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Review Article

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An Overview on Pediatric Meningitis Diagnosis and Management Approach

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ABSTRACT

Pediatric meningitis is a life-threatening infection and one of the pediatric emergencies. It has a high mortality rate ranging from 5% to 30%, with a high prevalence of central nervous system morbidity affecting up to 50% of pediatric meningitis cases. For that, the early detection of pediatric meningitis and early introduction of the appropriate Antibiotics can decrease mortality and morbidity. The objective of this review is to discuss Pediatric Meningitis pathogenesis, clinical features, etiologies, diagnosis, and management in clinical practice. PubMed database was used for articles selection, and the following keys were used in the mesh ((“meningitis"[Mesh]) AND (“assessment”[Mesh]) OR (“management"[Mesh])). Meningitis is considered to be one of the most serious infections that can affect the pediatric population with high morbidity and mortality. Most of the patients affected by meningitis present initially to the emergency department, and a comprehensive approach to these cases is crucial if one wants to lower the serious consequences of the disease.

Key words: *Pediatric meningitis, Neonatal meningitis, Lumbar puncture, Hydrocephalus*

INTRODUCTION

Pediatric meningitis is a life-threatening infection, and one of the pediatric emergencies is acute pediatric meningitis. It has a high mortality rate ranging from 5% to 30%, with a high prevalence of central nervous system morbidity affecting up to 50% of pediatric meningitis cases. For that, the early detection of pediatric meningitis and early introduction of the appropriate Antibiotics can decrease the incidence of mortality and morbidity [1]. Despite the inventions in vaccination, diagnosis, treatment, in 2015, there were 8.7 million cases of meningitis reported worldwide, with 379,000 deaths as a result of it [2, 3].

MATERIALS AND METHODS

PubMed database was used for articles selection, and the following keys were used in the mesh ((“meningitis"[Mesh]) AND (“assessment”[Mesh]) OR (“management"[Mesh])).
In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics: meningitis, non-invasive assessment.
Exclusion criteria were all other articles, which did not have one of these topics as their primary endpoint.
Around 90 publications were chosen as the most clinically relevant out of 1,202 articles indexed in the previous two decades, and their full texts were evaluated. A total of 31 of the 90 were included after a thorough examination. Additional research and publications were found using reference lists from the recognized and linked studies. Expert consensus recommendations and commentary were added where relevant to help practicing physicians assess meningitis most simply and practically possible.

RESULTS AND DISCUSSION

Meningitis is considered to be one of the life-threatening disorders that are most often caused by bacteria or viruses. The condition was universally fatal before the era of antibiotics [3]. Overall, the rate of meningitis cases has been declining since the initiation of the three vaccines against the most common meningeal pathogens (Streptococcus pneumoniae, Haemophilus influenza type b, and Neisseria meningitides) [4]. All around the world, bacterial meningitis is still considered to be a neurological emergency associated with high morbidity and mortality rates requiring urgent evaluation and management. Seizures, hearing loss, hydrocephalus, motor problems, and mental retardation, as well as more implied outcomes, including cognitive, behavioral, and academic difficulties, are observed after the recovery from meningitis in children [4].

Etiology by age group

Meningitis is a condition known as inflammation of the meninges. The meninges are the three membranes that cover the brain (the pia mater, arachnoid mater, and dura mater) that cover the enclosed canal and skull line the brain and spinal cord. On the other hand, Encephalitis is a condition where the brain parenchyma itself becomes inflamed [5]. Meningitis is caused by infectious and non-infectious processes (drug reactions, autoimmune diseases, paraneoplastic syndromes). The infectious organisms of meningitis may include bacteria, viruses (known as Aseptic meningitis), fungi, or parasites. The most common viruses causing aseptic meningitis are enteroviruses, mainly coxsackieviruses. Other causes of viral meningitis include echoviruses, Herpesviridae viruses, Human immunodeficiency virus (HIV), Mumps, Measles, and Poliovirus [2, 5]. Many bacterial pathogens can cause bacterial meningitis in children, including Listeria monocytogenes, Hemophilus influenzae type b (Hib), group B streptococcus, Escherichia coli, S. pneumonia, and Neisseria meningitis [2]. In a recent meta-analysis that was done to collect the available data on the organisms causing bacterial meningitis that was published globally in the last five years, the seven bacterial organisms most commonly causing meningitis are Streptococcus pneumonia, Escherichia coli, Group B Streptococcus, Haemophilus influenzae, Staphylococcus aureus, Neisseria meningitides, and Listeria monocytogenes were analyzed, and the results were stratified into the six geographical regions and seven age groups as determined by the WHO [6]. Coccidioides is an example of Fungal meningitis. Examples of parasitic meningitis include Strongyloides stercoralis, Angiostrongylus cantonensis, Baylisascaris procyonis, and Naegleria fowleri; Acanthamoeba. Moreover, meningitis can be due to non-infectious etiologies such as medications. Sulfa drugs and NSAIDs are examples of such drugs [1].

