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SEPSIS AND POSTPARTUM HEMORRHAGE

B. Das and S. Clark

INTRODUCTION

Sepsis and postpartum hemorrhage are linked by common predisposing factors, especially considering that secondary postpartum hemorrhage can follow infection of retained placenta or endometrium. Depending on the extent and severity of the condition, postpartum uterine infection is designated as postpartum endometritis, endomyometritis or parametritis. Postpartum endometritis may be divided into early-onset disease, occurring within the first 48 h, and late-onset disease, presenting up to 6 weeks postpartum. This chapter reviews the causes, pathogenesis and management of uterine sepsis.

CLINICAL RISK FACTORS

The most critical factor is the route of delivery. After vaginal delivery, the incidence of postpartum endometritis varies between 0.9 and 3.9%, but can increase to 12–51% after Cesarean section. Factors such as duration of labor, bacterial vaginosis and vaginal interventions are secondary predictors of post-Cesarean endometritis. Early rupture of the membranes, mid-forceps delivery, poor maternal health and soft tissue trauma act as 'relative risk factors' for uterine sepsis, although they are not present in most patients with such infections[1]. Indigent parturients are at higher risk of developing postpartum endometritis.

ETIOLOGICAL AGENTS

Postpartum uterine sepsis is thought to arise from an ascending infection caused by colonizing vaginal flora. Etiological agents include both aerobic and anaerobic micro-organisms and may consist of peptostreptococci, bacteroides, streptococci, enterococci and *E. coli*. Group A streptococcal endometritis, a rare cause in developed countries, usually occurs in early-onset disease (within the first 48 h of delivery), often with high temperature > 39°C (102.2°F). In contrast, *Chlamydia trachomatis* is involved with late-onset disease (from 2 days up to 6 weeks postpartum) in patients who deliver vaginally.

CLINICAL FEATURES AND INVESTIGATIONS

Postpartum endometritis is diagnosed by significant pyrexia associated with uterine tenderness or abnormal lochia in absence of other obvious sources of infection. Significant pyrexia is defined as oral temperature of 38.5°C (101.3°F) or higher in the first 24 h after delivery or 38°C (100.4°F) or higher, for at least 4 consecutive hours, in the first 24 or more hours after delivery. The first manifestation of fever may occur at night[2,3]. Uterine sepsis associated with late-onset disease and secondary postpartum hemorrhage usually presents as fever on days 10–12 after delivery.

Patients with suspected postpartum endometritis should have early clinical evaluation including bimanual pelvic examination to determine size, consistency and tenderness of the uterus and to detect any adnexal mass (ultrasound study may help, if available). Cesarean section/episiotomy wounds should be assessed for evidence of surgical site infection. Unremitting pain at the operative site may indicate necrotizing fasciitis, wherein urgent debridement is life-saving[3]. A distant site of infection, e.g. urinary or respiratory tract, should be ruled out.

Laboratory investigations (where facilities are available) include full blood count, transcervical cultures (aerobic and anaerobic) and one set of blood cultures, remembering that only 10–20% of patients with postpartum endometritis have bacteremia. The presence of bacteremia does not predict severity of infection or prolonged recovery. Transcervical cultures, although difficult to interpret because of contamination with vaginal flora, are helpful in those patients in whom initial therapy fails. Whenever possible, culture/antigen tests for chlamydia should be performed in patients with late-onset disease or those who are at high risk for acquisition of such infections.

ANTIBIOTIC THERAPY AND FURTHER MANAGEMENT

The aim of the antibiotics should be to provide bactericidal cover for aerobic Gram-positive cocci, Gram-negative bacilli and β-lactamase-producing anaerobes. Those antibiotics which have been used for prophylaxis should be avoided. Empirical treatment should be commenced as soon as possible. Parental treatment with once-daily intravenous gentamicin and intravenous clindamycin is an effective combination, especially in post-Cesarean section patients and those awaiting surgical interventions, including removal of retained placenta. Gentamicin levels need to be monitored. However, other alternatives, including extended-spectrum penicillins or second-generation cephalosporins (cefoxitin), have been used, albeit with greater failure rates than the combination of gentamicin and clindamycin[4]. Alternative antibiotic regimens are shown in Table 1. Intravenous clindamycin and intravenous once-daily gentamicin are the cheapest of the antibiotic regimen options, an important issue in countries with restricted resources.

Parental therapy is continued until the patient is pain-free, afebrile for 24–48 h, the leukocyte count returns to normal, and oral liquids and solids are tolerated. There is no need to continue with oral antibiotics after stopping parental treatment. Patients with positive cultures for chlamydia should receive a 7-day course of azithromycin or doxycycline, even if there is good response to the initial empirical antibiotic regimen. Azithromycin and doxycycline, although good antichlamydial agents, are bacteriostatic drugs and should not be used as first-line antimicrobial agents to treat endometritis.

