Conventional Cerebrospinal Fluid Investigations in the Diagnosis of Meningitis

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Summary

A 3-year prospective study is reported of the value of conventional cerebrospinal fluid (CSF) investigations in the diagnosis of meningitis. Of 739 cases of aseptic meningitis 74 (10 per cent) had a total CSF cell count $>500 \times 10^6$/l, a + or more of turbidity present on Pandy's test, a CSF total protein >0.8 Gl, or a CSF glucose <2.2 mmol/l and would have been inappropriately treated for bacterial meningitis using these criteria alone as would 18 (17 per cent) of 108 confirmed viral meningitis cases. Conversely, 10 (7 per cent) of 140 *N. meningitidis* cases, 3 (6 per cent) of 47 *H. influenzae* cases, and none of 34 *S. pneumoniae* cases had a total CSF cell count $<500 \times 10^6$/l, globulin absent or a trace on Pandy's test, a CSF total protein <0.8 G/l, a CSF glucose >2.2 mmol/l and no organisms visible on microscopy. In a tuberculosis meningitis group of 62 children, 55 (89 per cent) had either a + or more of turbidity on Pandy's test, a CSF protein >0.8 G/l, a CSF glucose <2.2 mmol/l or acid fast bacilli visible on microscopy. Pandy's test is a simple, but valuable aid to the selection of cases requiring the institution of antibiotic therapy.

The accurate early diagnosis of meningitis and the institution of appropriate therapy when necessary is a matter of great urgency. Despite the availability of a number of newer specific and non-specific aids to the rapid differential diagnosis of meningitis—countercurrent immunoelectrophoresis,[1] latex agglutination for a variety of antigens,[2,3] limulus lysate assay,[4] cerebrospinal fluid (CSF) lactate,[5] and lactate dehydrogenase determination[6]—conventional CSF investigations such as cell count, Gram's stain and microscopy, and Pandy's test for excess globulin still play an important role in initial decision making.

In the world as a whole today the majority of cases of meningitis in children will be diagnosed at small district hospitals or peripheral clinics, and it is at this level that immediate decisions must be made as to the likely diagnosis and the necessity for starting antibiotic therapy. Frequently, these decisions must be based upon conventional CSF investigations in conjunction with the patient's clinical condition. In this report we describe our experience with conventional CSF investigations in childhood meningitis as seen during a 3-year prospective study of all abnormal CSF specimens from pediatric patients submitted to the Department of Medical Microbiology at our hospital.

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Patients and Methods

Tygerberg Hospital is the teaching hospital of the University of Stellenbosch and is situated approximately 30 km from the centre of the City of Cape Town. Intermittent epidemics of meningococcal disease[7] and viral meningitis[8] occur locally, and tuberculosis is still prevalent[9] so that the accurate diagnosis of meningitis is an ever present problem. The period covered by this study was from July 1981 to June 1984, an interepidemic period in respect of meningococcal disease. Epidemiological details, criteria for selection of patients, and their inclusion in different groups have been presented previously.[10]

During the 3-year study period 1223 children <13 years of age were seen in whom the diagnosis of meningitis was made. In 739 cases (60 per cent) a diagnosis of aseptic meningitis was made and a viral aetiology confirmed in 108 of these cases by culture of a virus from the CSF. Septic meningitis cause unknown was diagnosed in 141 cases (12 per cent). In 140 cases (12 per cent) *N. meningitidis* was the causative organism, in 47 cases (4 per cent) *H. influenzae*, and in 34 cases (3 per cent) *S. pneumoniae*. Tuberculous meningitis (TBM) was diagnosed in 62 children (5 per cent) while in the remaining 60 children (5 per

TABLE 1
Conventional cerebrospinal fluid investigations in the diagnosis of meningitis

