

Group A Streptococcal Puerperal Sepsis with Retroperitoneal Involvement Developing in a Late Postpartum Woman: Case Report

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Group A beta-hemolytic streptococci cause a wide range of infectious diseases such as pharyngitis, impetigo, rheumatic fever, and even septic shock. Group A streptococcal puerperal sepsis is uncommon today, but recent reports indicate a reemergence of virulent strains can cause toxic-mediated shock and multiple organ failure. We present a case report of a 29-year-old postpartum woman after cesarean section who presented group A streptococcal puerperal sepsis. Furthermore, we discuss the GAS strain in this patient and its relation with close contact among family members. The group A streptococci (GAS) were isolated from the patient's retroperitoneal fluid and from her husband's throat swab, respectively. Both isolates were shown to be identical: M type 1. It is well known that exotoxin A produced by M1 or M3 serotypes of the organisms plays a crucial role in streptococcal toxic shock syndrome (STSS). We conclude that in this patient, close contacts of persons with GAS appear to be at risk for colonization with identical strains of STSS-causing GAS such as M1 or M3 serotypes. Therefore, the appropriate antibiotic including antibiotic prophylaxis for close contact should be considered.

GROUP A STREPTOCOCCAL PUERPERAL SEPSIS, once a frequent and feared complication of delivery, is now an uncommon peripartum infection.¹ Group A streptococcal puerperal infections have several presentations, ranging from asymptomatic to septic shock and multisystem organ failure. As such, infections with virulent strains of group A streptococci (GAS) can take an unpredictable course in which fever or mild somatic complaints might be the only warning signs before progression to life-threatening shock. Although the incidence of this disease has decreased these 30 years, there have been several reports of group A streptococcal puerperal sepsis during the past decade. Barnham et al. reported 6 cases of postpartum infection developed from 16 hours to 8 days postdelivery, which were detected over 20 years in North Yorkshire, U.K.² We describe a rare case of group A streptococcal puerperal sepsis presenting as a retroperitoneal infection in a post-cesarean section patient, which occurred in the late postpartum period.

Case Report

A 29-year-old woman, gravida two, para two, gave a birth to a healthy, full-term infant by cesarean section for arrest of descent (face presentation). Her prenatal course was uncomplicated including a negative vaginal-rectal culture for group B *Streptococcus*. She was discharged from the hospital on postpartum day 3 after an uneventful postoperative recovery.

Five weeks after the delivery, the patient presented to the emergency department with a 24-hour history of constitutional symptoms including fever (to 38°C), chills, and headache. As her husband and her 4-year-old daughter had positive throat cultures for group A beta-hemolytic streptococci (GAS) and were treated for GAS pharyngitis earlier that week, a throat culture was obtained from the patient. She was diagnosed with a viral upper respiratory tract infection, based on her negative throat culture. Her symptoms continued and she soon after developed abdominal pain and bilateral flank pain. Two days later, the patient visited the emergency department again, complaining of persistent fever, chills, and worsening abdominal and bilateral flank pain. At the time of presentation, she appeared nontoxic. She had a temperature of 37°C, blood pressure of 92/48 mm Hg, pulse was 124 beats per minute, and respiratory rate was 20 per minute. The abdominal examination showed generalized tenderness on palpation, most prominent in the midline, without guarding or rebound tenderness. In addition, the exam demonstrated costovertebral tenderness bilaterally, right greater than left. Her previous cesarean section incision did not demonstrate any erythema or

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discharge. The pelvic examination showed yellow to greenish discharge at the cervical os, which was thought to be lochia. The bimanual examination elicited cervical motion tenderness. The laboratory analysis was significant for a white blood cell count of $10,500/\text{mm}^3$ with 88 per cent neutrophils, hematocrit (HCT) of 34.2 per cent, and creatinine of 1.2 mg/dL. The urinalysis showed +3 bacteria, too numerous to count (TNTC) WBC, and TNTC granular cast. The patient was admitted to the hospital and started on intravenous Levofloxacin. Computed tomography (CT) of the abdomen and pelvis showed a fluid collection and inflammatory changes involving the right paracolic gutter and peri-aortic regions (Fig. 1).

