Tear analysis in radiologically isolated syndrome as new tool to predict risk to a clinical conversion

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ABSTRACT

- **Background**: In radiologically isolated syndrome (RIS), the detection of oligoclonal bands (OCBs) in cerebrospinal fluid (CSF) is critical for space dissemination validation associated with magnetic resonance imaging (MRI) multiple sclerosis (MS) diagnostic criteria published by Barkhof in 1997. It gives strength to RIS diagnosis compared with other incidental white matter T2 lesions. However, lumbar puncture for CSF collection is considered relatively invasive. Previous studies have demonstrated applicability of OCB detection in tears to the diagnosis of MS and CIS.

- **Objective** : To assess concordance between OCB detection in tears and in CSF.

- **Patients/methods**: We have prospectively included patients with RIS and compared results of CSF and tear OCB detection by isoelectric focusing (IEF). Tears were collected using a Schirmer strip.

- **Results**: We included prospectively 45 patients. For 3 of them, samples were non analyzable due to insufficient quantity of tears. OCBs were detected in CSF for 55% (25/45) and in tears for 50% (21/42) of patients. All patients with tears OCBs had CSF OCBs. One patient had a positive CSF and negative tears.

- **Discussion**: CSF OCB presence in RIS is considered to be predictive of conversion to a clinical event. Associated with spatial dissemination MRI criteria, their detection denotes a statistically significant increased conversion risk to clinical conversion. For OCB negative patients, a tears follow-up could help to early detection of CSF conversion.

- **Conclusion**: We suggest that tears OCB detection may replace CSF OCB detection as a diagnostic tool in patients with RIS. This would circumvent the practice of invasive lumbar puncture and probably will increase facilities for patients and neurologists to accept MRI T2 hypersignals investigations.

Rational

Several research studied tears in MS. Two of them showed its abnomality in multiple sclerosis. Among them :

- Tears analysis in MS (Coyle et al. Neurology, 1986) showed increased immunoglobulin G concentration in tears of MS patients.

- Silver stained isoelectrophoresis of tears and CSF in MS (Devos et al. 2001) found a concordance rate between tears and CSF of 83% in MS and of 86% in non MS patients, with a sensibility and a specificity comparable between tears and CSF.

- In RIS, either OCB or increased IgG index in CSF are predictive markers of the conversion risk to clinical event (Lebrun et al, Archive Neurol 2010).
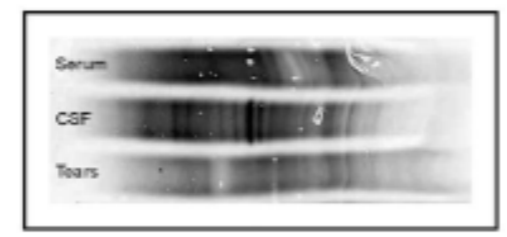
Comparison between Tears and CSF

Figure 1. Example of isoelectric focusing (IEF) with immunoblotting. Oligoclonal bands (OCBs) present in tears and CSF are pointed out.

Methods

- Diluted tears on Schirmer strip is the only reason of non analysable samples.
- It could be avoided by a shorter collection with maximum 10 millimeters of tears.

- Each RIS patient underwent a blood, CSF and tears collection

- Tears were collected by a Schirmer strip placed in the external corner of each eye

- Immunoglobulin G (IgG) oligoclonal bands (OCB) are detected by isoelectrofocusiong on agarose gel followed by an immunoblotting.

Results

All patients with tears-OCB had CSF-OCB.

The main limitation was for 3 patients, the lack of Tears.
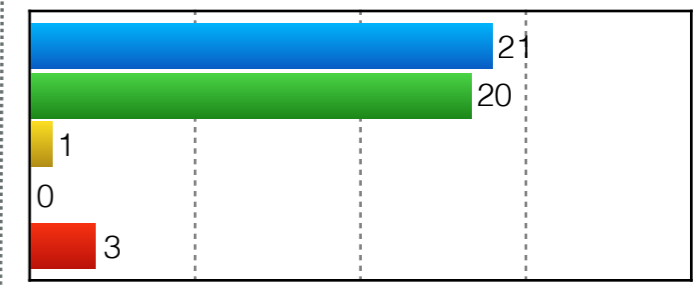
- CSF+ Tears+ : 21
- CSF- Tear : 20
- CSF+ Tears- : 1
- CSF- Tear : 0
- Tears NA : 3

Conclusion

We suggest than tears-OCB detection, if positive, may replace CSF-OCB detection in patients with radiologically isolated syndrome.

Lumbar puncture in this context could be avoided.

oligoclonal bands + If ≥ 3 OCB d'IgG compared with serum