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Are oligoclonal bands associated to lower retinal layer thickness at the time of relapsing remitting multiple sclerosis diagnosis? Evidence from an exploratory study

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Dear Editor,

The presence of oligoclonal immunoglobulin G bands (OCBs) in the cerebrospinal fluid (CSF) is still one of the most sensitive hallmark of ongoing inflammatory events in the relapsing remitting multiple sclerosis (RRMS), and the recent released MS diagnostic criteria underlined the importance of their detection for an early and prompt diagnosis [1].

It was suggested as patients without OCBs may show a more aggressive course of the disease, in terms of disability accrual and disease activity (new clinical relapses and/or new lesions at brain and spinal magnetic resonance imaging (MRI)), but conflicting data exist [2–5].

In the last decade, great attention was posed on data derived from optical coherence tomography (OCT) in RRMS assessment at the time of diagnosis and along the follow-up. It is now well characterized as retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thinning may occur in patients with RRMS, early in the course of the disease, and also independently of optic neuritis [6,7].

We conducted a retrospective analysis of the data collected at our tertiary MS centre of Catania, Italy. All data were included in a computerized database, iMed® software (iMed, Merck Serono SA; Geneva). We included all patients who received the diagnosis of RRMS (according to 2010 MS criteria [8]) between January 1st, 2016 and June 30th, 2016. The collected data included the CSF OCBs status and OCT evaluation. We excluded from the analyses the patients who experienced: a) optic neuritis, b) any ophthalmologic comorbidity and/or refractive errors of more than 6 diopters [9].

The aim of our study was to investigate if the presence of OCBs was correlated with retinal neuronal loss parameters in early-diagnosed RRMS. Also, we correlated the presence of OCBs with clinical, radiological and cognitive measures at the time of RRMS diagnosis.

1. Results

From a total sample of 180 patients, 80 matched the required criteria. Out of them, 64 had the presence of OCBs (group A) and 16 had no OCBs (group B). Differences were found about the two groups. In detail, group A had more T1 Gd+ and less T2 brain lesions than group B (for both, $p < .05$). About OCT data, group A showed lower RNFL and GCL than group B ($p < .05$). Correlation analysis showed a negative correlation among the presence of OCBs and both eyes RNFL ($\rho -313$, $p = .005$ for right eye and $\rho -268$, $p = .016$ for left eye) and also with GCL, monocularly ($\rho -318$, $p = .004$ for left eye). To determine whether the correlation was independent from age and from the significant baseline characteristics (number of T1 Gadolinium and T2 brain lesions), a corrected model was built. The correlation was confirmed between presence of OCBs and RNFL (both eyes) ($\rho -309$, $p < .001$ for right eye and $\rho -283$, $p < .001$ for left eye) and GCL ($\rho -271$, $p < .05$ for right eye and $\rho -282$, $p < .001$ for left eye). No correlations were found between presence of OCBs and clinical and cognitive parameters.

2. Discussion

In our RRMS cohort, the presence of OCBs was correlated to retinal layer thickness (assessed by OCT) at the time of diagnosis.

The detection of OCBs in the CSF gained renew interest in the 2018 MS diagnostic criteria, after that it received less emphasis in the McDonald criteria [8] and still less in the revised version [10]. OCBs are present in most of MS patients (up to 95%), and that implies intrathecal immunoglobulin synthesis and B cell related immune processes [11]. However, geographical difference exists, for example in Japan up to 45% of patients with RRMS showed no OCBs [12]. About a potential prognostic value of OCBs, there is debate whether MS clinical course may differ in patients with the presence of OCBs. In a retrospective case analysis on 69 patients, the time to get EDSS 6.0 (that means the use of assistance to walk) was significantly longer in patients without OCBs [3]. Long is debated about the time of OCB screening, as studies showed that OCB negativity is more common if assessed early in the disease course and it is well described as some patients with RRMS acquired OCBs along the disease course.

Some lines of evidence support the hypothesis that the presence of OCBs is related to brain tissue injury, describing a larger volumes of white matter lesions (independently of age, gender, disease course, disability, age of onset, disease duration, or therapies), and smaller gray matter volume in some brain areas (basal ganglia, cerebellum, and hippocampus) in patients with OCBs [13–16]

We first described a correlation between OCBs presence and retinal layer thickness.

Overall, a direct comparison among studies using OCT parameters is

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not simple, due to differences in the used technology and in the enrolled cohorts, as well for a lack of auto-rescan protocols and the absence of healthy control groups [17].

The findings of our study may lead to some questions. Firstly, could the presence of OCBs be considered marker of early neurodegeneration?

The presence of OCBs could be the mirror of a compartmentalized intra-central nervous system B cell responses, which have been described as associated with increased subpial demyelination and neuronal damage [18]. As recently discussed, the interaction of intra-central nervous system plasma cells (the source of OCBs), microglia and astrocytes may generate an environment which could initiate and perpetuate phenomenon of neurodegeneration [19].

Our study shows limits. This is a cross-sectional study in which a frame of the evolution of MS was taken at the time of diagnosis and not at the clinical onset.

Our findings may suggest that thinner retinal layer thickness and the presence of OCBs at the time of RRMS diagnosis may be used as potential combined biomarkers of early neurodegeneration in RRMS.

Further randomized studies which include extensive follow-up are needed to confirm our results.

Fundings

None.

Declaration of Competing Interest

Nothing to disclose.

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