Review Article

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Cerebrospinal Fluid Examination in Meningitis: Diagnostic Dilemmas

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Abstract

Cerebrospinal fluid examination is one of the most important investigation performed in the emergency department. It provides important diagnostic information but has a significant number of limitations also. Starting from the observation of color of CSF to latest invstigation like Polymerase Chain Reaction are useful in deciding the treatment. Properly interpreted tests can make cerebrospinal fluid a key tool in the diagnosis of a variety of diseases. Culture is the gold standard for determining the causative organism in meningitis. CSF findings are also useful in predicting the prognosis in acute bacterial meningitis

Keywords: Cerebrospinal Fluid; Lumbar Puncture; Meningitis.

Introduction

Acute Bacterial Meningitis (ABM) is themost common nervous system infection in children. The morbidity and mortality due to ABM in children is high when compared to other age groups. Another important factor determining the prognosis is early treatment; so early diagnosis and prompt treatment is crucial.

Cerebrospinal Fluid: "The liquid brain biopsy"

The most important tool in diagnosing meningitis is CSF examination. Children attending the pediatric department may already had taken oral or parenteral antibiotic, which may affect the CSF and confuse the physician. One can not repeat the procedure like routine blood or urine examination. Also there are many other factors which will affect CSF values.

Diagnostic dilemmas before lumbar puncture

Even though ABM is a common infection,under/ over diagnosis of this disease is not uncommon. It may be due to atypical signs in infant (unfortunately in infants, the infection is more common and serious) and altered clinical features due to prior antibiotic use. Other causes for false negative signs are given in Table 1.

Table 1: Causes of false negative neck sign

• In infants
• Prior antibiotic use
• Critically ill child
• Meningitis in a child with severe PEM
• Meningitis in severe immuno deficient conditions like HIV

On the other hand an anxious physician may over diagnosis it in any child with fever, headache and vomiting and may lead to unwanted and prolonged treatment. Sometimes clinician even more confused with false signs of meningeal irritation (Table 2).

Before performing lumbar puncture (LP) we have to stabilize the patient and look for any contraindications for doing LP. Contraindication

Table 2: Causes of false positive neck sign

Intracranial Causes	Extracranial Causes
Encephalitis	Meningism
Cerebral malaria	Upper lobe pneumonia
ICSOL-post fossa tumors	Tonsillitis
Brain abscess	Retropharyngeal abscess
Benign intracranial tension	Cervical vertebral problems
	Cervical lymphadenitis

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for doing LP is not common in children (Table 3). Fundus examination to rule out papilledema should be done. But absence of papilledema need not always rule out raised intracranial tension [1].

In uncomplicated meningitis where cerebral oedema is symmetrical, the chance for coning less unlike in a case of tumor or abscess where the pressure effect is unilateral and not uniform and chance for coning is high. In infants anterior fontanelle is open and chance of coning is rare. When papilledema is observed in a case of ABM, suspect venous sinus occlusion, subdural empyema, or brain abscess.

Table 3: Contraindication to lumbar puncture

1.	Obvious signs of increased ICT
2.	Clinically relevant cardiorespiratory compromise
3.	History or signs of bleeding disorder
4.	Infection at puncture site

In the following section we will discuss the common dilemmas in the CSF examination in a case of ABM in children.

CSF should be collected in 4 bottles-one each for biochemistry, cell count and Gram stain, culture test and for other tests (CRP, CSF Ag detection test, etc). In a well defined case of ABM, CSF is under high pressure, proteins will be high and sugar will be less than two third of the blood sugar. Gram stain(positive in 60-80% in untreated child) will help to identify the organism and culture will help to select the proper antibiotics.

Nowadays CSF CRP, rapid antigen detection tests, etc are available even in remote areas and many of these tests are useful in children previously treated with antibiotics. Even though all these facilities are available, rarely a practicing pediatrician may find it difficult to interpret a CSF result in his office practice.

Diagnostic dilemmas in CSF examination

CSF appearance may be turbid due to due to cells, bacteria, or blood. CSF will be turbid, when the WBC count is more than 200 per cmm or RBC count of more than 400 per cmm

Xanthochromic CSF: It will appear as early as 2-4 hrs.(oxyHb) or in a child with subarachnoid hemorrhage(bilirubin) by 12 hrs [2]. Xanthochromic CSF seen due to blood in the CSF, increased protein more than 150 mg%, hyperbilirubinemia of more than 15 mg% (in a newborn). Causes for xanthochromic CSF are given Table 4.

Table 4: Causes for xanthochromic CSF

1.	Subarachnoid hemorrhage(after 12 hrs).
2.	Blood in the CSF(traumatic LP with > 1Lakh RBC per cmm)
3.	Increased protein(> 150 mg%)
4.	Hyperbilirubinemia(> 15 mg%innewborn).
5.	In a child taking rifampicin

CSF Glucose: Normal CSF glucose is 40 – 80 mg and a ratio less than 0.5 abnormal. In a neonate CSF glucose 34-112 mg (ratio 0.7 to 0.9) and a ratio less than 0.6 is abnormal. Blood glucose should be estimated ideally 2-4 hrs prior to performing LP (3).

