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High Scored Thyroid Storm after Stomach Cancer Perforation: A Case Report and Review of the Literature

Dear Reviewers,

We thank the editor and reviewers of *World Journal of Clinical Cases* for reviewing our article. After carefully considering all of the reviewers' comments, we have made several corrections and clarifications in the manuscript. Our changes are summarized below:

Response to Reviewer #1

1. What is the clinical significance of high scored thyroid storm? The authors only described that there was no correlation between high score and mortality. Please discuss about the possible impact of high score on clinical significance. Or, what can we learn from these high-scored cases of thyroid storm?

Answer) We sincerely appreciate your comments to improve our manuscript. We acknowledge that we have not been clear the clinical significance of our case report. Therefore, we have added the following to the Discussion section:

Revised contents (Discussion section; last paragraph)

High fever and tachycardia are the main parameters of systemic inflammatory response syndrome, as per the criteria established in 1991[25]. In the Sepsis-3 criteria, newly established in 2016, PR and BT were not included [26]. Although PR and BT were excluded from the diagnostic criteria for sepsis, they are still important in managing sepsis. On the other hand, thyroid storm is not a major consideration in ICU. Therefore, when uncontrolled

fever or tachycardia is observed, it may be useful for the physician to consider evaluation of thyroid function. The reason is that sepsis-induced tachycardia and high fever are improved by appropriate sepsis management, but the signs induced by thyroid storm are different in treatment guidelines such as antithyroid agents, Lugol's solution and steroid etc.

2. Since the reported case is likely a patient of sepsis superimposed on thyroid storm. Presentation of sepsis may impede early diagnosis of thyroid storm. How did the authors make differential diagnosis between sepsis and thyrotoxicosis?

Answer) We acknowledge that such questions may arise. We obtained information related to the patient's hyperthyroidism through accurate history taking. Therefore, a thyroid function test, which is not normally performed, was performed before emergency surgery, and as a result, a fairly high level of fT4 was observed. In gastric perforation-induced sepsis, it is not common for body temperature to exceed 41 °C. We determined that the patient's symptoms were due to a thyroid storm rather than sepsis by past medical history taking, thyroid function test, and extremely high body temperature, which is not normally observed.

3. The level of T3/T4/fT4 on postoperative day 11 was higher than the data on postoperative day 6, despite treatment of antithyroid agents. What was the possible cause? The discrepancy between the clinical presentation and the thyroid function test should also be at least discussed in the section of Discussion.

Answer) We actively performed the following thyroid storm treatment on postoperative day 2: oral PTU 800mg, PTU enema 400mg and Lugol's solution 1.5mL. Because these treatments were performed simultaneously, it is presumed that the fT4 level decreased sharply. From postoperative day 4, the PTU dose was reduced to 200 mg. In the process of finding the appropriate PTU dose for the patient, it is presumed that the fT4 level on postoperative day

11 was higher than the fT4 level on postoperative day 6.

Response to Reviewer #2

1. Thyroid storm is well reported in literature. There is no correlation between the severity score and mortality neither the mentioned score has been externally validated.

No new information is gained.

Answer) We respect your comments and will do better research in the future.

Response to Reviewer #3

1. Abstract section CASE SUMMARY section: On the 2nd day in the ICU, his body temperature (BT) increased to 41.3 °C at 19:00, with the thyroid storm score peaking at 18:00 (BT; 41.2 °C, pulse rate [PR]; 138/min, irritable status). CASE PRESENTATION section: On the 2nd day in the ICU, the patient's BT increased to 41.3°C at 19:00, and the thyroid storm score peaked at 18:00 (BT 41.2 °C; PR 138/min); furthermore, he was irritable..... Score values/points should be described. Is the level highly associated with thyroid storms.

Answer) We appreciate your comments to improve the manuscript. As your suggestion, we have added score values/points of the case to the manuscript.

Revised contents (CASE SUMMARY section; line 54-56)

On the 2nd day in the ICU, his body temperature (BT) increased to 41.3 °C at 19:00, with the thyroid storm score (90 points) peaking at 18:00 (BT; 41.2 °C, pulse rate [PR]; 138/min, irritable status).

Revised contents (Case presentation section; 4th paragraph)

On the 2nd day in the ICU, the patient's BT increased to 41.3 °C at 19:00, and the thyroid

storm score peaked at 18:00 (BT 41.2 °C; PR 138/min); furthermore, he was irritable; had a Glasgow Coma Scale score of E3V1M5, with eye opening to speech, no verbal response, and localized motor response to pain; and complained of severe pain (Table 3). The patient's highest score for a thyroid storm was 90. The patient was administered a daily dose of oral PTU 800 mg, PTU enema 400 mg, intravenous glucocorticoids 40 mg, oral acetaminophen 650 mg, and oral Lugol's solution 1.5 mL. Subsequently, we performed bladder irrigation with cold saline using a Foley catheter and applied a hypothermic blanket to decrease the patient's BT.

2. DISCUSSION section: Therefore, these symptoms may be considered as signs of sepsis. Should the author discuss the diagnosis and differential diagnosis of hyperthyroid crisis (differentiate thyroid storm from sepsis).

Answer) We appreciate your comments to improve the quality of our manuscript. Therefore, we have added the following:

Revised contents (Discussion section; last paragraph)

High fever and tachycardia are the main parameters of systemic inflammatory response syndrome, as per the criteria established in 1991[25]. In the Sepsis-3 criteria, newly established in 2016, PR and BT were not included [26]. Although PR and BT were excluded from the diagnostic criteria for sepsis, they are still important in managing sepsis. On the other hand, thyroid storm is not a major consideration in ICU. Therefore, when uncontrolled fever or tachycardia is observed, it may be useful for the physician to consider evaluation of thyroid function. The reason is that sepsis-induced tachycardia and high fever are improved by appropriate sepsis management, but the signs induced by thyroid storm are different in treatment guidelines such as antithyroid agents, Lugol's solution and steroid etc.

Response to Reviewer #4

1. Dear author, your manuscript is neatly organized and systematic, but there are a few improvements to improve your manuscript. I suggest you add to the management of 'the other 17 cases reported in the literature' that you presented in this discussion. This can improve and open insight into the case further. Thank you

Answer) We sincerely thank you for your acceptance of our manuscript for publication.

We hope that the revised manuscript satisfies the requirements of *World Journal of Clinical Cases* and is now suitable for publication. We thank you once again for the constructive reviews and comments from the reviewers.

Sincerely,

Corresponding author

Jae-myeong Lee

E-mail: ljm3225@hanmail.net