

A confirmed case of toxic shock syndrome associated with the use of a menstrual cup

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Menstrual cups have been reported to be an acceptable substitute for tampons. These flexible cups have also been reported to provide a sustainable solution to menstrual management, with modest cost savings and no significant health risk.

The present article documents the first case of toxic shock syndrome associated with the use of a menstrual cup in a woman 37 years of age, using a menstrual cup for the first time. Toxic shock syndrome and the literature on menstrual cups is reviewed and a possible mechanism for the development of toxic shock syndrome in the patient is described.

Key Words: *Feminine hygiene products; Menstrual cups; Staphylococcus aureus; Toxic shock syndrome; Vaginal cups*

CASE PRESENTATION

A 37-year-old Caucasian woman presented to the emergency department with a two-day history of fevers, conjunctival hyperemia, abdominal cramps, myalgias, vaginal discharge and diffuse erythroderma prominent on her upper thorax, inner thighs and perineum. She had a history of Hashimoto's thyroiditis and chronic menorrhagia.

Ten days before her presentation, she began using The DivaCup (Diva International Inc, USA), a brand of menstrual cup for menstrual blood collection (Figure 1). She used appropriate hygiene when handling and changing the cup, but retrospectively reported causing a small abrasion during one of her initial insertions. Her subsequent menses became heavier and longer than normal. By day 7, she noticed an episode of black vaginal discharge followed two days later by yellow purulent discharge along with subjective fevers, at which point she stopped using the menstrual cup. She presented to the emergency department the following day, after continuing to feel unwell.

On initial examination, she looked unwell and had an oral temperature of 37.2°C, blood pressure of 98/65 mmHg and a heart rate of 132 beats/min. No other obvious source of sepsis was found during physical examination. Despite receiving aggressive intravenous fluid resuscitation and antibiotic therapy, including linezolid and piperacillin-tazobactam, she remained hypotensive for the next 24 h. Vaginal examination revealed yellow discharge and mild menstrual bleeding, but no cervical motion tenderness. The menstrual cup was not present because it had been removed before presenting to hospital. Her blood and urine cultures, methicillin-resistant *Staphylococcus aureus* screening, *Clostridium difficile* toxin assay and nasopharyngeal swab for respiratory viruses were negative (Table 1).

Un cas confirmé de syndrome du choc toxique causé par l'utilisation de la coupe menstruelle

Les coupes menstruelles sont considérées comme un substitut acceptable des tampons. Ces coupes flexibles sont également considérées comme une solution durable pour gérer les menstruations, entraînant de modestes économies, sans risque important pour la santé.

Le présent article rend compte du premier cas de syndrome du choc toxique chez une femme de 37 ans, qui utilisait une coupe menstruelle pour la première fois. Les chercheurs analysent le syndrome du choc toxique et les publications sur les coupes menstruelles et décrivent un mécanisme possible d'apparition du syndrome du choc toxique chez la patiente.

During the next 24 h, the patient clinically deteriorated; she had a temperature of 39.1°C, a blood pressure of 76/45 mmHg and a heart rate of 137 beats/min. She continued to receive aggressive intravenous fluids and was transferred to a high-acuity observational unit. Postadmission day 2, the patient developed a generalized morbilliform rash. The Infectious Diseases services were consulted. Subsequently, intravenous clindamycin was added to her antibiotic regimen with probable diagnosis of menstrual toxic shock syndrome (TSS).

Within 24 h of receiving clindamycin, her blood pressure had significantly improved. Desquamation of her skin rash began on postadmission day 4. The patient remained stable on her antibiotic regimen, ultimately being discharged in good health eight days postadmission. She remained stable for the next two weeks, at which point she was seen at the Infectious Diseases Outpatient Clinic at University Hospital, London Health Sciences Centre (London, Ontario). Control cultures including nasal swab for *S aureus* remained negative.

DISCUSSION

Menstrual TSS

The term 'toxic shock syndrome' was first coined in 1978 in a *Lancet* publication describing the symptom complex in children eight to 17 years of age with an acute febrile illness (1). It did not come to public attention until 1980, when an association between TSS and young menstruating women using tampons was discovered (2). Risk factors included the use of high-absorbency tampons and prolonged, continual usage (3). Cases occurring in men and nonmenstruating women were thereafter identified and it was recognized that TSS can occur in any population. There has been a recently published

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Figure 1 The DivaCup (Diva International Inc, USA) (a brand of menstrual cup)

TABLE 1
Laboratory results from initial assessment

Parameter (normal range)	Result
White blood cell count (4.0–10.0×10 ⁹ /L)	23.6×10 ⁹ /L
Hemoglobin (115–160 g/L)	72 g/L
Platelets 1(50–400×10 ⁹ /L)	107×10 ⁹ /L
International normalized ratio (0.9–1.1)	1.8
Fibrinogen (2.0–4.0 g/L)	4.79 g/L
Creatinine (<100 µmol/L)	106 µmol/L
Creatine kinase (<167 U/L)	346 U/L
Blood urea nitrogen (<8.3 mmol/L)	2.8 mmol/L
Alanine aminotransferase (<33 U/L)	52 U/L
Aspartate aminotransferase (<32 U/L)	72 U/L
Total bilirubin (3.4–17.1 µmol/L)	61.3 µmol/L
Potassium (3.5–5.0 mmol/L)	3.0 mmol/L
Magnesium (0.65–1.05 mmol/L)	0.34 mmol/L
Ionized calcium (1.09–1.30 mmol/L)	1.05 mmol/L
Urinalysis	20–30 leukocytes/high power field
Total beta human chorionic gonadotropin	Negative (<1 IU/L)
Blood cultures	Negative ×2
Urine culture	Negative

report of recurrent TSS in a 15-year-old girl even after she ceased to use tampons (4).

