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Case report

An overlooked cause of septic shock: Staphylococcal Toxic Shock Syndrome secondary to an axillary abscess

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ABSTRACT

Staphylococcal Toxic Shock Syndrome (TSS) is characterized by rapid onset of fever, rash, hypotension, and multiorgan system involvement. Clinical manifestations of staphylococcal TSS include fever, chills, hypotension, and a diffuse macular erythroderma followed by desquamation one to two weeks later. The disease came to public attention in the 1980s with the occurrence of a series of menstrual-associated cases. However, the relative incidence of staphylococcal TSS not associated with menstruation has increased, and still, it remains an overlooked cause of septic shock. We present the case of a healthy 19-year-old male that presented with fever, chills, malaise, near-syncope, and a non-fluctuant, mobile nodule in the left armpit. The patient developed septic shock requiring critical care. He underwent extensive investigations resulting negative except for PCR for the detection of MRSA, raising the suspicion for STSS. For that reason, antibiotics for staphylococcal coverage were started, after which he started to improve. Ultimately, the mobile nodule evolved to fluctuant access. Incision and drainage was performed, and cultures confirmed the presence of *Staphylococcus aureus*.

Introduction

Toxic shock syndrome (TSS) is a rare condition that can cause acute, progressive illness-associated multiple organ failure [1]. It is characterized by high fever, rash, hypotension, multiorgan failure (involving at least three or more organ systems), and desquamation, mainly of the palms and soles, one to two weeks after the onset of acute illness [2]. Other symptoms like severe myalgia, vomiting, diarrhea, headache, and nonfocal neurological abnormalities can also be present [2]. Among them, fever, rash, and gastrointestinal abnormalities (diarrhea or vomiting) are characteristic and essential for early diagnosis [3].

TSS is caused by exotoxin producing cocci. TTS Toxin type-1 (TSST-1) and Staphylococcal enterotoxin B are the most commonly implicated toxins responsible for STSS [4]. Between 70–80 % of individuals develop antibodies to TSST-1 by adolescence, and up to 95 % have such antibodies by adulthood. The people who lack antibodies by adulthood are more susceptible to TSS [5]. It represents the most fulminant manifestation of *Staphylococcus aureus* and group A streptococcus infections. Despite its elevated mortality, TSS has not achieved a high level of awareness among healthcare professionals [6].

TSS is classified as menstrual and nonmenstrual. Historically, the medical community has focused its attention on its relation to menstruation and tampon use [7,8]. However, nonmenstrual TSS cases have been documented with increasing frequency. Healthcare providers must realize the diversity of clinical settings in which TSS can develop [7]. We present a case of Staphylococcal Toxic Shock Syndrome in the setting of Staphylococcal abscess in a young male patient.

Case description

A 19-year-old male presented on October 3, 2020, with a two-day history of fever, malaise, headache, vomiting, and an episode of near-syncope. He had no relevant medical history. In the

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Emergency Department, he was confused with a 39.3 °C fever, a blood pressure of 124/66 mmHg, a pulse rate of 126 bpm, and an oxygen saturation of 100 % on ambient air. The physical exam showed a maculopapular rash spread in the legs and thigh. He had a >1 cm tender, solid, non-fluctuant, mobile nodule in the left armpit that had developed a few days back. On lung auscultation, normal breath sounds bilaterally were noted. No lymphadenopathy was seen. The initial labs were relevant for a white count of 26.9 k/mm^3 (4.0–11.0 k/mm^3) with left shift and neutrophils of 91 % with bands, a procalcitonin of 0.42 ng/mL (0.20−0.49 ng/mL), and a lactic acid of 3.1 mmol/L (0.7–2.0 mmol/L). Chest radiography showed no acute pulmonary disease. Infectious workup, including urine analysis, SARS-CoV-2 RT-PCR, and *Legionella* and pneumococcus urinary antigens, were negative. The patient was started on ceftriaxone and doxycycline for community-acquired pneumonia with atypical coverage and admitted to the general medical ward.

Given the presence of high fever with confusion, a lumbar puncture was performed. Further cerebrospinal fluid analysis did not show evidence of infection. A transthoracic echocardiogram was done to rule out infective endocarditis, which did not show evidence of vegetations. On admission day 2, the patient developed persistent hypotension with tachycardia and fever to 40 °C with a profound upper and lower extremities weakness. He was then transferred to the intensive care unit (ICU) with septic shock.