Neonates and infants

Neonates, premature infants, neonates, and infants younger than two months of age are at the highest risk for bacterial meningitis in the pediatric population [6]. The risk of developing bacterial meningitis is similar to the risk of sepsis in these patients and can be attributed to the lack of immunoglobulins that cross the placenta after 32-week gestation in the mother and possibly the impaired phagocytic ability of neutrophils and monocytes and the immature immune system in this young population [6]. Organisms that commonly cause neonatal meningitis are the same as the organisms that cause sepsis in this age group [7]. Risk factors in developing meningitis in neonates include maternal rectovaginal colonization with GBS, prematurity, very low birth weight (<1500g), premature rupture of membranes, invasive fetal monitoring, presence of external devices (e.g., reservoirs, shunts, catheters), prolonged rupture of membranes >18 hours, and prolonged hospitalization [7]. Despite the implementation of intrapartum prophylaxis, GBS remains the leading cause of early-onset neonatal meningitis, accounting for approximately 40% of cases [8]. Escherichia coli (E. coli) is considered to be the second most common etiology accounting for around 17.7% in Africa and 30% of cases in the USA [7] and is the main cause

of sepsis and early-onset meningitis in newborns with very low birth weight (<1500 g birth weight) [7]. In late-onset neonatal meningitis, E. coli and GBS are considered to be the two main causing organisms [9]. It is noted that the incidence of L. monocytogenes meningitis has been significantly reduced in this age group mainly because of the reduction in food-borne contamination, which leads to a reduction of listeriosis in pregnancy [9].

Children older than one year

IDespite the major reduction that happened to the incidence of meningitis in this age group that was attributed to the introduction of vaccines to the three most common meningeal pathogens, including:

S. pneumoniae and N. meningitides remain the most common organisms causing community-acquired bacterial meningitis, then followed by GBS and gram-negative bacilli organisms [10].

Pathogenesis

TThree layers are surrounding the brain called the meninges. The innermost layer is a thin impermeable layer called the Pia matter, which is tightly attached to the brain. Tiny blood vessels will pierce the Pia matter to provide nutrition to the brain. The intermediate layer is called the Arachnoid matter. Dura matter is the thick outermost layer that is attached to the skull [3].

Clinical manifestation

Children with meningitis usually manifest with the classical triad that includes fever, neck rigidity, and headache [11]. Other presentations include nausea, vomiting, photophobia, agitation, delirium, paralysis of the cranial nerves, and seizures. Children may have a positive Kernig sign that is knee pain and resistance that happens after extending the knee while the hip is flexed, or Brudzinski sign, which is flexion of the knees and hips that happens after forced passive flexion of the neck [3]. On the other hand, neonates present without the classical triad but rather present with non-specific signs and symptoms such as hyperthermia or hypothermia, lethargy, feeding intolerance, vomiting, and hypotonia. Bulging of the fontanelles is another sign that is present lately in neonates and is caused by the increase in the internal cranial pressure (ICP) [6]. The fundoscopic examination may show papilledema in children who have high intracranial pressure. Enterovirus meningitis children can have Maculopapular rash. On the other hand, pediatrics who are affected by meningococcal meningitis can have non-blanching purpuric rash or petechia. Moreover, they may present with disseminated intravascular coagulation, acute adrenal insufficiency, hypotension, and shock, which are the features of Waterhouse-Friderichsen syndrome. Flu-like symptoms and Upper respiratory tract symptoms such as sore throat can give a clue of viral meningitis [11]. Children may also present with seizures and focal neurological deficits, and that can give a clue of meningoencephalitis [11].

