Group A streptococcal cellulitis in the early puerperium

Celulitis izazvan streptokokom grupe A u ranom puerperijumu

Branka Nikolić*, Ana Mitrović*, Svetlana Dragojević-Dikić*, Snežana Rakić*, Zlatica Cakić*, Milena Saranović†, Milan Sikimić†

*University of Belgrade, †School of Medicine, Obstetrics and Gynecology Clinic

Volkonin 68, Broj 7 VOJNOSANITETSKI PREGLED Strana 607

Abstract

Introduction. Infectious diseases caused by *Streptococcus pyogenes*, a member of the group A Streptococci (GAS) are among the most common life threatening ones. Patients with GAS infections have a poor survival rate. Cellulitis is a severe invasive GAS infection and the most common clinical presentation of the disease associated with more deaths than it can be seen in other GAS infections. According to the literature data, most cases of GAS toxic shock syndrome are developed in the puerperium. However, there are two main problems with GAS infection in early puerperium and this case report is aimed at reminding on them. The first problem is an absence of awareness that it can be postpartal invasive GAS infection before the microbiology laboratory confirms it, and the second one is that we have little knowledge about GAS infection, in general.

Case report. A 32-year-old healthy woman, gravida 1, para 1, was hospitalized three days after vaginal delivery with a 38-hour history of fever, pain in the left leg (under the knee), and head injury after short period of conscious lost. Clinical picture of GAS infection was cellulitis. Group A *Streptococcus pyogenes* was isolated in vaginal culture. Rapid antibiotic and supportive treatment stopped development of streptococcal toxic shock syndrome (STSS) and potential multiorgan failure. Signs and symptoms of the infection lasted 25 days, and complete recovery of the patient almost 50 days. Conclusion. In all women in childbirth with a history of fever early after delivery, vaginal and cervical culture specimens should be taken as soon as possible. Early recognition of GAS infection in early puerperium and prompt initiation of antimicrobial drug and supportive therapy can prevent development of STSS and lethal outcome.

Key words: streptococcus pyogenes; puerperal infection; cellulitis; shock, septic; diagnosis; drug therapy; treatment outcome.

Apstrakt

Uvod. Infekcije koje izaziva *Streptococcus pyogenes*, predstavnik grupe A streptokoka (GAS), spadaju među one koje mogu da ugroze život. Bolesnici sa razvijenom infekcijom izazvanom GAS imaju nisku stopu preživljavanja. Celulitis je ozbiljna, invazivna GAS infekcija. To je najčešća klinička prezentacija GAS infekcije sa češćim smrtnim ishodom u odnosu na ostale GAS infekcije. Prema podacima iz literature, najveći broj slučajeva toksičnog sindroma u sklopu GAS infekcije razvije se u puerperijumu. Postoje dva problema vezana za GAS infekciju u ovom periodu, pa je i cilj ovog prikaza bio da se na njih, još jednom, podsetimo. Prvi problem vezan je za lekare koji najčešće nisu svesni da se radi o invazivnoj GAS infekciji, pre nego što im mikrobiološka laboratorija to ne potvrdi, dok se drugi odnosi na, generalno, slabije znanje o GAS infekciji.

Prikaz bolesnika. Bolesnica, stara 32 godine, prvorotka, bola febrilna nakon parturitiona, zbog febrilnosti koja se održavala 38 sati, bola u levoj potkolenici i povrede na glavi koju je zadobila u toku kratkotrajnog gubitka svesti. Klinička slika GAS infekcije bio je celulitis. *Streptococcus pyogenes* grupe A izolovan je u kulturi vaginalnog brisa. Brzo uključivanje antibiotika i suportivne terapije spriječilo je razvoj streptokokog toksičnog sindroma (STSS), kao i potencijalnu multiorgansku disfunkciju. Znaci i simptomi infekcije bili su prisutni 25 dana, dok je potpuni oporavak bolesnice trajao gotovo 50 dana. Zaključak. Kod svih porodilja koje su febrilne nakon porodljava, trebalo bi što je pre moguće uraditi kulturu iz vaginalnog i cervikalnog brisa. Rano prepoznavanje GAS infekcije i brzo započinjanje antimikrobne i suportivne terapije može da spreči razvoj STSS i, poslije, smrtni ishod.

