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CLINICAL VIGNETTE

A Classic Case of Toxic Shock Syndrome Due to a Not So Classic Organism, *Clostridium sordellii*

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Introduction

Toxic shock from *Clostridium sordellii* is a rare and fatal syndrome that has resulted from childbirth, abortion, and gynecological procedures. We present a tragic case of a woman who died from Clostridial toxic shock syndrome within 24 hours of her hospitalization in order to raise awareness of this fatal disease.

Case

A 33-year-old previously healthy female presents with 3 days of fever and lower abdominal pain. About 1 week prior to presentation, the patient underwent a medically induced abortion for a 6-week non-viable pregnancy with 800 μg of vaginal miso-prostol. She initially developed heavy bleeding, which subsided after 4 days, and abdominal cramping. Due to worsening pain, she presented to the Emergency Department (ED) 2 days prior to presentation. At that time, ultrasound showed a thickened "endometrial stripe" but no evidence of intra-uterine pregnancy. White blood cell (WBC) count was elevated to 20 x 10^3. She was given one dose of levofloxacin in the ED, and after consultation with gynecology, she was discharged home on doxycycline due to a penicillin allergy. Despite antibiotics, she continued to have worsening abdominal pain along with nausea and vomiting. She also had new fevers up to 101.6 F. Prompting return to the ED.

Upon presentation, she was afebrile but tachycardic to 142 bpm with blood pressure of 131/80. She was breathing at 20 breaths per minute at 97% on room air. Physical exam was notable for tenderness to palpation in her mid-abdominal region. Initial laboratory studies were significant for leukocytosis at 57.62 x 10^3 with 75% neutrophils, hemoconcentration with hematocrit at 52.3%, and thrombocytosis with platelets elevated to 509 x 10^3. Creatinine was elevated at 0.95 mg/dL compared to her baseline of 0.56 mg/dL. Lactate was also elevated to 37 mg/dL. Computerized tomography (CT) scan of the abdomen and pelvis showed small to moderate free peritoneal fluid and small pleural effusions along with an abnormal density of the myometrium at the level of the uterine fundus. Patient was given a dose of IV ceftriaxone and piperacillin/ tazobactam. Then, the decision was made to go to the operating room for dilation and curettage (D&C) for possible retained products of conception and then to the Intensive Care Unit for close monitoring, where the patient was started on gentamicin and clindamycin.

After her D&C, the patient remained tachycardic. Aggressive volume resuscitation and pain control were initiated; however, the patient remained in sinus tachycardia with heart rate in the 160-170s bpm. Her blood pressure and urine output were also steadily declining. Repeat laboratory studies were notable for worsening leukocytosis with WBC 113.29 x10^3 and lactate at 50 mg/dL. Arterial blood gas showed metabolic acidosis with a pH of 7.2, a partial pressure of carbon dioxide of 30 mmHg and a bicarbonate concentration of 12 mmol per liter. More fluids were given, and antibiotics were further broadened to add vancomycin and meropenem. IVIG was also ordered for concern for toxic shock syndrome. Despite these measures, she continued to deteriorate over the next three hours, requiring intubation, multiple pressors, and continuous renal replacement therapy (CRRT). Unfortunately, as emergent plans were being made for emergent hysterectomy for source control, she suffered a cardiac arrest and died. Tissue cultures from her D&C were positive for pan-sensitive *Clostridium sordellii (C. Sordellii)*. Blood cultures were negative. Autopsy was performed, which found a large volume of cloudy serosanguineous fluid, fibropurulent exudates, and mesenteric and pelvic lymphadenopathy, demonstrating infection and peritonitis, along with a hemorrhagic and necrotic uterus, right ovary, and right fallopian tube. Post-mortem cultures grew gram positive anaerobic rods, consistent with *C. sordellii*.

Discussion

Toxic shock syndrome (TSS) is characterized by a rapid onset of severe illness that results in fever, hypotension and end-organ damage. Symptoms occur typically in otherwise healthy individuals and are the consequences of toxin production by the bacteria. Many of the reported cases have been due to methicillin-susceptible *Staphylococcus aureus* (*MSSA*), however, other organisms can cause TSS.[1]

Clostridium sordellii is a gram-positive, spore-forming obligate anaerobe, which is carried vaginally in 0.5-10% of healthy women.[2] It was first isolated in 1922 from gangrenous wounds in humans and has been associated with pneumonia, endocarditis, peritonitis, arthritis, and myonecrosis.[3] Fulminant toxic shock syndrome due to *C. sordellii* results from specific exotoxins.[4] Patients initially present with nonspecific signs about 2-7 days although can occur up to 2 months after delivery

or abortion. They then develop severe tachycardia and refractory hypotension but lack fevers. Lab studies show a leukemoid reaction with WBC in the 40 to 200 x 10^3 and hemoconcentration. Imaging may show pleural and peritoneal effusions due to capillary leakage. Blood cultures are typically negative.[2-5]

Early diagnosis is challenging due to the rare nature of the infection and the non-specific presenting symptoms. One study investigating the presence of *Clostridium sordellii* and *Clostridium perfringens* in the vagina and rectum of women found 3.4% of women who were positive for *C. sordellii.*[6] Recent gynecologic surgery was associated with the presence of this organism. Interestingly, 94.7% of the women with *C. sordellii* were negative for the pathogen on their two-week follow-up visit. The study also identified that only two of the 238 *C. sordellii* isolates contained the lethal toxic gene, and none had the hemorrhagic toxic gene. In light of the rare and transient nature of *C. sordellii* in the vagina and rectum, there is no recommendation to screen to prevent infection.

Antibiotics are an important part of management, and older studies suggest that *C. sordelli* is susceptible to B-lactams, clindamycin, tetracycline, and chloramphenicol but not to aminoglycosides and sulfonamides.[2] Adding clindamycin can potentially suppress toxin synthesis. An anti-toxin may also be beneficial; however, none currently exists for use in humans. Otherwise, surgical debridement or extraction of infected tissues may be necessary for diagnosis, source control, and removal of toxins.

Despite the current available treatments, the overall mortality rate has been 100% for *C. sordellii* infections associated with medical-induced and spontaneous abortions as well as childbirth.[2] Most patients die from hypotension and multi-organ failure within hours to days after initial presentation. The key to treatment is prevention and early diagnosis. In 2005, the US Food and Drug Administration issued a public health warning about mifepristone/misoprostol-induced abortion and its association with *C. sordellii*-related deaths. Current guidelines from the American Congress of Obstetricians and Gynecologists give a level A recommendation for use of mifepristone and misoprostol as part of the medical abortion regimen for first-trimester abortions.[7] There is, however, no support to use prophylactic antibiotics to prevent infection. A large retrospective study was conducted by Planned Parenthood Federation of America, Inc, which showed a decrease in serious infection rate when switching from vaginal to buccal misoprostol and a further decrease when adding a 1 week treatment course of doxycycline to the abortion regimen.[8] A subsequent report showed that the serious infection risk increased to the rate noted prior to routine doxycycline administration, suggesting that the addition of the antibiotic might have been a period effect.[9] Additionally, adherence to the antibiotic regimen was poor throughout the entire study period. Therefore, there is no strong evidence to warrant the use of prophylactic antibiotics for medical abortion.

Conclusion

Toxic shock syndrome due to *C. sordellii* is a devastating yet extraordinarily rare syndrome affecting young, healthy women. To improve the morbidity and mortality of this potentially fatal disease, physicians need to be able to identify the key clinical features of this syndrome and quickly intervene. More studies, however, need to be done to understand the pathogenesis of the organism and develop novel treatment strategies.

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