Investigations

The standard gold test for meningitis is through the lumbar puncture and cerebrospinal fluid (CSF) analysis **(Table 1)**, which includes white blood cell count, culture, protein, glucose, and polymerase chain reaction (PCR) in some cases. CSF is obtained by performing a lumbar puncture (L.P.), and the opening pressure can be measured [11].

Additional testing must be considered and tailored on suspected etiology [1, 12]

- Viral: Specific PCRs and Multiplex test
- Fungal: India ink stain for Cryptococcus and CSF fungal culture
- Mycobacterial: Mycobacterium culture and CSF Acid-fast bacilli smear.
- Lyme disease: CSF burgdorferi antibody
- Syphilis: VDRL

Table 1. The CSF findings in bacterial, fungal, and viral meningitis

	Appearance	Openin Pressure mmHg	WBC (Cell/uL)	Protein (mg/dl)	Glucose (mg/dL)
Normal	Clear	90- 180	< 8	15- 45	50- 80
Bacterial Meningitis	Turbid	Elevated	>1000- 2000	>200	<40
Viral Meningitis	Clear	Normal	<300; Lymphoctic predominance	<200	Normal
Fungal Meningitis	Clear	Normal- elevated	<500	>200	Normal- Low

In ideal situations, the L.P. should be performed before starting antimicrobials. Nonetheless, when there is a high clinical suspicion for bacterial meningitis in severely ill patients, antibiotics should be administered before performing the lumbar puncture test [3]. Indications for performing Computed Tomography (C.T.) of the Head before L.P. The current guidelines indicate the use of empiric antibiotics and supportive care without performing L.P. if an increase in the intracranial pressure or impending brain herniation is suspected [3].

Signs and symptoms of increased intracranial pressure [12]

- Lethargy
- New-onset seizures
- Focal neurologic deficit
- Glasgow coma scale (GCS) less than 11
- Altered mental status

It is crucial to keep in mind that a normal head C.T. does not rule out an increase in the intracranial pressure. When the clinical symptoms are consistent with possible brain herniation, regardless of the head C.T. is normal or not, L.P. must be avoided, and the appropriate treatment should be started as soon as possible. Blood work-up, including serum electrolytes, blood culture, renal and liver function, serum glucose, and HIV testing [12].

Treatment

Supportive care and antibiotics therapy are critical in all cases of bacterial meningitis [13-16]. The type of antibiotic of choice depends on the suspected organism causing meningitis. The physician must take into account the past medical history of the patient and the patient's demographics to be able to make the best choice of treatment with the highest antimicrobial coverage [17-19].

Current empiric therapy

Neonates - Up to 1 month old [11]

- Ceftriaxone IV and Ampicillin IV
- Gentamicin IV and Acyclovir IV

Older than one month old [17]

- Ceftriaxone IV and Ampicillin IV.

Adults (18 to 49 years old) [17]

- Vancomycin IV and Ceftriaxone IV.

Adults older than 50 years old or immunocompromised patients [17]

- Vancomycin IV and Ceftriaxone IV, and Ampicillin IV

Meningitis in patients with penicillin allergy [17]

- Vancomycin IV and Moxifloxacin IV

Fungal (Cryptococcal) meningitis [20]

- Flucystine Oral and Amphotericin- B IV

CONCLUSION

Meningitis is considered to be one of the most serious infections that can affect the pediatric population with high morbidity and mortality. Most of the patients affected by meningitis present initially to the emergency department, and a comprehensive approach to these cases is crucial if one wants to lower the serious consequences of the disease. When bacterial meningitis is the main differential to the case, antibiotics treatment must be started even before having the routine laboratory investigations. Preventing meningitis in children can be achieved by educating the public about the importance of vaccinations in the pediatric population [21].

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