Ključne reči: streptococcus pyogenes; infekcija, puerperijum; celulitis, šok, septic; dijagnoza, lečenje lekovima; lečenje, ishod.

Introduction

Group A *Streptococci* (GAS) cause infections of public health meaning. Clinical picture varies from local infections such as pharyngitis or vaginitis to severe invasive GAS cellulitis, meningitis, myositis and, even, multiorgan failure as streptococcal toxic shock syndrome (STSS) or necrotizing fasciitis (NF). Infectious diseases caused...
by the group A Streptococcus pyogenes, known as “flesh eating bacteria”, are among the most common life threatening ones. The presence of bacterial egzotoxyns in blood can cause generalized intoxication and shock syndrome with cytotoxic effect and fatal outcome within 48–96 hours. Bacteriemia occurs in only 0.3% of febrile patients \(^1, 2, 4\).

Besides fever, hypothermia, hypotension, tachycardia, hypopalbuminemia, oliguria can be observed and have to be carefully monitored \(^1, 3, 4\).

Literature data suggest that letal outcome is possible within 30 days from the confirmation of Streptococcus pyogenes presence in any culture specimen. Good prognosis of GAS infection depends of early recognition and intensive antimicrobial and supportive treatment which must last until signs of the infection are completely retired. Extremities, trunk and pelvis are most often GAS infected. Cellulitis, an invasive GAS infection, is the most common clinical presentation of the disease. Compromising subcutaneous tissue, fascia and adipose tissue it is associated with serious sequels and more deaths (30%) than other GAS infections \(^1-3, 9-11\). Thirty-day survival after a positive culture specimen has been confirmed is significantly reduced among patients in whom the developed STSS and 26% of these patients die with a day of specimen collection \(^1, 2, 8\).

Severe pain may be the only early symptom of streptococcal myositis and cellulitis. According to the literature most STSS develop in puerperium within 42 days \(^1, 2, 6\).

There are two problems with GAS infection, and this case report is aimed at reminding on them. The first problem is the absence of awareness that it can be postpartum invasive GAS infection before the microbiology laboratory confirms it. The second one is that we have little knowledge about GAS disease, in general \(^4, 9\).

**Case report**

A 32-year old woman, gravida 1, para 1, hospitalised on the day 3 after delivery with a 38-hour history of fevers (38–40.3ºC), and pain in the left leg under the knee. There were no edema, redness or visible skin abrasions or minor local trauma on the left leg. Also, the patient had a head injury in occipital region that she did not mentioned because she hardly remembered what had happened during a period of mental changes when she had felt down. Head injury was discovered during the external examination (3 sutures placed). Her pregnancy and labour were uneventful prior to these symptoms.

On the hospital day 1 her blood pressure and pulse were 100/65 mmHg and 130 beats/minute, respectively. Laboratory values included white blood cell count of 20.3 × 10⁹/L, hematocrit of 33%, platelet count of 215 × 10⁹/L, and C reactive protein (CRP) of 459 mg/L (referent value 0–5 mg/L). Hypoalbuminemia was also associated with the mentioned laboratory values. Blood, vaginal and cervical culture, urinalysis, and urine culture were performed before the antibiotic treatment. This is a part of standard procedure in patients in puerperium with more than 24 hours of faver history.

Antibiotic (ceftriaxon 2 × 2 g intravenously), albumin, and electrolyte solutions containing salts were administrated. During the first 6 days 6 liters of electrolyte solutions were given. There were no changes in systolic blood pressure. Renal function was not compromised.

On the hospital day 2, body temperature of the patient was 38–39.2ºC. The patient had more intensive pain along the whole left leg followed with edema and redness. Because of intensive pain in the left leg with limited mobility the patient was examined by vascular surgeon. Thrombophlebitis and deep venous thrombosis were excluded. Unilateral cellulitis cruris was confirmed. The skin was without abrasions. There were no clinical or laboratory data for STSS (not for organ damage, including renal failure, adult respiratory distress syndrome, disseminated intravascular coagulation and serious mental changes). Blood pressure was 110/65 mmHg, white blood cell count had decreasing rate (14.0 × 10⁹/L), while CRP was increased (463.7 mg/L).

