

DR VINCENT M. AQUINO (Orcid ID : 0000-0001-6102-3669)

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I. Title

Toxic Shock-Like Syndrome Following Third Molar Extraction: Case Report

II. Authors

Vincent M. Aquino, D.D.S. (Corresponding Author)

Resident, Department of Oral and Maxillofacial Surgery

Detroit Receiving Hospital

University Health Center Suite 2F

4201 St. Antoine St.

Detroit, MI 48201

716-983-6028

vincenta@buffalo.edu

Joseph M. Hildebrand, D.D.S.

Chair, Department of Oral and Maxillofacial Surgery

Children's Hospital of Michigan

University Health Center Suite 2F

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4201 St. Antoine St.
Detroit, MI 48201
810-348-1923
drjmp@sbcbglobal.net

Joshua Hester
Medical Student
Wayne State University School of Medicine
540 E. Canfield Ave.
Detroit, MI 48201
203-676-7727
Joshua.hester333@gmail.com

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IV. Abstract

Streptococcal toxic shock-like syndrome(TSLS) is a rare and fatal infection associated with *Streptococcus pyogenes* (group A streptococcus). While there are

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documented cases of TSLS, it is rarely observed following extraction on non-infected wisdom teeth. We describe the diagnostic criteria and successful treatment of a case of TSLS resulting in multi system organ failure following uncomplicated extraction of his wisdom teeth in a healthy 18-year-old male.

V. Keywords

Toxic shock syndrome; group A streptococcus; GAS; Streptococcus pyogenes; postoperative complications; third molar extraction; wisdom teeth; multi organ failure

VI. Main Text

Introduction

Staphylococcal Toxic shock syndrome (TSS) and streptococcal toxic shock-like syndrome (TSLS) are fatal conditions characterized by the rapid onset of unstable vital signs with multi-organ system failure. They are caused by two gram-positive organisms, *Staphylococcus aureus* and group A streptococcus (GAS), which produce exotoxins that can crosslink T-lymphocytes and antigen presenting cells resulting in cytokine release.¹ Although these syndromes have a similar pathogenesis, they both differ in their clinical presentations. First the inoculation site between the two bacteria differ, which can aid in the diagnostic process. *Staphylococcus aureus* is able to enter the blood system through breeding sites, most commonly prolonged placement of nasal packing following rhinoplasty or tampons during menstruation. Patients with GAS usually present afebrile, making it more difficult to identify clinically, while those infected with *Staphylococcus aureus* present with a profound fever. Lastly, TSS caused by GAS ultimately has a more progressive course, leading to a higher mortality rate than staphylococcus.^{1,2}

GAS is a beta hemolytic bacterium which utilizes humans as its only natural reservoir. GAS has the ability to produce a range of mild (i.e. pharyngitis, impetigo) to severe infections, such as cellulitis, necrotizing fasciitis, and TSLS.³ While mild infections have a high prevalence in young adults and may be treated conservatively with outpatient antibiotics, patients with invasive GAS have a mortality rate of 23% within seven days of onset.⁴ The mortality rate increases two-fold following the onset of TSLS, although some studies have demonstrated approximately a four-fold increase.^{5,6}

It is imperative that TSLS be recognized immediately and that intervention is initiated once suspected, in order to provide the best chance of survival. Here we present a case in which a patient developed TSLS following routine extraction of non-infected wisdom teeth without complications.

Case report

An 18-year-old male, with a past medical history of asthma, was sent to the emergency department (ED) twenty-four hours following exposure and bond of tooth #27 and the surgical extraction of third molars #16, 17, and 32 under intravenous (IV) sedation. Prior to arrival, the patient was evaluated by the treating surgeon at an outside facility and administered fluids, but due to the rapid progression of his symptoms and concern for airway maintenance, he was sent to the hospital for further assessment. Patient presented to the ED with septic shock including multi-organ system failure, as well as severe right facial edema, extending infraorbitally and into the submandibular spaces. He was hypotensive, tachycardic, and tachypneic. However, he was afebrile with no leukocytosis (Table I). Despite the vital signs and laboratory values resembling severe dehydration, which could have been attributed to lack of oral intake prior to a general anesthetic procedure, the patient was unresponsive to fluids raising the concern for a more serious etiology. Due to the patient's dysphagia, dyspnea, and extensive edema, concern for airway compromise increased. A computed tomography (CT) scan was obtained in order to

