PedsCases Podcast Scripts

This is a text version of a podcast from Pedscases.com on "Meningitis." 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.

Meningitis

Developed by Linda Ding and Dr. Mel Lewis for PedsCases.com.
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Hi my name is Linda and I am a third year medical student at the University of Alberta. This podcast was developed under the guidance of Dr. Melanie Lewis, a general pediatrician at the Stollery Children's hospital. Today we will be discussing one of the core topics in pediatrics – infectious meningitis!

The objectives of this podcast are:

1) Discuss the etiology and epidemiology of meningitis in different age groups.
2) Explore the clinical presentation and physical exam in different age groups.
3) Review the pertinent investigations and how they can differentiate between bacterial and viral meningitis
4) Discuss the management of bacterial and viral meningitis according to the most recent guidelines
5) List the acute complications and long term sequelae of meningitis

But first of all, let's start with a case! A 6 month-old boy is brought to the Emergency department by his parents, who state that he has been sleepy and hard to rouse for the past day. For the past week he has been fighting cold symptoms with fever, runny nose, cough, and for the past couple of days has been pulling at his ear. His vital signs are: Temp 39.1^{o}C, HR 170, RR 30, BP 75/48, O2 Sat 99% on RA. On exam he is lethargic and responds only to painful stimuli, his anterior fontanelle feels full, his left ear is red and bulging, his pupils are reactive. He has normal heart sounds, cap refill, breath sounds, and a soft abdomen. He has no rashes. He has poor tone in all of his limbs, and his reflexes are brisk. His parents are worried because they have never seen him like this. As an astute medical student your spidey-senses are tingly that this could be serious. What do you do now? What investigations are you considering? What initial management would you start on? And after the initial management, what possible short- and long-term sequelae do you need to consider?

Introduction

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First let's start with the basics. Meningitis is inflammation of the meninges, most commonly due to an infectious cause, which is what this podcast will focus on. It is a severe, life-threatening disease with potentially life long sequelae and hence should always be part of the differential for anyone that presents looking very toxic, lethargic, irritable, or hypotonic.

Etiology and Epidemiology

Infectious meningitis can be caused by bacteria, viruses, or even fungi. Due to limited timing, this podcast will focus mainly on bacterial meningitis, given the associated high morbidity and mortality, as well as viral meningitis which is common in the pediatric population.

Among neonates, the incidence of bacterial meningitis is between 0.2-0.5/1000 live births. The most common organisms are *Group B Streptococcus* (GBS), *E.Coli*, and *Listeria monocytogenes* in order of prevalence, the so called GEL organisms, if acronyms are your thing. The risk factors for meningitis in this age group include preterm birth, low birthweight, chorioamnionitis, maternal GBS status, prolonged labour, and PROM.

Among infants >1 months of age, *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenza type B* (Hib) are the most common causes of bacterial meningitis. Since the introduction of pneumococcal, Haemophilus Type B and meningococcal vaccine the incidence of bacterial meningitis has decreased drastically, with a current overall incidence of 1.38/100000. Although the incidence is as high as 10/100000 among infants less than 1 years of age. Risk factors for bacterial meningitis in this age group includes mechanical factors such as CNS trauma, cochlear implants, ventricular shunts, and medical factors such as asplenia, primary immune deficiency, chronic renal disease, and sickle cell disease.

Aseptic meningitis also known as viral meningitis, is diagnosed when there are signs and symptoms of meningitis, moderate elevation of CSF white blood cells and no growth of bacteria. The most common cause of meningitis by far is viral pathogens including: enteroviruses, arboviruses (especially West Nile virus and La Crosse virus), and most importantly HSV-2, which can cause meningoencephalitis in neonates.

History

The presentation of viral and bacterial meningitis are similar. Like many diseases in young infants, the history can be very nonspecific. It is important to ask about symptoms such as inconsolable irritability, poor feeding, and lethargy, which does not simply mean that the baby is sleepy, but that the baby is hard to rouse. It is also important to ask about symptoms of increased intracranial pressure and meningeal inflammation such as vomiting, apnea, and seizures. Temperature dysregulations, which can be either fever or hypothermia, are common, but not necessary.

In an older child, the symptoms become more specific, and it is important to ask about any history of fever, headache, lethargy, photophobia, vomiting, back pain or stiff neck, and any changes in mental status.

In all ages it is important to ask about past medical history including: recent illness, any chronic illness, or any head or facial trauma. On past surgical history it is important to know whether there are central nervous system shunts or cochlear implants. On the birth history one should ask specifically about maternal GBS status, any maternal STIs, chorioamnionitis, premature rupture of membranes, or perinatal infections, especially in an infant <1 months of age. It is very important to ask about immunizations as that can affect the likelihood of the pathogens. The medication history is also extremely important, paying particular attention to any recent NSAID use, recent IVIG transfusions since those can cause symptoms similar to meningitis, any immunosuppressive agents use such as prednisone, or recent antibiotic use which can influence the susceptibility profile. Any exposure related risk factor such as a sick contacts, day care, chance of TB exposure, and travel history should also be elicited. Finally, it is important to ask about child care exposures in consideration of chemoprophylaxis among those exposed.

