PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "**Management of Early Onset Bacterial Sepsis.**" These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Management of Early Onset Bacterial Sepsis

This podcast was developed by Dr. Jonathan Hagel & Dr. Ann Jefferies for PedsCases.com. January 11, 2017.

Introduction

PedsCases Script – Management of term infants at increased risk for early onset bacterial sepsis

Hi everyone, my name is Jonathon Hagel, a third year paediatrics resident at SickKids Hospital in Toronto, affiliated with the University of Toronto. This podcast was produced in conjunction with PedsCases and the Canadian Paediatrics Society (CPS), and aims to summarize the recently published 2016 CPS position statement on management of term infants at increased risk for early onset bacterial sepsis. This podcast was developed with Dr. Ann Jefferies, a staff neonatologist and Professor in the Department of Paediatrics at the University of Toronto. Dr. Jefferies is the lead author of the CPS statement we are going to review. For more information and to see the full CPS position statement please visit www.cps.ca. A written summary of these cases can also be found on pedscases.com.

Case Presentation

To put this podcast in context, let's start with a clinical vignette. You are working at a community hospital and are called to assess a newborn infant with tachypnea, subcostal retractions, tracheal tug and nasal flaring. The baby is 38+2 weeks' GA, born two hours ago by spontaneous vaginal delivery. As you walk to the patient room, you think of a broad differential diagnosis of tachypnea and accessory muscle use in a newborn infant that includes sepsis, transient tachypnea of newborn, meconium aspiration syndrome, respiratory distress syndrome, along with must rule out diagnoses of pneumothorax and congenital heart disease. You wonder if the most likely diagnosis is sepsis and consider the risk factors, diagnosis, and management of this disease process.

The objectives of this PedsCases podcast are:

1. To outline risk factors for early onset bacterial sepsis
2. To identify appropriate monitoring/investigation strategies for infants at increased risk for early onset sepsis
3. To outline empiric antibiotic therapy in infants treated for sepsis
4. To describe a management algorithm for infants at increased risk for early onset sepsis

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Definitions

Before we begin, let's briefly discuss key definitions of this topic. First, **early onset sepsis** is defined as sepsis occurring within the first seven days of life with the majority of infants becoming symptomatic within 24 hours of birth. Early onset sepsis usually results from vertical transmission and, consequently, is associated with organisms that colonize the birth canal. **Intrapartum antibiotic prophylaxis (IAP)** refers to treatment of group B streptococcus (GBS) colonized mothers with IV antibiotics prior to delivery. Following the implementation of universal maternal screening for GBS colonization and implementation of IAP, the incidence of early onset GBS (EOGBS) infection has decreased although there has been no decrease in the incidence of early onset sepsis caused by other pathogens and no change in the incidence of late onset GBS disease.

An important caveat of this podcast is that it only provides updated recommendations for the care of term (≥37 weeks' GA) newborns with risk factors for early onset sepsis during the first 24 hours of life. Therefore, first determine if your patient fits these criteria before deciding if these guidelines are applicable.

Maternal risk factors for early onset sepsis

Understanding the factors that put term infants at increased risk for sepsis is important in influencing our monitoring and management of these infants. Let's begin by talking about these risk factors. It is important to note that risk factors are additive meaning the presence of more than one risk factor increases the likelihood of early onset sepsis. There are 5 well documented risk factors for early onset sepsis.

1. Maternal intrapartum GBS colonization during the current pregnancy
2. GBS bacteruria at any time during the current pregnancy
3. A previous infant with invasive GBS disease
4. Prolonged rupture of membranes >18 hours
5. Maternal intrapartum fever (Temperature ≥38˚C)

The final two risk factors have "dose-dependent" rather than dichotomous relationships with increasing the risk of early onset sepsis. That is, the duration of ruptured membranes and degree of maternal fever increase the risk of early onset sepsis.

Current guidelines recommend screening pregnant women for GBS colonization at 35-37 weeks' GA and providing IAP for those who screen positive as well as those with GBS bacteruria or a previous GBS infected infant. Adequate IAP consists of at least one dose given at least 4 hours before birth of either IV penicillin G or ampicillin OR IV cefazolin if the mother is allergic to penicillin with low risk of anaphylaxis. Those mothers with high risk of anaphylaxis can be treated with IV clindamycin or IV vancomycin but this management should be considered inadequate IAP when managing the neonate.