On the hospital days 3–4, two blood cultures were negative for GAS. Also, skin, throat, cervical and urine cultures were negative for GAS. Vaginal culture was positive for the group A Streptococcus pyogenes, sensitive to ceftriaxone and clindamycin.

As above mentioned, ceftriaxon was administrated (2 × 2 g, intravenously) on the hospital day 1, then continued in a dose of 2 g, daily. Clindamycin (3 × 300 mg, intravenously) was added to the therapy on the hospital day 3. Blood pressure was 115/70 mmHg, white blood cell count and CRP had decreasing rate (12.4 × 10⁹/L, and 382.9 mg/L, respectively). Throat and chest exams were done and no pathological changes were confirmed. Repeated exam of the skin culture remained negative.

After 6 days of the antibiotic treatment redness, edema and pain were localized under the knee with a limited mobility of the left leg. These changes had slow regression during next 20 hospital days. White blood cell count showed decreasing rate to 7.7 × 10⁹/L, as well as CRP which started to decrease significantly after the hospital day 11 (109.3 mg/L). Repeated exams of vaginal and cervical cultures remained negative.

On the hospital day 9 localised painful redness under the left knee stayed unchanged (Figure 1). Blood pressure increased to 165/95 mmHg. Antihipertensive therapy was administrated during the next two weeks and blood pressure was normalised. The patient had problem with high pressure during the last trimester of pregnancy. Hypotension during the first days of hospitalization was one of the early symptoms for invasive streptococcal infection. Body temperature remained at 37.4–37.8ºC in spite of antibiotic treatment given according to the antibiogram.

From the hospital day 10 meropenem (3 × 0.5 g, intravenously) and vancomycin (2 × 1 g, intravenously) were administrated instead of ceftriaxone and clindamycin. Also, vancomycin was administrated orally (125 mg, daily) to prevent pseudomembranous enterocolitis. Two days after, her body temperature was 37.2ºC. The patient was subfebrile until the 25th day of hospitalization when the patient became afebrile.

---

Nikolić B, et al. Vojnosanit Pregl 2011; 68(7): 607–610.
Pain and redness withdrawed on the hospital day 26. Edema lasted 10 days more (Figure 2). Walking was normalized after edema withdrawal (Figure 3) and under the professional controlled exercises which lasted two weeks. From the beginning of the disease to the complete recovery of the patient, the treatment lasted almost 50 days.

**Discussion**

The most common initial symptoms of streptococcal infection are pain and fever, followed with nausea, vomiting and diarrhea. Severe pain may be the only early symptom for streptococcal myositis and cellulitis. Bacteriemia occurs in only 0.3% of febrile patients. GAS bacteremia is rare event among persons 14–40 years old, but puerperal sepsis account for most bacteremia in this age group. Infection usually involves one extremity. Twenty percent of patients have an influenza-like syndrome. Confusion is present in 55% of patients, and some of them can in to a coma. Necrotizing fasciitis or myositis is present in 70% of patients, and a diffuse scarlatine-like erythema in 10% of patients.

The nature of *Streptococcus pyogenes* infection can be dramatic and severe. The most common early clinical signs of soft tissue infection in puerperium are fever, strong pain or/and localized erythema. Also hypotension, hypotermia, hypoalbuminemia, hypocalcemia, mild leucocytosis, increased serum creatinin, need serious diagnostic and treatment approach. Specimens have to be collected from the vagina (in puerperium), nose, throat, and skin. Urinalysis, urinoculture, and hemoculture, also have to be done. Streptococcal infections and sequels treatment and recovery can last more than 4 weeks.

The presented patient had the history of 38-hour fever, pain, hypotension, hypoalbuminemia and conscious lost with head injury in a short period before the hospitalization. Also, there was no visible tissue trauma before cellulitis developed. The full recovery of the patient lasted 50 days.

Puerperal GAS infection can appear as cellulitis within 42 days after delivery. According to the reported results in literature, cellulitis, the most common GAS infection, has been associated with more deaths (30% patients) compared with other forms of the disease. Survival during 30 days after positive culture confirmation has been significantly reduced among patients in whom STSS developed, and approximately 28% of these patients have died within a day of culture specimen collection.

