Tripolitana Medical Journal; 2017, Vol. 6, No. 2, pp. 47 - 51

Research Article

ISSN 2077-5628

Pattern of Childhood Meningitis; Diagnosis and Treatment

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Received 20 June 2017/Accepted 7 October 2017

ABSTRACT

Acute bacterial meningitis is a medical emergency requiring immediate diagnosis and treatment. Streptococcus pneumoniae and Neisseria meningitis are the most common and most aggressive pathogens of meningitis. Twenty four of forty four patients admitted with suspected meningitis had fulfilled criteria of the disease, their age ranged between 50 days and 12 years. Twelve of them were males with male: female ratio 1:1. All laboratory investigations were done as a part of the daily routine work. Most patients presented with fever and vomiting. Headache was common at and after 4 years of age. From 24 patients with meningitis 79% were pyogenic and 21% were aseptic. CSF culture demonstrated the growth of one organism like *E.coli, Enterobacter cloacae*, Gram negative diplococci, *Streptococcus pneumniae* and *klebsiella pneumonia*. Brain images (CT scan or MRI) showed presence of complication such as brain abscess, subdural collections and dilatation of ventricles in 4 patients.

The classical symptoms and signs of bacterial meningitis may be absent. A high index of suspicions for bacterial meningitis in the child with convulsion and fever is paramount. The most appropriate management is a lumbar puncture, when there are no contraindications, analyzing CSF and to start immediately parenteral antibiotics. When the results of the cerebrospinal fluid (CSF) culture and susceptibilities are known, therapy can be narrowed to cover the specific pathogen identified. In general, Penicillin G or Ampicillin is preferred for group B streptococcal meningitis, Ampicillin for Listeria monocytogenes meningitis, and Ampicillin plus either an Aminoglycoside or Cefotaxime for Gram negative meningitis.

Keywords- *Viral meningitis; Bacterial meningitis; Cerebrospinal fluid..*

INTRODUCTION

Since the widespread use of the vaccine for Haemophilus influenzae type B, *Streptococcus pneumoniae* has replaced it as the most common cause of acute community-acquired bacterial meningitis in industrialized countries. Despite modern antibiotics and improved critical care, bacterial meningitis is still an unresolved problem in clinical medicine. Although highly effective antibiotics kill bacteria efficiently, in pediatric age; many probabilities of outcomes varied significantly by etiologic bacteria, e.g. mortality: Haemophilus influenzae, 3.8%; Neisseria meningitidis, 7.5% Streptococcus pneumoniae 15%.[1]

Some studies in adults showed high mortality rates up to 34%.[2] Up to 50% of the survivors suffer from long-term sequelae.[3-6] A hallmark of bacterial meningitis is the recruitments of highly activated leukocytes into the CSF. Beside bacteria, viruses, fungi and noninfectious causes as in systemic and neoplastic disease as well as certain drugs can induce meningeal inflammation. Usually the inflammatory process is not limited to the meninges surrounding the brain but also affects the brain parenchyma (meningoencephalitis).[7] The incidence of the disease varies from 1.1 to 2 in 100,000 per year in the US and in Western Europe[5,8,9], but up to 12 in 100,000 per year in Africa.[10] Early clinical features of meningitis are non-specific, especially in young children; the symptoms include fever, poor feeding, vomiting lethargy, irritability and convulsions. In addition; the important clinical signs are the bulging fontanelle, fever, drowsiness and purpuric rash.

In older children the more classic signs are the neck stiffness, headache and photophobia. The specific signs of Kernig's, Brudzinski, and nuchal stiffness are often absent in young children.[11]

In children, Nigrovic et al.[12] documented that the neck stiffness in children present in 40% and altered mental status present in 13%. The key to the diagnosis of bacterial meningitis is the proof of bacteria in the CSF by Gram staining or a positive bacterial culture. Detection rates in the CSF may be as high as 90%, while about 50% positive results are observed in blood cultures. PCR has an important role in strain identification mostly in meningococcal diseas.[13] Lower cell counts and a mixed pleocytosis are observed with L. monocytogenes, M.

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tuberculosis and fungi; also, they may be found in partially or insufficiently treated meningitis. The aim of the study is to ascertain and document the facts of the clinical and laboratory findings in childhood meningitis leading to more responsible management decisions.

MATERIALS AND METHODS

This case series study; done in end of 2016 to reviews of children were admitted with meningitis in the pediatric departments, Tripoli Medical Centre, University of Tripoli. Out of the forty four patients with diagnosis of meningitis; 24 patients fulfilled the required criteria for the disease. The youngest patient was 50 days and the oldest was 12 years of age. All laboratory investigations were done at the centre as part of their daily routine work including complete blood count (CBC) and random blood sugar (RBS). Criteria used for diagnosis is presence of abnormal CSF results. For the bacterial meningitis (CSF sugar less than 45% or CSF /blood sugar ratio less than 66%; protein more than 45% ; and cells more than 5/mm^3; positive CSF Gram stain preparation or/and positive CSF culture.