In the light of her clinical presentation and radiographic findings, the patient was taken to the operation room for diagnostic laparoscopy with a presumed diagnosis of intra-abdominal sepsis secondary to perforated appendix or tubo-ovarian abscess. At laparoscopy, purulent peritoneal fluid was aspirated and sent to the laboratory for Gram stain and culture. As laparoscopic evaluation revealed no intra-abdominal source, the operation was converted to a midline celiotomy for complete exploration. Exploration revealed an inflammatory process involving the retroperitoneum extended cephalad from the iliac bifurcation to the superior mesenteric artery (SMA) takeoff from the aorta. This process was characterized by fibrinous exudates with a small amount of purulent material at the SMA. Gram stain and cultures were obtained from this material as well. No obvious source of perforation or infection was present during the exploration. The low transverse cesarean section incision was well healed. The right ovary was edematous without evidence of abscess or infection. Gram stain of the retroperitoneal fluid revealed rare gram-positive cocci. Postoperatively, empiric antibiotic therapy was begun with imipenem/cilastin and metronidazole in the intensive care unit (ICU). On postoperative day 2, the culture of the retroperitoneal fluid yielded sparse GAS. Based on these findings, the antibiotic regimen was changed; metronidazole was discontinued and clindamycin was started. The patient re-

mained febrile with temperatures postoperatively while on this antibiotic regimen. Evaluation including chest X-ray, urinalysis, urine culture, blood culture, and lower extremity ultrasound were obtained to evaluate the fever, which revealed no abnormal findings. The incision site showed no signs of infection. On postoperative day 6, the patient was transferred to the floor. With the patient still febrile, drug fever was suspected. Therefore, on postoperative day 10, all of intravenous antibiotics were discontinued. The patient became afebrile the following day. The patient made a slow, steady recovery and was discharged from the hospital after a 2-week admission.

Discussion

Group A beta-hemolytic streptococci commonly cause pharyngitis and cutaneous infections such as impetigo and erysipelas. GAS may also cause necrotizing fasciitis, septicemia, or complications of rheumatic fever such as glomerulonephritis and erythema nodosum. It has been reported that a reemergence worldwide of more virulent strains of GAS can cause septic shock and disseminated intravascular coagulation (DIC).³⁻⁵ GAS puerperal sepsis occurs when *Streptococcus pyrogenes* colonizing the genital tract or acquired nasocormally invades the endometrium, adjacent structures, lymphatics, and bloodstream. Cesarean section has been noted as a risk factor for serious puerperal infection.⁶ At the time of cesarean delivery, an incision is made in the myometrium, thus allowing bacteria to adhere to the cut surface of the myometrium as well as to enter the lymphatics and veins. Suture placed in the uterine muscle may also act as a nidus for infection. In addition, the creation of dead space permits collection of blood and serum, which serve as an ideal environment for the bacterial growth.⁷ High fever in the early postpartum is a classic manifestation; however, it has been reported that fever can occur as late as 7 days postpartum.⁸ A lack of pelvic symptoms is common. Later, flu-like symptoms with vague somatic complaints can progress rapidly to septic shock. Invasive infection can be complicated by pelvic cellulitis, septic ovarian vein thrombosis, peritonitis, or pelvic abscess.⁹

Puerperal sepsis caused by GAS has been reported in different locations.^{2, 8-15} Several reports have demonstrated that group A streptococcal puerperal sepsis might be associated with cesarean section, and all of cases occurred in the early postpartum period (from 6 hours to 8 days after the delivery).^{2, 13-14} However, one report described peritonitis and multiple organ failure secondary to group A streptococcal sepsis at 2-month postpartum after normal delivery.¹² Specific serotypes of GAS are strongly associated with obstetric infections. Barnham et al. reported six cases of group A streptococcal puerperal sepsis, in four of which serotyping was done.² Serotyping of isolates from four cases showed T1M1 (in one), T2R28