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Investigations for early onset sepsis

Bacterial Cultures
A positive neonatal blood culture remains the gold standard for diagnosis of neonatal sepsis. An LP should be performed at the outset when there is a **strong clinical suspicion** of early onset sepsis or when signs of meningitis (seizures, bulging fontanelle, irritability, altered neurological status) are present. An LP must also be done whenever the blood culture is positive. Sometimes, the LP may be performed after initiation of antibiotics because the patient to too unstable to tolerate the procedure earlier, with the possibility of a negative culture. Here pleocytosis, low glucose, and/or elevated protein may be observed with meningitis and should influence management decisions. In term infants, CSF with a WBC count >20-25 cells/mm^3 is considered abnormal.

Biomarkers
Previously, a complete blood count (CBC) after 4 hours of birth was recommended to help guide management of infants at increased risk of early onset sepsis. A low WBC count (<5 x 10^9/L) or low absolute neutrophil count (ANC <1.5 x 10^9/L) is more likely to be associated with EOS than an increased ratio of immature to total neutrophils (I:T ratio >0.2) or a high total WBC (>30 x 10^9/L). However, the positive predictive accuracy and sensitivity of all WBC indices is low, particularly for asymptomatic babies, and are not helpful for ruling in or ruling out sepsis in these babies.

The diagnostic accuracy of a single C-reactive protein (CRP) at the time of initial investigation for sepsis is poor and a normal result should not delay the initiation of antibiotics for a symptomatic infant. Serial CRP measurements may helpful in deciding how long to continue empiric antibiotic therapy but a single elevated CRP should not be used to prolong the duration of empiric antibiotic therapy.

It is important to note that clinical signs are more sensitive and predictive than any lab test. All symptomatic infants should be treated for early onset sepsis.

The first question to ask yourself when determining the management of infants at increased risk of early onset sepsis is: is this infant well or unwell?

Return to Case

Remember our case?

Further history reveals the mother is 33 years old, G2P2, GBS unknown, rubella immune, HIV, syphilis, and HBsAG negative. Her membranes were ruptured 20 hours prior to delivery and she received multiple doses of IV penicillin. The physical exam of the infant is significant for respiratory distress with tachypnea, subcostal indrawing, and nasal flaring. There is also tachycardia and delayed capillary refill time. This infant has clinical signs concerning for sepsis. Investigations should be done immediately including a CBC, blood culture, LP and CXR given respiratory symptoms. Empiric antibiotic therapy with ampicillin and an aminoglycoside should be initiated without delay.

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Management of Unwell Infants

Initial signs of sepsis in newborns may be subtle and include respiratory distress, temperature instability, acidosis, and tachycardia, or they may be more obvious like seizures, hypotonia, lethargy, poor peripheral perfusion, and hypotension. Because invasive disease can progress quickly, all infants with clinical signs of sepsis must be treated immediately with IV antibiotics followed by prompt investigation that includes a CBC, blood culture, LP, and a chest x-ray if respiratory distress is present. **No screening tests have sufficiently high sensitivity to prevent therapy in a symptomatic neonate**. Clinical signs are more predictive than laboratory investigations. A CBC is indicated in this instance to provide further information about the disease state including WBC and platelet indices but should not influence management. Negative GBS cultures or GBS positive mothers with adequate IAP should not influence management in symptomatic neonates.

Infants with only respiratory distress who appear stable and lack perinatal risk factors for sepsis can be observed closely for up to 6 hours to determine whether respiratory distress resolves before investigating for sepsis and starting antibiotics.

Empiric antibiotic therapy should be directed toward the most common bacteria associated with EOS. In term infants born in Canada and the United States, the most common pathogen is GBS followed by Esherichia coli, Stretopcoccus viridans, Staphylococcus aureus and Haemophilus influenza. Ampicillin and an aminoglycoside provide coverage for GBS, E.coli and most other common pathogens.

Now let's change the case …

You examine your patient who is now 2 hours old born to the same 33 years old G2P2 mother, GBS unknown, whose membranes were ruptured 20 hours prior to delivery. You find that the baby's respiratory distress has resolved. She is not tachycardic, she is warm, well perfused, and neurologically appropriate. On auscultation of her lungs you hear good air entry bilaterally and the chest is clear. Given her well status and only one risk factor for sepsis, you decide to watch and wait with close observation over the next couple of hours before investigating further.