At that point, the white count increased to 41.7 k/mm^3, liver enzymes were aspartate aminotransferase (AST) 113 IU/L (13–39 IU/L) and alanine aminotransferase (ALT) 151 IU/L (7.0–52.0 IU/L), creatinine kinase (CK) was 319 IU/L (30–223 IU/L), high sensitivity troponin was 27 pg/mL (0–20 pg/mL) and inflammatory markers were also found elevated, including a D-dimer of 1067 ng/mL FEU (0–500 ng/mL FEU), a C-reactive protein of 18 mg/dL (<1.0 mg/dL), an erythrocyte sedimentation rate 42 mm/h (0–17 mm/h), an interleukin-6 of 1620 pg/mL (0.0–6.0 pg/mL), and a fibrinogen of 625 mg/dL (163–463 mg/dL). A repeat SAR-CoV-2 RT-PCR and IgG antibodies were sent due to the high suspicion for COVID-19 given the ongoing pandemic setting that later turned back negative again. Looking for an infectious source, other investigations were sent, including respiratory viral panel, PCR assay for identification of methicillin-resistant *S. aureus* (MRSA), gonococcus and *Chlamydia* DNA probe, HSV1 and 2 antigen/antibodies, hepatitis panel, *Rickettsia* and *Brucella* antibody agglutination, EBV IgM and IgG VCA antibodies and PCR, CMV antibodies, West Nile Virus antibody panel, Lyme IgM and IgG antibodies Western Blot, Syphilis screen, interferon release assay for tuberculosis, malarial smear, and *Histoplasma* galactomannan urine antigen quantitative by enzyme immunoassay (EIA). Rheumatological panels were also ordered, including C3 and C4 complement levels, antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (P-ANCA and C-ANCA), and rheumatoid factor. Further imaging studies, including magnetic resonance imaging of the spine to rule out spinal or paravertebral abscess, CT of the head to rule out intracranial infections, and CT chest and abdomen for the presence of any new lung involvement or intraabdominal infection. All these investigations ultimately resulted in negative, except for the MRSA PCR screen. Considering this finding, the patient was started on intravenous (IV) vancomycin.

On day 4 of admission, the white count and the lactic acid started trending down, fever decreased, vitals became stable, and the patient was discharged from the ICU. He still had the left armpit pain, and the nodule seen in admission was noted to evolve into an abscess with fluctuance. He also appeared flushed and had nonspecific erythrasma on the lower limbs with deep palmar erythema, raising the suspicion for staphylococcal TSS. Incision and drainage of the abscess was performed and sent for culture. The patient gradually improved, rashes started to have central clearance, and he started to have flaky skin, especially in the palms. The patient was monitored a few days more for possible generalized desquamation and then discharged in stable condition with oral amoxicillin-clavulanate for 14 more days. At the time of discharge, his diffuse erythroderma was nearly resolved except for his palms and soles. He also had some flakiness along with pinkish coloration in the palms. The rash started to improve while the patient was on vancomycin; hence vancomycin-induced rash, which typically involves the face, neck, and upper torso, was deemed unlikely. Cultures from the wound then became available, showing methicillin-susceptible *Staphylococcus aureus*. Thus, the definitive diagnosis of staphylococcal TSS secondary to the abscess was made.

Discussion

We present the case of a healthy 19-year-old male who developed staphylococcal toxic shock syndrome secondary to a staphylococcal axillary abscess. Toxic shock syndrome is a clinical diagnosis of exclusion, for which a case definition was created by the Centers for Disease Control 40 years ago. A confirmed TSS case is defined by the presence of all major criteria and three or more minor criteria, along with exclusionary evidence of other disease processes. Major criteria are fever ≥38.8 °C, a diffuse, macular erythrodermic rash, skin desquamation 1–2 weeks after onset of illness (particularly palms and soles), and hypotension. Minor criteria include the involvement of three or more organ systems [9–11]. Of note, menstruation does not play a role in the diagnosis. Our patient presented initially with febrile illness and a maculopapular rash on the lower extremities, and later during the hospital course, developed desquamation on his palms, fulfilling major criteria. He also had vomiting, confusion, muscular weakness with elevated CK, and elevated liver enzymes, fulfilling minor criteria for TSS. Other infectious diseases were ruled out, including COVID-19, while methicillin-sensible *S. aureus* was isolated from an axillary abscess. Although the diagnosis was finally obtained, and the patient had a good outcome, there was a significant delay in the diagnosis and treatment. Hence, physicians must familiarize themselves with the clinical presentation to entertain a possible diagnosis of TSS early in the course of evaluation of any seriously ill patient [10].