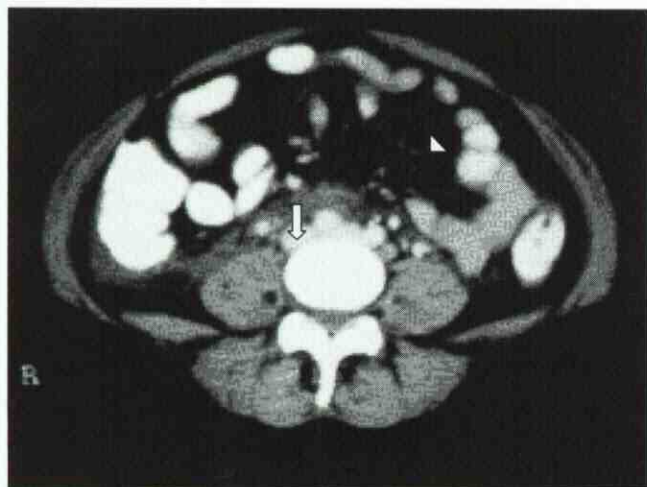


FIG. 1. Computed tomography shows a fluid collection (arrow) and inflammatory changes (arrowhead) involving the right paracolic gutter and peri-aortic regions.

(two), and T25M75 (one). Serotype T28R28 has been proven to have a special affinity for mucosal cells in the female genital tract in another study.¹⁶ Therefore, these findings strongly suggest that serotype T28R28 can contribute to group A streptococcal puerperal sepsis. Streptococcal toxic shock syndrome (STSS) due to GAS is attributed to exotoxin A produced by M1 or M3 serotypes of the organism.¹⁷ The exotoxin produces rapid skin and soft tissue necrosis, fever, septic shock, and multiple organ failure. The mortality rate of STSS is still more than 50 per cent, and STSS can occur sporadically or via close contacts of infected patients.¹⁸ STSS in the setting of a family outbreak was reported in Japan in 1997.¹⁹ This study demonstrated that patients with STSS were associated with transmission of GAS among family members, confirmed by serologic M and T typing (M1T1, M3T3, M12T12). Furthermore, the study showed pharyngitis as the primary manifestation in the majority of family members.

The GAS isolates from our patient and her husband were tested for M precipitation type (M type) by DNA macrorestriction endonuclease analysis using pulsed-field gel electrophoresis (PFGE). The patient's isolation site was retroperitoneal fluid and her husband's site was throat swab. Both isolates were identical; M type 1. This finding strongly suggested that group A streptococcal puerperal sepsis in the patient was transmitted by GAS among one of the family members.

In summary, we describe a unique case of group A streptococcal puerperal sepsis with retroperitoneal involvement in a post-cesarean section patient. It is noted that in our case, the onset of group A streptococcal puerperal sepsis was late postpartum period; 5 weeks after the delivery. Group A streptococcal puerperal sepsis is uncommon today, but recent reports indicate a reemergence of virulent strains can cause rapid tissue invasion, toxin-mediated shock, and multiple organ failure. There are two possibilities for the entry of GAS in postpartum patients; one pathway is via the genital tract despite a lack of local symptoms. The other pathway is the hematogenous route, possibly from pharyngeal or cutaneous primary sites.

In our case, the spread of virulent strain of GAS among family members was demonstrated by using PFGE genotyping. Close contacts of persons with GAS appear to be at risk for colonization with identical strains of STSS-causing GAS such as M1 or M3 serotypes. Therefore, antibiotic prophylaxis for close contact should be considered, especially if there are intimate contacts between a patient with STSS and his or her family members, health care workers, and others. Although invasive infection with GAS can have a high mortality, aggressive treatment with immediate surgical intervention and the appropriate antibiotic is effective, and the outcome may be favorable.