Physical Examination

For all ages, it is important to first assess the vitals, conduct a quick survey of the ABCs to ensure the baby is stable, and assess the level of consciousness with the pediatric Glasgow Coma Scale.

It is then essential to do a complete head to toe physical. On general appearance the baby may be less active and disinterested in its surroundings. In the head and neck area pay special attention to symptoms of increased intracranial pressure such as papilledema, diplopia, unilateral or bilateral dilated, poorly reactive pupils, or a bulging fontanelle in infants. The Cushing triad is a late finding of increased ICP, with hypertension, bradycardia, and irregular respirations. A head circumference should also be obtained. On the respiratory exam it is important to note the presence of any respiratory difficulty and increased work of breathing such as grunting, nasal flaring, indrawings, and any adventitious breath sounds. On the cardiovascular exam it is important to get an idea of perfusion status. On the MSK exam it is important to note the presence of any rashes, and any joint involvement which can be present with GBS or meningococcal infections. One may notice through the exam that the infant does not wish to be handled and prefers to remain motionless. Kernig and Brudzinskis signs are usually not present in a young infant.

For an older child, along with all of the above, it is possible to elicit a positive Kernig and Brudzinski signs. To elicit the Brudzinski sign, have the patient lie in the supine position, and then passively flex the neck. A positive Brudzinskis sign is when the passive flexion of the neck causes a reflex flexion of the patients' hips and knees. To elicit the Kernig signs, have the patient flex their hips and knees to a right angle while in a supine position, and then slowly passively extend the knee. A positive Kernigs sign is when there is the appearance of resistance or pain during the extension of the knee. Both

movements stretch the nerve roots through inflamed meninges leading to pain in the lower extremities. A more thorough neurological exam is also possible in an older patient, looking specifically for signs of cranial nerve 3, 4, and 6 palsies, and any focal neurological deficits, which can be present with bacterial meningitis.

Investigation

There are some basic investigations one must order if meningitis is high on the differential. CBC with a differential may show an elevated white count. However, remember sometimes WBC can be normal, and in neonates it may even be low. Serum electrolytes, creatinine, and glucose should be obtained for detecting possible syndrome of inappropriate anti-diuretic hormone (SIADH), as well as monitoring for fluid administration. ESR and CRP may be elevated. Blood cultures and urine culture should be obtained.

It is essential to perform a lumbar puncture if meningitis is high on the differential, unless there are absolute contraindications. Contraindications include: an unstable patient, presence of a coagulopathy or the presence of signs and/or symptoms of elevated intracranial pressure (ICP). The cerebrospinal fluid (CSF) glucose, protein, and CSF leukocyte count and differential will help differentiate between a bacterial and viral cause of infection. Typically, the glucose is decreased and the protein increased in bacterial meningitis, CSF leukocytes are elevated with a neutrophil predominance – often >90% polymorphonuclear lymphocytes (PMNs). The CSF findings of a viral infection, do not have that distinct pattern. Often the glucose and protein are normal with only minimal or moderate elevation of CSF WBCs. The white cell count differential however can show <50% PMN if the infection has been occurring for >48 hrs. A viral PCR panel could be included as well. Hence when sending CSF specimens at least 4 tubes should be obtained and sent to the lab for: Cell count and differential, gram stain and bacterial culture, glucose & protein, and viral PCR.

Management

It is essential to remember that meningitis is a SERIOUS disease with SEVERE comorbidities and management needs to be started on an empiric basis BEFORE any lab work come back. For neonates, the empiric treatment consists of ampicillin and gentamicin, with gentamicin covering for *E. coli*, and ampicillin covering GBS and listeria. It is also possible to use ampicillin and cefotaxime as empiric treatment. If the CSF cultures come back indicating the presence of GBS or listeria, then consider stepping down the antibiotic therapy to penicillin G. The duration of antibiotic for GBS or listeria is 14 days minimum for uncomplicated meningitis, and at least 21 days for *E. coli* positive meningitis.

As for infants >1months of age, there is a very nice CPS guideline on the management of bacterial meningitis. The gist of it is as follows: Empirical treatment should consist of ceftriaxone OR cefotaxime, along with vancomycin to cover for penicillin resistant *S.pneumoniae*. Consider adding ampicillin to cover for listeria if the patient is at risk or

immunocomprominsed. After the LP culture comes back it is possible to tailor the antibiotic therapy a little bit more: If the culture results show *s.pneumoniae*, then change antibiotic to penicillin G or ampicillin if the bug is penicillin susceptible. Continue with ceftriaxone or cefotaxime if it is penicillin resistant. Treatment duration is 10-14 days. If the bug is *n. meningitidis*, then use Pen G or ampicillin if susceptible, and ceftriaxone or cefotaxime if not, and the treatment duration is 5-10 days. If the bug is HiB, then use ampicillin if susceptible, and ceftriaxone or cefotaxime if not. The treatment duration is 7-10 days. Hence basically to summarize, if the bug is susceptible, use Pen G or ampicillin, if not then continue with ceftriaxone or cefotaxime.