Investigation	Aseptic meningitis (%)	Viral meningitis (%)	*N. meningitidis* (%)	*H. influenzae* (%)	*S. pneumoniae* (%)	Other organisms (%)	TBM (%)	Neonatal bacterial meningitis (%)
Cell count $>500 \times 10^6$/l	50/739 (7)	13/108 (12)	110/136 (81)	34/46 (74)	23/33 (70)	19/47 (40)	2/62 (3)	17/25 (68)
Pandy's test + or more	17/699 (2)	6/108 (6)	102/130 (78)	35/45 (78)	29/33 (88)	12/47 (26)	44/61 (72)	20/21 (95)
Protein >0.8 G/l	14/699 (2)	7/108 (1)	106/127 (83)	36/43 (84)	30/31 (97)	33/42 (79)	45/59 (76)	16/16 (100)
Glucose <2.2 mmol/l	10/736 (1)	1/108 (1)	103/135 (76)	33/45 (73)	24/32 (75)	27/48 (56)	39/61 (64)	20/28 (71)
CSF blood glucose ratio <0.4	14/461 (3)	6/ 80 (7)	82/104 (79)	23/31 (74)	20/22 (91)	10/19 (53)	30/38 (79)	11/15 (73)
Organisms seen on microscopy	—	—	91/140 (65)	22/47 (47)	29/34 (85)	29/60 (48)	5/62 (8)	22/33 (67)

TBM = Tuberculous meningitis.

cent) a variety of Gram-negative and Gram-positive organisms were identified mainly in infants <3 months of age.

Routine CSF examination was carried out in the Department of Medical Microbiology and Chemical Pathology upon arrival of the specimens in the laboratory. CSF cell counts were done in a Fuchs–Rosenthal counting chamber. Cells were not routinely counted beyond 500×10^6/l. Counts greater than this were reported as predominantly lymphocytes or polymorpho-nuclear leucocytes. Total CSF protein was determined by a sulphosalicylic acid method, while glucose levels in both blood and CSF were determined by a glucose oxidase method (Beckman glucose analyser®). CSF glucose levels were not determined below 1.0 mmol/l and a value of 0.9 mmol/l was used for the determination of the CSF blood glucose ratio for those values reported as <1.0 mmol/l. Pandy's test for excess globulin was scored as absent, trace, +, + +, + + +.[11]

Results

The results of individual conventional CSF investigations in the different groups of patients are summarised in Table 1.

In 16 of the 50 aseptic meningitis cases with a CSF cell count $>500 \times 10^6$/l polymorphonuclear leucocytes predominated. Of the major bacterial pathogens (*N. meningitidis*, *H. influenzae*, and *S. pneumoniae*), 48 cases (22 per cent) had a cell count $<500 \times 10^6$/l and, of these, 28 had a predominance of lymphocytes. In the TBM group 53 cases (85 per cent) had a predominance of lymphocytes.

In the 'septic meningitis cause unknown' group (which is not included in Table 1) 63 children (45 per cent) had a CSF cell count $<500 \times 10^6$/l. Of the 126 children in this group in whom total CSF protein was determined, 81 (64 per cent) had a value >0.8 G/l while Pandy's test was carried out in 132 cases and a + or more of globulin found in 60 cases (45 per cent). CSF glucose was determined in 137 cases and 54 (39 per cent) had a CSF glucose value of <2.2 mmol/l while only 28 of 87 cases (32 per cent) had a CSF/blood glucose ratio of <0.4.

Blood culture

Blood culture was positive in 39 of 107 cases due to *N. meningitidis* (36 per cent), in 31 of 38 cases due to *H. influenzae* (82 per cent), 18 of 23 cases due to *S. pneumoniae* (78 per cent), and in 26 of 39 cases due to 'other organisms' (67 per cent). In four cases due to *N. meningitidis*, seven cases due to *H. influenzae*, and in four due to *S. pneumoniae* the CSF culture was negative and the blood culture positive. In the 'other organisms' group 10 organisms were identified solely by blood culture and nine of these cases were due to *Staphylococcus aureus*.

Conventional CSF diagnostic criteria combined

The sensitivity of individual CSF criteria in detecting a possible bacterial or tuberculous infection varied from as low as 8 per cent for the detection of acid fast bacilli in the CSF in cases of TBM to 97 per cent in respect of a CSF total protein >0.8 G/l in *S. pneumoniae* cases. In practice, however, criteria will not be assessed individually, but as a group.

