Chorioamnionitis and Endometritis

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Contents

This update emphasizes need for sepsis evaluation in patients with chorioamnionitis or endometritis who have a positive sepsis screen.

Summary of Recommendations

- Chorioamnionitis
  - Definition of suspected chorioamnionitis: maternal fever PLUS one of the following: maternal leukocytosis (> 15,000/mm^3), purulent cervical drainage, or fetal tachycardia; however ACOG notes that diagnosis of suspected intraamniotic infection *may also be made in the absence of maternal fever* when other associated clinical signs and symptoms are present.[6]

    - Antibiotics: Ampicillin 2g IV q6h (not allergic to PCN) **PLUS** gentamicin 5mg/kg IV q24h (IBW) x 1 dose
    - Duration of treatment: No additional postpartum doses with vaginal delivery; give single postpartum dose with Cesarean delivery.
- Endometritis
    - Clindamycin 900mg IV q8 hours **PLUS** gentamicin 5mg/kg IV q24 hours, based on IBW **PLUS** ampicillin 2g IV q6h (for suspected enterococcus or GBS colonization with clindamycin resistant organism)
    - Duration of treatment: Give until the patient is afebrile for 24 hours
- **Patients that have a positive sepsis screen and chorioamnionitis or endometritis should receive a full sepsis evaluation per the hospital sepsis protocol/algorithm.**

Chorioamnionitis

Background

Chorioamnionitis complicates approximately 4% (1-10%) of term deliveries and 15-41% of preterm deliveries.[1]

Risk factors include:

a. Nulliparity
b. Longer length of labor/membrane rupture
c. Meconium-stained amniotic fluid
d. Genital tract pathogens such as group B strep

Both number of vaginal exams and intrauterine pressure catheters (IUPC) have been disproven as risk factors for the development of chorioamnionitis.[2,3]

Diagnosis

ACOG recommends three categories for classification of intraamniotic infection: 1) isolated maternal fever, 2) suspected intraamniotic infection, and 3) confirmed intraamniotic infection.[4,5]

*Intrapartum fever**

a. Single oral temperature >39°C *or*
b. An oral temperature of 38-38.9°C that persists for greater than 30 minutes

Other causes of fever can include of neuraxial anesthesia, prostaglandins, and other sources of infection (i.e. pyelonephritis, influenza)

Suspected intraamniotic infection

Maternal fever *plus one or more* of the following:
a. Maternal leukocytosis (WBC >15,000/mm^3)
b. Purulent cervical drainage
c. Fetal tachycardia

It is important to note that absence of maternal fever does not rule out intraamniotic infection, and delay in treatment due to lack of fever can significantly worsen the patient's clinical course. **The diagnosis of suspected intraamniotic infection may also be made in the absence of maternal fever when other associated clinical signs and symptoms are present.[6]**

Confirmed intraamniotic infection:

Either of the following:

a. Positive amniotic fluid test result obtained before or at the time of delivery[#]
   i. Glucose <15mg/dL
   ii. WBC >30 cells/mm^3
   iii. LDH > 400
   iv. Organisms on Grams Stain or culture
b. Placental pathology demonstrating placental infection or inflammation
c. Patients who have a Positive Sepsis Screen and chorioamnionitis should receive a full sepsis evaluation.

Management

Once chorioamnionitis has been diagnosed clinically, antibiotics should be administered. Typical pathogens are polymicrobial, with the most common being group B strep, gram negative anaerobes and vaginal flora.[7] **If patients meet suspected sepsis criteria, full sepsis evaluation should be performed, similar to any other infection source.**

Antibiotic Selection

Recommended regimen[8-11]

Ampicillin[*] 2g IV q6h (not allergic to PCN) **PLUS** gentamicin[#] 5mg/kg IV q24h (IBW) x 1 dose

- See Ideal Body Weight (IBW) in appendix

Mild penicillin allergy

Cefazolin 2g IV q6h **PLUS** gentamicin 5mg/kg IV q24h (IBW) x 1 dose

Severe penicillin allergy

Gentamicin 5mg/kg IV q 24h **PLUS** [clindamycin 900mg IV q8h **OR** Vancomycin[€] 1g IV q12h]

Duration of treatment

- Post-vaginal delivery: no additional doses are required; but if given anyway, clindamycin is NOT indicated.
- Post-Cesarean delivery: one additional dose of chosen regimen is indicated to reduce the risk of post-operative endometritis, add clindamycin 900mg IV OR metronidazole 500mg IV for at least one additional dose.