RESULTS

Nineteen (79%) patients diagnosed as bacterial meningitis while 5 patients (21%) were aseptic without any record of deaths. The gender was equal in distribution and the age of patients ranged from 50 days to 12 years in septic meningitis. In aseptic meningitis all patients were above one year of age (Table 1). Seven patients (36%) with bacterial meningitis had received antibiotic treatment prior to laboratory diagnosis. In bacterial meningitis; **Table 2:** Symptoms and clinical signs in meningitis

the presenting symptoms and signs on admission were fever (89%), neck stiffness (37%), headache (21%) and convulsions (16%), bulging anterior fontanelle (15%), kernings and Brudzinski's signs (15%). While fever (100%), vomiting (100%), headache (100%) and neck stiffness (80%) were the main presentation in aseptic meningitis (Table 2). Lucokytosis is a characteristic in 14 patients (74%), but neutrophelia was found only in 7 cases with septic meningitis, on the other hand, leukocytosis documented in only 2 cases in aseptic meningitis with mixed lymphocytosis and neutrophelia (Table 3). The key to the diagnosis of meningitis is the CSF analysis; in our cohort, all patients with bacterial meningitis had pleocytosis, as well as low CSF sugar. We noted in patients with bacterial meningitis, that CSF protein levels were varied between minimum 4 and highest 2100 mg%. Only one patient had positive gram stain and 6 cases (31.5%) had positive CSF culture with growth of one organism; *E.coli*, Entrobacter cloacae, Gram neagative *Diplococcic*, *Streptococcus pneumiae*, *Pseudomonas paucimobilis*, *Klebsiella pneumonia* (Table 4). Three of these six patients had prior antibiotic treatment.

In aseptic meningitis CSF pleocytosis is evident in all patients, and CSF blood sugar ratio was more than 50%.

Table 1: Age distribution of patients according to type of meningitis

Age	Bacterial n=19	Aseptic n=5
1 m- 1 year	12	-
2- 4years	3	1
5- 8years	-	3
9-12years	4	1

Table 2: Symptoms and clinical signs in meningitis

Symptoms	Bacterial n 19	%	Aspect n 5	%
Fever	17	89.4	5	100
Vomiting	10	52.6	5	
Poor feeding	6	31.5	-	
Headache	4	21	5	100
Parotid swelling	-	-	4	80
Irritability	4	21	-	-
Seizures	3	15.7	1	-
Neck stiffness	7	36.8	4	80
Brisk reflexes	4	21	-	-
Bulging fontanelle	3	15.7		
Kerning/Brudzinski's signs	3	15.7	3	60

Table 3: with blood coli in count with meningitis

WBC Count	Bacterial n 19	Aseptic n 5
Normal (Range 4000-11.500/mm^3)	5	3
Lucocytosis	14	2
Neutrophilia	7	0
Lymphocytosis	4	0
Neutrophilia+ Lymphocytosis	3	2

Table 4: CSF parameters in bacterial meningitis

Age sugar ratio	Prior Therapy CSF protein mg/dL	Cells/mm³ Gram Smear	CSF/blood CSF Culture	%	Aspect n 5	%
51 d	-	119	30%	70	-ve	-ve
2 m	-	16	15%	395	-ve	+ve
2.5 m	-	400	34%	4	-ve	-ve
4 m	-	490	54%	46.4	-ve	+ve
6 m	-	28	35%	53	-ve	-ve
6 m	+	22	14%	21	-ve	+ve
7 m	+	194	56%	15	-ve	-
8 m	-	235	49%	23.7	-ve	+ve
8 m	-	12	18%	48.5	-ve	-ve
8 m	+	191	30*	5	-ve	-ve
8 m	+	15	37*	17	-	-ve
1 yr	-	48	5%	20	-ve	-ve
1.5 yr	-	114	75%	4	-ve	-ve
2.5 yr	-	370	4%	235	+ve	+ve
4 yr	-	958	5%	1000	-ve	-ve
11 yr	+	32	60%	34	-ve	-ve
12 yr	-	546	24%	2100	-ve	+ve
12 yr	-	86	45%	33	-ve	-
12 yr	-	123	25%	178.5	-ve	-ve

In addition, all CSF culture and Gram stain were negative (Table 5). The brain images (CT scan or MRI) were not a routine; they were performed in 4 patients and it showed the presence of complications such as brain abscess, subdural collections and dilatation of ventricles. The choice of antibiotic depends on the organism isolated. In most cases the initial treatment was empirical. In all cases of bacterial meningitis a broad spectrum Cephalosporin (Cefotaxime or Ceftriaxone) was started in children over 3 months old. Ampicillin was added in young infants (less than 3 months old) to cover Listeria monocytogenes.

DISCUSSION

Acute bacterial meningitis in childhood is known to be associated with significant mortality, complications and long-term neurological sequelae.[14] In our study, out of 44 patients admitted as meningitis only 24 fulfilled the criteria of diagnosis. 21% were aseptic meningitis. In literatures, study from Oman[15] documented that only 13% were viral while in other studies; the viruses were a common causative agents of meningitis.[16] On the other hand, 79% of our patients had bacterial meningitis. This result is similar to literature[17,18] but it is much higher than Husain study et al.[16] in Canadian children (79%, 11% respectively $P < 0.05$). In reference to age, ⅔ of our patients with septic meningitis were less than one year of age and those less than 5 years old had the highest proportion.

