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Gas6/TAM system: potential prognostic biomarkers for Multiple Sclerosis

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Introduction:

The protein growth arrest specific 6 (Gas6) and its tyrosine kinase receptors Tyro-3, Axl, Mer (TAMs) are ubiquitous proteins involved in regulation of inflammation and apoptotic body clearance. Gas6 and TAMs have been associated with neuronal remyelination and stimulation of oligodendrocyte survival. However, few data are available on their role in multiple sclerosis (MS).

Objectives/Aims:

In this study we evaluated if soluble levels of these molecules, determined at MS diagnosis in cerebrospinal fluid (CSF) and serum, correlated with progression with short-term disease severity.

Methods:

We conducted a retrospective cohort study enrolling 64 patients with different forms of MS, the Radiological Isolated Syndrome (RIS), the Clinical Isolated Syndrome (CIS) and Relapsing-Remitting (RR). At diagnosis, we collected serum, CSF, and clinical-radiological data: lesion load, spinal cord, and gadolinium-enhancing (Gad+) lesions, and expanded disability status score (EDSS). During the last clinical follow-up EDSS, MS *s*everity score (MSSS) and Age-Related MS severity (ARMSS) were assessed. Gas6 and TAMs were determined by ELISA kit (R&D Systems), while neurofilaments (NFLs) levels, for neuronal damage assessment, by SimplePlexTM fluorescence-based immunoassay. Statistical analyses were conducted with STATA software to determine Mann–Whitney, Kruskal-Wallis test and Spearman's rank correlation coefficient significance.

Results:

At diagnosis, RIS and CIS showed higher values of sMer and sTyro-3, compared to RRMS ($p = 0.007$ and $p = 0.018$). Serum sAxl was higher in patients untreated or first-line disease modifying treatments (DMTs) versus patients with high-efficacy DMTs ($p = 0.04$). Moreover, serum Axl was associated with EDSS ≤ 3 at diagnosis ($p = 0.037$) and EDSS progression in patients with EDSS ≤ 3 ($p = 0.017$). Similarly, high levels of Gas6 in CSF were associated with EDSS ≤ 3 at diagnosis ($p = 0.04$), and high levels of Gas6 in serum to a lower MSSS (r2 = -0.32 and $p = 0.01$). Results significances were confirmed by multivariate analyses. In our cohort, serum and CSF NFLs levels were confirmed as markers of disability in EDSS ($p = 0.005$ and $p = 0.002$) and MSSS (r2 = 0.27 and $p =$

0.03; r2 = 0.39 and $p = 0.001$).

Conclusion:

Taken together, our results suggest that Gas6 and its receptors, particularly Axl, might have a neuroprotective role and prognostic potential in MS.

Disclosures:

Nothing to disclose