Aphasia Semantic Variant (PPA-SV) Versus Limbic Predominant Age-Related TDP-43 Encephalopathy (LATE): A Case Report

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Objective: Primary progressive aphasia semantic variant (PPA-SV) is an atypical dementia subtype on the frontotemporal dementia (FTD) spectrum. PPA-SV is clinically defined by naming and semantic deficits, with progressive language decline that generalizes to other domains over time. Typically, it presents as an early-onset dementia with TDP-43 pathology, but 33-46% of PPA-SV cases display initial onset after age 65 with potentially different clinical features. Limbic Predominant Age-Related TDP-43 Encephalopathy (LATE), a more recently discovered neurodegenerative entity, is defined by an older age of onset, hippocampal sclerosis/atrophy, and TDP-43 pathology with a gradually progressive amnestic profile that expands to other cognitive deficits over time. The authors present a case report with overlapping features and suspected TDP-43 neuropathology ante-mortem for two reasons: first, to highlight the need for clinical criteria to formally diagnose LATE, and second, to address a gap in the literature on the possible clinical differences of late-onset PPA-SV.
Participants and Methods: The authors present a case of a 78-year-old Indian bilingual man (English dominant) with 18 years of education, noncontributory medical history, and gradually progressive cognitive complaints reported over the past few years who was seen for outpatient neuropsychological evaluation. Prior workup was notable for negative amyloid PET scan, negative p-tau 217 blood test, and abnormal brain MRI revealing marked bilateral hippocampal atrophy with ex vacuo ventriculomegaly and minimal cerebrovascular disease. He scored 23/30 on prior MMSE, was diagnosed with amnestic MCI, prescribed Namenda and Exelon, and complained of minor memory and word-finding difficulties with reportedly intact IADLs and no signs of NPH.
Results: Neuropsychological testing revealed a profound dysnomia (RBANS Naming raw score = 1/10), and he provided 0 words on two semantic fluency tasks but 15 words on letter fluency. Receptive vocabulary score was also impaired (PPVT-4, <1st %). Memory performance also demonstrated rapid forgetting of information (RBANS List Recall raw = 0/10, Story Recall raw = 0/12) with no benefit to recognition cues (RBANS List Recognition raw = 12/20), but slightly better visual memory recall, albeit still impaired (RBANS Figure Recall raw = 4/20). Grooved pegboard scores were significantly worse with right-hand than left-hand. Irregular word reading (NAART = 16th %ile) was significantly below expectations and thought to reflect more of a surface dyslexia rather than a cultural confounder given that he has lived in the US for over 50 years and his occupational and educational history was completed in English.
Conclusions: Results support the clinical utility of neuropsychological evaluation in the differential diagnosis to support a predominant clinical syndrome of PPA-SV despite overlapping features with LATE and suspected TDP-43 pathology. This case report highlights the diagnostic issue with the lack of literature describing the typical clinical progression or suggested diagnostic criteria of LATE. These findings also indicate that late-onset PPA-SV may include greater memory deficits earlier in the course, but this may also be a clinical masquerade that is more reflective of the extent of language deficits. Further research on late-onset manifestations of PPA-SV and LATE consensus clinical guidelines is advised.

Categories: Dementia (Non-AD)
Keyword 1: dementia - other cortical
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58 Right Anterior Temporal Lobe Atrophy is Associated with Informant-Reported Socioemotional Dysfunction in Patients with Frontotemporal and Early Onset Alzheimer's Dementia

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Objective: Abnormalities in social and emotional behavior are the major diagnostic criteria for behavioral variant frontotemporal dementia (bvFTD). Investigators have attributed their behavioral disturbances to disease in mesial prefrontal and related networks, such as the salience network. This study examined the main neural correlates of informant-reported socioemotional dysfunction among patients with bvFTD compared to those with early-onset (before age 65) Alzheimer's Disease (EOAD).
Participants and Methods: Participants included 13 patients with bvFTD and their caregivers and 18 patients with EOAD and their caregivers. The caregivers consisted of a spouse, family member, or other informant who resided with the patient. They completed the informant-based Socioemotional Dysfunction Scale (SDS), a 40-item scale which rates common disturbances in social and emotional behavior on a five-point Likert scale (1-5). The patients underwent magnetic resonance imaging (MRI) with tensor-based morphometry (TBM) analysis of the 3D T1-weighted MRI scans. Computations of mean Jacobian values within select regions of interest (ROIs) in frontal and temporal lobes generated numerical summaries of regional volumes, and voxel-wise regressions created 3D statistical maps of the association between tissue volume and SDS total scores. Statistical analyses included independent samples t-tests group differences in ROIs and SDS scores, Pearson correlations between SDS scores and brain volumes, and multiple regression of ROIs with SDS scores and group as predictor variables.
Results: Compared to the EOAD group, the bvFTD group had significantly higher SDS scores ($p < .001$; $d = 2.24$), smaller frontal lobe volumes (specifically dorsolateral-prefrontal cortex, $p = .003$; $d = 1.24$), and larger temporal lobe volumes (specifically hippocampus, $p = .014$; $d = 0.979$). Within the bvFTD group, higher SDS scores were associated with a smaller right anterior temporal lobe (ATL; $p = .005$; $r = -.729$), especially the lateral ATLs ($p = .002$; $r = -.776$), and a smaller bilateral orbitofrontal cortex (OFC; $p = .016$; $r = -.650$). In contrast, within the EOAD group, higher SDS scores were associated with a smaller right parietal cortex ($p = .030$; $r = -.542$). In the entire sample (both bvFTD and EOAD), higher SDS scores was associated with a smaller lateral ATL volumes ($p = .019$; $r = -.431$). Regression analyses confirmed that SDS score predicted lateral ATL volume ($p = .041$; $b = -.262$) after controlling for diagnosis ($p < .001$; $b = -.692$).
Conclusions: These findings are consistent with greater socioemotional dysfunction, smaller frontal, and larger mesial temporal regions in bvFTD, when compared to EOAD. The findings, however, suggest that positively disturbed socioemotional behavior in bvFTD, as reported by caregivers, results from involvement of the right temporal lobe and the lateral temporal region, with further contribution from disease in OFC. The association of SDS scores and ATL volume across diagnostic groups suggests that this region is instrumental in socioemotional functioning and that the SDS may have diagnostic value in distinguishing the "right-temporal variant" of bvFTD.

Categories: Dementia (Non-AD)
Keyword 1: dementia - other cortical
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59 Objectively-Measured Performance on Tests of Episodic Memory and Executive Function in Autopsy-Confirmed Chronic Traumatic Encephalopathy

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