The term “Staphylococcal TSS” was used for the first time in 1978, but there are reports of the syndrome in the literature as early as 1927 [6,7]. Staphylococcal TSS came to prominence in the early 1980s in the US in association with highly absorbent tampons among young, healthy women, with high rates of vaginal cultures yielding *S. aureus* [6]. Since then, the medical community has focused on its relation to menstruation and tampon use [8]. However, recent evidence has shown that nonmenstrual SST could be more frequent than previously thought, and most importantly, some studies have shown higher mortality than menstrual TSS [7,12]. Nonmenstrual TSS may result from any primary infection or colonization with a toxin-producing *S. aureus* strain. It can arise after skin or mucous membrane breakdowns, associated with abscesses or burns, and after surgical procedures [6]. Our patient was found to have an axillary abscess due to methicillin-sensible *S. aureus*. In fact, axillary abscesses account for 16 % of all cutaneous abscesses, and most of these are caused predominantly by *S. aureus* [13]. TSS should be considered in patients with shock and infection with *S. aureus* [6].

Epidemiological studies have shown that the incidence of both menstrual and nonmenstrual TSS has been stable compared to the peak observed in the late 1980s, but the relative incidence of nonmenstrual TSS has increased [14,15]. Although the initial presentation of patients with nonmenstrual TSS may not differ clinically from menstrual TSS, they display differences in demographics, epidemiological characteristics, morbidity, and

mortality. Patients with nonmenstrual TSS make up a heterogeneous group with a wide range of ages, antecedent events, and *S. aureus* infections [7,8]. In contrast to menstrual TSS, nonmenstrual TSS can affect both men and women and is not limited by the reproductive age, affecting patients from infancy to old age [7,8,12]. Nonmenstrual TSS is associated with more pronounced fever and rash in early illness and more severe hematological, renal, and neurological complications [6,8]. In 46%–52% of the cases, skin or soft tissue infection is identified as the cause, although commonly, no source of infection is confirmed [7,14,15]. Finally, while some studies have found no difference in mortality between menstrual and nonmenstrual TSS [8,15], other reports have shown significantly higher mortality among patients with nonmenstrual TSS, with mortality rates ranging from 5 % to 22 % [12,14].

For critically ill patients with sepsis or septic shock, time is of the essence. Inadequate and delayed initial antibiotic therapy increases mortality in patients with septic shock [6,16]. The clinical characteristics of staphylococcal TSS overlap with those of septic shock: sepsis that results in tissue hypoperfusion and life-threatening organ dysfunction and may overlap at early phases. Three elements are critical: administrations of broad-spectrum intravenous antimicrobials for a suspected pathogen within 1 h after the diagnosis of sepsis; for patients with hypoperfusion, the administration of 30 mL/kg of IV crystalloid within 3 h; and anatomic source control as rapidly as is practical [16]. The antibiotic regimen choice is based on in-vitro studies and theoretical principles rather than evidence-based guidelines from clinical trials. It is generally accepted that the empiric treatment should include a β-lactam agent and vancomycin or linezolid, given the high prevalence of MRSA, pending results from blood cultures and cultures from the suspected source [6,17]. Clindamycin should also be considered, as in-vitro models have been shown to suppress *S. aureus* toxin production [6]. If an organism is finally identified, antibiotic stewardship should be performed. Observational data have shown a mortality benefit using IV immunoglobulin: however, no randomized controlled trials support its use [6,17]. Our patient was initially treated with ceftriaxone and azithromycin in the context of a young patient presenting with sepsis during the ongoing COVID-19 pandemic. As expected, he did not improve until later in the hospital course when vancomycin was started due to a positive PCR screen for MRSA, and source control was performed by surgery. Ultimately, he was discharged on oral amoxicillin-clavulanate after MSSA was identified.

In conclusion, nonmenstrual TSS now has a relatively higher incidence than menstrual TSS. No single diagnostic test is available to identify patients with TSS. Hence, physicians must be familiar with the clinical presentation of TSS to entertain a possible diagnosis early in the evaluation of any seriously ill patient with septic shock and possible or confirmed infection with *S. aureus*.

Ethical approval

Our institution does not require ethical approval for case reports.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor of this journal.

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Bidhya Poudel: Conceptualization, Writing - original draft, Writing - review & editing. **Qishuo Zhang:** Writing - review & editing. **Angkawipa Trongtorsak:** Writing - review & editing. **Bimatshu Pyakuryal:** Writing - review & editing. **Goar Egoryan:** Writing - review & editing. **Mina Sous:** Writing - review & editing. **Rizwan Ahmed:** Writing - review & editing. **Daniela Patricia Trelles-Garcia:** Writing - review & editing. **Maria Adriana Yanez-Bello:** Writing - review & editing. **Valeria Patricia Trelles-Garcia:** Writing - review & editing. **Jonathan J. Stake:** Conceptualization, Supervision. **Guillermo Rodriguez-Nava:** Conceptualization, Supervision, Project administration, Writing - review & editing.

Declaration of Competing Interest

None.

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