Additional Work Up and Management

Sources have evaluated the need for routine blood cultures in the setting of chorioamnionitis. In general, they do not appear to change the management or course of illness and therefore **blood cultures should not be**

[#] *Even in combination, these tests have reported false positive rates of 67%.[6] Often culture can take >24-28 hours to return, making amniocentesis impractical in the diagnosis and management of chorioamnionitis. Therefore, the use of amniocentesis is likely only useful in very premature gravidas with an uncertain clinical diagnosis.*

[*] If patients have previously been on penicillin for GBS, it is reasonable to continue PCN (dosing unchanged) and add gentamicin OR change the regimen to ampicillin and gentamicin. While PCN has reasonable gram-positive coverage, ampicillin has broader gram positive and negative coverage. The addition of gentamicin, however, also covers these gram-negative bacteria.

[#] Numerous studies have evaluated gentamicin dosing in pregnancy, and it appears the 24 hour dosing is superior to the q 8 hours regimen. Ideal body weight (IBW) is a more accurate measure than total body weight in determining gentamicin dosing. See appendix for IBW formula.

[€] Vancomycin should be used if patient is colonized with GBS that is resistant to clindamycin or erythromycin, or with GBS where no sensitivities are available.

obtained routinely *unless the patient has a Positive Sepsis Screen*.[9] Patients that have a positive sepsis screen and chorioamnionitis should receive a full sepsis evaluation per the hospital sepsis protocol/algorithm. Due to potential neonatal benefits, antenatal corticosteroids and magnesium sulfate for neuroprotection can be considered for patients with preterm chorioamnionitis, **although delivery should not be delayed** for these interventions.[12]

In general, a patient's labor course need not be dramatically altered by a diagnosis of chorioamnionitis.[13£]

Complications

Complications related to chorioamnionitis include:

1. Increased rates of operative delivery or cesarean delivery
2. Hemorrhage (atony)
3. Postpartum infection
4. Sepsis
5. ICU admission
6. Neonatal sepsis, pneumonia, meningitis and increased rates cerebral palsy

The leading risk factor for preterm *neonatal sepsis* is clinical chorioamnionitis, with an odds ratio of 25.[14] In the setting of PPROM, chorioamnionitis increases the neonatal morbidity rate from 18-55%.[15] Additional adverse outcomes have been reported, including 5-minute Apgar score of 3 or less, sepsis, and seizures.[13,16] Data regarding association between chorioamnionitis and cerebral palsy and long-term neurodevelopmental outcomes is conflicting.[12]

£ In 2004, the MFMU evaluated whether there is an optimal duration between diagnosis of chorioamnionitis and need to deliver. They evaluated term patients, all of whom underwent cesarean, with a 12% incidence of chorioamnionitis. While maternal complications such as uterine atony, need for blood transfusion and ICU admission did increase with increasing duration between diagnosis and delivery, after logistic regression, the only factor remaining significant was atony. The only neonatal factor that was significant with duration of chorioamnionitis was 5-minute Apgar <3.

Postpartum Endometritis

Postpartum endometritis is an infection of the decidua. It is typically a polymicrobial infection[17] that develops within the first week postpartum. In 15% of cases, it can be late in onset and develops 1-6 weeks postpartum. It can rarely also include pathogens such as HSV and CMV.

Definition and Diagnosis

Postpartum fever over 38 ˚C in association with one or more of the following: uterine tenderness, foul smelling lochia and leukocytosis of >12,000 after exclusion of another site of infection, which develop within the first 5 days after delivery.[18] It has also been defined as a single temperature of over 38.3˚C, (101 ˚F) on a single occurrence or two temperatures over 38˚C on two separate occasions, in addition to the above associated clinical symptoms .[19] *Clinical judgment should be applied, and therapy not delayed in gravidas who are febrile with systemic symptoms suggestive of infection.*

Route of delivery is a strong predictor of the likelihood of developing endometritis, with rates reported after vaginal delivery (<3%), non-laboring cesarean (7%), and cesarean delivery after trial of labor (30%).[20]

Risk factors

- Cesarean delivery
- Prolonged rupture of membranes
- Chorioamnionitis
- Bacterial vaginosis
- Long duration of labor
- Meconium-stained amniotic fluid
- Manual removal of the placenta
- Maternal diabetes
- Maternal anemia
- Preterm delivery
- Operative vaginal delivery
- Immunosuppression
- Colonization with GBS
- Nasal colonization with Staph Aureus

Symptoms:

- Postpartum fever >38.0˚ C
- Maternal tachycardia
- Fundal tenderness, midline abdominal pain
- Purulent lochia

Differential Diagnosis

Other causes of postpartum fever should be evaluated and excluded, based on physical exam and evaluation, including but not limited to:

- Urinary tract infection/pyelonephritis
- Pneumonia
- Mastitis/breast abscess

- Surgical site infection
- Deep venous thrombosis/pulmonary embolus
- Infections unrelated to pregnancy: influenza, COVID, appendicitis, C Difficile, Gastritis
- Septic pelvic thrombophlebitis

Prevention

- Antibiotic prophylaxis prior to skin incision in cesarean deliveries reduced the prevalence of post-cesarean endometritis.[21] Please refer to the perinatal guideline entitled "Timing of Prophylactic Intravenous Antibiotics for Cesarean Delivery" for more details.
- Spontaneous placenta extraction.[22*]

Management

Broad spectrum coverage is recommended, to include gram positive, gram negative, and anaerobic bacteria. Recent antibiotic exposure should also be taken into account.[23,24] **Patients that have a positive sepsis screen and endometritis should receive a full sepsis evaluation per the hospital sepsis protocol/algorithm.**

Antibiotic selection

Recommended regimen:

- Clindamycin 900mg IV q8 hours **PLUS** gentamicin 5mg/kg IV q24 hours, based on IBW **PLUS** ampicillin 2g IV q6h (for suspected enterococcus or GBS colonization with clindamycin resistant organism) until the patient is afebrile for 24 hours

Penicillin allergy:

- Clindamycin 900mg IV q8 hours **PLUS** gentamicin (5mg/kg IV q24 hours, based on IBW) **PLUS** Vancomycin 1.5gm IV q12h (PCN allergic patients with GBS colonization with clindamycin resistant organism or suspicion of MRSA)[#]

Renal dysfunction

- Consult Infectious Disease

Duration of treatment

- The optimal duration of treatment has not been demonstrated in randomized controlled trials. **BCM OB/Gyn Perinatal Guidelines Committee recommends continuation until the patient is afebrile for 24 hours.**
- Oral therapy is not required after successful parenteral therapy.[25,26]
- If bacteremia was discovered by blood cultures, treatment should be as appropriate for that pathogen (ie extended oral antibiotic treatment for 7-14 days is often recommended).

Considerations if treatment fails

Defined as persistent fever without improvement 48 hours after *actual* initiation of treatment. Complete history and physical exam should be reviewed, and further workup dictated by these findings. This may include:

- Evaluation of the incision
- CT scan
- Blood cultures

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[*] Data are lacking whether antibiotic prophylaxis in the setting of manual extraction of the placenta decreases postpartum febrile morbidity.

[#] Vancomycin is not appropriate coverage alone for enterococci.

- Echocardiogram
- Ultrasound

Possible sources of the persistent fever may include:

- Other etiologies of the fever (abscess, wound infection, septic pelvic thrombophlebitis, retained products of conception)
- Resistant organisms or secondary infection (see above section on addition/changing of antibiotics)
- Bacteremia
- Inappropriate antibiotic dosing (i.e., if the patient is receiving Gentamicin q 8 hours, levels may be non-therapeutic)
- Drug Fever

There are other, less typical causes of endometritis that can be potentially lethal. **These include Group A Strep infection, Staph Toxic Shock Syndrome (TSS), and Clostridium.** These tend to have onset within 24-48 hours of delivery, and require aggressive fluid resuscitation, antibiotics and source control.[27,28]

- Group A strep endometritis/sepsis is typically associated with high fever, hypotension, and multi-organ failure.[23] Historical data indicates that hysterectomy is required to clear this infection due to the microabscesses created by the bacteria. However, more recent case reports exist indicating in some circumstances aggressive medical treatment and/or IVIG may be successful without operative management.
- Staph TSS is characterized by high fever, hypotension and diffuse rash and desquamation. It is often accompanied by multi-organ involvement.
- *Clostridium sordelli* is often rapid in onset of shock with progressive refractory hypotension, generalized massive edema and evidence of hemoconcentration, in the absence of fever.
- *Clostridium perfringens* can be considered in a severely ill person with evidence of intravascular hemolysis. It may cause myonecrosis (‘gas gangrene’) which can be identified on imaging.

Appendix

Ideal Body Weight Calculations:

Ideal Body Weight = 45.5 kg + 2.3kg for each inch over 5 ft

For obese individuals: IBW + 0.4(TBW-IBW)

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