Failure to respond to the initial antibiotic regimen in 48 h or clinical deterioration requires further clinical evaluation and investigations to rule out another site of infection and complications (see Figure 1). The antibiotic regimen needs to be altered, preferably after reviewing transcervical culture and sensitivity results (see Table 2).

PREVENTION OF UTERINE SEPSIS

Strategies to prevent uterine sepsis include improved obstetric care and the use of prophylactic antibiotics in high-risk patients, as well as

Table 1 Initial antibiotic therapy[1,2,4]

Day 1
1. Clindamycin 900 mg 8-hourly + intravenous gentamicin 5 mg/kg body weight* once daily
or
2. Intravenous piperacillin–tazobactam 4.75 g 6-hourly
or
3. Intravenous metronidazole 500 mg 8-hourly + intravenous gentamicin 5 mg/kg body weight* once daily
or
4. Ampicillin–sulbactam 3.1 g 6-hourly + intravenous gentamicin 5 mg/kg body weight* once daily

*Monitor gentamicin level

Day 1

↓

Specimen collected: transcervical swab for aerobic organism and chlamydia* – blood culture	Empirical antibiotics, e.g. i.v. gentamicin + i.v. clindamycin	Surgical intervention if clinically relevent

*Specimen for *Chlamydia trachomatis* to be obtained on patients with:

(a) late onset of disease or
(b) high risk for acquisition of this infection

Day 3

Patient on empirical antibiotic

↙ ↘

Afebrile

Continue i.v. antibiotics until:

·Patient afebrile × 24–48 h

·Pain-free

·Normal cell count

Febrile

·Clinical evaluation

·Rule out other source of infection

·Urine, wound swab for culture and sensitivity (if facility available)

·Imaging ± surgical intervention

Altered antibiotic regimen (see Table 2) or specific antimicrobial therapy as per culture results, e.g. i.v. benzyl penicillin and i.v. clindamycin for Group A streptococci

Figure 1 Flow chart of treatment regimens for patient with suspected uterine sepsis and postpartum hemorrhage[1,2,4]

coverage of planned or emergency surgical interventions. In areas with limited resources, education with the emphasis on a clean environment and simple infection control measures like hand-washing, cleaning the genital area, preferably with mild detergents/disinfectant, and minimizing the number of vaginal examinations all play an important role in reducing uterine infection.

The risk of infection increases with postpartum hemorrhage especially if the blood loss is greater than 1 liter. If uterine sepsis occurs,

Table 2 Altered antibiotic regimen[1,4]. In all cases, the therapy should ideally be guided by culture results

If the patient deteriorates *or* Day 3 onwards if patient continues to be febrile on initial regimen:
Initial antibiotic regimen + another antimicrobial agent = altered regimen
1. Intravenous clindamycin + intravenous gentamicin* + intravenous ampicillin 1–2 g 6-hourly
or
2. Intravenous piperacillin–tazobactam + intravenous gentamicin 5 mg/kg* once daily)
or
3. Intravenous metronidazole + intravenous gentamicin* + intravenous ampicillin 1–2 g 6-hourly
or
4. Intravenous ampicillin–sulbactam + intravenous gentamicin intravenous metronidazole 500 mg/8 hourly
The choice of antibiotics in the altered regimen may be determined by transcervical isolates (where culture facilities are available), cost and availability of antimicrobial agents.

*Monitor gentamicin levels

such hemorrhagic consequences can be devastating: collapse can lead to death, as discussed elsewhere in this book. In many developing countries, the majority of deliveries do not occur in a facility with a skilled attendant. Traditional birth attendants (TBAs) need to recognize the consequences of delayed referral. Local and international organizations that aim to provide resources to educate TBAs, increase access to skilled attendants and to facilities for prompt care of postpartum hemorrhage and sepsis all help to decrease maternal mortality in these countries.

CASE STUDY

A 28-year-old primigravida presented at 41/40 weeks with a history of prolonged latent phase of labor. She underwent a Cesarean section as she failed to respond to 8-h oxytocin infusion, commenced after artificial rupture of the membranes. Prior to the procedure, the patient received intravenous cefuroxime and intravenous metronidazole as she was found to be pyrexial (38.7°C). At Cesarean section, she had offensive grade 1 meconium liquor; the placental membranes were found to be adherent but were successfully removed. A live baby with good Apgar score was delivered; however, the patient had primary postpartum hemorrhage due to uterine atony. The patient lost 6 liters of blood and a B-Lynch compression suture was inserted to stay the continual bleeding. The patient received a total of 7 units of blood and 4 units of fresh frozen plasma. The patient continued to be pyrexial, her white blood cell rose from 10 000 to 25 000; lochia was offensive and a transcervical swab grew *E. coli* and anaerobes. She was therefore administered an intravenous clindamycin and once-daily intravenous gentamicin regimen for uterine sepsis. Gentamicin levels were regularly monitored and the patient was discharged after 8 days intravenous therapy, having being ambulant, afebrile and pain-free for 48 h. The baby remained well.

References

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