Joint Event on 19th Global Neuroscience and Neurology Conference and 13th Global Neurologists Meeting on Neurology and Neurosurgery November 07-08, 2019, Frankfurt, Germany - Systematic review of clinicopathological correlations in logopenic progressive aphasia

Sheng Yuan Kan

University of Edinburgh Medical School, United Kingdom

Systematic Review of Clinicopathological correlations in logopenic progressive aphasia: Logopenic aphasia (lvPPA) is characterised by impaired word-retrieval and sentence repetition. It is usually associated with AD pathology, but other pathologies have been reported. The objectives of this study were to estimate the prevalence of different neuropathology in autopsied lvPPA cases and evaluate the performance of new criteria in predicting Alzheimer's Disease (AD) pathology in lvPPA patients. In this systematic review, we developed search strategies to identify studies which reported clinical cases of lvPPA and neuropathology investigation results. The included studies were analysed for reporting quality, demographics, clinical criteria and pathological diagnosis. Out of 2459 articles screened, 35 studies reported 200 lvPPA patients in total. Reporting quality were good for clinical criteria (100%) and neuropathology (91.4%), moderate for gender, age at onset and duration (60%) and poor for ethnicity (5.7%). The neuropathology findings in lvPPA are 74% AD, 20% Frontotemporal Lobar Degeneration (FTLD-TDP=14%, FTLD-Tau=6%), 2% Dementia with Lewy Bodies (DLB), 2% Creutzfeldt-Jakob disease (CJD) and 2% others. The positive predictive value of new criteria is 9% higher, but not statistically significant (p>0.05). This study confirmed the prevalence of different neuropathologies among lvPPA patients, with AD pathology being the most prevalent. We also showed that more studies are published using the new criteria and suggested the importance of multimodal diagnostic approach due to the low positive predictive value (77%) of the consensus clinical criteria. To explore the predictive value of impaired repetition for AD pathology in broadly defined lvPPA spectrum (non-naPPA/svPPA). Background: The logopenic variant (lvPPA) of primary progressive aphasia (PPA) presents core features of word-finding difficulty and impaired repetition, differently from semantic (svPPA) and non-fluent/agrammatic (naPPA) variants. Impaired repetition results from phonological loop dysfunction associated with temporo-parietal disease, which is often relatively spared in frontotemporal lobar degeneration (FTLD) compared to Alzheimer's disease (AD) pathology.

Methods: We reviewed charts of all sufficiently documented autopsy-confirmed PPA cases (n=37), excluding those who met naPPA (n=6) or svPPA (n=6) criteria. Six patients met lvPPA criteria. We identified three additional phenotypes, i.e. lvPPA+ (logopenic core features with >1 naPPA/svPPA features, n=10), lvPPA- (lvPPA with word-finding difficulty but spared repetition, n=5), and mixed (word-finding difficulty, spared repetition and ≥1 svPPA/naPPA features, n=4). We evaluated baseline phonological loop function (i.e. qualitative report of repetition and quantitative digits-forward score) in pathology-defined subgroups. In the more modern literature, Mesulam reported several cases of slowly progressive aphasia.[3] In 2001, Mesulam defined PPA as an aphasic impairment of language that must be the dominant deficit for the first 2 years after symptom onset.[4] This language deficit must be insidiously progressive in nature without an identifiable cause, which rules out non-neurodegenerative etiologies such as stroke or malignancy. Minimal memory, visuospatial, executive or social difficulty should be observed during the first 2 years, thereby eliminating neurodegenerative conditions such as typical Alzheimer disease

(AD). The existing clinical criteria for the diagnosis of PPA and associated syndromes have limitations. For example, specific clinical features have received minimal validation in patients with known pathology. In addition, clinical criteria such as the 2-year rule are arbitrary, and no empirical evidence exists to support this particular duration of disease. The recognition of PPA is important for the development of more-appropriate criteria for its diagnosis. This review focuses on the ascertainment of PPA and determination of its histopathological basis during life. First, the clinical characteristics of the three main PPA syndromes are described. Second, studies evaluating pathology in patients with PPA are reviewed. The identification of a specific PPA syndrome provides considerable information about its etiology, but many cases exist in which the clinical syndrome does not correspond to the expected pathology. Finally, biomarker studies that further define the histopathological basis of PPA are described. Neuroimaging and biofluid biomarkers will be valuable tools for establishing the pathological basis of PPA during life, particularly as a diagnosis made solely on clinical findings has a number of short-comings. As etiology-specific agents become available to treat PPA, identification of the histopathological abnormalities causing PPA in an individual patient becomes increasingly important. Clinical trials have already been designed for patients with frontotemporal lobar degeneration (FTLD) syndromes such as PPA,5 but a necessary trial prerequisite-diagnostic accuracy-remains elusive.

Results: Full lvPPA criteria predicted pure AD in 4/6 (66.7[percent]) cases (1/6 AD-mixed, 1/6 FTLD-TDP). Qualitatively, repetition was impaired in a higher frequency of patients with pure AD (11/14, 78.6[percnt]) compared to AD-mixed/FTLD (5/11, 45.5[percent]).