Numerous GAS infection cases develop within 24 to 72 hours after minor nonpenetrating trauma proraging to severe septic shock syndrome with hypothermia, hypotension, multiorgan failure, disseminated intravascular coagulation and death. Rapid antibiotic and supportive treatment has a great impact on GAS infection outcome. A number of studies show that penicillins and cephalosporins have proven efficacy in treating of GAS infections. According to investigations showing penicillins failure in the presence of numerous streptoccoci and that serious GAS infections treated with penicillins respond less well to them and are associated with high mortality and morbidity rates, cephalosporins and clindamycin have become antibiotics of choice. Cephalosporins have proven efficacy in cellulitis treatment caused by *Streptococcus pyogenes*. Our results in preveting STSS development in this case confirm it. Beta-lactam antibiotics continue to be very effective for GAS infections because of a prolonged effect after treatment and very rare resistancy.
However, prolonged treatment of sequels may need the use of other antimicrobial drugs as we done in this case administering meropenem and vancomycin.

Conclusion

In all women in childbed with a history of fever early after delivery, vaginal and cervical culture specimens should be taken as soon as possible. Early recognition of group A *Streptococcus pyogenes* infection or GAS invasive disease according to microbiology confirmation and prompt initiation of antibiotic and supportive therapy are very important in prevention of developing STSS and fatal outcome in these patients.

Acknowledgement

We thank the personnel of the Microbiology Laboratory, Obstetrics and Gynecology Clinic “Narodni front”, Belgrade, for their professional assistance in performing microbiologic analyses.

REFERENCES

1. Lamagni TL, Neal S, Keshishian C, Alhaddad N, George R, Duckworth G, et al. *Streptococcus pyogenes* infections, United Kingdom, 2003-2004. Emerg Infect Dis 2008; 4(2): 202–9.
2. *Streptococcal toxic-shock syndrome: spectrum of disease, pathogenesis, and new concepts in treatment*. Emerg Infect Dis 1995; 1(3): 69–78.
3. Lamagni TL, Darenberg J, Luis-Harari B, Siljander T, Efstratiou A, Henriques-Normark B, et al. Epidemiology of severe *Streptococcus pyogenes* disease in Europe. J Clin Microbiol 2008; 46(7): 2359–67.
4. Rainbow J, Jewell B, Danila RN, Becrud D, Beall B, Van Beneden C, et al. Invasive group a streptococcal disease in nursing homes, Minnesota, 1995-2006. Emerg Infect Dis 2008; 14(5): 772–7.
5. O’Loughlin RE, Robinson A, Cieslak PR, Lynfield R, Gerber MA, Craig A, et al. The epidemiology of invasive group A streptococcal infection and potential vaccine implications: United States, 2000-2004. Clin Infect Dis 2007; 45(7): 853–62.
6. Neal S, Beall B, Ekholm K, Henriques-Normark B, Jair A, Johnson D, et al. International quality assurance study for characterization of *Streptococcus pyogenes*. J Clin Microbiol 2007; 45(4): 1175–9.
7. Lamagni TL, Neal S, Keshishian C, Powell D, Potz N, Pebody R, et al. Predictors of death after severe *Streptococcus pyogenes* infection. Emerg Infect Dis 2009; 15(8): 1304–7.
8. *Centers for Disease Control and Prevention*. Active bacterial core surveillance report. Emerging Infections Program Network, Group A Streptococcus, 2004. Atlanta: The Centers; 2005 [cited 2007 Jun 4]. Available from: http://www.cdc.gov/ncidod/dbmd/abcs/survreports/gas04.pdf
9. Lamagni TL, Efstratiou A, Voutin-Varkila J, Jair A, Schalden C. The epidemiology of severe *Streptococcus pyogenes* associated disease in Europe. Euro Surveill 2005; 10(9): 179–84.
10. *World Health Organization*. Programme on streptococcal diseases complex. Report of a consultation; 1998 Feb 16–19; Geneva. EMC/BAC/98.7. Geneva: WHO; 1998.
11. Schalden C. European surveillance of severe group A streptococcal disease. Euro Surveill 2002; [cited 2007 Jun 4]. Available from: http://www.eurosurveillance.org/ew/2002/020829.asp

Received on April 22, 2010.
Revised on July 8, 2010.
Accepted on July 20, 2010.