attached in this letter is the answers to reviewers.

We will be grateful to your positive evaluations on the manuscript.

Thank you for your time and supports.

Best regards.

Yours sincerely,

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## **Responses to Reviewers' comments**

We are very grateful to reviewers for reviewing our manuscript (Manuscript NO.: 62178) and advising valuable comments to improve the scientific level of the paper. We have carefully considered these comments and suggestions and accordingly responded to the comments.

### **Reviewer #1 (03725838):**

This is an interesting case with perfect treatment, and which might be contribute to the complications of capecitabine and lapatinib.

**Response:** Thank you for your positive feedback on our study.

### **Reviewer #2 (03453355):**

This article described a rare but potentially life-threatening adverse event Stevens Johnson Syndrome and concurrent Hand Foot Syndrome during capecitabine treatment. It suggests that medical oncologists need to pay attention to the fatal effect when prescribe capecitabine. And the effective treatment of this case through steroids further provided evidence of its usefulness in SJS management.

**Response:** Thank you for your kind review. We are pleased that steroids were useful for SJS treatment in this case.

### **Reviewer #3 (05265182):**

In this paper, The authors present a case report describing Stevens Johnson Syndrome And Concurrent Hand Foot Syndrome During Treatment With Capecitabine. Though it is interesting, there are still some important points. major comments

**Response:** Thank you for your detailed and important comments. With your comments, there will be an improvement in our manuscript.

1. In general, Stevens Johnson Syndrome And Concurrent Hand Foot Syndrome During Treatment With Capecitabine are not common, but not rare. As their references, there are many similar situations have been reported before. This case dose not put more information in this field.

**Response:** Thank you for your comment. We agree with you that HFS is commonly reported after using capecitabine. There are also some reports of SJS that occurred after the use of capecitabine.

Capecitabine and lapatinib therapy was performed every 3 weeks in this patient. The patient was visitted to the hospital only on the prescription day. After taking capecitabine and lapatinib for 4 weeks (after initiating the second cycle of capecitabine and lapatinib) mild erythema developed on her hands and feet, but she did not come to the hospital. And we figured out this side effect by taking her medical history after hospitalization. After the symptoms got worse, she came to our clinic (6 weeks after taking capecitabine and lapatinib). At that time there were already erythema and blisters on her trunk, buttocks, hands and feet. She was diagnosed with SJS and hospitalized for treatment. As time went on, we noticed that the hands and feet and other parts of the treatment process were different. Then we realized that she was accompanied by HFS.

Oncologists who practice chemotherapy are often only interested in the patient's cancer. However, oncologists should always be alert about patients' adverse events, such as SJS, which can be fatal to patients. I reflect on myself through case presentation. In addition, If this case is announced, I think it will be helpful in the diagnosis and treatment of patients who have SJS and concurrent HFS in the future.

And, in the process of reviewing, the sentence in line 14 on page 8 was corrected because there was an error in the English translation process. Please understand that we are not native speakers.

“However, our patient had more acral and atypical lesions, which were initially

distributed symmetrically on the face, upper trunk, and proximal limbs, while the distal limbs were relatively spared." -> "However, our patient had more acral and atypical lesions, which were initially distributed symmetrically on the distal limbs, while the face, upper trunk, and proximal limbs were relatively spared."

2. The author mentioned the patient developed Stevens Johnson Syndrome And Concurrent Hand Foot Syndrome six weeks after Capecitabine chemotherapy. Her symptoms were already very serious at the time of treatment. The authors need to explain the evolution of the symptoms in the past six weeks.

**Response:** Thank you for your comment. After initiating the second cycle of capecitabine and lapatinib, she had mild erythema in her hands and feet, but she did not visit the clinic. Only after her symptoms got worse, she came to our clinic. We regretted the delay in treatment because we didn't provide enough education about the side effects.

Following your comment, I added and changed the following sentence to the *History of present illness*.

"Four weeks after taking capecitabine and lapatinib, erythema was developed on her hands and feet, but she did not visit the clinic. After approximately 6 weeks of capecitabine plus lapatinib treatment, she complained of worsening of erythema, edema, and bullae not only her hands and feet but also on her upper arms, trunk, and buttocks."

3. The author mentioned the patient's symptoms improved significantly after treatment, however, they mentioned "she unfortunately died 2 months later because of multisystem organ failure". What is the specific cause of death? Is it related to Stevens Johnson Syndrome And Concurrent Hand Foot Syndrome?

**Response:** Thank you for your comment. Her death was not directly related to SJS and HFS. However, there was an indirect relation. Unfortunately, while doing treatment

for SJS and HFS, her general condition was bad and she was tired of chemotherapy. So we were unable to resume another chemotherapy regimen. While we stopped chemotherapy to wait for her general condition to improve, her liver and lung metastasis got worse. In addition, her renal function was decreased to the level required for dialysis, but the patient refused dialysis and died due to pulmonary and renal failure.

Following your comment, I added and changed the following sentence to the *OUTCOME AND FOLLOW-UP*.

“The patient’s skin lesions improved after systemic steroid therapy and conservative treatment. However, her condition was not suitable for chemotherapy during SJS and HFS treatment. Her lung and liver metastasis progressed further, and her renal function decreased, and she died 2 months later because of pulmonary and renal failure.”

4. There are some mistakes in the manuscript. The author needs to review the full text carefully and revise them. for example: a. In the cover letter, “ I am pleased to submit an original research article entitled ..... Case report” for consideration for publication in Journal of Breast cancer."It needs to be corrected to “ I am pleased to submit a case report entitled ..... Case report” for consideration for publication in World Journal of Clinical Cases."b. In the first paragraph of discuss, "Nevertheless, our experience and other reports suggest that capecitabine may also be associated with the development of potentially life-threatening dermatological conditions, such as SJS. Sendur et al.[2] and Jadhav et al.[7] " The orders of references are wrong.

**Response:** I'm really sorry for making a basic mistake that shouldn't be made. Unfortunately, the cover letter couldn't be modified. We checked all referneces as well as the references you mentioned.

**Science editor:**

**1. Please provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement.**

We provided and uploaded the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement in the revision.

**2. The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.**

Thanks for your advice. We provide the original figures and arrange the figures using PowerPoint to ensure that all text portions can be reprocessed by the editor.

Dear editor,

Thank you for your comments. I have attached revised files for the issues you mentioned. We are also grateful to the reviewer who gave us the re-review. Thank you for your time and supports.

Best regards.

Yours sincerely,

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