determine airway patency and evaluate abscess formation. Unfortunately, due to the patient's elevated creatinine and decreased glomerular filtration rate levels, IV contrast was unable to be utilized. Prior to CT, the patient was continued on IV fluids and, started, empiric antibiotic therapy, including ceftriaxone, clindamycin, and vancomycin according to the recommendations of the infectious disease service.

CT without IV contrast revealed extensive diffuse bilateral edema involving the sublingual, submental, and submandibular regions (Figure 1). The oropharyngeal area was obliterated due to elevation of the tongue with patency of the remaining airway. However, a definitive abscess was unable to be determined due to lack of IV contrast. The decision was made to perform an emergency incision and drainage in the operating room under general anesthesia. Cultures were taken and sent for appropriate interpretation. Following the conclusion of the case the patient remained intubated and was transferred to the ICU for monitoring. Analysis of the cultures from a nonsterile site revealed GAS with susceptibility to beta-lactam antibiotics. Given the observed cultures and the clinical presentation on arrival, a diagnosis of TSLs was made. Since methicillin resistant staphylococcus aureus (MRSA) was not observed, vancomycin was discontinued.

By hospital day five (post-op day four), all of the patient's symptoms appeared to have subsided. There was no facial swelling and the patient's vitals were within normal limits. Therefore, the patient was discharged on amoxicillin/clavulanic acid. Approximately twenty-four hours following discharge, he returned to the ED with increased facial swelling, similar to that observed when he initially presented. However, upon arrival at this hospital visit he was hemodynamically stable. The patient was started on the same IV antibiotic regimen previously prescribed. A CT with IV contrast was obtained at this visit, which was inconclusive for abscess formation. Patient was once again brought to the operating room for an incision and drainage. The previous surgical sites were reopened and dissected appropriately. Serous fluid was encountered with minimal purulence which was cultured and sent for appropriate interpretation. Penrose drains

were secured and patient was extubated this time. Once again cultures grew GAS. Patient was discharged after two weeks, following placement of a peripherally inserted central catheter (PICC) to receive IV infusions of ceftriaxone as outpatient.

At the patient's follow-up visit, two days after discharge, increased right facial swelling was noted with erythema and desquamation. Patient was sent once again to the hospital to be admitted and evaluated for recurrent abscess. Patient was hemodynamically stable with no leukocytosis and afebrile. Patient was brought to the operating room for the third and final time for incision and drainage. More purulent drainage than was previously seen was noted. During this admission, clindamycin was discontinued and the beta-lactam antibiotic of choice was switched from ceftriaxone to ertapenem. An improvement in swelling was observed, in addition to a subjective improvement reported by the patient. Patient was once again discharged and the infectious disease service placed the patient on a fifty-day course of ertapenem as outpatient treatment. The patient has now finished that course with complete resolution of symptoms. It is important to note that the patient had a complete immune work-up, which produced no significant findings.

Discussion

Encountering a case of this severity serves as a reminder of the many considerations involved in its proper management. The first and most important phase is properly identifying the postoperative infection, in addition to initiating therapy. The next step is initiating the appropriate management prior to and following the final diagnosis. The final step is to determine the etiology, thereby reducing the risk of similar complications in the future.

Following surgical extraction of multiple wisdom teeth, one of the most common complications is swelling. It can be easy to affirm significant edema twenty-four to forty-eight hours postoperatively as expected if a patient contacts the surgeon with this concern.

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In a case report by Leavitt et al,⁷ it was demonstrated that early onset of postoperative fever occurred concomitantly with significant edema. Therefore, neither excessive postoperative edema nor immediate postoperative fever should be overlooked. In this case, differentiating between postoperative edema versus an invasive infection was crucial, especially since the patient was afebrile at initial presentation, thus decreasing the suspicion for infection.

