Oligoclonal Band Number Correlates with Relapses and Progression in Multiple Sclerosis

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Introduction

Oligoclonal bands (OCBs) in the cerebrospinal fluid (CSF) are a reliable laboratory abnormality in multiple sclerosis (MS), found in greater than 90% of patients. Their presence has been shown to have predictive value with respect to clinically isolated syndrome (CIS) evolving into clinically definite MS (CDMS) as well as worse prognosis if noted early in a relapsing disease course. OCBs have been incorporated into the latest version of McDonald Criteria for MS diagnosis. The predictive value of OCBs has, to date, been incompletely explored.

While most studies examine the presence or absence of OCBs with regard to prognosis, only a few small studies have investigated correlations between the number of OCBs on single disease metrics. A study of 44 MS patients split into two groups, EDSS<3.5 and EDSS>7.5, found that a lower number of OCBs suggested a favorable prognosis. A separate study found that CIS patients were 2.5x more likely to develop CDMS with 8-12 OCBs compared to <8 OCBs.

The goal of this study was to examine relationships between the number of OCBs and markers of relapses as well as progression, both clinical and radiographic, in short-term follow-up as this would be a time for early intervention.

Methods

Through screening of lumbar punctures with OCB testing from 2010-2014 at the University of Pennsylvania's three hospitals, 204 MS patients were identified. Further inclusion criteria were:

1) A diagnosis of relapsing-remitting MS
2) Adherence to a DMT initiated within three months of diagnosis
3) Two years of follow-up clinical visits and imaging

There criteria yielded 128 patients. Four disease course metrics were quantified over a two-year period proximal to the diagnosis:

	Activity	Progression
Clinical	Annualized relapse rate (by # steroid prescriptions, IV or PO)	Ambulatory assist (cane-1, walker-2, wheelchair-3)
Radiographic	Annualized relapse rate (by # new lesions, enhancing or non-enhancing, in the brain, C-spine, or T-spine)	Accelerated (>1%) total brain volume loss (measured on T1 MPRAGE using SIENA)

Subsequently, the number of OCBs were examined.

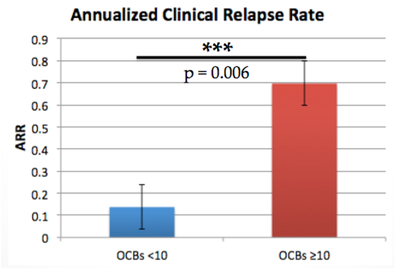
Unpaired, two-tailed t-tests were used for comparative analyses. Significance was determined with p<0.05.

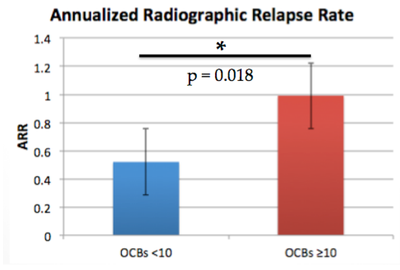
Results

- 118/128 (92%) MS patients were OCB+ (2 or more bands)
- Range of OCBs was 0-23
- Non-linear relationship was suspected, and the cohort was divided into two groups: OCBs <10 (62) and ≥10 (66).

	Bands < 10	Bands ≥ 10
# steroid Rx	17	46

	Bands < 10	Bands ≥ 10
# New lesions	48	107



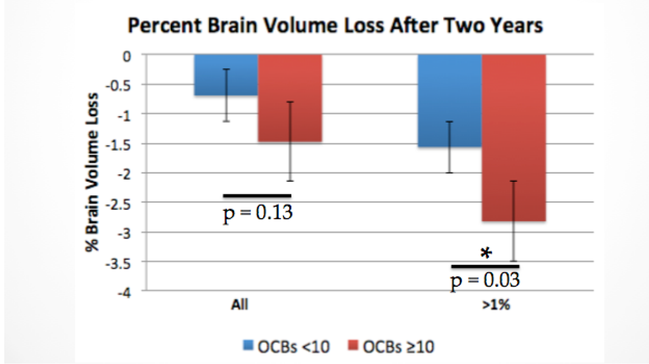


- Examination of clinical activity after two years, patients with ≥10 OCBs had significantly higher annualized clinical and radiographic relapse rate.

Degree of Assist	Bands < 10 Baseline	Bands <10 Post 2yrs	Bands ≥ 10 Baseline	Bands ≥ 10 Post 2yrs
No assist	51	49	50	45
Cane	10	12	15	18
Walker	1	1	1	3
Wheelchair	0	0	0	0
Total	62	62	66	66
P-value		0.08		0.007

- Regarding progression, use of a new or more advanced assistive device was higher for patients with ≥10 OCBs.

	Bands < 10	Bands ≥ 10
% Brain volume loss (all)	-0.692	-1.566
% Brain volume loss >1%	-1.475	-2.822



- While brain volume loss was not significantly different with all patients in both groups, examination of those with accelerated progression (>1% brain atrophy) was significantly greater in patients with ≥10 OCBs.

Conclusions

This study shows significantly greater relapses and progression, both clinical and radiographic, for patients with high levels (≥10) of OCBs early in the MS disease course.

In light of the recent revision to the McDonald Criteria in 2017, OCBs can satisfy the criteria for separation in time and, in the correct clinical setting, would lead to an MS diagnosis. The findings in this study support that quantification of OCBs may help to identify patients with more aggressive MS and may therefore guide selection of a stronger DMT earlier on in the MS disease course.

Limitations of this study include:
- Retrospective design with lack of a control group
- Insufficient sample to evaluate the effect of individual treatments
- Evaluation of clinical relapses/progression relative to time of diagnosis rather than disease onset
- More qualitative measures of clinical progression
- Use of brain volume loss as a proxy for radiographic progression without a known standard

Future Directions

To expand on this study, the aims of future research would be to:
- Broaden the data capture to beyond four years
- Perform further stratification of OCBs
- Study individual treatments at different numbers of OCBs to correlate with disease activity and progression
- Establish more quantitative measures of clinical progression such as extrapolating EDSS from clinical notes and exams
- Investigate and correlate other measures of brain volume studied in MS patients such as gray matter volume or thalamic volume

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