

The Clinical Value of Commonly Used Spinal Fluid Diagnostic Studies in the Evaluation of Patients with Suspected Multiple Sclerosis

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Abstract

Objective: This study was designed to evaluate the diagnostic value of cerebrospinal fluid (CSF) oligoclonal banding and immunoglobulin G (IgG) production in the diagnosis of multiple sclerosis.

Study Design: Spinal fluid changes in patients with suspected multiple sclerosis were compared with clinical data to determine sensitivity, specificity, and predictive value of the procedures. The results were evaluated in terms of cost compared with clinical utility in the managed care environment.

Patients and Methods: The CSF oligoclonal banding and CSF IgG index were measured in 50 patients being evaluated for possible multiple sclerosis at a multispecialty group practice clinic.

Results: CSF oligoclonal banding had a sensitivity of 75% and a specificity of 92% in the diagnosis of multiple sclerosis. The CSF IgG index had a sensitivity of 75% and a specificity of 95% in the diagnosis of multiple sclerosis.

Conclusions: Although neither test would identify 100% of patients with multiple sclerosis, the combination of CSF oligoclonal banding and an elevated CSF IgG index correctly identified most patients with multiple sclerosis and excluded all patients without the disease in this patient population.

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Multiple sclerosis is a disease of unknown etiology that is characterized by inflammatory plaques scattered throughout the white matter of the nervous system. It is a common neurologic disease with serious prognostic implications. The diag-

nosis of multiple sclerosis is made based on clinical evidence, with laboratory studies providing confirmatory information.¹ Spinal fluid changes have been important in the past but have assumed a secondary role with the advent of magnetic resonance imaging (MRI), a noninvasive technique that can demonstrate plaques. MRI is a valuable tool for diagnosis; however, despite its high sensitivity, it has low specificity.²

With managed care assuming an ever-increasing role in medicine, it has become very important to look at each diagnostic test in terms of cost versus clinical utility. Physicians often make such judgments intuitively (eg, "worthless test") and adapt their practice to their own clinical experience. However, the move to capitation will require that physicians evaluate laboratory studies in a more systematic manner and decide exactly how useful a procedure is in making the diagnosis or in following the clinical course of the patient.³

Currently, most laboratories use either oligoclonal banding or some measure of immunoglobulin G (IgG) production in the spinal fluid to aid in the confirmation or exclusion of a diagnosis of multiple sclerosis. Cerebrospinal fluid (CSF) analysis is most useful in patients with atypical presentation; this is especially true in patients older than 50 years when MRI studies are most problematic because of changes associated with aging.¹ Although these procedures are adopted based on the results of studies at major medical centers involving large numbers of patients, considerable variation in methods can exist. Each laboratory should compare its own diagnostic results against published standards.

The purpose of the present study was to examine the clinical utility of these two procedures (CSF oligoclonal banding and IgG production) in the diagnosis of multiple sclerosis in patients seen in a multispecialty group practice clinic. These data will allow conclusions to be drawn regarding the sensitivity, specificity, and predictive value of these studies in "real-world" conditions.

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... METHODS ...

We studied 50 consecutive patients who had a lumbar puncture for evaluation of possible multiple sclerosis at our institution between August 14, 1990, and August 23, 1993. The patients ranged in age from 15 to 77 years, with a mean and median age of 44 years. There were 30 women and 20 men in the group.

Oligoclonal banding was performed by moving boundary electrophoresis on an agarose gel strip. Discrete bands were visually examined, and comparisons were made between serum and spinal fluid proteins separated in the medium.

The IgG index was calculated by measuring IgG in serum and spinal fluid (using rate nephelometry; Beckman Instruments, Brea, CA) and albumin in the serum and spinal fluid (using the Beckman CX7 automated chemistry analyzer; Beckman Instruments). The following ratio was then constructed:

$$\text{IgG index} = \frac{\text{CSF IgG/serum IgG}}{\text{CSF albumin/serum albumin}}$$

Beckman controls and calibrators were used on both instruments, and all controls were in accordance with manufacturer specifications.

Patients were divided into four classes after a chart review by a neurologist (A.B.F.) who was blinded

to the result of spinal fluid analysis but was aware of other diagnostic studies, including MRIs of the brain done at our institution or elsewhere before referral. Because these patients were evaluated by different members of the Department of Neurology, specific quantitative criteria were not used in each case. The reviewing neurologist made his judgment based on clinical details noted in the record. On the basis of this review, patients were classified as having definite multiple sclerosis (I), probable multiple sclerosis (II), possible multiple sclerosis (III), and not multiple sclerosis (IV). For purposes of statistical calculations, patients in Class I and Class II were considered to have multiple sclerosis, and patients in Class III and Class IV were considered not to have multiple sclerosis.

