Atypical parkinsonism mimicking prion diseases: diagnostic challenges and predictive clinical features from the Italian Creutzfeldt-Jakob disease and related disorders Registry

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Objective: Prion diseases (PrDs) are neurodegenerative disorders characterized by abnormal prion protein aggregates[1]. Early diagnosis is challenging due to their marked clinical heterogeneity[2]. Evidence of PrDs mimicking atypical parkinsonisms mostly comes from case reports and small case series. In this study, we investigated clinical and demographic features at onset, as well as disease manifestations over time, that may distinguish PrDs from other neurodegenerative disorders in patients with suspected PrDs and a phenotype resembling atypical parkinsonism.

Methods: We retrospectively analysed demographic, clinical, instrumental, biomolecular and pathological data from 531 of 6665 patients referred to the Italian Registry for Creutzfeldt-Jakob disease and related disorders. Multiple logistic regression models were used to identify clinical features at onset and disease-course manifestations associated with neuropathologically confirmed or RT-QuIC supported PrDs. Comparisons were made with other neuropathologically defined neurodegenerative disorders, with a separate sub-analysis focusing on the Lewy Body Disease (LBD) subgroup.

Results: Based on neuropathological findings, clinical features and biomarkers, 78 patients were classified as definite PrDs, 112 as probable and 97 as possible PrDs. Seventy patients were diagnosed with definite non-prion disease. Of these, 53 had a confirmed non-prion neurodegenerative disease, while 17 had miscellaneous diagnoses. In particular, a diagnosis of definite LBD was established in 39 patients. Pure AD pathology was observed in 5 patients. PSP-specific pathology was identified in 4 patients, CBD was diagnosed in 1 patient and MSA in 4 patients (**Fig 1**). Remaining cases did not meet criteria for probable or possible PrD during follow-up and were excluded. **Discussion:** Results of multiple logistic regression models demonstrated that cerebellar signs at onset were independent predictors of PrDs, whereas a slower progression of cognitive decline and an older age at onset were associated with non-prion neurodegenerative diseases (**Fig 2**). During disease progression, cerebellar signs, akinetic mutism, dystonia and visual disturbances were associated with PrDs.

Conclusions: These findings highlight the importance of considering PrDs in the differential diagnosis of rapidly progressive parkinsonian syndromes and underscore the diagnostic value of specific clinical features at onset and throughout the disease course.

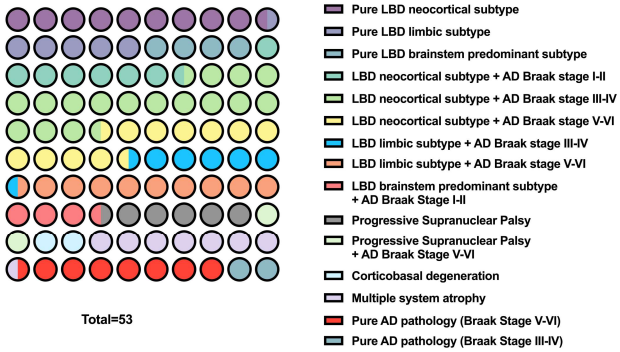

Fig 1. Neuropathological diagnoses of patients with definite neurodegenerative diseases

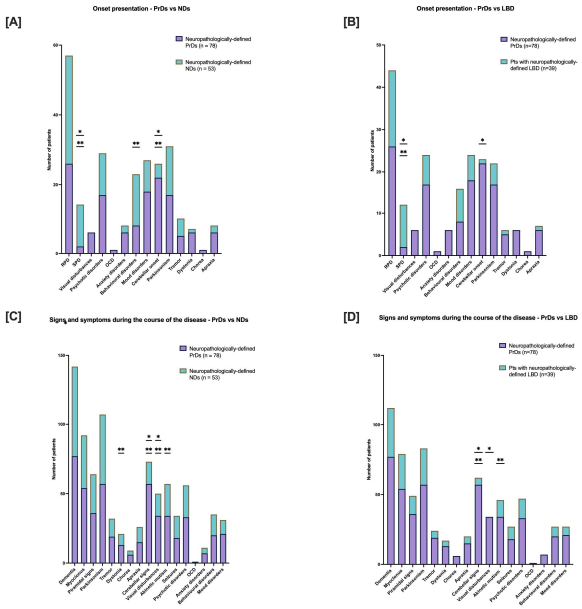

Fig 2. Signs and symptoms in patients with definite prion disease, non-prion neurodegenerative diseases and Lewy body pathology at onset and during disease course

References

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