Case report

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Toxic shock syndrome related to the use of a menstrual cup in a pediatric patient

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Abstract

Menstrual cups, made of hypoallergenic rubber or silicone, were first marketed in the 1930's but have become increasingly popular. Menstrual cups may be less expensive, more environmentally friendly and potentially a safer alternative to tampons and menstrual pads, although the safety of these cups is unknown. We report a case of a 17.5-year-old female who developed probable toxic shock syndrome related to use of The DivaCup®. We suggest that women presenting with signs and symptoms of toxic shock syndrome be asked specifically about their use of a menstrual cup in addition to tampons, because it may be a risk factor and present requires prompt removal for source control.

Key words: Pediatric, menstrual cup, toxic shock syndrome, TSS.

Case presentation

A 17.5-year-old female presented to an urgent care after one day of fever, chills, vomiting, diarrhea, low back pain, and a mild sore throat. On initial exam, she was febrile to 39.2 °C, hypotensive, and throat swab was Strep A positive. Despite 3 liter boluses of normal saline, upon arrival in the emergency department, she was tachycardic (114-121 bpm) and hypotensive (78-90/34-40 mmHg), but her fever resolved. Initial labs are shown in **Table 1**.

She was started on ceftriaxone and vancomycin and transferred to the pediatric intensive care unit. The admitting intensivist noted an erythematous rash and added clindamycin. She initially denied tampon use, but on hospital day 2 the patient revealed that she was using a DivaCup® for menstrual collection. It was promptly removed and found to contain purulent material. She stated that she normally cleaned it every 8 hours with soap and water and boiled it in hot water monthly for added cleanliness. Pelvic imaging was consistent with general inflammation but free of intra uterine infection or pelvic inflammatory disease. Vaginal cultures grew moderate methicillin sensitive Staphylococcus aureus, toxic shock syndrome toxin-1 (TSST-1) positive, staphylococcal enterotoxins serotype B (SEB antibody) positive, and staphylococcal enterotoxins serotype C (SEC antibody) positive. Blood and urine cultures were negative.

Based on the Centers for Disease Control and Prevention (CDC) definition of non streptococcal toxic shock syndrome (TSS), this patient with a probable case. She met criteria for fever, diffuse rash, hypotension, and multisystem involvement including gastrointestinal, muscular, and renal involvement. Cultures were also positive for an organism positive for toxins and enterotoxins known to cause TSS. The patient never had documented desquamation, which precludes the classification of confirmed toxic shock syndrome.

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An infectious disease physician was consulted on hospital day 3, and antibiotics were adjusted to nafcillin, clindamycin, and vancomycin. Vancomycin and clindamycin were discontinued on hospital days 5 and 6, respectively. On hospital day 8 and date of discharge, antibiotics were changed to cephalexin 500 mg PO TID for nine more days for a total treatment course of 14 days. Patient and family were thoroughly counseled that patient should not use tampons or other internal menstrual devices. She began combination oral contraceptives two months after discharge and was considering intrauterine device (IUD) placement. Patient has not had documented reinfections or long-term sequelae from her infection and hospitalization.

Discussion

TSS was first characterized in 1978 by Todd and colleagues as a combination of high fever, headache, confusion, hypotension, scarlitiniform rash, and subcutaneous edema. (1) Additional symptoms included sore throat, vomiting, diarrhea, and shock. During recovery, all patients had fine desquamation of skin, specifically on the hands and feet. From 1979-1980, there was an increased number of TSS cases leading to increased epidemiologic studies. (2) The first surveillance report and case-controlled study was published in Wisconsin in 1980. Researchers found that 37 of 38 patients with reported symptoms meeting case definition were previously healthy women with a mean age of 24.5 years. (3) Thirty-five (95%) of these women developed onset of toxic shock symptoms during menses, prompting the term menstrual toxic shock syndrome. This study found a statistically significant association between TSS and tampon use similar to other cases series and surveillance data at that time.

However, as noted by Shands, et al the estimated incidence of toxic shock syndrome of 6.2 per 100,000 menstruating women per year was low compared to the 70-80% of American women who used tampons, suggesting that tampon use by itself was not directly causing TSS. (3,4) Subsequent studies suggested that tampons' chemical structures and/or absorbencies were associated risk factors. (5) A tampon analysis in 1987, again, showed that users of tampons had elevated risk compared to non-users, but regardless of chemical composition, increasing absorbency increased the odds ratio for TSS. (6) Reingold, et al found a 34% increased risk for every 1-g increase in absorbency. (5) Surveillance studies plotted a declining trend in menstrual TSS cases after Rely® tampons were removed from the market, manufacturers decreased tampon absorbency, and the FDA required standardized tampon labeling. This was also following a time of increased awareness that led to active surveillance in 1986. (2)

With heightened surveillance and case control trials on toxic shock syndrome, came increased laboratory reports on the causative organism. All but one patient in Todd's study grew phage group 1 Staphylococcus aureus from mucosal sites. (1) From 1979-1996, 90% of women who had TSS and vaginal cultures taken grew Staphylococcus aureus. (2) The current understanding is that S. aureus produces super antigens, Sags, which increase a patient's risk for developing TSS. (7) Staph strains can produce one or more Sag proteins including TSST-1. The TSST-1 antigen was isolated from vaginal cultures in a 17-year-old female who died from menstrual TSS and from a 13-year-old female with recurrent menstrual TSS despite tampon cessation. (8,9) TSST-1 was the most commonly identified super antigen in an epidemiological observation study from 2000-2006. (10) Other Sags include staphylococcal enterotoxins serotypes A, B, C, D, E, which can stimulate >20% of host T cells, leading to cytokine storm and inflammation within tissues and organs. (7) Since the 1980s, there have been reports of toxic shock syndrome caused by M type (1,3,11,12, and 28) superantigens from invasive Streptococcus pyogenes infections, although with somewhat different diagnostic criteria. (11)

