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Survival from *Clostridium* toxic shock syndrome: Case report and review of the literature



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ABSTRACT

INTRODUCTION: Clostridial toxic shock is a rare syndrome traditionally described in case studies and reviews as a uniformly fatal condition associated with post-partum and post-abortion. Clostridium sordellii was first mentioned in scientific literature as a human pathogen in 1922 when Argentinian microbiologist Alfredo Sordellii identified the organism in gangrenous wounds. Over the past century, there has been infrequent discussion and little awareness surrounding this serious condition. Information about patients who survived C. sordellii toxic shock is essentially nonexistent.

PRESENTATION OF CASE: A 31-year old post-partum female who underwent caesarian section 17 days prior, presented with abdominal pain and septic features. She underwent six operations/procedures over the next 17 days and was hospitalized for 25 days before discharge to her home with a successful outcome. DISCUSSION: This case provides insight on the process of identifying and managing complications associated with clostridial toxic shock syndrome. Out of now, 16 reported cases of *C sordellii* gynecologic infections in the world literature, our patient is the second patient to survive infection by this organism. More research is needed to provide clinicians with evidence-based approaches for managing these unique cases.

CONCLUSION: We present a case report of a rare toxic shock syndrome in a post-partum female caused by Clostridium sordellii. Her survival is notable among 16 patients with whom this infection now has a documented 87.5% mortality rate. Aggressive surgical measures and optimized intensive care management may have contributed to this patient's survival.

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1. Introduction

Clostridium sordellii is a gram positive, anaerobic, spore-forming bacillus found ubiquitously in soil that presents as a rare yet serious pathogenic potential in humans. Case reports have identified *C sordellii* as the culprit in bacteremia, necrotizing soft tissue infections, orthopedic tissue graft infections, and female upper reproductive tract infections since its 1922 debut in medical literature on gangrenous wounds [1]. Case reviews have demonstrated that postpartum and post-abortion women are a group susceptible to *C sordellii* infections [2–8]. As many as 18% of healthy women are colonized with a clostridia species but only about 3% are *C. Sordellii*, as a component of their normal vaginal flora, believed to be introduced

by way of recto-vaginal transmission [8,9]. The organism gained attention in 2005 when the US Food and Drug Administration investigated its association with mifepristone-induced abortions after five California women died, but authorities were unable to demonstrate an epidemiologic linkage [10]. A recent 2016 case report commented that up to 10% of healthy women harbor C. sordellii in their vagina, and while most strains are nonpathogenic, those that are virulent can cause fatal infections through toxin-induced septic shock rapidly followed by end-organ failure; identification of C. sordellii has occurred by cultures, mass spectrometry, and other molecular methods. Due to the danger of this syndrome, they argue for the necessity of rapid C sordellii testing for women [11]. A large multicenter trial by Chong et al., on over 4000 women revealed only about 3% colonized with C. sordellii and in this group of 238 patients, only 2 had the lethal toxin. This group concluded that it would be inadvisable and ineffective to use any screening or prophylactic approach to try to prevent [18].

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A. Elkbuli et al. / International Journal of Surgery Case Reports 50 (2018) 64-67

Basic science research has revealed two highly virulent *C. sordellii* toxins that mediate a systemic inflammatory response: lethal toxin (TcsL) and hemorrhagic toxin (TcsH). The lethal toxin triggers apoptotic mechanisms by exerting its effects on GTPases involved in mitochondrial function, cytoskeletal integrity, and cell cycle checkpoints [12]. Sequelae from these molecular alterations are devastating to endothelial cells, contribute to vascular compromise, and ultimately lead to systemic hemodynamic instability. The host response by uterine macrophage involves secretion of interleukin-10 (IL-10), an anti-inflammatory cytokine that may mask the development of infection and account for the fact that many patients are afebrile [13].

Patients generally present with signs of clinical sepsis and rapidly deteriorate to an almost invariably fatal toxic shock syndrome. The *C. sordellii* toxic shock syndrome inconsistently manifests as a triad of tachycardia, hypotension, and lack of fever [2]. The afebrile nature of this syndrome can be used in some cases to suggest *clostridium* as the etiology for toxic shock classically associated with severe staphylococcal and group A streptococcal infections. Laboratory results in clostridial shock typically show a remarkably high leukemoid reaction with white blood cell counts as high as 200,000 cells/µl in some cases.

Workup with aerobic and anaerobic cultures and gram stain of gynecological tissue may narrow the differential diagnoses and allow for targeted treatment. As obligate anaerobes, clostridia are fastidious organisms and often difficult to grow and isolate in culture. Definitive diagnosis of *C. sordellii* is dependent on immune-histochemical (IHC) staining and molecular methods such as polymerase chain reaction (PCR) because other species of clostridia like *C. perfringens* can inhabit the upper female reproductive tract and mount a concurrent infection. This case has been reported in line with the SCARE criteria [14].

