50 Years of Progressive Supranuclear Palsy

Other clinical presentations

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In 1963 J.C. Steele, J.C. Richardson and J. Olszewski described eight cases of progressive supranuclear palsy (PSP) with a clinical syndrome, which is now termed Richardson’s syndrome (RS). Several atypical phenotypes have been described since then. In 2005, a single-center systematic analysis of 103 definite PSP cases highlighted a second distinct PSP phenotype, namely PSP with parkinsonism (PSP-P). In 2007, the same group described six definite PSP cases manifesting as pure akinesia with gait freezing (PSP-PAGF).

Further single-centre clinico-pathological studies with smaller numbers of patients have identified additional PSP phenotypes, e.g. PSP with corticobasal syndrome (PSP-CBS), frontotemporal dementia (PSP-FTD), progressive non-fluent aphasia (PSP-PNFA) and cerebellar ataxia (PSP-C).

In a multi-centric, multi-national cohort of 100 autopsy-confirmed patients, we studied the phenotypic spectrum of PSP by retrospective chart review. Only 24% of cases presented as RS and more than half of the cases either showed overlapping features of several pre-described phenotypes, or features not fitting proposed classification criteria for PSP phenotypes. Classification of patients according to predominant clinical features in the first 2 years of the disease course allowed a more comprehensive description of the phenotypic spectrum. When analysing the predominant clinical features in the first 2 years of the disease, the most common predominance types were PSP-RS, -PI (predominant postural instability), -OM (predominant oculomotor dysfunction), -P, -FTD and -CBS, capturing almost the entire population, while many of these patients developed other features later in the disease course. Thirteen cases remained unclassified.

In terms of prognosis, the mildest clinical course was observed in PSP-P. After 10 years, PSP-P patients had the lowest frequency of supranuclear gaze palsy, frontal dysfunction, cognitive decline and dysphagia, and they survived significantly longer than patients of any other predominance type did. Cumulative mortality after 5 years was about 30% in PSP-RS, PSP-CBS and PSP-FTD, but only in 5.3% PSP-P and 0% in PSP-OM.

In summary, the phenotypic spectrum of PSP may be broader and more variable than previously described in single-centre studies. Thus, too strict clinical criteria defining distinct phenotypes may not reflect this variability. A more pragmatic clinical approach using predominance types could potentially be more helpful in the early recognition and for making prognostic predictions for these patients.
References