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Improvement in Tc-99m HMPAO brain SPECT findings during donepezil therapy in a patient with pure akinesia

Gorsev G. YENER,* Gamze Çapa KAYA,** Vesile ÖZTÜRK* and Gulden AKDAL*

*Department of Neurology, Dokuz Eylül University, Medical School, Izmir, Turkey
**Department of Nuclear Medicine, Dokuz Eylül University, Medical School, Izmir, Turkey

A 58-year-old man presented with a history of disturbance in initiating gait. His history revealed meningoencephalitis five years prior to admission. Neurological examination included gait disturbance as difficulty in initiation and a hesitating speech with many freezing episodes and micrographia. Magnetic resonance imaging (MRI) showed diffuse hyperintensity of frontal subcortical white matter on T2 weighted images. He was diagnosed with PA. L-Dopa up to the dosages of 1000 mg/day and selegiline 10 mg/day were given. First brain SPECT using technetium-99m labeled D,L-hexamethylpropylene amine oxime (Tc-99m HMPAO) was performed when he was taking L-dopa and selegiline. In visual evaluation, hypoperfusion in bilateral frontoparietal cortex was seen (Fig. 2). Treatment with L-dopa and selegiline produced no benefit. Donepezil 10 mg/day was begun. This therapy regimen resulted in dramatic clinical improvement within several days that was confirmed by blinded raters who watched the patient's video recordings. During this response second brain perfusion SPECT study was repeated during donepezil therapy. Markedly increased perfusion in bilateral frontoparietal cortex was observed. This is the first case of PA to develop possibly after an episode of bacterial pneumococcal meningoencephalitis and who responded to donepezil as documented by changes in clinical findings and Tc-99m HMPAO brain SPECT studies.

Key words: pure akinesia, Tc-99m HMPAO brain SPECT, donepezil

INTRODUCTION

PURE AKINESIA (PA) is a clinical syndrome characterized by disturbances of gait, speech and handwriting. The absence of rigidity, rest tremor, dementia, or response to L-dopa is among the other features PA.[1] The relationship of PA to progressive supranuclear palsy (PSP)[1,2] has been emphasized, but non-degenerative etiologies have also been reported.[3,4] Hypoperfusion in the frontal cortex has been demonstrated in previous studies.[4,5] This case report determines improvement in brain SPECT findings in a patient with PA during donepezil therapy.

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For reprint contact: Gamze Çapa Kaya, M.D., Dokuz Eylül University, School of Medicine, Department of Nuclear Medicine, Inciralti, 35340 Izmir, TURKEY.

E-mail: gamze.capa@deu.edu.tr

CASE REPORT

A 58-year-old man presented with a history of disturbance in initiating gait. His history revealed meningoencephalitis five years prior to admission, diabetes mellitus, and daily alcohol consumption. Neurological examination included gait disturbance as difficulty in initiation and a hesitating speech with many freezing episodes and micrographia. He had no rigidity, gaze paralysis, or static tremor. Laboratory investigations including total blood count, electrolytes, BUN, creatinine, hepatic enzymes, thyroid function tests, vitamin B_{12}, and tests for HIV, syphilis, hepatitis, Brucella, and Lyme were within normal limits. Wechsler memory tests, Stroop color word interference tests, controlled oral word association test, verbal fluency, Luria's hand sequences, and Benton line orientation test were within normal limits. Magnetic resonance imaging (MRI) showed diffuse hyperintensity of frontal subcortical white matter on T2 weighted images

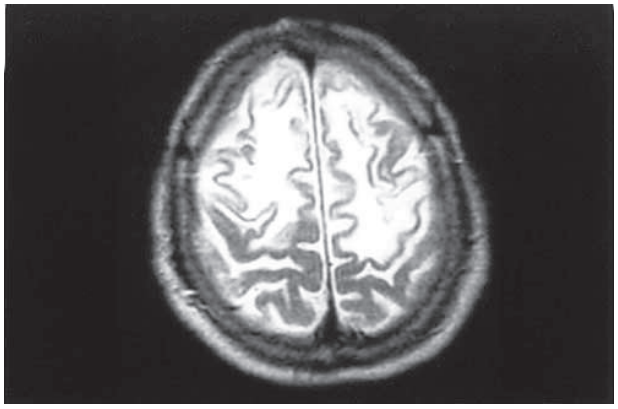

Fig. 1 Diffuse frontal subcortical hyperintensity on T2 weighted MRI images.

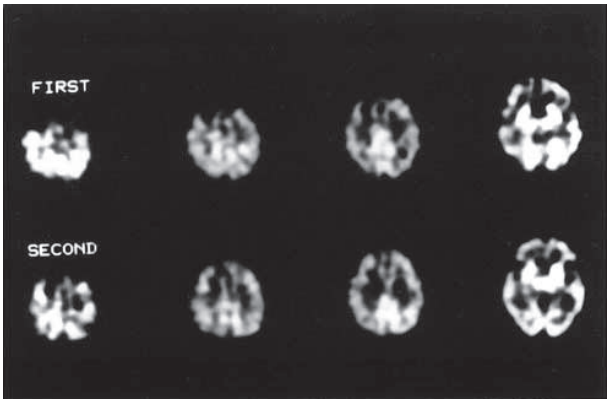

Fig. 2 The first SPECT images (before donepezil therapy) showed decreased perfusion in bilateral frontoparietal cortex (*upper images*). The second SPECT during donepezil showed markedly increased perfusion in bilateral frontoparietal cortex (*lower images*).

