

Dear Editor-in-Chief:

2021-04-20

The enclosed manuscript, “Streptococcal toxic shock syndrome after hemorrhoidectomy – a mortality case report” is respectfully resubmitted to the World Journal of Clinical Cases. We thanks for reviewer’s suggestion for our report. In this version, we tried our best to answer the critiques point by point. The changes in the revised manuscript were labeled by underline. We hope that reviewers can accept these responses with the manuscript.

Best Regards

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**Responses to reviewer 1#:**

Thank you so much for your careful review and wonderful suggestion. We tried our best to answer the critiques point by point. The changes in the revised manuscript were labeled by underline.

**Question 1:** The case is clearly described and adequately documented, although I recommend that abbreviations be defined at first use, since not everyone will understand them as a matter of course.

**Answer:**

Yes, we had recheck our manuscript. For the phrase first occurrence in the article, we will write the full text, followed by the abbreviation of the word in parentheses. In page 3, line 38 (abstract paragraph), we re-written as "Streptococcal toxic-shock syndrome (STSS) after hemorrhoidectomy are rare but may be catastrophic.", and in page 6, line 91 (Introduction paragraph), we re-written as "Streptococcal toxic shock syndrome (STSS) occurs as a serious complication of invasive group A streptococcus (GAS) and 30 - 70% of patients die in spite of aggressive treatments."

**Question 2:** The description of the clinical evolution of this patient shows a change from hypotension to hypertension shortly before clinical deterioration and death. Up to this point, the subjective perception of the patient as to discomfort was the main guidance to the clinical team. Things were considered more serious when relatives reported a confused state of mind in the patient. Laboratory tests showing extensive systemic abnormalities were performed after that increase in awareness of risk for

sepsis. I wonder whether an increased level of suspicion might allowed for earlier therapeutic intervention, perhaps preventing fatal deterioration. AT any rate, the authors are to right in publishing their observations, so that awareness of this risk in other practitioners may be increased.

**Answer:**

Thank you so much for your careful review and wonderful suggestion.

Group A Streptococcus (GAS; Streptococcus pyogenes) is an aerobic gram-positive coccus that causes a broad array of infections. Toxic shock syndrome (TSS) occurs as a complication of invasive GAS disease in approximately one-third of cases [1-4].

Secreted molecules thought to contribute to pathogenesis include the hemolytic toxins streptolysin O and streptolysin S; enzymes such as hyaluronidase, streptokinase, nicotinamide-adenine dinucleotidase, deoxyribonucleases; and pyrogenic exotoxins. Streptococcal pyrogenic exotoxins are virulence factors with capacity to induce lymphocyte blastogenesis, potentiate endotoxin-induced shock, induce fever, suppress antibody synthesis, and act as superantigens [5].

Back to our present case, after the operation, the patient was sent back to the ward of general surgery and vital signs were similar to those from preoperative examination. On the morning of day one post operation, his temperature was 36.4 °C, however, his blood pressure was 85/50 mm Hg with normal pulse rate (pulse was 83

beats per minute). On examination, the patient had good spirits and fair activity without any discomfort except for moderate wound pain (VAS= 5). The wound showed mild swelling and no pus or bloody discharge. On day two post operation, persistent hypotension (76/54 mmHg) with increased pulse rates to 108 beats per minute was noted. At this point in time, the patient is experiencing persistent low blood pressure, after differential diagnosis of hypovolemic, cardiogenic, metabolic, obstruction, or neurogenic hypotension, we should immediately think about the possibility of toxic shock syndrome, and intervene in active treatment as soon as possible, including the use of antibiotics.

#### **References:**

1. Kiska DL, Thiede B, Caracciolo J, Jordan M, Johnson D, Kaplan EL, Gruninger RP, Lohr JA, Gilligan PH, Denny FW Jr. Invasive group A streptococcal infections in North Carolina: epidemiology, clinical features, and genetic and serotype analysis of causative organisms. *J Infect Dis.* 1997; 176:992-1000.
2. Nielsen HU, Kolmos HJ, Frimodt-Møller N. Beta-hemolytic streptococcal bacteremia: a review of 241 cases. *Scand J Infect Dis.* 2002; 34:483-6.
3. Ispahani P, Donald FE, Aveline AJ. *Streptococcus pyogenes* bacteraemia: an old

enemy subdued, but not defeated. J Infect. 1988; 16:37-46.

4. Defining the group A streptococcal toxic shock syndrome. Rationale and consensus definition. The Working Group on Severe Streptococcal Infections. JAMA. 1993; 269:390-1.
5. Barsumian EL, Schlievert PM, Watson DW. Nonspecific and specific immunological mitogenicity by group A streptococcal pyrogenic exotoxins. Infect Immun. 1978; 22:681-8.

**Responses to science editor:**

Thank you so much for your careful review and wonderful suggestion. We tried our best to answer the critiques point by point. The changes in the revised manuscript were labeled by underline.

1. We had add "Table 1" in our manuscript.
2. In page 16, line 283 – 287, we had described "author contributions".
3. In "Case Presentation" section, we had re-written according to the guidelines for manuscript preparation (page 7-8).

#### **Responses to company edito-in-chief**

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