Vaginal devices were first patented in the United States in 1867, which included menstrual collection, contraception, and uterine/pelvic support. (12) Disposable menstrual products were introduced in 1896 and became widely available due to increased advertising of Kotex® pads and tampons in the 1920s and 1930s. While the social constraints of menstruation have begun to decrease, these taboos still reduce many women's quality of life in developing countries. (12) Efforts to produce inexpensive solutions included the first menstrual cup, which was patented in 1937. Despite their long history, there are few study reports that evaluate safety and acceptability of cups. Available studies have not showed significant changes in vaginal cultures including staphylococcus colonization and normal flora alterations. (13) A recent safety study in 2017 in Kenya did not detect any cases of toxic shock syndrome among 177 cup users with a Staphylococcus aureus prevalence of 9.6%. None of the cup users tested positive for the TSST-1. (14)

Staphylococcal toxic shock syndrome (not streptococcal) has been a national reportable disease since

1983. The 2011 CDC definition is presented in **Table 2**. (15) At this time, the only case of toxic shock related to a menstrual cup was published in 2015. A 37-year-old female presented to an Ontario hospital with fever, abdominal cramp, myalgia, vaginal discharge, and erythroderma. She reported using the DivaCup® (Diva International Inc, USA) ten days prior to her presentation. She remained in septic shock for 24 hours despite aggressive fluids and antibiotics. All cultures were negative, and she developed a morbilliform rash. Antibiotics were adjusted to include clindamycin for probable menstrual toxic shock syndrome, and she began to improve. (16)

The subject of this report specifically denied ever using tampons but was not specifically asked and did not volunteer the presence of a menstrual cup. Despite delayed removal of the device (day 2), she improved clinically with fluid resuscitation and appropriate antibiotics and made a full recovery. The early addition of the protein synthesis inhibiting antimicrobial clindamycin is thought to have a direct, more rapid effect on toxin production than other anti-staphylococcal agents and may improve survival but should not be used as a single agent.

Toxic shock syndrome has been reported with both Staphylococcus aureus and Streptococcus pyogenes infections from multiple sources, and identification and control of the infectious site is critical to improve outcomes. Our patient met probable classification for toxic shock syndrome and grew methicillin sensitive, TSST-1 positive, SEB (antibody) and SEC (antibody) positive Staphylococcus aureus from her vagina. The incidence of menstrual cup associated toxic shock syndrome remains unknown, but this case leads us to suggest that women presenting with signs and symptoms of toxic shock syndrome be asked specifically about their use of a menstrual cup and if present requires prompt removal for source control.

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Table 1. Initial laboratory results

Parameter	Result
White blood cell count	16.4 x10^3/ul
Bands	58%
Hemoglobin	11.5 g/dl
Platelets	237 x10^3/ul
Creatinine	1.7 mg/dl
Blood urea nitrogen	18 mg/dl
Creatinine kinase	776 U/l, 1337 U/l
International normalized ratio	1.56
Total bilirubin	0.3 mg/dl
Alanine aminotransferase	22 U/l
Aspartate aminotransferase	21 U/l
Urinalysis	58 leukocytes/high powered field
Urine cultures	Multiple organisms
Blood cultures	Negative x2
Vaginal cultures	Moderate methicillin sensitive Staphylococcus aureus TSST-1: Positive SEB (antibody): positive SEC (antibody): positive

Legend: TSST-1=toxic shock syndrome toxin-1; SEB=staphylococcal enterotoxins serotype B; SEC=staphylococcal enterotoxins serotype C.

Table 2. Centers for Disease Control and Prevention 2011 case definition for toxic shock syndrome (other than Streptococcus)

Clinical criteria An illness with the following clinical manifestations • Fever: temperature greater than or equal to 102.0 °F (greater than or equal to 38.9 °C) • Rash: diffuse macular erythroderma • Desquamation: 1-2 weeks after onset of rash • Hypotension: systolic blood pressure less than or equal to 90 mmHg for adults or less than fifth percentile by age for children aged less than 16 years • Multisystem involvement (three or more of the following organ systems): o Gastrointestinal: vomiting or diarrhea at onset of illness o Muscular: severe myalgia or creatinine phosphokinase level at least twice the upper limit of normal o Mucous membrane: vaginal, oropharyngeal, or conjunctival hyperemia o Renal: blood urea nitrogen or creatinine at least twice the upper limit of normal for laboratory or urinary sediment with pyuria (greater than or equal to 5 leukocytes per high-power field) in the absence of urinary tract infection o Hepatic: total bilirubin, alanine aminotransferase enzyme, or aspartate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory o Hematologic: platelets less than 100,000/mm^3 o Central nervous system: disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent
Laboratory criteria for diagnosis Negative results on the following tests, if obtained: • Blood or cerebrospinal fluid cultures (blood culture may be positive for Staphylococcus aureus) • Negative serologies for Rocky Mountain spotted fever, leptospirosis, or measles
Case classification Probable • A case which meets the laboratory criteria and in which four of the five clinical criteria described above are present Confirmed • A case which meets the laboratory criteria and in which all five of the clinical criteria described above are present, including desquamation, unless the patient dies before desquamation occurs

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