Increased public awareness and change in the composition of tampons to less-absorbent materials led to a substantial decrease in the incidence of menstrual TSS over the next decade (3).

Menstrual TSS is a severe, multisystem, toxin-mediated disease associated with multiorgan failure (Table 2) (5). Considering these criteria, the clinical findings of our patient and her laboratory data fulfill the criteria of a 'confirmed' case.

S aureus TSS toxin 1 (TSST-1) is responsible for multiorgan failure in nearly all (95%) patients with menstrual TSS. (6). This toxin acts as a superantigen, stimulating excessive and nonconventional T cell

TABLE 2
Centers for Disease Control and Prevention (Georgia, USA) 2011 case definition for toxic shock syndrome (other than *Streptococcus*) (5)

Clinical criteria

An illness with the following clinical manifestations:

- Fever: temperature $\geq 102.0^{\circ}\text{F}$ ($\geq 38.9^{\circ}\text{C}$)
- Rash: diffuse macular erythroderma
- Desquamation: one to two weeks after onset of rash
- Hypotension: systolic blood pressure ≤ 90 mmHg for adults or less than fifth percentile for children <16 years of age

Multisystem involvement (≥ 3 of the following organ systems):

- Gastrointestinal: vomiting or diarrhea at onset of illness
- Muscular: severe myalgia or creatine phosphokinase level at least twice the upper limit of normal
- Mucous membrane: vaginal, oropharyngeal or conjunctival hyperemia
- Renal: blood urea nitrogen or creatinine at least twice the upper limit of normal for laboratory or urinary sediment with pyuria (≥ 5 leukocytes per high-power field) in the absence of urinary tract infection
- Hepatic: total bilirubin, alanine aminotransferase enzyme or aspartate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory
- Hematological: platelets $< 100,000/\text{mm}^3$
- Central nervous system: disorientation or alterations in consciousness without focal neurological 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 that meets the laboratory criteria and in which four of the five clinical criteria described above are present

Confirmed

- A case that 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

activation and, subsequently, cytokine expression (7). Superantigens bypass normal major histocompatibility complex-restricted antigen recognition and activate 30% of host T cells, while conventional antigen presentation activates only approximately 0.01% of the host T cell population (8). Eventually, significant cytokine release causes multiorgan failure. Detection of TSST-1 is not required for the diagnosis of TSS and this test is only available in some research laboratories.

Treatment includes active fluid resuscitation, early use of vasopressors and appropriate antimicrobial therapy. Clindamycin has been demonstrated to reduce the expression of superantigens (9). Theoretically, clindamycin suppresses the protein synthesis and, as a result, more effectively inhibits toxin production compared with vancomycin, which inhibits cell wall synthesis. Linezolid has also been successfully used to treat nonmenstrual TSS and has been shown to decrease TSST-1 production (10). To our knowledge, we report the first case of menstrual TSS that was successfully treated with combination of linezolid and clindamycin. Although rapid clinical improvement has been previously described with the use of linezolid in TSST-1-producing *S aureus*, our patient remained hypotensive while receiving linezolid (10). Her blood pressure significantly improved only after the addition of clindamycin. She did not require intravenous immunoglobulin. Although both clindamycin and linezolid inhibit

bacterial protein synthesis and, therefore, toxin production, our patient remained hypotensive until clindamycin was included in her antibiotic regimen. Further experimental and comparative studies are required to determine the inhibitory effects of these two medications against TSST-1.

Menstrual cups

Menstrual cups are a reusable alternative to conventional tampons. Designed to collect rather than absorb menstrual flow, they are made of silicone and worn internally (Figure 1). In a recent multicentre randomized controlled trial by Howard et al (11), the use of tampons was compared with The DivaCup in a total of 110 women. The results demonstrated that overall satisfaction was higher among users of The DivaCup, with 91% of users stating they would continue using it. The present case report identified increased vaginal irritation with The DivaCup compared with tampons, but was not powered to detect a difference in infectious complications (11).

Tierno (12) explained the probable reasons for the association between hyperabsorbable tampons and TSS as follows:

1. Accumulation of blood in the polyester foam cubes and chips of carboxymethylcellulose.
2. Increase of vaginal pH in menstruation from 4.2 to around 7.4.
3. Existence of both oxygen and carbon dioxide in the vagina during menstruation.

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These three main factors provide a condition for *S aureus* growth. In a narrative review, Vostral (13), concluded that the gelled carboxymethylcellulose, in essence, acted like agar in a petri dish, providing a medium on which the bacteria may grow. Menstrual cups are made of silicone or rubber, and carboxymethylcellulose is not used in their structure. Silicone itself does not support microbiological growth. However, because of accumulation of blood, menstrual cups appear to provide a medium for bacterial growth with the same three conditions mentioned above. Menstrual blood in the uterine environment is sufficient to promote the growth of *S aureus* in the lower genital tract. As such, the menstrual cup appears to provide a necessary milieu for *S aureus* growth during menstruation. Our patient began using the menstrual cup approximately 10 days before presentation. This duration appears to be sufficient for *S aureus* growth. High placement of a previously handled cup, an abundant volume of menstrual blood and mucosal irritation within the vagina may be considered as other probable contributing factors.

To our knowledge, the present report is the first to detail the association between a menstrual cup and menstrual TSS. We present here a rare case in a 37-year-old woman who met all six Centers for Disease Control and Prevention (Georgia, USA) criteria (5) for confirmed TSS after wearing a menstrual cup for the first time.

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