Management of Well-Appearing Infants

Asymptomatic term infants with risk factors have a very low incidence of early onset sepsis (~1%), although this incidence is still higher than that for the general birth population. Given this, clinicians must use the combination of risk factors and exposures to determine which infants warrant invasive investigations. When infants are discharged home, there must be ready access to health care and trustworthy parents that understand the signs of sepsis and when to seek medical care.

Management of well appearing infants can be broken down into five broad categories:

a. Infants of GBS+ mothers with adequate IAP may be discharged home in 24 hours provided other discharge criteria are met.

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b. Infants of GBS+ mothers without adequate IAP and no additional risk factors should have close in-hospital observation. This can be achieved by doing vital signs q3-4h for at least 24 hours. **A CBC is no longer indicated as sensitivity of clinical signs is higher than that of WBC indices.** This is a new recommendation – a change from the previous CPS statement about terms infants at risk for sepsis. These infants can be discharged at 24 hours if parents are counseled about signs of sepsis, there is ready access to health care, and parental understanding of when to seek medical care. Otherwise these infants should be observed for 48 hours

c. Infants born to GBS+ mothers with other risk factors (regardless of IAP) – there is insufficient information to guide management, therefore clinicians should consider the severity of each factor as well as intrapartum antibiotic exposure, and the clinical status of each infant to determine an individualized management plan. A CBC after 4 hours of life may be helpful.

d. GBS-/unknown +risk factors – these patients should be managed as GBS positive when a single risk factor is present, that is, in hospital observation with vitals q3-4h for 24 hours. Individualized care is appropriate when multiple risk factors exist as there is not enough evidence to help clinicians make an evidence based decision.

e. Chorioamnionitis (acute inflammation of the fetal membranes) is diagnosed on the basis of maternal temperature >38˚C plus 2 other signs (uterine tenderness, maternal or fetal tachycardia, foul/purulent fluid, maternal leukocytosis). The incidence of EOS in infants exposed to chorioamnionitis is low (< 1%). Although both the CDC and AAP currently recommend that all term infants born to women with suspected chorioamnionitis have cultures and antibiotics, alternative approaches are reasonable because studies show that well appearing infants born to mothers with chorioamnionits have very low rates of early onset sepsis. Therefore, if term infants are well, close hospital observation for at least 24h, without further investigation and antibiotic therapy is a reasonable approach.

Summary

Let's finish with some key take home points on management of infants at increased risk for early onset sepsis:

The number one take home point of this CPS statement is that clinical signs are the most important and more predictive than lab tests.

Second, all symptomatic infants must be investigated and treated for early onset sepsis

The management strategy of newborn infants ≥37 weeks' GA at increased risk for early onset sepsis can be divided into two broad categories and that is whether they appear well or unwell.

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Unwell Infants

1. Infants with **clinical signs** of sepsis must have a full septic work up including a CBC, blood culture, lumbar puncture +/- CXR if the presence of respiratory symptoms exists and empiric antibiotic therapy with ampicillin and an aminoglycoside should not be delayed.
2. Of note, infants with only respiratory signs and without risk factors for sepsis may be observed for up to 6h prior to initiating investigations or empiric antibiotic therapy.

Well Infants

1. WBC indices with a differential or C-reactive protein should not be routinely used screening or diagnostic tests for early onset sepsis or to rule out early onset sepsis
2. For GBS-positive mothers with adequate IAP and no additional risk factors, OR mothers who are GBS-negative or GBS-unknown with one other risk factor and adequate IAP – infants do not require investigation or treatment for sepsis and can be discharged home at 24 hours so long as they remain well, meet other discharge criteria, and parents understand signs of sepsis and when to seek medical care
3. For GBS-positive mothers with inadequate IAP and no additional risk factors OR mothers who are GBS-negative or GBS-unknown with one other risk factor and inadequate IAP – infants should be observed closely in hospital with vital sign checks every 3-4h but may be discharged home after 24 hours provided they remain well and meet the same criteria as above
4. Multiple risk factors for sepsis and/or chorioamnionitis – infants should be treated using an individualized approach and at a minimum observed in hospital for 24 hours with vital signs every 3-4h. A CBC after 4h of life may be helpful, particularly if the WBC<$5x10^9$/L and ANC<$1.5x10^9$/L

Conclusion

That concludes our podcast on infants at risk of EOS, brought to you by PedsCases and the Canadian Pediatric Society.

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