... RESULTS ...

Oligoclonal banding was positive in 9 of the 12 patients with multiple sclerosis and in 3 of the 38 patients without multiple sclerosis. This test had a sensitivity of 75% and a specificity of 92%. It had a positive predictive value of 75% and a negative predictive value of 92%.

An elevated IgG index was noted in 9 of the 12 patients with multiple sclerosis and in 2 of the 38 cases without multiple sclerosis. The IgG index had a sensitivity of 75% and a specificity of 95%. This test had a positive predictive value of 82% and a negative predictive value of 92%.

Both oligoclonal banding and the IgG index correctly identified 9 of the 12 patients with multiple sclerosis. All nine were considered abnormal by both procedures. The absence of oligoclonal banding correctly identified 35 of the 38 patients without multiple sclerosis. A normal IgG index correctly identified 36 of the 38 patients without multiple sclerosis. However, the misidentified patients (ie, false positives) were not the same. Thus, although both procedures were equally useful at identifying patients with multiple sclerosis, they did confuse three patients who did not have the disease. However, it should be noted that none of these "false positives" were considered abnormal by both procedures.

... DISCUSSION ...

This study found two commonly used laboratory procedures to be equally effective in the diagnosis and exclusion of multiple sclerosis in clinical practice in a multispecialty group clinic. Both procedures were capable of identifying patients with multiple

Table. Cost Comparisons for Neurologic Evaluation with and without Cerebrospinal Fluid Analysis

CPT Code	Description	MAC (\$)
With CSF Analysis		
99244	Neurology consultation	127.19
70551	MRI without contrast	440.02
62270	Lumbar puncture	61.63
82724	CSF IgG index	12.85
83916	CSF oligoclonal banding	27.79
Total		669.48
Without CSF Analysis		
99244	Neurology consultation	127.19
70551	MRI without contrast	440.02
Total		567.21

CPT = Current Procedural Terminology; MAC = Medicare allowable charges; MRI = magnetic resonance imaging; CSF = cerebrospinal fluid; IgG = immunoglobulin G.

sclerosis and excluding patients without multiple sclerosis, with the results similar to national published figures. Oligoclonal banding had a sensitivity of 75% and a specificity of 92%; it had a positive predictive value of 75% and a negative predictive value of 92%. Calculation of the IgG index had a sensitivity of 75% and a specificity of 95%. The test had a positive predictive value of 82% and a negative predictive value of 92%. None of the 38 patients without multiple sclerosis had both oligoclonal banding and an elevated IgG index. Thus, both procedures were very similar in sensitivity, specificity, and predictive value. Although neither test would identify 100% of patients with multiple sclerosis, the combination of oligoclonal banding and an elevated IgG index correctly identified most patients with multiple sclerosis and excluded all patients without multiple sclerosis.

For comparative purposes, we looked at the results of MRI studies in these same groups of patients who were evaluated at our institution. We found that the MRI had a sensitivity of 89% and a specificity of 94%. In general, improved MRI methods and more experienced neuroradiologists have led to improved sensitivity and specificity with neuroimaging.

Our current recommendation for evaluation of a patient with suspected multiple sclerosis is for an MRI after a careful neurologic examination. This procedure will confirm or exclude the diagnosis in the vast majority of patients. If a diagnosis can be made with these findings, CSF analysis is not indicated. Oligoclonal banding and IgG index studies of the spinal fluid should be reserved for those patients in whom the diagnosis is uncertain because of equivocal or ambiguous findings. The table details the cost comparison for evaluation with and without CSF analysis using Medicare allowable charges. Adding the CSF analysis, including the cost of lumbar puncture by the neurologist, will increase the cost of the work-up by approxi-

mately 18%. This analysis will be necessary, however, in only a minority of patients seen at a tertiary care center.

From a managed care standpoint, it is reasonable to question whether both spinal fluid tests are needed in the evaluation of patients with suspected multiple sclerosis. The diagnosis of multiple sclerosis is often made on the basis of an abnormal MRI in the appropriate clinical setting in patients who have never had a lumbar puncture. Thus, the value of CSF analysis is not in the usual or typical patient being evaluated for multiple sclerosis but in the more difficult clinical situation where both diagnosis and exclusion are equally important.⁴ Here, utilization of both procedures provides useful information to the clinician responsible for patient care.

In summary, our study showed that oligoclonal banding and IgG index of the spinal fluid are useful and complementary diagnostic procedures in the clinical diagnosis of multiple sclerosis in a multispecialty group practice setting.

... REFERENCES ...

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