In This Issue: The Non-Alzheimer Dementias

Whereas Alzheimer's disease accounts for the largest percentage of patients with dementia, non-Alzheimer dementias may account for up to 40% of dementias,[1] and an additional percentage of dementias may be related to a mixture of Alzheimer's and non-Alzheimer neuropathology. In this issue of *The Journal of Clinical Psychiatry*, Bradley F. Boeve, M.D., considers the clinical and neuropathologic features, evaluation, and management of the neurodegenerative and prion diseases that cause non-Alzheimer dementias, their known genetic risk factors, and the still-evolving terminology used to describe some of these conditions.

While the list of non-Alzheimer dementias may be daunting, physicians should resist the temptation to ignore these problems until definitive disease-specific medication treatments come along. Why? Patients with the non-Alzheimer dementias have potentially important differences in their cognitive, noncognitive behavioral, and associated neurologic features; in their onset age and clinical course; and in some of their caregiving challenges and needs. For instance, the frontotemporal dementias may be confused with late-life depression, may not respond well to cholinesterase inhibitors, and may be associated with behavioral changes that are especially frustrating for caregivers who do not understand these changes as part of the patient's disorder. They also may have modes of inheritance and genetic causes that could be helpful for families to understand. Patients with dementia with Lewy bodies, one of the most common non-Alzheimer dementias and commonly associated with visual hallucinations, may be unusually sensitive to the extrapyramidal side effects of antipsychotic medications.

Researchers continue to make scientific progress in the understanding of non-Alzheimer dementias. For instance, more than 30 mutations in the gene encoding the microtubule-associated protein tau have been shown to cause a condition known as familial frontotemporal dementia with parkinsonism linked to chromosome 17 (FTD-17), neuropathologically characterized by neurofibrillary inclusions composed of hyperphosphorylated tau. Earlier this year, mutations in another gene on chromosome 17 encoding the protein progranulin (*PGRN*) were shown to cause another form of frontotemporal dementia, neuropathologically characterized by inclusions composed of ubiquitin rather than hyperphosphorylated tau,[2,3] raising the possibility that this growth factor is necessary for neuronal survival. These scientific discoveries may provide targets at which to aim new disease-slowing and prevention therapies for these less common forms of dementia.

While it can be difficult to make the diagnosis of non-Alzheimer dementias, clinicians should be on the lookout for forms of dementia with atypical symptoms or neuropsychological findings, an unusually early age at onset or a strong familial pattern. Sometimes, referral to a memory loss specialist, brain imaging (e.g., fluorodeoxyglucose positron emission tomography in making the distinction between Alzheimer's disease and frontotemporal dementia[4]), genetic testing (with appropriate genetic counseling), other laboratory tests, or neuropathologic examination may be indicated to support the right diagnosis. While judicious use and empirically justified

continuation of medications are helpful in certain cases, patients and families afflicted by non-Alzheimer dementias may also benefit from careful consideration of those nonpharmacologic treatment strategies designed to lessen the impact of their particular, intolerably distressing and disabling symptoms.

If you have suggestions or comments regarding this special section please feel free to contact me at Eric.Reiman@bannerhealth.com.

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REFERENCES

1. Leifer B. Early diagnosis of Alzheimer's disease: clinical and economic benefits. J Am Geriatr Soc 2003;51:S281–S288
2. Baker M, Mackenzie IR, Pickering-Brown SM, et al. Mutations in progranulin cause tau-negative frontotemporal dementia linked to chromosome 17. Nature 2006;442:916–919
3. Cruts M, Gijselinck I, van der Zee J, et al. Null mutations in progranulin cause ubiquitin-positive frontotemporal dementia linked to chromosome 17q21. Nature 2006;442:920–924
4. US Dept Health Human Services. Centers for Medicare and Medicaid Services. Decision Memo for Positron Emission Tomography (FDG) and Other Neuroimaging Devices for Suspected Dementia (CAG-00088R); September 15, 2004. Available at: http://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=92. Accessibility verified Nov 10, 2006