2. Presentation of case

We present a case of a 31-year-old healthy female with no significant past medical history and a past surgical history of a previous cesarean section at term, two years prior. She had an uneventful second cesarean section at term and presented 17 days delivery. Her presenting complaints were; three days of suprapubic abdominal and bilateral flank pain accompanied by dysuria, nausea, vomiting, and diarrhea. She was afebrile but noted subjective rigors and chills. Her caesarian surgical incision was well healed and without evidence of cellulitis or infection. Her presenting vital signs were significant for hypotension. Initial laboratory results revealed a leukocytosis of 23,000 white blood cells/µl with a left shift. She had an elevated serum lactate of 4.1 mmol/liter. She was given intravenous fluid volume resuscitation and empiric broad spectrum intravenous antibiotic therapy in the emergency department and admitted to the Intensive Care Unit (ICU).

The admitting diagnosis was sepsis without an established source. The obstetrics & gynecology and general surgery team provided consultation. Unremarkable urologic and radiologic examinations as well as a clean urinalysis made urosepsis unlikely. Gynecologic and intra-abdominal origin were considered in the etiology.

Postpartum sepsis was entertained and she was taken to the operating room. A gynecologic surgeon performed a suction dilation & curettage (D&C) while a general surgeon laparoscopically examined the intra-abdominal viscera for a potential source, with no clear etiologic findings.

Despite the D&C, a procedure that should have identified and alleviated most uterine infectious sources, her white blood cell count rose to 42,000 cells/ μ l overnight and her septic shock worsened. Her white blood cell count tripled that day to become a

leukemoid reaction of 112,000 cells/ μ l. She also developed disseminated intravascular coagulation (DIC). Potential infection with Clostridium species including sordellii was considered in the differential.

With rapid clinical deterioration, obstetrics & gynecology and general surgery took the patient back to the operating room on admission day two for another visual inspection and performed a supra-cervical hysterectomy with bilateral salpingectomy. Her abdomen was left open because of development of abdominal compartment syndrome. Clinically the specimen revealed a grossly enlarged, engorged and discolored uterus while the initial pathologic review showed acute and chronic endo-myometritis with necrotic features along with acute salpingitis. The omental fat that was adherent to the uterus and was resected with it en-bloc showed gross necrosis and hemorrhage. Necrotic gynecologic tissue established the puerperal septic source and raised the index of suspicion for C. sordellii infection. Pathology performed microscopic examination of the tissue but did not reveal microorganisms. Specimens from this operation as well as from the previous D&C were sent to the United States Centers for Disease Control and Prevention (CDC) for further investigation. She was given intravenous immunoglobulin (IVIg) was given for a course of three days. A small European study suggested that patients that receive IVIg as adjunctive therapy in toxic shock syndromes have a decrease in the sepsis-related organ failure, although there was no statistical difference in mortality compared to patients that received placebo [15].

On hospital day five with her condition improving, general surgery took her to the operating room for exploratory laparotomy with abdominal washout and application of a vacuum-assisted closure (VAC) device to the wound. She was returned to the operating room on admission day seven for another abdominal washout, application of a Wittmann temporary abdominal fascia Velcro prosthetic patch (Starsurgical, Burlington, WI) and wound VAC. Five days later on admission day 12, she underwent another exploratory laparotomy with abdominal washout and tightening of the Wittmann abdominal fascia patch and placement of a wound VAC. On admission day 14, she underwent her fifth abdominal washout, this time with closure of the abdominal fascia.

White blood cell counts remained above 40,000 until admission day six. Over the next thirteen days in the ICU, her white blood cell count slowly normalized with a prolonged intravenous antibiotics course (Fig. 1). After 17 days of treatment in the ICU, she was transitioned to the surgical floor; she stayed in the hospital for another week until her discharge on admission day 25. She was successfully discharged with a walker for ambulation and arrangements for physical therapy home visits because she was de-conditioned. Follow up in the clinic; she was doing well a month out.

3. Discussion

With numerous interventions, this remarkable case had a positive outcome. Our patient is the second person to survive a *C. sordellii* gynecological infection out of 30 reported cases in the world medical literature. She underwent a supra-cervical hysterectomy with bilateral salpingectomy, laparoscopic abdominal washout, three exploratory laparotomies with abdominal washout, and a fascial closure procedure for a total of six operations. Massive fluid resuscitation was utilized to treat severe septic shock. The surgical critical care team managed her critical condition for 17 days in the ICU and infectious disease orchestrated a course of broadspectrum intravenous antibiotic and immunoglobulin therapy.

Our case is the only case where *C. sordellii* infection happened post-partum via Caesarean section. Most commonly, they occur after childbirth, or more recently, with medically induced abortions due to the theory that this bacterium colonizes the vagina, and the

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