

Figure 1. Magnetic resonance imaging (MRI) scan, axial fluid attenuated inversion recovery (left), axial diffusion-weighted (middle), and computed tomography (right) scans. Note the subtle hypodensity in the temporal lobe and markedly greater signal on MRI.

established based on clinical presentation, neuroradiology, routine CSF analysis, and electroencephalography. Our case is highly unusual, with early neuroimaging abnormalities and near-normal routine CSF findings. PCR confirmed HSE the same day. This case emphasizes the importance of early neuroimaging in elderly patients suspected of having HSE without CSF abnormalities.

PCR detection of HSV DNA in CSF is presently considered to be the reference standard but may be negative during the first 24 to 48 hours after onset of symptoms. Also, PCR sensitivity can diminish 5 to 7 days after commencing antiviral treatment.^{3,4} EEGs show temporal lobe involvement as well as characteristic PLEDs and are fairly sensitive, particularly during the first 48 hours, although lacking specificity.⁵ Several publications have recently reported on the diagnostic value of diffusion-weighted MRI, suggesting that it is more sensitive than conventional T2-weighted sequences in the early detection of HSE, although conclusive studies have not yet been performed.⁶

CT scans typically reveal hypodensities in the temporal lobes and frontal lobes (uni- or bilaterally), rarely with hemorrhagic components, and show gadolinium enhancement only during later stages of the disease. T2-weighted and MRI imaging studies, as well as fluid attenuated inversion recovery and diffusion-weighted sequences, commonly show more-extensive abnormalities corresponding to tissue edema, often including the inferior frontal and medial temporal lobes, and insular cortex and often sparing the basal ganglia. The neuroradiological findings in this patient are typical for HSE, although they appeared unusually early. Diagnostic tools are evolving but presently do not offer high enough sensitivity to exclude the presence of HSV in the early stages of the disease. Our case report suggests that conventional MRI should be performed early in the absence of other diagnostic clues.

The efficacy of acyclovir 10 mg/kg given every 8 hours for 21 days has been proven in two randomized clinical trials.^{7,8} The effect of dexamethasone as an adjuvant treatment on survival and neurological sequelae of HSE in adults is being studied in the German trial of Acyclovir and Corticosteroids in Herpes Simplex Encephalitis, which is planned to conclude in 2011. In our patient, early acyclovir treatment—before a pleocytosis appeared—did not have a significant effect on outcome.

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HOW TO MANAGE OVERACTIVE BLADDER IN ELDERLY INDIVIDUALS WITH DEMENTIA? A COMBINED USE OF DONEPEZIL, A CENTRAL ACETYLCHOLINESTERASE INHIBITOR, AND PROPIVERINE, A PERIPHERAL MUSCARINE RECEPTOR ANTAGONIST

To the Editor: Although urinary incontinence inevitably occurs in advanced stages of dementia of any etiology, urinary urgency or frequency (also called an overactive blad-

der, OAB) occurs more commonly in dementia with Lewy bodies (DLB)¹ and vascular dementia (also called multiple cerebral infarction)² (both > 80%) than it does in Alzheimer's disease (AD) (40%).³ Comorbidity of AD and vascular etiologies is not uncommon. Acetylcholinesterase (AChE) inhibitors for dementia and anticholinergics for OAB have been widely used, although a combination of these medications is believed to be contradictory. Thus, there have been no established regimens to treat a patient who has dementia and OAB together.

Twenty-six cognitively impaired older individuals were prospectively recruited (AD in 7, multiple cerebral infarction in 5, DLB in 5, frontotemporal dementia in 1, AD and multiple cerebral infarction in 8; of these, 5 with mild cognitive impairment, 19 with dementia, 17 with difficulty walking). They were seven men and 19 women, mean age 78 (range 62–88), already taking 5 mg per day (according to the drug formula in Japan) of donepezil hydrochloride, a central AChE inhibitor, for 7 months (range 3–20 months), but all still had OAB. The patients were started on 20 mg per day (according to the drug formula in Japan) of propiverine hydrochloride, a peripheral muscarinic receptor antagonist, for OAB. A urinary questionnaire (a part of the modified Functional Independence Measure,⁴ filled basically by the caregivers), Mini-Mental State Examination (MMSE; 0–30 scale), and the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog; 0–70 scale)⁵ were completed before and 3 months after the addition of propiverine. Statistical analysis was performed using the Student paired *t*-test and the chi-square test. At the first assessment, the patients showed a mean nighttime urinary frequency of 3.1 times and a daytime frequency of 5.9 times, and urinary incontinence was observed in 14 of 26 patients. Urinary incontinence occurred more than once a day in 11 patients, more than once a week in two, and more than once a month in one. Mean MMSE and ADAS-cog scores were 19.4 and 18.6, respectively (Figure 1). At the second assessment, none of the patients had discontinued the propiverine treatment because of dry mouth, constipation, delusion, or agitation. The patients showed a mean nighttime frequency of 2.5 times ($P < .05$) and a daytime frequency of 5.7 times (not significant), and urinary incontinence was observed in 12 of 26 patients ($P < .01$). Daily incontinence disappeared in 36% of patients with daily incontinence. Mean MMSE and ADAS-cog scores were 19.3 and 18.8, respectively (not significant) (Figure 1). There was no correlation between the changes in urinary symptoms and age, sex, underlying diseases, gait function, or MMSE or ADAS-cog scores.