In severe hyperglycemia(if the child had received glucose containing fluids before LP or in DKA) the ratio is 0.4 and a ratio less than 0.3 abnormal.Very low CSF glucose is associated with high incidence of hearing defect and is a poor prognostic sign in ABM.

CSF glucose can be decreased in 3.5% of children with aseptic meningitis. Other conditions where one will get low CSF sugar is given in table 5.

Table 5: Conditions associated with low CSF sugar

1.	Mumps
2.	HSV infection
3.	Varicella-zoster
4.	Lymphocytic choreo meningitis
5.	Fungal meningitis
6.	Widespread neoplastic involvement of the meninges
7.	Subarachnoid hemorrhage

CSF Protein: Normally protein content in the CSF is less than 40 mg% and in neonate it may as high as 150 mg%. The adult range of 18 to 58 mg per dL (0.18 to 0.58 g per L) is reached between six and 12 months of age [3]. A protein level of above 150 mg per dL can cause xanthochromia. "Cob-web" appearance of CSF is due to high level of CSF protein ie. 1.5 gm/L. It may be normal in initial stages of ABM and misleading in traumatic tap. Protein may be high in Guillian- Barre syndrome, multiple sclerosis, in spinal block (TBM) and parameningeal infiltrations. In viral meningitis, CSF protein is less than 100mg/dl, almost never more than 250 mg%.

CSF cell count: In normal child the CSF cell count is less than 5 cells per cmm with no polymorph. In a newborn the normal cell count may be as high as 30 cells per cmm and upto 60% polymorphs. Presence of plasma cells and eosinophils in the CSF is always abnormal. Very low count indicate severe meningitis. Cell count tends to fall over time and

decreased if measured after 1 hour. So a physician doing a lumbar puncture should examine his patients's CSF without delay. After a generalized seizure, there is chance for CSF pleocytosis. But the rise in cell count is usually less than 80 cells per cmm. CSF pleocytosis may confuse a treating pediatrician, especially when he will do CSF study in a child with fever and seizure. Anyway one has to rule out CNS infection, before attributing CSF pleocytosis due to seizure. CSF lymphocytosis (of more than 50%) can occur in 13–32% of bacterial meningitis [4]. So if general condition of the patient is not improved in 24-48hrs of antibiotic treatment, repeat LP. If there is polymorph treat it as pyogenic meningitis. In 1-13% of TBM, predominant polymorph is seen. In viral meningitis predominant polymorphonuclear leucocytos is seen in 1/3 of children and usually gets converted to lymphocytosis in 24-48 hrs [5]. The CSF cell count in viral meningitis is seldom exceeds 1000 percmm. (except in mumps).

Gram stain: This is one of the most useful part of CSF examination, but unfortunately not performed routinely. We can identify the organism and can start appropriate antibiotic while awaiting for the culture and sensitivity test. The positivity is 60-80% in untreated bacterial meningitis [6]. Positivity is less in pretreated patients.

CSF Culture: Culture will be positive in CSF is up to 80% in good centers. Send blood also for culture. It will be positive in 60-80% in untreated children. Always send CSF for culture even when the fluid appears to be crystal clear and acellular. Similarly one can do CSF culture and sensitivity test in a case of traumatic LP (one useful test in a case of blood stained CSF).

Metabolic changes in CSF in bacterial meningitis: Various metabolic changes will occur in CSF in ABM (Table 6).

Table 6: Metabolic changes in CSF in ABM

Increased
CSF lactate
LDH
CRP
CPK
Aspartate transaminase
Vasopressin
Ferritin
Decreased
CSF pH

All these tests are not readily available or not reliable, but can be do in specific cases or in research institutions

Tests to differentiate septic from aseptic meningitis: Many tests are available, but none of them are uniformly reliable. Bacterial antigen tests are very useful. Latex agglutination test has a sensitivity 81% for detecting Hib, 50-70% for pneumococcal and 30-70% for N. meningitis. The specificity for these 3 antigens are about 90-96%. Antigen tests are useful when the child had received prior antibiotic treatment [6].

Detection of bacterial DNA by PCR is very sensitive, but is very costly and not freely available. Limulus lysate test (useful in gram negative infection, with a positive rate: 70- 90%) and CSF lactic acid (more than 35 mg% in bacterial meningitis with a predictive value of less than 30%) are rarely performed.

CSF CRP level: It is one of the test commonly performed nowadays. It is non-specific and is elevated in 95-100% of ABM. It elevated in 60% of non-bacterial meningitis also.CRP also elevated in inflammatory and necrotic conditions. A negative CRP excludes bacterial meningitis,while a positive test need not always indicate an infection. High CRP value both in blood and CSF got very high sensitivity and specificity.

