Brigham Young University
Department of Microbiology and Molecular Biology

The Relationship Between the Presence of Oligoclonal Bands and the Multiple Sclerosis Severity Score

[1]Holly Jensen, [3]Joshua C. Denny, [1]Mary F. Davis
[1]Department of Microbiology and Molecular Biology, Brigham Young University, Provo, UT, USA, 84602. [2]Department of Epidemiology and Biostatistics, Case Western Reserve University, Cleveland, OH, USA, 44106.
[3]Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, TN, USA, 37232.

ABSTRACT

Oligoclonal bands (OCB) stem from immunoglobulins in the serum or cerebrospinal fluid (CSF). If OCBs are found in CSF and not serum, they are indicative of multiple sclerosis (MS), a disease characterized by nervous system damage. The clinical progression of MS can be measured by the Expanded Disability Status Scale (EDSS) which rates the severity on a scale of 1 to 10.

The purpose of this study is to determine if the appearance of OCBs is related to an increased EDSS. Using the electronic medical records (EMR) from Vanderbilt University Medical Center of twenty-four patients, a statistical analysis of the relationship between the presence of OCBs within ten years after diagnosis with the highest recorded EDSS was performed.

After performing a two-sample T test, the data indicated that patients with OCBs had a higher average EDSS ($EDSS_{w/OCB}$ = 4.78) than those without ($EDSS_{w/out\ OCB}$ = 4.50) although it was not statistically significant (p = 0.86). A χ^2 test indicated patients with an EDSS higher than the average EDSS of our patient set ($EDSS_{avg}$ = 4.7) were more likely to have OCBs than those with an EDSS lower than the average, although it was not significant (p = 0.65). These results suggest there is no relationship between the appearance of OCBs and a higher EDSS.

STUDY POPULATION

BioVU is a resource of over 180,000 leftover blood samples from outpatients that have been collected and used to extract DNA, and each sample is linked to the individual's clinical data through a "synthetic derivative" of their de-identified EMR.

Patients in BioVU are representative of all patients that come to VUMC, in that they come from diverse regions of the country, varied ethnicities and health statuses, and are of all ages. We have limited our study to patients 18 years or older. EMR usage at Vanderbilt dates back to 1997, so we have over 10 years worth of clinical information for many patients.

Most of the MS patients in our study have been seen at the Multiple Sclerosis Clinic by one of three physicians. The Vanderbilt MS Clinic was established in 1994 and up to 30 patients are seen each day. In general, patients at the MS Clinic are seen twice a year. Additionally, some patients in our study were seen at Vanderbilt in other clinics for other reasons but also have a diagnosis of MS.

BACKGROUND

Multiple sclerosis is an autoimmune disease characterized by inflammation and axonal demyelination which can lead to neurodegeneration in the patient. The progression of this degeneration is measured on the Expected Disability Status Score (EDSS) (table 2). The presence of the antibodies in cerebral spinal fluid (CSF) appear as oligoclonal bands (OCB) on a protein electrophoresis (fig 1). Over 95% of MS patients have OCBs in their CSF and not serum making this clinical finding strongly indicative of MS, although it is not diagnostic.[1]

Sample Population	Number in Sample	Percent of Sample	Average EDSS
Patients w/ OCB	20	83.3%	4.78
Patients w/out OCB	4	16.7%	4.50

Table 1 – A summary of the sample population.

Expanded Disability Status Scale		
Score	Description	Functional Systems (FS)
1.0	No disability, minimal signs in one FS	Pyramidal, Cerebellar, Brainstem, Sensory, Bowel and Bladder, Visual, Cerebral, Other
1.5	No disability, minimal signs in more than one FS	
2.0	Minimal disability in 1 FS	
2.5	Mild disability in 1 or Minimal disability in 2 FS	
3.0	Moderate disability in 1 FS or mild disability in 3 - 4 FS, though fully ambulatory	
3.5	Fully ambulatory but with moderate disability in 1 FS and mild disability in 1 or 2 FS; or moderate disability in 2 FS; or mild disability in 5 FS	
4.0	Fully ambulatory without aid, up and about 12hrs a day despite relatively severe disability. Able to walk without aid 500 meters	
4.5	Fully ambulatory without aid, up and about much of day, able to work a full day, may otherwise have some limitations of full activity or require minimal assistance. Relatively severe disability. Able to walk without aid 300 meters	
5.0	Ambulatory without aid for about 200 meters. Disability impairs full daily activities	
5.5	Ambulatory for 100 meters, disability precludes full daily activities	
6.0	Intermittent or unilateral constant assistance (cane, crutch, or brace) required to walk 100 meters with or without resting	
6.5	Constant bilateral support (cane, crutch, or brace) required to walk 100 meters without resting	
7.0	Unable to walk beyond 5 meters even with aid, essentially restricted to wheelchair, wheels self, transfers alone; active in wheelchair about 12 hours a day	
7.5	Unable to take more than a few steps, restricted to wheelchair, may need aid to transfer; wheels self, but may require motorized chair for full day's activities	
8.0	Essentially restricted to bed, chair, or wheelchair, but may be out of bed much of day; retains self care	
8.5	Essentially restricted to bed much of day, some effective use of arms, retains some self care functions	
9.0	Helpless bed patient, can communicate and eat	
9.5	Unable to communicate effectively or eat/swallow	
10.0	Death due to MS	