(Fig. 1). He was diagnosed as PA. L-Dopa up to the dosages of 1000 mg/day and selegiline 10 mg/day were given. First brain perfusion SPECT was performed when he was taking L-dopa and selegiline. 925 MBq technetium-99m D,L-hexamethylpropylene amine oxime (Tc-99m HMPAO) was injected intravenously with the patient lying supine position in a quiet and dimmed room. Imaging was performed 30 minutes after the injection with a three headed gamma camera (GE, Medical Systems, Neurocam, Horsholm, Denmark) equipped with high resolution collimators. A total of 128 frames were obtained in 64 × 64 matrices, 35 s/frame and over 360°. The coronal and sagittal planes were obtained following reconstruction of 2 pixel slices in the transaxial plane. SPECT images were evaluated visually and semi quantitatively. Semi quantitative analysis was done by drawing irregular regions of interest (ROIs') corresponding to symmetrically identical right and left cortical regions. The ROI boundaries were drawn along the outside surfaces of the brain and internally followed the division between the gray and white matter. ROI was first identified for the first brain SPECT slices and then moved to the same side on the second brain SPECT slices. The lesions to cerebellum ratios were calculated in three consecutive slices. In visual evaluation, hypoperfusion in bilateral frontoparietal cortex was seen (Fig. 2). Lesions to cerebellum ratio for left frontoparietal cortex and right frontoparietal cortex were 0.66 and 0.57, respectively. Treatment with L-dopa and selegiline produced no benefit. Donepezil 10 mg/day was begun. This therapy regimen resulted in dramatic clinical improvement within several days that was confirmed by blinded raters who watched the patient's video recordings. During this response second brain perfusion SPECT study using Tc-99m HMPAO was repeated. Markedly increase perfusion in bilateral frontoparietal cortex was observed (Fig. 2). Semi quantitative evaluation also demonstrated increased lesions to cerebellum ratios for bilateral frontotemporal cortex during therapy response (0.81 and 0.76 for left and right frontoparietal cortex, respectively).

DISCUSSION

In our case, diagnosis of PA was supported by a gait disorder with start hesitation and freezing, speech hesitation and freezing, and micrographic handwriting. He lacked rigidity, static tremor, dementia, and any response to L-dopa. At the time of the acute pneumococcal meningoencephalitis, computerized tomography (CT) showed diffuse hypodensity in the frontal-subcortical white matter and curvilineer gyral contrast enhancement in the frontal and parietal regions. Our patient's gliosis in frontal subcortical white matter in MRI may be related to the CT image during the meningoencephalitis episode, and may also cause the hypoperfusion on SPECT. His follow-up for two years did not result in PSP, yet we cannot be certain that our case will not develop any degenerative disease in future.

PA can be a limited form of PSP[1,2] and may be seen in Lewy body dementia,[6] pallido-nigro-luysian atrophy,[7] or in non-degenerative disorders including subcortical white matter infarct.[3] The common findings in most cases include hypometabolism or hypoperfusion seen in frontal lobes.[4,5] Changes in striatum have also been reported due to primary central nervous system lymphoma primary involving the globus pallidus[3] and thalamic infarction.[8] We observed a case of PA with diffuse frontoparietal hypoperfusion on SPECT images and frontal subcortical gliosis on MRI images possibly after an episode of bacterial pneumococcal meningoencephalitis.

Brain SPECT studies have been used to investigate differences between progressive supranuclear palsy, cortico-basal degeneration and multiple system atrophy.[9–14] Hypoperfusion in the frontoparietal lobe and basal ganglia on brain perfusion SPECT often supports

the diagnosis of progressive supranuclear palsy.[12,15] Frontal hypoperfusion has been shown in patients with PA, an atypical manifestation of progressive supranuclear palsy, using brain SPECT in limited number of case reports.[4,5,8] Watanabe et al. demonstrated a significant increase in brain activitiy in the right cingulated cortex after tandospirone therapy using activational SPECT study with Tc-99m ethyl cystienate dimmer during gait. In our case report, increased perfusion in the bilateral frontoparietal cortex was demonstrated after donepezil therapy comparing with SPECT findings before donepezil therapy.

Treatment options in PA are limited. In this patient, we observed a temporary, but dramatic relief with donepezil. During tandospirone citrate therapy, marked improvement in clinical findings in a patient with pure akinesia was reported previously.[5] This is the first case of PA that developed possibly after an episode of bacterial pneumococcal meningoencephalitis and who responded to donepezil as documented by changes in clinical findings and Tc-99m HMPAO brain SPECT studies.

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