Even under relatively primitive conditions it should be possible for the physician to undertake a CSF cell count, to do Pandy's test for excess globulin, and to examine the CSF microscopically for bacterial organisms following Gram's stain. If a total CSF cell count of $>500 \times 10^6$/l and a Pandy's test score of a + or more are accepted as indicating a possible bacterial infection then 64 cases of aseptic meningitis (9 per cent) had a feature of bacterial infection. Of the 108 confirmed viral meningitis cases 18 (17 per cent) had either a + of globulin or more in the CSF or $> 500 \times 10^6$/l cells present.

Conversely, amongst the confirmed bacterial meningitis cases 11 *N. meningitidis* cases (8 per cent), four *H. influenzae* cases (8 per cent), one *S. pneumoniae* case (3 per cent), and eight cases due to 'other organisms' (13 per cent) had either no globulin present with Pandy's test or only a trace, $< 500 \times 10^6$/l cells in the CSF and no bacterial organisms seen on microscopy following Gram's stain.

If the total CSF protein and CSF glucose values are now also brought into consideration, and a CSF total protein value of > 0.8 G/l and a CSF glucose value of < 2.2 mmol/l accepted as indicating possible bacterial infection then an additional 10 aseptic meningitis cases had one or more features of bacterial infection, a total of 74 cases (10 per cent). No further false positive cases were detected in the confirmed viral meningitis cases. With the additional aid of the CSF total protein and CSF glucose values one further *N. meningitidis* case, one further *H. influenzae* case, one further *S. pneumoniae* case , and one further case due to 'other organisms' would be detected. Thus, overall conventional CSF investigations had a sensitivity of 93 per cent in detecting possible bacterial infection and a specificity of 90 per cent in differentiating bacterial from aseptic meningitis. If the confirmed viral meningitis cases are considered separately then specificity falls to 83 per cent.

Discussion

It should be the aim of the physician undertaking lumbar puncture in a child with symptoms and signs suggestive of meningitis to initiate appropriate therapy at the earliest opportunity in all possible cases of bacterial or tuberculous meningitis. Conventional CSF investigations alone will, however, neither identify all cases of bacterial or tuberculous meningitis, nor always differentiate aseptic, or viral meningitis from bacterial, or tuberculous meningitis. Despite this clinicians in many parts of the world must make important therapeutic decisions based on the results of these investigations in conjunction with the patient's clinical condition.

Although the sensitivity and specificity of individual conventional CSF investigations in the detection of bacterial or tuberculous meningitis is well established, they are seldom considered as a group as they would be in clinical practice. Our results indicate that relying on conventional CSF investigations as a group appropriate treatment would be initiated in 93 per cent of bacterial meningitis cases, while 10 per cent of aseptic meningitis cases (but 17 per cent of confirmed viral meningitis cases) would be inappropriately treated.

In doubtful cases more sophisticated specific techniques such as countercurrent immunoelectrophoresis and latex agglutination may be applied. Even these investigations may however at times give false negative results so that the clinician should at all times be guided by the patient's clinical condition, and when in doubt treat for bacterial (or tuberculous meningitis) and reconsider the evidence once the patient's condition has stabilized.

Pandy's test has been described as 'obsolete' by some[12] while others regard it as 'still useful'.[13] We are of the latter opinion. Although its interpretation is subjective it is inexpensive, easy to perform at the bedside or in the emergency room and the finding of a + or more of turbidity should be a strong indication to the physician that the case is probably not one of aseptic or viral meningitis. In our patients a + or more of globulin was present in the CSF in 80 per cent of children presenting with meningitis due to one of the major pathogens (*N. meningitidis*, *H. influenzae*, or *S. pneumoniae*) and 72 per cent of TBM cases. Two per cent of cases in the aseptic meningitis group as a whole and 6 per cent of the confirmed viral meningitis cases had a + or more of globulin present in the CSF. Thus, the finding of a + or more of globulin in the CSF is an indication that antibiotic therapy may be required.

Finally, when no organisms are identified on Gram's stain of the CSF and the CSF is clear with a cell count of $< 500 \times 10^6$/l, but 'septic' features are found such as a + or more of globulin on Pandy's test or a total CSF protein > 0.8 G/l or a glucose of < 2.2 mmol/l consideration must be given to the possible presence of TBM. This is particularly true in the developing world where tuberculosis is prevalent, but care is also needed in developed countries where the diagnosis may not be initially considered because of its rarity.[14]

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