Association of choroid plexus enlargement with intrathecal inflammation in early multiple sclerosis

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BACKGROUND

The choroid plexus acts as a gateway for immune cell trafficking, allowing selective entry of lymphocytes and monocytes into the cerebrospinal fluid. Through the secretion of cytokines and chemokines, it orchestrates communication between the peripheral immune system and the CNS.

AIM OF THE STUDY

To assess the association between choroid plexus (CP) volume and cerebrospinal fluid (CSF) markers of intrathecal inflammation in multiple sclerosis (MS) patients.

METHODS

We included 149 patients with relapsing and progressive MS (109F/40M, mean age 38.4±11.9 years). All underwent lumbar puncture, clinical evaluation including Expanded Disability Status Scale (EDSS; median 1.0, range 0–7), and 3T brain MRI within 3–6 months of their first clinical episode. All patients tested positive for CSF-restricted oligoclonal bands. CSF levels of 68 inflammatory markers were analyzed using a multiplex immunoassay. CP segmentation in the lateral ventricles was performed using the Aschoplex deep learning-based ensemble model (https://gitlab.dei.unipd.it/fair/aschoplex/) applied to T1-weighted images. These images were lesion-filled and processed with FreeSurfer v7.3.1 to estimate total intracranial volume (TIV), used to normalize CP volume and account for inter-individual variability in brain size.

Tab. 1. Demographical and clinical characteristics of the patients enrolled in the study

	PwMS = 149
Gender (F/M)	109F/40M
Age (years)	38.4±11.9
EDSS score	*1,0; (0-7)

Data are reported as mean, standard deviation
** Data are reported as median (range)*

RESULTS

Through linear logistic regression adjusted for age and sex, we found that the increase in certain cytokines involved in pro-inflammatory pathways is correlated with an increased plexus volume *(Fig.1)*. Similarly, we observed reduced levels of cytokines involved in regulatory processes associated with increased choroid plexus volume *(Fig. 2)*. The correlation matrix *(Fig. 3)* reveals strong clustering among elevated cytokines, indicating they function as a coordinated inflammatory network. The weaker correlations among reduced cytokines suggest independent regulatory pathway failures. Gene Ontology enrichment analysis *(Fig. 4)* confirmed these markers are involved in neuroinflammatory responses, cytokine-cytokine receptor interactions, and ERK/MAPK signaling pathways - all critical for neuroinflammation progression.

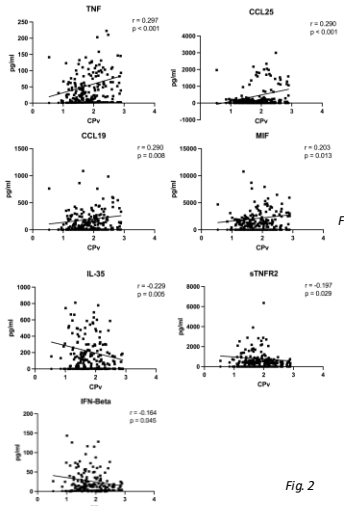

Fig. 1

Fig. 2

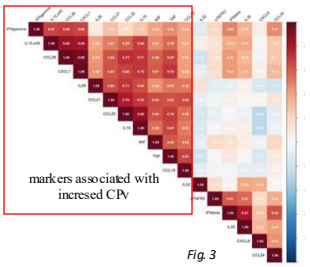

Fig. 3

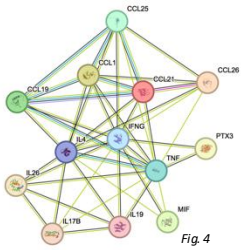

Fig. 4

DISCUSSION AND CONCLUSIONS

Our findings show that choroid plexus enlargement reflects early compartmentalized inflammation in MS. Its association with CSF inflammatory markers highlights the plexus as a key neuroimmune interface. Choroid plexus morphology appears to actively regulate neuroimmune processes, making it a potential therapeutic target and non-invasive biomarker for intrathecal inflammation, and offering new insights into MS pathogenesis.

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