In order to make a diagnosis of TSLS, the following criteria, outlined by Brieman et al,⁸ must be met. Colonies of GAS must be isolated from the infected site, and the patient must be hypotensive (≤ 90 mmHg systolic) with two or more of the following signs: renal impairment, coagulopathy, liver involvement, acute respiratory distress syndrome, erythematous macular rash that may desquamate, or soft tissue necrosis. If the colonies were obtained from a sterile site, then it is considered a definitive diagnosis, but if they originated from a nonsterile site, then it is considered a probable diagnosis (definitive diagnosis comes once other etiologies have been excluded). In the case presented, the patient's systolic blood pressure was less than 90 mmHg, and he had renal impairment and a coagulopathy. Cultures grew a GAS from a nonsterile site; therefore, once other etiologies were ruled out a definitive diagnosis of TSLS was made.

As exhibited in this case, there was clinical and laboratory evidence to support the diagnosis of TSLS. Thus, it was important to begin prompt antibiotic therapy to aid in hemodynamically stabilizing the patient.⁹ While mild GAS infections are highly susceptible to penicillin, invasive GAS infections, such as TSLS, require a beta lactam antibiotic other than penicillin. Following onset of TSLS, it is shown that penicillin is less efficacious than ceftriaxone and clindamycin.^{9,10} In the case presented, a virulent organism was suspected leading to a differential diagnosis of TSLS, MRSA, and necrotizing fasciitis. Ceftriaxone was recommended due to the decreased efficacy of penicillin, along with vancomycin for MRSA. Clindamycin was also administered for its anti-microbial activity and its toxin suppression effect during the acute phase of the TSLS.⁹⁻¹¹

The etiology of GAS infections following third molar extractions is one that has been hypothesized, but no substantial evidence has been provided to support these theories. Considering humans' ability to be a natural reservoir in the oropharynx, it is plausible that contamination of extraction sites can produce a severe infection. However, if this were the source, it would be expected that the complication rate of GAS infections would be higher. Another possibility is contamination of surgical equipment by surgical staff given GAS's ability to lay dormant on the skin. The final consideration would be a recent or active GAS infection, such as pharyngitis. In the described case, the patient had a diagnosis of GAS pharyngitis one month prior to the procedure. This was revealed by the patient following admission to the hospital, and not disclosed prior to surgical intervention. Other cases have also shown family members with a recent diagnosis of GAS, while some have not provided a cause.⁷

The case presented is uncommon on account of the low prevalence of TSLS in the general population follow dental procedures. It emphasizes the importance and urgency of evaluating postoperative complications due to their potential to be life threatening. Excessive edema within forty-eight hours postoperatively, with or without a fever, should not be overlooked. Early recognition, appropriate diagnosis, and immediate intervention are imperative when any GAS infection is suspected, especially TSLS.

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VIII. Table with title footnotes

TABLE I. VITAL SIGNS AND LABORATORY VALUES ON ADMISSION

	Patient	Normal
Temperature (Celsius)	36.6	36.5-37.3
Blood Pressure (mmHg)	72/53 [†]	90/60-120/80
Pulse (beats/minute)	140 [†]	60-100
Respiratory Rate (breaths/minute)	30 [†]	12-18
O ₂ Saturation (%)	100	≥95%

Laboratory values on admission		
INR	2.16 [†]	0.8-1.2
PT (seconds)	22.5 [†]	11-15
PTT (seconds)	35.3	25-40
BUN (mg/dL)	26 [†]	7-18
Creatinine (mg/dL)	2.21 [†]	0.6-1.2
GFR (mL/min/1.73m ³)	47 [†]	90-120 [‡]

Abbreviations: INR, International Normalized Ratio; PT, Prothrombin Time; PTT, Partial Thromboplastin Time; BUN, Blood Urea Nitrogen; GFR, Glomerular Filtration Rate.

† Denotes abnormal values

‡ Denotes value based on patient's age

IX. Figure Legends

Figure 1. Axial views of the maxillofacial computed tomography (CT) scan without intravenous contrast obtained upon admission.



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