

Case Report

Multi-System Organ Failure Secondary to Group A *Streptococcal Sepsis* in a Non-Pregnant Female

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Abstract

Background: While Group A Streptococcal sepsis is a well-described cause of peripartum morbidity and mortality, it is significantly less common among non-pregnant patients.

Case presentation: We report a rare presentation of Group A Streptococcal sepsis in a 45-year-old non-pregnant female. The patient presented in multi-system organ failure three days after an assault. Clinical course was complicated by cardiac arrest with PEA on admission and ROSC after one round of CPR, severe hypotension requiring multiple pressors, metabolic encephalopathy, renal failure requiring continuous renal replacement therapy, and acute left upper extremity ischemia with unsuccessful thrombectomy. Endometrial biopsy showed purulent material and gram-positive cocci consistent with *streptococcus pyogenes*. A total abdominal hysterectomy was performed for source control.

Outcomes: Postoperatively, the patient developed a gastrointestinal bleed and Heparin was stopped to control bleeding. She subsequently developed multiple arterial emboli with worsening necrosis of all extremities. Her family made the decision to transition to comfort care and the patient passed away shortly after.

Recommendations: In instances of multisystem organ failure of unknown cause, clinicians should consider gynecologic origin for both source and complications of infection. Obtaining early tissue samples for diagnosis can be a critical component in achieving appropriate source control.

Keywords: Organ failure; Group A Streptococcal sepsis; Non-pregnant Female; Uterine infection

Introduction

Streptococcus pyogenes, Group A Streptococcus (GAS), is a significant cause of uterine infection, with incidence of invasive GAS-related deaths increasing in recent years to approximately 75,000 cases annually worldwide [1]. Clinical diagnosis is often missed or delayed until the patient manifests signs of systemic shock and organ failure as the source is not usually immediately apparent [2]. Among women, GAS is seen most commonly in the peripartum period, resulting in significant maternal morbidity and mortality [3]. A study by Mason et al. [3] found that postpartum patients are 25 times more likely to have invasive GAS infections than nonpregnant patients. However, non-pregnancy related invasive GAS uterine infection can have just as devastating of consequences, though it has been less well described in the literature.

The most common entry points for *streptococci* include the vagina, pharynx, mucosa, and skin [4]. For invasive GAS uterine infection, the most common associations outside of pregnancy and childbirth include invasive gynecologic procedures and intrauterine devices. Patients are equally likely to present with gastrointestinal symptoms as they are to have genitourinary symptoms, often masking the diagnosis for some time [5]. Additionally, primary genital colonization with

streptococcus pyogenes is rare, making it more likely that patients with this infection have a different primary source of infection.

In addition to uterine infections, other sources of invasive *strep pyogenes* have been described in prior case reports. Manalo et al. [3] describe a case of a 26-year-old female with GAS peritonitis and tubo-ovarian abscess. Of note, their patient had engaged in oral sex with a partner who had recently had a GAS upper respiratory infection [1]. Paulson et al. [5] cite a case of toxic shock syndrome secondary to necrotizing pelvic inflammatory disease in a postmenopausal woman. Despite the potential devastating consequences of GAS sepsis among nonpregnant patients, understanding of its diagnosis and management is still underrepresented in the literature. Diagnosis and management of one manifestation of this infection is described in the following case to bring awareness to a potential cause for patients presenting with severe systemic illness.

Case Presentation

A 45-year-old female presented to the Emergency Department with lethargy after an assault three days prior. At the time of assault, the patient was evaluated and had a negative CT head. She was treated with doxycycline for a possible infected posterior scalp wound. The patient presented again three days later reporting body aches and decreased urine output. She had no known medical problems prior and reported lack of regular medical care. Upon arrival *via* EMS, patient was on a non-rebreather as she was hypoxic and tachycardic. Blood pressure could not be obtained until the patient received one liter of fluids. CT head, cervical spine, chest, abdomen, and pelvis were performed. These were significant for heterogeneous enhancement of the left kidney, uterine enlargement with internal multilobulated mass-like hypoattenuation centrally, and bilateral adnexal complex cystic masses. Patient's labs returned significant for a high anion gap metabolic acidosis and acute kidney injury. She was admitted to the Intensive Care Unit for further workup and management of metabolic

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encephalopathy.

