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Neurodegeneration and inflammation in Parkinson's disease: an insight from blood biomarkers

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Background and aim of the study: Parkinson's disease (PD) is the second most frequent neurodegenerative disorder and is characterized by a great phenotypical heterogeneity. Alfa-synuclein deposition plays a crucial role in PD development but also other mechanisms, including inflammation, seem to underlie PD pathogenesis and progression [1]. Recently, great attention has been put on biomarkers which could follow disease initiation and progression to both monitor disease progression and understand underlying pathophysiological mechanisms [2-3].
Our aim was to measure blood levels of neurodegeneration and inflammation biomarkers and correlate them with clinical and demographic data.

Materials and Methods: We consecutively enrolled PD patients and evaluated them by means of validated clinical scales (UPDRS, Hoehn and Yahr staging, MMSE, NMSQ). Then, serum levels of selected biomarkers (Neurofilament light chain, BDNF, IL-1β, IL5, IL-6, IFN, TNF-a, IL4 and IL10) were essayed using commercially available kits on an ELLA™ automated immunoassay system (Bio-Techne, San Jose, CA, USA). Descriptive statistics, parametric and non-parametric tests were used when necessary. Spearman correlation test was used to correlate clinical-demographical data and biological measures.

Results: 104 patients were enrolled with a mean age of 66.55 years and disease duration ranging from 0 to 29 years, with a mean of 8 +/-5 years. NfL levels showed a positive correlation with disease duration and UPDRS III score (respectively rho 0,348, p=0.014 and rho 0,258 and p=0.047). A correlation analysis between inflammatory markers and disease duration showed a trend in increase of pro-inflammatory citokynes in the first years, with a tendency to peak at 5 years from diagnosis and then a decrease. patietns with short disease duration (< 5years) had significantly lower consentrations of IL5, IL10 and IL17.

Discussion: In this study we confirm the role of NfL as a marker of disease progression, confirming its reliability also if measured in the serum of PD patients. If combined with more specific markers, it could play a significant role in monitoring disease progression and also be predictive of conversion to a clinical manifest phase in prodromal patients. Moreover, we also found an interesting trend showing an increase of pro-inflammatory cytokines in the earliest phases of the disease, followed by a decrease in the following years.

Conclusion: This study shows the association between serum NfL and disease burden and the tendency to manifest a pro-inflammatory status in patients in the earliest phases of the disease.

References:
[1] Lindestam Arlehamn CS, Dhanwani R, Pham J, Kuan R, Frazier A, Rezende Dutra J, Phillips E, Mallal S, Roederer M, Marder KS, Amara AW, Standaert DG, Goldman JG, Litvan I, Peters B, Sulzer D, Sette A. α-Synuclein-specific T cell reactivity is associated with preclinical and early Parkinson's disease. Nat Commun. 2020 Apr 20;11(1):1875. doi: 10.1038/s41467-020-15626-w. PMID: 32313102; PMCID: PMC7171193.

[2] Halloway S, Desai P, Beck T, Aggarwal N, Agarwal P, Evans D, Rajan KB; and the Chicago Health and Aging Project. Association of Neurofilament Light With the Development and Severity of Parkinson Disease. Neurology. 2022 May 31;98(22):e2185-e2193. doi: 10.1212/WNL.0000000000200338. Epub 2022 Apr 13. PMID: 35418452; PMCID: PMC9162164.
[3] Parnetti L, Gaetani L, Eusebi P, Paciotti S, Hansson O, El-Agnaf O, Mollenhauer B, Blennow K, Calabresi P. CSF and blood biomarkers for Parkinson's disease. Lancet Neurol. 2019 Jun;18(6):573-586. doi: 10.1016/S1474-4422(19)30024-9. Epub 2019 Apr 10. PMID: 30981640.