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XLVI CONGRESSO NAZIONALE
10-13 OTTOBRE 2015 – GENOVA

Diagnosis of Neuromyelitis Optica Spectrum Disorders (NMOSD) in clinical practice. Sensibility and specificity of different NMO antibodies detecting assays

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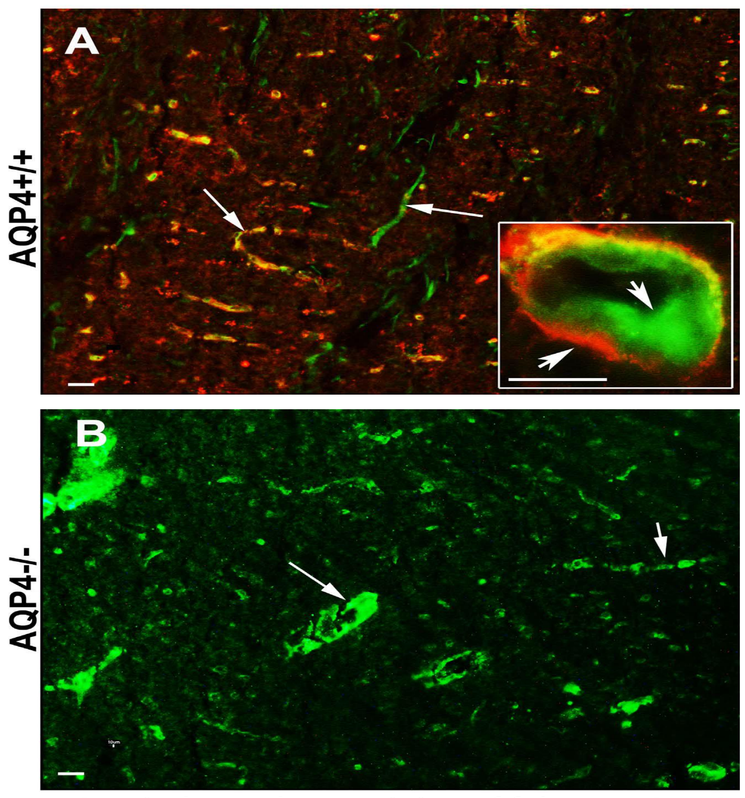
Introduction

The identification of serum anti-Aquaporin-4 (AQP4) antibodies is crucial in the evaluation of patients with suspected Neuromyelitis Optica Spectrum Disorders (NMOSD) in clinical practice[1]. Cell based assay (CBA) is known to be more sensitive and specific in comparison to the assay based immunofluorescence on monkey cerebellum sections (IF), but the latter test continue to be used often in clinical setting.

Recently, we demonstrated that: 1) homemade CBA targeting AQP4-M23 isoform is more sensitive and specific than commercial CBA targeting AQP4-M1 isoform, 2) false NMO-IgG positivity may occur using a tissue-based IF test [2]

Objective

To evaluate the sensitivity and the specificity of different assays in detecting serum anti-AQP4 antibodies in a cohort of patients screened for NMOSD.