Patient's specific clinical presentations of our patients are similar to other studies except for convulsion. A significant observation in our cohort is the infrequent occurrence of seizures (16%).

CSF analysis remains the definitive tool for diagnosis of meningitis. The changes of the biochemical composition of the CSF help in the diagnosis and even the differentiation of the type of meningitis either bacterial or viral. In the current study the differential leukocyte count was not done. Moreover, there was discrepancy of CSF protein levels and as a result it was difficult to correlate them to the type of meningitis. Gram smear is a simple and quick procedure for the detection of bacteria in CSF and is positive in bacterial meningitis. If Gram smear test is

Table 2: Symptoms and clinical signs in meningitis

Age	Cells/	CSF/bl Sugar ratio	CSF protein mg/dL	Gram Smear	CSF culture
18 m	16	100%	27	-ve	-ve
5 yr	200	75%	470	-ve	-ve
7 yr	200	60%	3.4	-ve	-ve
7 yr	>650	50%	17	-ve	-ve
	66	65%	-	-ve	-ve

positive, the expected CSF culture positive results rising to 90%. Surprisingly, in our study, CSF Gram stain was negative nearly in all patients. Several factors influence the sensitivity of Gram stain. Laboratory techniques used to concentrate and stain CSF can greatly influence reliability. In addition, Cyto-centrifugation increases the ability to detect bacteria. Greater numbers of colony-forming units (CFU) per mm^3 of CSF increase the likelihood of a positive a positive result. Staining will be positive 25 percent of cases if fewer than 1,000 CFU per mm^3 are present and in 75 percent of cases if more than 100,000 CFU per mm^3 are present.

CSF cultures were positive in 31.5% of bacterial meningitis. The bacteria recovered from CSF cultures in acute pyogenic meningitis were *E.coli, Enterobacter cloacae*, Gram negative *Diplococci, Streptococcus pneumoniae*, *Pseudomonas paucimobilis* and *Klebsiella pneumoniae*. Some of these organisms are not a common causative agent of meningitis and can be attributed to improper handling of the specimens, shortage of laboratory materials or to antibiotic abuse. Moreover, H influenzae was not recovered at all probably due to introduction of the vaccine. Both CSF gram stain smears and CSF cultures were negative in aseptic variety. Unfortunately new diagnostics modalities such as PCR are not available in our hospital. PCR is helpful in the diagnosis of CNS infections including partially treated meningitis and is a golden standard for the diagnosis of viral meningitis. In a recent study the PCR; a sensitivity of 87% and a specificity of 100% were reported in children with meningococcal disease .[23,24] Neuro-imaging study (CT scan and MRI) are typically used to identify and monitor complications of meningitis, such as hydrocephalus, subdural effusion, empyema, and infarction and to exclude parenchymal abscess and ventriculitis.[25] Early identification of CNS complications and fast neurosurgical intervention as in case of subdural empyema or cerebral abscess improve the outcome. Broad spectrum antibiotics; is obligatory to prevent CNS complications. Antibiotic therapy used in our patients with bacterial meningitis followed international protocols. There has been a worldwide increase reported in infection with Penicillin and Cephalosporin resistant strains of S. pneumoniae, for example in Europe, South Africa, Asia and the United States of America.[26-28]

The American Academy of Pediatrics recommended combination therapy, initially with Vancomycin and either Cefotaxime or Ceftriaxone for all children 1 month of age or older with definitive or probable bacterial meningitis. Penicillin G, Ampicillin is preferred for group *B Streptococcal meningitis*. Ampicillin is recommended for *Listeria monocytogenes meningitis* for the children less than one month of age.

Steroids have anti-inflammatory effects and decrease the release of various cytokine. They inhibit the transcription of mRNA for TNF-a and IL-1, and the production of prostaglandins and PAF, reduce vasogenic cerebral oedema, and reduce the production of inducible nitric oxide synthase.[29,30]

The use of corticosteroids in bacterial meningitis has been debated for more than 40 years. Recent meta-analysis of steroid use in bacterial meningitis support the use of Dexamethasone at a dose of 0.4 mg/kg given every 12 hours for a total duration of two days proved to be safe and efficacious as the dose of 0.15mg/kg given every six hours for four days.[31]

CONCLUSION

Healthcare professionals should be aware that classical signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis. Proper use of appropriate antibiotics can treat the meningitis and decrease the complications of meningitis. The most appropriate management is a lumbar puncture and analyzing the cerebrospinal fluid to start the parenteral antibiotics. With positive results of CSF culture, specific antibiotic therapy can be narrowed to cover the specific pathogen identified. Failure of isolation of H. influenzae supports our national vaccination program.

ACKNOWLEDGMENTS

The authors would like to express their deepest gratitude to Prof. Mostafa BenHalim and to the Pediatric Department Team of Tripoli Medical Center.

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