Over the next several hours, the patient's clinical condition deteriorated rapidly. She was intubated, started on continuous renal replacement therapy, and placed on broad spectrum antibiotics. Her blood cultures grew gram positive cocci in pairs and the gynecology team was consulted for evaluation of a possible infectious source. The initial pelvic exam revealed no obvious pathology or foreign objects. Testing for gonorrhea, chlamydia, vaginal pathogen panel, HSV, HIV, syphilis, and an endometrial biopsy were obtained. A transvaginal ultrasound was performed and showed a tubo-ovarian complex without bowel wall thickening or fat stranding. The vaginal culture returned with *streptococcus pyogenes* and, on hospital day six, the endometrial biopsy returned with evidence of pus with limited endometrial glands and autolysis. The gram stain from the endometrial biopsy was significant for gram positive cocci. At this point, the decision was made to proceed with surgical management for attempted source control as the patient was not improving despite aggressive medical management.

The patient underwent an exam under anesthesia, total abdominal hysterectomy, bilateral salpingo-oophorectomy, and cystoscopy. Postoperatively, she developed a gastrointestinal bleed and heparin was stopped to control bleeding. She subsequently developed multiple arterial emboli with worsening necrosis of her arms and legs. Her family made the decision to transition to comfort care and the patient passed away shortly after.

Outcomes and Implications

Group A streptococcal toxic shock syndrome has rarely been associated with uterine infection after uterine procedures or instrumentation but is more often seen in cases in the peripartum period. Invasive GAS can be associated with toxic shock syndrome resulting in multi-organ failure soon after symptom onset. In the presented patient, it remained unclear whether the source of her infection was related to a primary genital tract infection or was secondary to a laceration after her recent assault.

Because the exact mechanism of streptococcal toxic shock syndrome is not entirely understood, diagnosis and treatment often require multidisciplinary care and aggressive surgical management. Complications associated with this diagnosis have led to an overall mortality rate of 33% despite antibiotics and supportive therapy [6-8]. Increasing awareness of GAS sepsis in the nonpregnant population may improve clinicians' ability to promptly diagnose and treat the condition.

While rare, there are some factors found among women who develop GAS. In one study, women with low estrogen levels, such as those who were post-menopausal or those who were lactating, accounted for 2/3 of GAS-positive cases [9]. It is thought that low estrogen leads to thinning of the vaginal wall and increased pH, making it easier for bacteria to multiply. Additionally, risk factors such as number of people in the home, diabetes, cardiac disease, cancer, and steroid use have been found to increase risk among people older than age 45 [10]. Despite this, between 1/5 and 1/3 of cases still occur in individuals with no predisposition to severe infection [11].

Severe infection with *streptococcus pyogenes* may continue to be on the rise as the bacteria has been showing a newly re-established virulence in the last several decades. The bacteria produce exotoxins that lead to massive cytokine release and septic shock [12]. Because of this, it is possible that this organism will continue to cause systemic infection

through a variety of transmission methods. Transmission can occur from oral to genital route or, in the case of our patient, may have transmitted from skin infection to hand and then genitalia.

While the source of GAS sepsis and toxic shock syndrome can often be difficult to determine, cases such as this show that vaginal cultures and consideration of endometrial biopsy should be performed as part of the initial workup. One barrier, however, to this method of diagnosis is that culture results and endometrial biopsy samples can take several days to be analyzed, time which a patient may not have if their clinical course is deteriorating rapidly. Therefore, a combination of blood and urine cultures, endometrial aspiration for gram stain and culture, and imaging, such as ultrasound, MRI, or CT scan, should be performed. Unremarkable imaging, however, does not rule out the genital tract as a source of infection [13].

In instances of multisystem organ failure of unknown cause, clinicians should consider gynecologic origin for both a source of infection and a cause of complications. Obtaining early tissue sampling for diagnosis can be a critical component in achieving appropriate source control.

Recommendations

The intensity and severity of illness after infection with GAS necessitates aggressive workup for sources of infection and rapid administration of antibiotics for source control. Surgical management, including debridement or removal of affected organs, such as the uterus, may also be crucial in preventing severe morbidity and mortality. Overall, a high index of suspicion and evaluation of all possible sources of infection are crucial for timely diagnosis and treatment of this potentially fatal condition.

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