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Parkinson and Gaucher in real life: results from the clinical practice of a panel of experts

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Introduction: GBA mutation represents the most important genetic risk factor for Parkinson’s disease (PD). Homozygous or compound heterozygous mutations cause Gaucher’s disease (GD) – the most common recessive lysosomal storage disorder [1]. Incidence of GD among PD is unclear, such as the role of the mutation in the PD pathogenesis in patients with or without GD.

Objectives: Investigate the experience of an Italian group of 24 PD experts on screening patients using Dried Blood Spot tests (DBSt) and a criteria list for identifying GBA and GD-PD.

Methods: Participants were equipped with a suspicion index of neurological (PD or LBD cases with pain, RBD, neuropsychiatric issues, dysautonomia, early fluctuations) and general (organomegaly, fractures/bone pain, hematological issues) criteria. Participants obtained and tested DBSt for CGase activity, substrate (LysoGB1) accumulation and GBA status as for GD routine [2].
Results: 336 patients were screened (age 33–93). 63/336 (18.7%) had a heterozygous GBA mutation: 7 L444P (11%), 11 N370S (17.5%), 19 E326K or T369M (30%), 26 (41%) other rarer variants. Mean GCase activity and LysoGB1were 4.64 nMol/h/ml and 5.08 ng/ml. Two patients had compound heterozygous mutations (T369M/N370S, E326K/C342F) and a LysoGB1 over the reference.

Intriguingly, 8/63 presented abnormal LysoGB1 despite having normal GCase activity and heterozygous mutations. The large part of centers screened PD (>75%), but also LBD (<25%) cases. The role of neurological criteria on selecting cases was largely over the 50%, while the use of general criteria was frequently of 50% or lower. The most relevant criteria for identify GBA-PD cases were considered early fluctuations/psychiatric symptoms and hematological issues.

Conclusions: Large genotype-phenotype studies on GBA PD are already available [3], however there is still the unmet need to identifying GBA-PD. Here we provide early evidence of the use of a suspicion index in selecting GBA-PD cases, but a further prospective study is warranted.

References:

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