The Importance of Screening for FTD in ALS

Once thought to be extremely rare, frontotemporal degeneration (FTD) is now recognized to be the cause of 10% to 20% of all dementia cases. Onset can occur any time from the third to ninth decade, but is most common between ages 45 and 65, earlier than the average age of onset of Alzheimer's disease.

FTD can co-occur with ALS, most commonly due to mutations in the C9orf72 gene, as well as from mutations in TARDP or FUS. In these cases, FTD and ALS can be thought of as two ends of a clinical spectrum, with many patients developing first one and then the other, with the evolution and intensity of each variable from person to person, even within a single family.

Management of ALS/FTD poses special challenges to the family, and to the physician, according to Rick Bedlack, MD, PhD, Director of the Duke University ALS Clinic, and Director of Advocacy and Outreach for the CReATe Consortium. "Patients with ALS and FTD are more likely to be non-compliant with evidence-based care options such as good nutrition and non-invasive ventilation, compared to patients with ALS alone," he says. In addition, patients with ALS and FTD in general do not survive as long as patients with ALS alone. "For these reasons, it is important for ALS clinicians to screen for FTD."

While there is not yet a consensus among experts about the best way to screen for FTD, many clinics use a standardized tool such as the ALS Cognitive Behavioral Screen (ALS-CBS) or the Edinburgh Cognitive and Behavioral ALS Screen (ECAS). If results are abnormal, the patient should be referred for detailed neuropsychological testing.

Links:
ALS-CBS: http://www.cpmcri-currents.org/sites/default/files/shared/ALS%20CBS%202014%20non-copyrighted.pdf

ECAS:
https://www.era.lib.ed.ac.uk/handle/1842/6592

Although both the ALS-CBS and the ECAS can be used as screening tools to identify patients in need of more thorough neuropsychological evaluation, the ECAS serves not only as a screen, but also as a brief assessment.

In addition to cognitive and behavioral testing (including caregiver/informant-based assessments), a full FTD work-up would include a detailed medical history, family history, social history, neurological exam, brain imaging study (such as MRI), EMG, and bloodwork (B12, copper, TSH, and in some cases testing for syphilis and HIV). Genetic testing for C9orf72, TARDP and FUS may also be considered.

The discovery of a common genetic basis for many cases of FTD and ALS has led to a major realignment between two fields that have been largely separate in the past, Dr. Bedlack notes. “Investigators from the fields of FTD and ALS have come together to begin to understand the shared biology of these two diseases. This unprecedented collaboration has led to the discovery that dysfunction in RNA processing and protein homeostasis is an emerging theme in both these diseases. This work is still in a pre-clinical phase, but in the next few years it is quite likely that we will see trials in our clinics manipulating these shared mechanisms open to both patient groups.”

The CReATe Consortium is helping to lay the groundwork for those trials, and for a deeper understanding of ALS, ALS-FTD, and related diseases, through combining detailed clinical phenotyping (including not just motor assessments, but also detailed cognitive and behavioral testing) with genotyping and biological-fluid based biomarker development. Patients can become involved in this important work by enrolling in a new CReATe-sponsored clinical trial. You can learn more about this trial at https://www.rarediseasesnetwork.org/CREATE/8001.htm