Table 2 – The criteria of each score in the EDSS. [2]

METHODS and RESULTS

Using the data from Vanderbilt Medical Center, we found the results of OCB testing and the highest recorded EDSS of 24 patients. The EDSS ranged from 1 to 9 among these patients. 20 of the patients had OCB present, and 4 did not (table 1). We ran a two sample t-test and a chi-squared test on the data in order to determine the relationship between the presence of OCB and EDSS.

We first looked at the average EDSS of patients with OCB ($EDSS_{avg}$ = 4.78) verses the average EDSS of patients without OCB ($EDSS_{avg}$ = 4.50) (table 3). The EDSS of those with OCB was higher on average; however, it was not statistically significant (p = 0.86).

We then looked at the average EDSS of the sample population ($EDSS_{avg}$ = 4.7), and compared patients with an EDSS higher than the average with patients with an EDSS lower than the average and ran a chi-squared test. We found that patients with a higher EDSS were more likely to have OCB than those with a lower EDSS; however, it was again not a statistically significant difference (p = 0.65) (table 4).

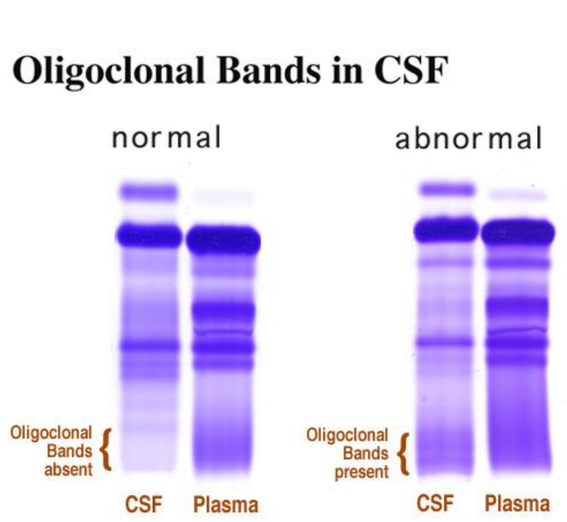

Figure 1 – An image of protein electrophoresis of normal CSF and abnormal CSF. The presence of OCBs in CSF is indicative of MS. [3]

	EDSS W/OCB	EDSS W/OUT OCB
Mean	4.78	4.50
Variance	4.88	8.17
Observations	20	4
df	4	
t Stat	0.18	
P(T<=t) two-tail	0.86	
t Critical two-tail	2.78	

Table 3 – Results from a two-sample t-test looking at the relationship between the presence or lack of OCB and EDSS.

	Observed	Expected
High RDSS w/OCB	12	10.8
Low EDSS w/OCB	8	9.2
High EDSS w/out OCB	1	2.2
Low EDSS w/out OCB	3	1.8
		p = 0.65

Table 4 – Results from a χ^2 test analyzing EDSS and the presence of OCB.

CONCLUSIONS

While the results of this study were not statistically significant, they did indicate a potential relationship between OCB and EDSS. With a larger sample size, a significant relationship might be able to be determined. Other factors of MS, such as age at onset and relapsing remitting verses progressive MS, might also be able to be linked to the presence of OCBs in the first 10 years of disease. This would allow physicians to gain a better understanding of MS allowing for better treatment for the patient.

SOURCES

[1] Link, Hans; Huang, Yu-Min (2006). Oligoclonal bands in multiple sclerosis cerebrospinal fluid: An update on methodology and clinical usefulness. Journal of Neuroimmunology, 180(1-2), 17-28.
[2] Kurtzke, JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 1983;33(11):1444-1452.
[3] Rose, J., MD, & Houtchens, M. (n.d.). [Oligoclonal Bands in CSF in a Patient with Multiple Sclerosis]. Retrieved from https://library.med.utah.edu/kw/ms/mml/ms_oligoclonal.html

The dataset(s) used for the analyses described were obtained from Vanderbilt University Medical Center's BioVU which is supported by institutional funding, the 1S10RR025141-01 instrumentation award, and by the CTSA grant UL1TR000445 from NCATS/NIH.