At all ages if HSV is a concern, then acyclovir should be added. The usual treatment duration is 21 days. At the end of 21 days, a follow up CSF HSV DNA PCR should be done to confirm the sterility of the CSF fluid.

Routine use of steroid in meningitis management remains controversial except in the case of Hib meningitis. For all ages, some experts recommend giving dexamethasone 0.6mg/kg/day administered every 6 hours, with the first dose at initiation of antibiotic, for a total duration of two days. There is evidence that steroids reduce hearing loss in the case of Hib meningitis.

In terms of discharge planning, the patients are safe for discharge if they have been clinically and neurologically stable, able to tolerate enteral fluids, and have been afebrile for 24-48 hours. It is not necessary to have completed the full course of antibiotic prior to discharge if the patients can finish their course of antibiotic as outpatients with home IV therapy.

Short- and Long-Term Sequelae

In the immediate period, up to 70% of children with bacterial meningitis require fluid resuscitation, usually done with normal saline. Seizures occur in approximately 20-30% of patients with bacterial meningitis. Subdural effusions can complicate the course of meningitis in 10-40% of babies with meningitis. Treatment is supportive as long as the babies are showing that they are improving with the course of antibiotic. SIADH is common in babies with bacterial meningitis, and close monitoring of urine output and osmolality, serum electrolytes and osmolality is required. The treatment consists of fluid restriction, however, it is important to ensure that there are no clinical findings suggestive of hypovolemia or dehydration.

Fortunately, most babies that are treated on time go on to recover fully with no long term effects, however risk of comorbidities still exist. In particular hearing loss is present in 20-30% of the babies with *s. pneumoniae* meningitis, 10% if meningococcal meningitis, and 5% if HiB meningitis. There is also a risk of developing cognitive and developmental disability, hemiparesis, quadriparesis, CN palsies, epilepsy, cortical blindness, hydrocephalus, diabetes insipidus, and hypothalamic dysfunction with delays in treatment. The longer these babies remain untreated the greater the risk of these

morbidities, which is why it is important to start them on empiric treatment as soon as possible!

Chemoprophylaxis

So what happens to everyone that had been exposed to the index case? If *N. meningitidis* was cultured, then prophylaxis is recommended for everyone in the household, and everyone at daycare that had been exposed to the patient. Rifampin is usually used for both kids and adults. Ceftriaxone or ciprofloxacin can also be considered for adults. If HiB was cultured, then only unimmunized or under-immunized children under four years of age, and immunocompromised individuals of all ages that were in the same household as the index case should have prophylaxis with rifampin. If *s. pneumoniae* was cultured then no prophylaxis is needed.

Conclusion

Now you know all about meningitis, how to recognize it and how to manage it appropriately. Let's return to the case that we started at the beginning of the podcast!

Recognizing the severity of the situation, the baby was immediately admitted to the hospital. An urgent LP was done which showed WBC 1250 x 10^6 cells/L with predominance of PMNs, glucose 0.7 mmol/L, and protein 1.3 g/L. The baby was started immediately on empiric ceftriaxone and vancomycin, as well as dexamethasone. One day later the LP culture came back positive for *s. pneumoniae* that was penicillin sensitive and the antibiotic was narrowed to Penicillin G. After 5 days on the antibiotic the baby looked much better, more awake and alert, with better tone, flatter anterior fontanelle, and remained afebrile, you decided to discharge the patient. A plan was made to finish the remaining course of antibiotic as outpatients.

Now let's finish up this podcast by reviewing some key points for meningitis:

1) Among neonates the most common cause of bacterial meningitis is GBS, *E. coli*, and listeria
2) Among older babies the most common cause of bacterial meningitis is *s.pneumoniae, n. meningitidis*, and HiB
3) Clinical manifestation of meningitis in a younger child is often nonspecific.
4) LP can help differentiate between bacterial and viral causes of meningitis.
5) Empiric therapy for suspected bacterial meningitis in a neonate is ampicillin and gentamycin OR ampicillin and cefotaxime.
6) Empiric therapy for suspected bacterial meningitis in a non-neonate includes ceftriaxone OR cefotaxime, PLUS vancomycin.
7) Sensorineural hearing loss occurs in 30% of children with pneumococcal meningitis or in 10% of those with meningococcal meningitis.
8) Dexamethasone is given to those with HiB meningitis for reducing risk of hearing loss.
9) Chemoprophylaxis with rifampin is given to those with potential exposure to child with meningococcal or HiB meningitis

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Thank you so much for listening!

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