P154

Phenotypical and molecular characterisation of a cohort of patients with GBA-related Parkinson's disease: focus on dysautonomic symptoms

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Introduction: GBA is presently considered the most important genetic risk factor for Parkinson's disease (PD). A previous multicentric study (2020) revealed a significant prevalence of monoallelic variants of GBA (14,3%) in Italian PD patients, but centers from North-East of Italy were not included.

Objective: To assess clinical and genetic features of a cohort of patients with GBA-related-PD followed at Padova University and to compare them with results from previous studies. To assess potential differences in the clinical phenotype of GBA-related PD vs idiopathic-PD.

Methods: 20 patients with GBA-related-PD were included. Mutations were classified according to pathogenicity (ACMG guidelines) and clinical phenotyping was performed with motor and non-motor assessment scales, including COMPASS-31 for dysautonomia. The results were compared with a cohort of early-onset genetically-negative PD patients, matched for age, sex and disease duration. Lastly, results were compared with another group of late-onset idiopathic-PD patients with longer disease duration, not genetically tested.

Results: Mutational frequency of GBA was 11,76% (20/170). Patients with GBA-related-PD showed an earlier onset (mean 45.2 years), positive family history in 35% of cases and bradykinetic-rigid presentation in 65% of cases, with motor and non-motor complications over disease course, such as cognitive decline (75%), psychiatric disturbances (80%) and dysautonomia. The comparison with the two control groups demonstrated a higher severity of GBA-related-PD in terms of cognitive symptoms (p1=0,0003, p2=0,0002), disease progression (H&Y: 2,54, p1=0,00988, p2=0,02852) and dysautonomia, as confirmed by the higher average scores of COMPASS-31 (34,12400723, p=0,03662).
The most common mutations were N370S (9 patients) and D409H (4 patients), classified as mild and severe, respectively, according to residual GBA enzymatic activity. Other previously reported mutations were L444P and IVS2+1, both severe.

Conclusions: Our results are in line with previous research and demonstrate that GBA-related-PD has peculiar features compared to idiopathic, genetically-undetermined forms, particularly regarding cognitive and dysautonomic symptoms.