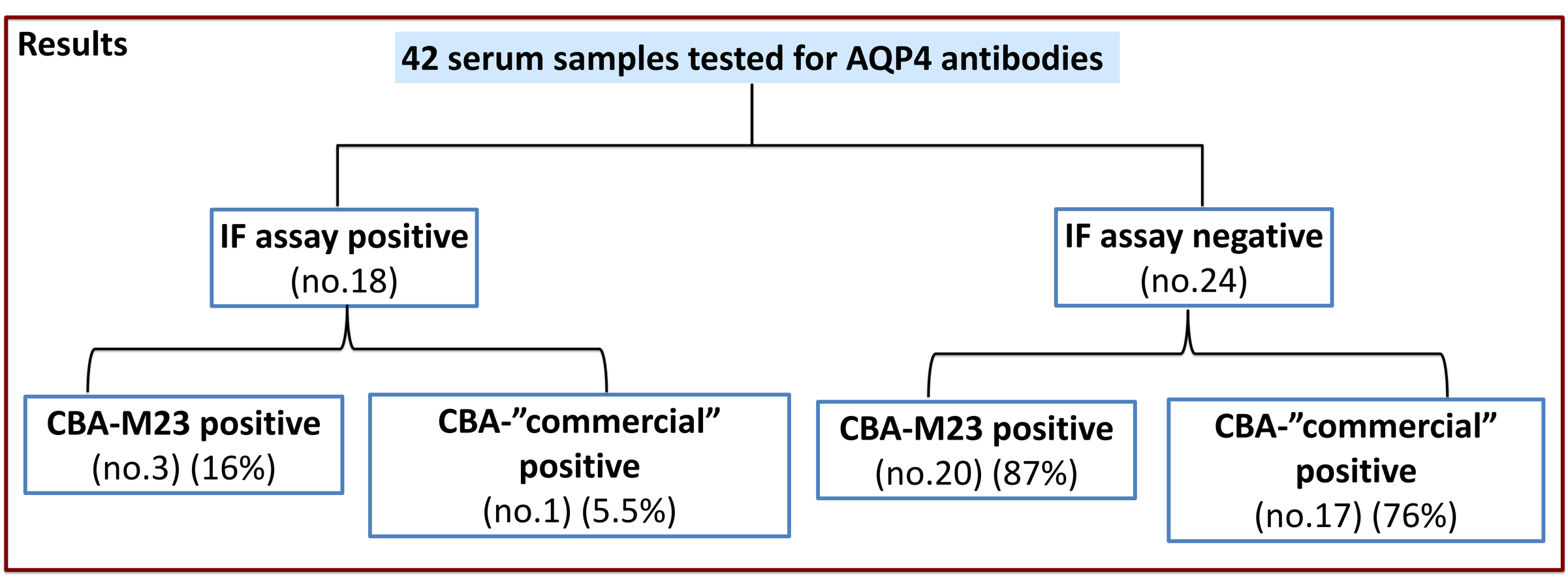
AQP4 independent staining of false NMO-IgG positive sera

WT (A) and **AQP4 knockout** (B) mouse brain sections were stained with a serum showing NMO IgG-like staining at low magnification. Inset (A) shows that the serum staining (green) is restricted to endothelial cells of the brain capillaries and not to astrocyte processes stained red by AQP4 antibodies. (B) Staining of AQP4-/- mouse endothelial cells of the serum under analysis[2].

Material and Methods

Forty-two consecutive serum samples derived from 27 patients with suspected NMOSD, enrolled in a clinical setting, were screened for anti-AQP4 antibodies using two commercial kits (IF and CBA, Euroimmune) and one homemade CBA specific for AQP4 M-23 isoform (CBA-M23).

Results



Twenty-three sera belonged to patients who developed NMO during three years follow-up. All of them were CBA positive and only 4 were IF positive.

None of the patients "IF positive" and "CBA negative" developed NMO at follow-up. The **sensitivity** of the **IF assay** in our cohort was 13%, whereas the **specificity** of the IF assay was 21%.

Five of 23 CBA positive sera were positive only by using handmade CBA-M23 and not by commercial CBA kit.

These sera belonged to patients with clinically mild NMOSD (2 CRION, 1 NMOSD associated to celiac disease).

Conclusions

Our prelimanary results highlight that IF assay has low sensitivity and specificity in detecting serum anti- AQP4 antibodies and it is worthless in clinical setting in patients with NMOSD. Furthermore, our preliminary data suggest that the use of CBA-M23 assay can further improve anti-AQP4 antibodies detection in patients with highly suggestive clinical features of NMOSD and negative results of CBA commercial kit.

References
(1) Wingerchuk DM Neurology 2015;85:1–13
(2) Pisani et al. PLOSone 2013; 8(11): e79185