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Clinical and pathological aspects of FTLD-FUS and FET proteinopathies

Abnormal intracellular accumulation of the DNA/RNA binding protein fused in sarcoma (FUS) is a characteristic feature of familial amyotrophic lateral sclerosis caused by FUS mutations (ALS-FUS). FUS is also a component of the pathological inclusions in most cases of tau/TDP-negative frontotemporal lobar degeneration where FUS co-localizes with the other FET family proteins, TAF15 and EWS (FTLD-FUS/FET). FTLD-FET includes three sporadic conditions with overlapping but distinct clinical and neuropathological features. Neuronal intermediate filament inclusion disease (NIFID) and basophilic inclusion body disease (BIBD) both present with various combinations of pyramidal/extrapyramidal movement disorders and FTD. In contrast, atypical FTLD-U (aFTLD-U) has a more consistent and highly unusual phenotype characterized by early-onset, severe progressive psychobehavioral abnormalities without significant language or motor dysfunction. Here we will review the clinicopathological correlations of the various FET proteinopathies, including some unusual cases that expand the phenotypes.

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