Two other situations where CSF may confusing the pediatricians are 1) CSF changes in partially treated pyogenic meningitis and 2) Problem of traumatic tap in a suspected case of bacterial meningitis

1) CSF changes in partially treated pyogenic meningitis: The first changes that will happen after antibiotic use in a case of ABM is negative Gram stain and sterile CSF culture. These changes can happen with in 24 hrs of antibiotic treatment. CSF glucose reaches normal on the 3rd day in 80% of patients but protein remains elevated even after 10th day, in up to 40% of patients [7].

Prior antibiotic use does not affect total WBC count, CSF protein and CSF glucose. So even if the child had received antibiotic, all these investigations should be done. Same is almost true in a case of traumatic CSF. Oral antibiotics with poor blood brain penetration usually not affect the CSF results [8].

Prior antibiotic use decrease in the percentage of polymorph in CSF. In this situation bacterial antigen tests have certain advantages-Antigen tests do not depend up on viable organism in the CSF. So they may give positive results even when gram stain and culture are negative [9].

CSF may be normal in ABM (up to 6%) and in such cases, CSF becomes abnormal in 24 hours. So it is important to do repeat LP, if one strongly suspecting ABM clinically.

2) Problem of traumatic tap in a suspected case of bacterial meningitis: It is a known fact that holding the child in a perfect position is more difficult than inserting the LP needle. Even an experienced person sometimes find it difficult to get CSF sample without trauma. Correction in the form of subtracting 1 WBC for every 700 RBCs and subtracting 1 mg/dl from total protein for every 1000 RBCs are some common methods used [10]. Always remember that CSF glucose, Gram stain and culture are not altered by traumatic tap, provided contaminant is less than 2 lakhs RBC/ cmm. One may get red blood cells in CSF as in case of herpez simplex meningitis even without trauma.

When to do repeat LP?

In uncomplicated case of ABM there is no indication for repeat LP [11]. The various indications to repeat LP is given in Table 7.

Table 7: Indication for repeat LP

1.	Lack of clinical improvement in 24-48 hrs.
2.	Gram negative meningitis
3.	Beta lactam resistant organism
4.	Recurrent Meningitis
5.	Meningitis in a newborn

CSF findingsand prognosis: Various parameters in CSF will give an idea about the prognosis. It will give a rough idea about the overall outome to the treating physician. CSF factors associated with poor prognosis is given in Table 8 [12].

Table 8: CSF findings associated with poor outcome in ABM

High bacterial count in CSF
Very low or high CSF leucocyte count
High CSF protein level
Very low CSF sugar
Delay in CSF sterilization

Summary

Complete and careful CSF examination without delay is the rule. Sometimes CSF results may confuse the physician especially in partially treated case of meningitis.A repeat LP is rarely indicated and neuro imaging has limited value in uncomplicated meningitis.

References

1. Sencer W. Lumbar puncture in the presence of papilledema. J. Mt Sinai Hosp. 1956;23: 808–10.
2. Fishman RA. Cerebrospinal fluid in diseases of the nervous system. 2d ed. Philadelphia: Saunders, 1992.
3. Conly JM, Ronald AR. Cerebrospinal fluid as a diagnostic body fluid. Am J Med 1983;75(1B):102-8.
4. Arevalo CE, Barnes PF, Duda M, Leedom JM. Cerebrospinal fluid cell counts and chemistries in bacterial meningitis. South Med J 1989;82:1122-7.
5. BonsuBK,HarperMB. Differentiating acute bacterial meningitis from acute viral meningitis among children with cerebrospinal fluid pleocytosis: A multivariable regression model. Pediatr Infect Dis J. 2004;23:511-17.
6. Zunt JR, Marra CM. Cerebrospinal fluid testing for the diagnosis of central nervous system infection. Neurol Clin 1999;17:675-89.
7. Dean A. S, Mark M. R, Demitri A. F. Cerebrospinal Fluid Analysis Am Fam Physician 2003;68:1103-8.
8. Durand ML, Calderwood SB, Weber DJ et al. Acute bacterial meningitis: A review of 493 episodes. N. Engl. J. Med. 1993;328:21–8.
9. Feign and Cherry. Text book of Pediatric Infectious Diseases, 6thEdn Saunders, 2009.pp.481-499.
10. Buruma OJ, Janson HL, Den Bergh FA, Bots GT. Blood stained cerebrospinal fluid: Traumatic puncture or haemorrhage? J. Neurol. Neurosurg. Psych. 1981;44:144–7.
11. Addy DP. When not to do a lumbar puncture.Arch. Dis. Child 1987;62:873–5.
12. Kaplan SL. Clinical presentations, diagnosis, and prognostic factors of bacterial meningitis. Infect Dis Clin North Am 1999;13:579-94.