Evaluation of the Use of Oligoclonal Bands in the Diagnosis of Multiple Sclerosis at Moffitt Hospital

Introduction

Multiple sclerosis is an inflammatory disease of the central nervous system characterized by primary destruction of myelin. Several etiologies, including autoimmunity and viruses, have been suggested (1), but the cause of this disorder still remains unknown. The diagnosis is primarily based on the neurologic history, findings on neurologic examination and, to a lesser extent, results of special examinations, such as laboratory tests (2). The most commonly utilized of these tests are detection of CSF oligoclonal bands and determination of the CSF IgG index (the ratio of CSF IgG to CSF albumin/the ratio of serum IgG to serum albumin) (2). Approximately 90% of patients with clinically definitive multiple sclerosis and 30-40% of those with possible multiple sclerosis have abnormal (two or more bands in the CSF not present in the serum) (3) oligoclonal bands (2). These seem to correlate with the number of plasma cells in multiple sclerosis plaques (4). The IgG index is reported to be elevated in 80-90% of patients with definitive multiple sclerosis (5). The IgG index is a standardized procedure while oligoclonal band interpretation is often confusing with dispute between independent observers. This survey was performed to determine whether evaluation of oligoclonal bands in the CSF yielded any additional information in patients with multiple sclerosis, information that could have or did aid in their diagnosis.
Although patient data for 1989 cannot be scanned by diagnosis/laboratory test using the UC computer system, data from 1986-7 is available. Reports come only from inpatients; outpatients are not included in the database. Patients who met one of the four following criteria were selected for manual review: (1) Patients with a diagnosis of multiple sclerosis, (2) Patients with a diagnosis of demyelinating disorders, (3) Patients who had the oligoclonal band test, (4) Patients who had a CSF IgG/albumin index performed.

Thirty-eight patients had oligoclonal band electrophoresis analysis without evaluation of the IgG/albumin index, two of which were positive. These carried the diagnosis of paralysis agitans (Parkinson's Disease) and hemiplegia NOS. None of these patients carried a diagnosis of multiple sclerosis/demyelinating disease.

Thirty-eight patients had IgG/albumin index evaluation without oligoclonal band analysis. Eleven of these were read as positive (IgG/albumin ratio > .60. None of these patients carried a diagnosis of multiple sclerosis/demyelinating disease. Diagnoses of the patients with positive indices included Hodgkin's Disease, pseudotumor cerebri, viral meningitis, encephalopathy NOS, progressive multifocal leukoencephalopathy, convulsions NOS, cerebral embolism and cerebellar ataxia.

There were a total of 149 patients who had both IgG/albumin index and oligoclonal banding. Results:

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<th>Oligo +</th>
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<tbody>
<tr>
<td>IgG index +</td>
<td>11</td>
<td>29</td>
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<td>IgG index -</td>
<td>10</td>
<td>99</td>
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Of the ten patients in which the oligoclonal banding was positive and the IgG/albumin index was negative, no cases of multiple sclerosis or demyelinating diseases were present. Diagnoses included chronic meningitis, lymphoma, acute infectious polynuertis, cryptococcal meningitis, cerebrovascular disease, toxic encephalopathy, hemiplegia NOS, and acute myelogenous leukemia.
Of the twenty-nine patients with a positive IgG/albumin index and negative oligoclonal banding, two patients received a diagnosis of multiple sclerosis and six were described as having clinical features which may be consequences of multiple sclerosis. Other diagnoses included epilepsy, acute infective polyneuritis, Werdnig-Hoffman Disease (Infantile Muscular Atrophy), coma and stupor, Behcet's Syndrome (vasculitis), encephalitis NOS, encephalopathy NOS, cervical spondylitis with myelopathy, systemic lupus erythematosis, spinal cord disease NOS, meningitis NOS, giardiasis, cerebral arteritis, cerebral artery occlusion, myesthenia gravis, viral encephalitis and subarachnoid hemorrhage.

Of the eleven patients that had both positive oligoclonal banding and IgG/albumin index, only one carried a diagnosis of multiple sclerosis and one had clinical features possibly compatible with multiple sclerosis. Other diagnoses included toxic encephalopathy, meningitis NOS, acute myelogenous leukemia, amnestic syndrome with psychosis, acute polio, cerebral arteritis, epilepsy, systemic lupus erythematosis and viral infection NOS.

Of the 99 patients with negative IgG/albumin index and negative oligoclonal banding, two carried a diagnosis of multiple sclerosis and three of CNS demyelination.

1989

Oligoclonal bands and IgG/albumin indices were reviewed manually over an eleven month period (1/89-11/89). Both outpatients and inpatients were included. Only patients with both oligoclonal banding and IgG/albumin index were included. A total of 85 patients were reviewed. Results:

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<tr>
<td>IgG index +</td>
<td>7</td>
<td>20</td>
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<td>IgG index -</td>
<td>5</td>
<td>53</td>
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Of the five patients in whom the oligoclonal band test was positive and the IgG/albumin index was negative, only one was given a diagnosis of multiple sclerosis. It should be noted, however, that the IgG index of this patient was .58 (reference range 0.29-0.59). Furthermore, review of the agarose elecrophoresis results revealed that at the time of testing, there was considerable disagreement as to whether or not the specimen should be reported as positive. Depending on who reviewed the results, this specimen might well have been reported as negative or "one band". In the remaining four patients, the diagnoses were: (1) Questionable cyclosporine neurotoxicity, (2) Progressive spastic quadriplegia, (3) Hepatic failure and encephalopathy, (4) Mixed Seizure Disorder.

Of the twenty patients in whom the IgG/albumin index was positive and the oligoclonal band test was negative, approximately five were described as having clinical features that could have been compatible with the consequences of multiple sclerosis, but no diagnoses of multiple sclerosis were made. In the other patients, diagnoses included CNS vasculopathy and seizure disorder, left basal ganglia infarct, "progressive encephalopathy", pituitary abscess, mixed seizure disorder, HIV encephalopathy, chronic viral meningitis, "probable ischemic dementia", lupus cerebritis, Gullian-Barre Syndrome and brainstem glioma.

Of the seven patients in whom both tests were positive, one patient appeared to have clear-cut multiple sclerosis and another had clinical features possibly consistent with multiple sclerosis. Other diagnoses included ARC, "chronic meningitis of unknown etiology", polyarteritis nodosa, Krabbe's disease and pituitary tumor.

Additionally, one patient in whom the oligoclonal banding and IgG/albumin index were both negative carried the diagnosis of multiple sclerosis.

Conclusions
This review looked at approximately three years of oligoclonal banding and IgG/albumin index data during which time these tests were performed in parallel on a total of 234 patients. Of these patients, oligoclonal banding was positive in one patient diagnosed as having multiple sclerosis that was not detected by IgG/albumin index, and, even in that case, the interpretation of the oligoclonal bands is questionable, and the level of the IgG/albumin index is near the decision point.

In any event, the positive predictive value for a diagnosis of multiple sclerosis of either test is very low (9% for oligoclonal banding, 5% for IgG index > .60) and remains low even when both tests are positive (11%). At least three cases of clinically obvious multiple sclerosis were missed by both laboratory parameters. It is thus easy to see that the laboratory data adds relatively little to the clinical diagnosis.

The IgG/albumin index is a far more standardized and reproducible test while oligoclonal banding is highly subjective and very labor intensive. In view of these results and the fact the oligoclonal banding offered so little additional data to that supplied by the IgG/albumin index, a strong case is made for discontinuing oligoclonal band analysis at Moffitt Hospital. It utilizes time and resources in the laboratory while having very little, if any, clinical utility.

Bibliography