REFERENCES

1. Charles D, Larsen B. Streptococcal puerperal sepsis and obstetric: a historical perspective. *Rev Infect Dis* 1986;8:411-22.
2. Barnham M, Weightman N. Bacteraemic *Streptococcus pyogenes* infection in the peri-partum period: now a rare disease and prior carriage by the patient may be important. *J Infect* 2001;43:173-6.
3. Swingle GR, Bigg MA, Hewitt BG, et al. Disseminated intravascular coagulation associated with group A streptococcal infection in pregnancy. *Lancet* 1988;i:1456-67.
4. Stevens DL. Streptococcal toxic-shock syndrome: spectrum of disease, pathogenesis, and new concepts in treatment. *Emerg Infect Dis* 1995;1:69-78.
5. Perez-Trallero E, Marimon JM, Montes M, et al. Clonal differences among erythromycin-resistant *Streptococcus pyogenes* in Spain. *Emerg Infect Dis* 1999;5:235-40.
6. Nathan L, Peters MT, Ahmed AM, et al. The return of life-threatening puerperal sepsis caused by group A streptococci. *Am J Obstet Gynecol* 1993;169:571-2.
7. Sebastian F. Infectious disease relations to cesarean section. *Obstet Gynecol Clin North Am* 1988;15:685-95.
8. Silver RM, Heddleston LN, McGregor JA, et al. Life-threatening puerperal infection due to group A streptococci. *Obstet Gynecol* 1992;79:894-6.
9. Gourlay M, Gutierrez C, Chong A, et al. Group A streptococcal sepsis and ovarian vein thrombosis after an uncomplicated vaginal delivery. *J Am Board Fam Prat* 2001;14:375-80.
10. Anteby EY, Yagel S, Hanoch J, et al. Puerperal and intra-partum group A streptococcal infection. *Infect Dis Obstet Gynecol* 1999;7:276-82.
11. Helmig RB. Life-threatening puerperal sepsis caused by group A streptococci. *Ugeskr Laeger* 2000;162:2891-2.
12. Vuilleumier H. Streptococcal toxic shock syndrome revealed by a peritonitis. Case report and review of the literature. *Swiss Surg* 2001;7:25-7.
13. Schummer W, Schummer C. Two cases of delayed diagnosis of postpartal streptococcal toxic shock syndrome. *Infect Dis Obstet Gynecol* 2002;10:217-22.
14. Kankuri E, Kurki T, Carlson P, et al. Incidence, treatment and outcome of peripartum sepsis. *Acta Obstet Gynecol Scand* 2003;82:730-5.
15. Tanguy M, Malledant Y, N'Guyen Q, Tropres H, Pangui E, Grall JY. Fetal maternal streptococcus A infection after cesarean section. *Ann Fr Anesth Reanim* 1990;9:447-9.
16. Stalhammar-Carlalmalm M, Areschoug T, Larsson C, et al. The R28 protein of streptococcal pyogenes is related to several group B streptococcal surface proteins, confers protective immunity and promotes binding to human epithelial cells. *Mol Microbiol* 1999;33:208-19.
17. Miyoshi-Akiyama T, Zhao J, Kikuchi K, et al. Quantitative and qualitative comparison of virulence traits, including murine lethality, among different M types of group A streptococci. *J Infect Dis* 2003;15:1876-87.
18. Group A Streptococcal (GAS) Disease—General Information. Atlanta: Centers for Disease Control and Prevention, 2001.
19. Ichijima S, Nakashima K, Shimokata K, et al. Transmission of streptococcus pyogenes causing toxic-shock-like syndrome among family members and confirmation by DNA macrorestriction analysis. *J Infect Dis* 1997;175:723-6.