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Co-existing proteinopathies in globular glial tauopathy

State of the art: Globular glial tauopathies (GGT) belong to the group of frontotemporal lobar degenerations and have overlapping clinical, genetic and pathological features to other neurodegenerative disorders. To date, co-existing proteinopathies have only been reported in a small proportion of GGT cases.

Methodology: An international multicentric study was initiated to collect and evaluate GGT cases. This study focused on the prevalence and type of co-existing proteinopathies including Ab, TDP-43 and a-synuclein, which were examined in multiple brain regions.

Results: The cohort comprises 73 pathologically confirmed GGT cases collected from 17 centres as part of the GGT consortium. 36 (49%) cases had Ab plaques, which included Thal phases 1 or 2 (n=16), phases 3 or 4 (n=14), and phase 5 (n=6). Cerebral amyloid angiopathy was found in 16 cases (22%). TDP-43 pathology was observed in 22 cases (30%). Limbic predominant age-related TDP-43 encephalopathy (LATE) neuropathological change was observed in 17 cases (23%; stage 1=3 cases, stage 2=10 cases, stage 3=4 cases). An additional 5 cases had an unusual constellation of neuronal and non-neuronal TDP-43 pathology that could not be classified. Lewy bodies were found in 12 cases (16%), which included one case with amygdala-predominant, four cases with brainstem-predominant, five cases with limbic-predominant, one case with neocortical-predominant Lewy bodies, and one case that could not be classified into current criteria.

Conclusion: This study highlights the spectrum of co-existing proteinopathies in GGT. Evaluating mixed pathologies has implications for biomarker and therapy development and for determining clinicopathological correlations.