To the best of the authors' knowledge, this is the first report to show that addition of 20 mg per day propiverine to 5 mg per day donepezil improved OAB without any cognitive change. Although there were no larger such studies previously, two case reports are available, and the results suggested con and pro, respectively. One⁶ reported three cases taking 5 mg per day of donepezil, 6 mg per day of rivastigmine, and 10 mg per day donepezil, respectively. All patients developed delusion and agitation after starting 4 mg per day of tolterodine, a muscarinic receptor blocker, for OAB. **Discontinuation of tolterodine reversed these events completely.** Another study⁷ reported one case taking 10 mg per day of donepezil and 6 mg per day of tolterodine

for OAB (details not known). After the dose of tolterodine was titrated to 4 mg per day, the subject came to have nocturia that might cause poor sleep and agitation. More recently, a retrospective study of 3,536 nursing home residents taking central AChE inhibitors, of whom 10.6% were prescribed anticholinergics together, found no differences in cognitive function between groups of AChE inhibitors alone and AChE inhibitors with anticholinergics, although the subjects scored only from 0 to 10 on the Minimum Data Set used for cognitive assessment.⁸ Propantheline and oxybutynin have been used to treat urinary incontinence in patients with dementia but without detailed cognitive assessments. Oxybutynin is known to produce cognitive problems⁹ because it is more lipophilic and more apt to penetrate the blood-brain barrier than other anticholinergic agents, including propiverine.¹⁰ Although the current study was a pilot study, it calls for an experimental study to determine whether the combined use of a "central" AChE inhibitor and a "peripheral" muscarine re-

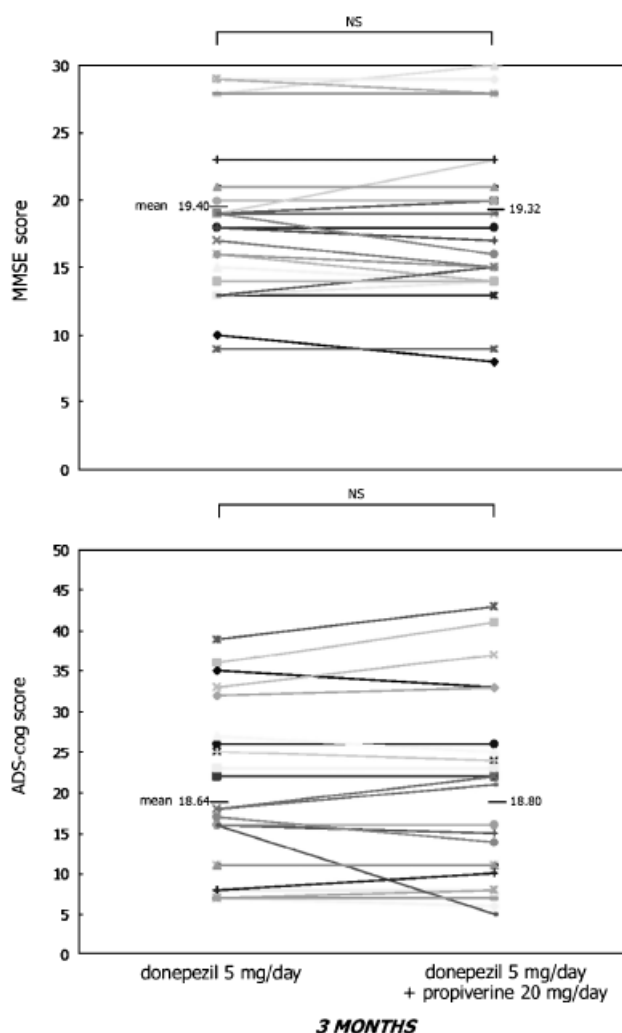


Figure 1. Mini-Mental State Examination (MMSE; range 0–30, lower scores indicating worse cognition) and Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog; range 0–70, higher scores indicating worse cognition) scores before and after the addition of propiverine to donepezil. NS = not statistically significant.

ceptor antagonist would be pharmacologically sound as site-directed therapy, because many elderly patients and their caregivers seek medical care for dementia and OAB together. This combination therapy therefore could become an option in patients who suffer from dementia and OAB together.

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GLUCOSE IMPAIRMENT IN OLDER ADULTS WITH DIABETES MELLITUS AND NON-ST ELEVATION ACUTE MYOCARDIAL INFARCTION IS LINKED TO MYOCARDIAL NECROSIS AND SYSTOLIC DYSFUNCTION

To the Editor: Impaired glucose tolerance is linked to greater cardiovascular mortality rate, and glucose level has been established as an independent risk factor for cardio-