Limbic-Predominant Age-Related TDP-43 Encephalopathy (LATE) Dementia

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Introduction

LATE is a recently defined and under-recognized dementia subtype. Thus far, it has been definitively diagnosed only on autopsy studies with misfolded deposits of TDP-43, a proteinopathy also involved in other cognitive disorders, within the memory centers of the brain. LATE, however, tends to differ by affecting the medial temporal lobes of the brain and typically presents itself in patients over the age of 80. Symptoms of LATE mirror those of Alzheimer's or other dementias, including memory problems, difficulty with word finding and decision-making, and wandering. Supportive care is the mainstay of management at this time, as with most dementias, including increased physical activity, a healthy diet, alcohol and smoking cessation, and management of a patient's other comorbid conditions.

Case Presentation

80-year-old Caucasian male who presented to his Primary Care Provider with chief complaint of roughly one year of memory loss with progressive worsening for two months.

PMHx :

Coronary artery disease status-post stenting, thoracic abdominal aortic dissection status-post multiple repairs and aortic valve replacement, chronic kidney disease, atrial fibrillation on Eliquis, hyperlipidemia, and heart block status-post permanent pacemaker placement

Symptoms :

(+) Difficulty with name recall, word finding, new information processing, confusion with date and time, forgetfulness, use of repetitive questions

(-) Mood or behavioral issues, problems with IADLs, sleep disturbances

Prior Imaging :

CT Head (2 yrs prior) : Small vessel ischemic disease changes

Workup with PCP :

(+) SLUMS scoring 13/30

(-) CBC, CMP, Lipid panel

Secondary Workup with Geriatrician :

(+) PET CT: Posterior predominant cortical hypometabolism with relative sparing of both posterior cingulate and occipital cortex consistent with LATE

(-) TSH, Vitamin B12

Management :

Daily Donepezil with cognitive and safety education

Imaging

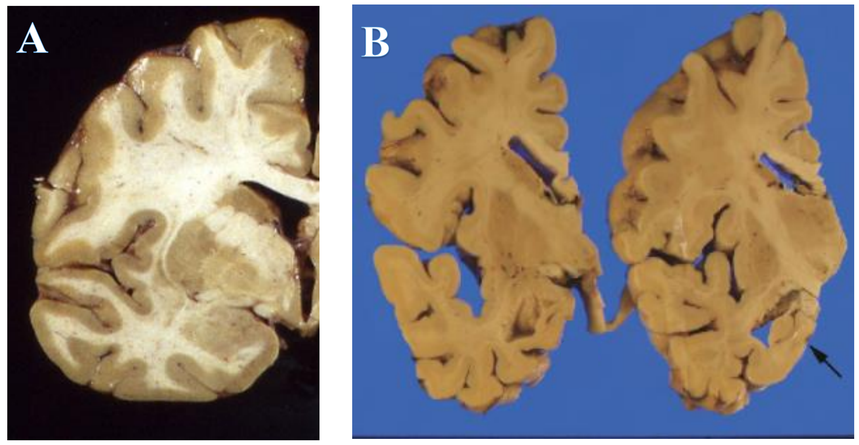

Figure 1: Autopsied Brains **(A):** Normal brain with intact hippocampus[1] **(B):** Brain with medial temporal lobe thinning and severe atrophy of hippocampus (arrow)[2]

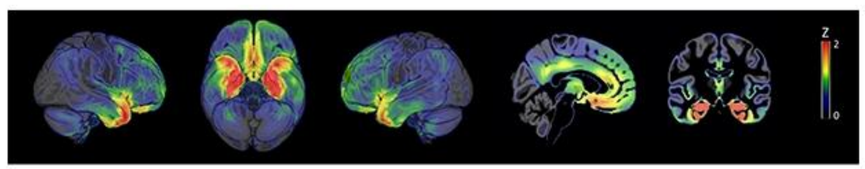

Figure 2: FDG-PET pattern of hypometabolism of LATE within the temporolimbic region of the brain[3]

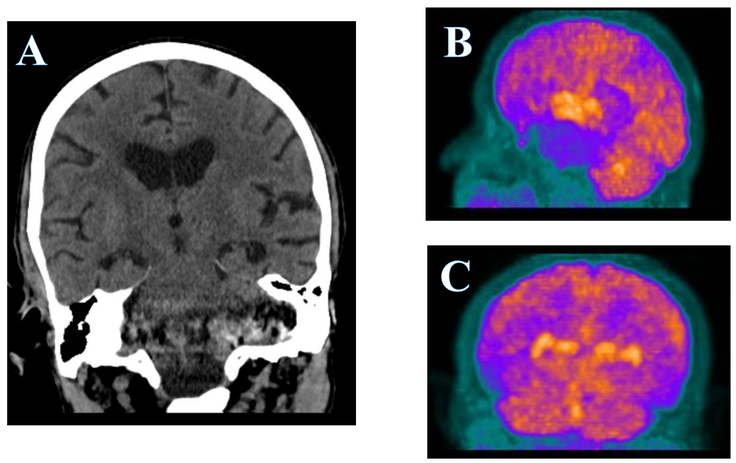

Figure 3: Patient Imaging **(A):** CT Head 2 years prior to current presentation **(B)/(C):** PET-CT with hypometabolism within the temporolimbic region of brain

Discussion

This case illustrates the reality of mimics of Alzheimer's Dementia and the importance of diagnostic imaging and biomarkers to differentiate such subtypes. Given new developments in MRI and PET imaging, new biomarkers are emerging to help differentiate LATE from other subtypes as opposed to current clinical diagnostics. Similarly, there is a need for further development of other TDP-43 specific radiotracers, biofluid markers, and genomic identifiers to hopefully lead to new treatment targets and subsequent modalities to improve patient outcomes.

What's Next?

Biomarkers :

TDP-43 within astrocytic exosomes >> microglial exosomes

Genetics :

Risk alleles ApoE carriers or TMEM106B

FDG-PET :

Hypometabolism patterns: temporolimbic in LATE versus temporoparietal in AD

Trials:

Vasodilators (Nicorandil) to treat hippocampal sclerosis in patients with memory problems. Criteria involved elevated tau and reduced hippocampal volumes without amyloid.

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Figures:

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