Value of Second Lumbar Puncture in Confirming a Diagnosis of Aseptic Meningitis

A Prospective Study

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• **In patients with viral meningitis, polymorphonuclear leukocytes sometimes predominate in the CSF on initial examination. In a prospective analysis of this phenomenon, 16 consecutive patients with viral meningitis were followed up with serial CSF studies. The percentage of polymorphonuclear leukocytes showed a significant fall between initial and second examinations (41.75 ± 27.0 to 8.6 ± 8.78 [mean ± 2 SD], $P < .001$), while total WBC counts and the protein and sugar content levels remained unchanged. Based mainly upon this "polymorph shift," antibiotic therapy was correctly withheld from 100% of patients reexamined. On subsequent examinations, the percentage of polymorphonuclear cells remained low. All patients recovered completely without any specific treatment. In otherwise healthy subjects with the aseptic meningitis syndrome, antibiotic therapy can be withheld even when polymorphonuclear cells predominate on initial CSF examination. If suspicion arises regarding the diagnosis, another examination will demonstrate a significant fall in polymorphonuclear cells if the initial impression was correct.**

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The diagnosis of viral meningitis is usually made when mononuclear pleocytosis in the CSF accompanies a febrile illness with signs of meningeal irritation. However, when polymorphonuclear cells predominate on initial CSF examination, differentiation from incipient or partially treated bacterial meningitis is vital. In 1973, Feigin and Shackelford[1] pointed out that while standard textbook references state that this early polymorphonuclear predominance is only transient, no previous studies had clarified this pheonomenon, and no specific guidelines were available for the management of this situation. Based on a retrospective review of selected pediatric patients with aseptic meningitis, they suggested that a shift towards mononuclear predominance might be demonstrated in 94% of cases if a second lumbar puncture were performed between 12 and 72 hours after the initial examination.

We report what we believe is the first prospective analysis of this phenomenon by serial CSF examinations in a group of patients with viral meningitis.

PATIENTS AND METHODS

Sixteen patients seen consecutively in a three-month period with the clinical syndrome of viral meningitis (benign febrile illness of acute onset, signs of meningeal irritation, and CSF pleocytosis) were included in the study. None had received prior antibiotic therapy, and all recovered completely with no specific treatment.

Cerebrospinal fluid was obtained by atraumatic lumbar puncture on admission and was tested for total and differential cell counts, protein and sugar content, Gram stain and acid-fast bacilli cultures. No viral studies were performed.

Symptomatic treatment with bed rest, analgesics, antipyretics, and fluids was provided. Lumbar puncture was repeated within 18 to 36 hours in all patients whose condition did not show obvious clinical improvement (ten patients). In this group, antibiotic therapy was still withheld on the basis of a shift to mononuclear predominance (see "Results"). Another CSF examination was performed on 11 patients just prior to discharge (five to 12 days); all patients were asymptomatic at that time. Twelve patients were seen two to six weeks later, and CSF examinations were performed on seven of these. Statistical analysis for significance employed the Student *t* test.

RESULTS

Included in the study were ten female and six male patients with a mean age of 23 ± 8.1 (1 SD). Clinical features included severe generalized headache (16 patients), fever (16 patients), vomiting (13 patients), signs of meningeal irritation (16 patients), preceding upper respiratory tract infection (5 patients), parotid swelling (1 patient), and erythematous facial rash (1 patient). No patient had an altered sensorium, focal neurological deficit, or relevant ophthalmoscopic findings. All patients were children or young adults with no other major concomitant illnesses.

The results of serial CSF examination are displayed in the Table. Total

Serial CSF Findings in Viral Meningitis

Laboratory Studies	Normal Values	Values at Initial and Subsequent Examinations*			
		Admission (n = 16)	18-48 hr (n = 10)	5-12 Days (n = 11)	2-6 wk (n = 7)
WBCs/cu mm	0-5	201.00 ± 178.50	210.00 ± 165.3	92.00 ± 73.20	2.70 ± 0.70
Polymorphonuclear cells, % of total	0-1	41.75 ± 29.00	8.60 ± 8.78	9.00 ± 22.29	0.00
Protein concentration, mg/dL	14-45	48.38 ± 13.60	38.50 ± 18.24	34.50 ± 12.22	26.67 ± 4.99
Sugar level,† mg/dL	44-100	66.22 ± 8.61	73.20 ± 11.58	60.81 ± 10.81	68.67 ± 7.63

*Values in mean ± 1 SD.
†All patients had blood sugar values within normal limits.

cell counts were initially elevated and showed no significant fall until follow-up at two to six weeks. The percentage of polymorphonuclear cells showed a significant fall on second examination, 18 to 48 hours later ($P = .001$), and remained low at five to 12 days after the initial examination. At two to six weeks, no polymorphonuclear cells were present in any specimen.

Cerebrospinal fluid sugar values showed no significant deviation outside the normal range. No patient had elevated blood sugar values during the illness. Cerebrospinal fluid protein values tended to be high-normal to high and showed a significant fall only on subsequent examinations at two to six weeks ($P = .01$).

All patients were completely well at subsequent examinations.

COMMENT

Early studies of aseptic meningitis[2,3] revealed that in as many as two thirds of the patients, the number of polymorphonuclear leukocytes in the CSF might exceed the number of mononuclear leukocytes in the initial phase of the illness. In a study of St Louis encephalitis with features of meningitis, a similar polymorphonuclear predominance was present early in the disease process, and a shift to mononuclear predominance was noted after the sixth day.[4] However, early repeated CSF examinations were not described in any of these studies, and the correct approach to this clinical quandary remained unclear. Feigin and Shackelford analyzed this question in their retrospective review of five years' records.[1] Of 590 cases with meningitis reviewed, in only 48 did the patients not receive major antibiotic therapy and so become eligible for evaluation. A second lumbar puncture had been performed in these patients in a period ranging from six to 72 hours later. No significant changes in total cell count or protein and sugar content of the CSF were seen during the early phase of the illness. The only significant finding was a shift from polymorphonuclear cells to mononuclear cells, which occurred in 87% of patients within eight hours, and in 94% at 12 hours.

In the present study, a prospective evaluation of the clinical value of this "polymorph shift" has been performed. Sixteen consecutive previously untreated patients with the clinical syndrome of viral meningitis were managed with symptomatic measures only, although polymorphonuclear cells predominated in the majority. All patients not showing obvious clinical improvement underwent a second lumbar puncture within 18 to 48 hours. Further antibiotic therapy was correctly withheld in all of these patients solely on the basis of the shift to mononuclear cell predominance ($P < .001$). Total cell counts and sugar and protein content showed no significant changes throughout the acute phase of the illness. Subsequent CSF examinations showed that the fall in percentage of polymorphonuclear cells persisted.

We have, therefore, confirmed the value of the polymorph shift in a prospective manner. Antibiotic therapy can be withheld from otherwise healthy children and young adults with the syndrome of viral meningitis even when polymorphonuclear cells predominate in the CSF. If rapid clinical improvement does not occur, or if other suspicions arise regarding the diagnosis, another lumbar puncture performed at 18 to 48 hours after the first will demonstrate a shift to mononuclear cells in up to 100% of patients, if the initial impression was correct.

It must be cautioned, however, that our patients had not received antibiotic therapy prior to admission. Partially treated pyogenic meningitis, although it can usually be distinguished from aseptic meningitis,[5] may require a different approach.[6]

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