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CASE REPORT

The Application of Proton Magnetic Resonance Spectroscopy and Cerebral Perfusion Single Photon Emission Computed Tomography for the Diagnosis of Frontotemporal Dementia in Brothers

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ABSTRACT

Extensive data have shown that magnetic resonance spectroscopy is valuable for the diagnosis of common dementias. Cerebral perfusion single photon emission computed tomography has proven characteristic perfusion defect patterns in patients with Alzheimer's disease and frontotemporal dementia. This report is of 2 brothers with frontotemporal dementia. The elder brother was diagnosed with frontotemporal dementia at the age of 57 years. Imaging studies showed that he had unilateral left frontotemporal atrophy by magnetic resonance imaging, depressed N-acetyl aspartate:creatine ratio and raised myoinositol:creatine ratio by magnetic resonance spectroscopy, and asymmetrical left frontotemporal hypoperfusion by cerebral perfusion single photon emission computed tomography. His brother presented with memory loss at the age of 48 years and was suspected to have familial inheritance of frontotemporal dementia. He had similar magnetic resonance spectroscopy pattern and single photon emission computed tomography findings, although no morphological changes were evident at routine magnetic resonance imaging brain study. These patients demonstrate that magnetic resonance spectroscopy is sensitive for early screening for dementia, and cerebral perfusion single photon emission computed tomography has the unique ability to differentiate frontotemporal dementia from Alzheimer's disease.

Key Words: *Dementia; Magnetic resonance spectroscopy; Tomography, emission-computed, single-photon*

INTRODUCTION

Extensive data have demonstrated that proton magnetic resonance spectroscopy (MRS) is invaluable for the diagnosis of common dementias. However, the MRS metabolite ratios of Alzheimer's disease (AD) and frontotemporal dementia (FTD) are similar, with decreased N-acetyl aspartate (NAA) and raised myoinositol (MI) relative to creatine (Cr) in the brain.[1] Differentiation of these 2 entities by MRS therefore seems difficult in the early stages, when the respective clinical features have not matured. Cerebral perfusion single photon emission computed tomography (SPECT) has already demonstrated a characteristic perfusion deficit pattern for AD and FTD, namely bilateral symmetrical parietotemporal hypoperfusion for AD and asymmetrical frontotemporal hypoperfusion for FTD.[2]

This report is of 2 brothers with dementia. The elder brother had a typical FTD clinical presentation, MRS pattern, and cerebral perfusion pattern on SPECT. The younger brother was clinically suspected to have early dementia, with an abnormal MRS pattern and cerebral SPECT contributing to the diagnosis of early FTD in the presence of a strong family history.

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CASE REPORT

Patient 1

A 57-year-old man presented in 2005 with poor memory and personality changes for the previous 2 years. His wife noted that he was irritable and had speech problems. He had a family history of dementia, as his father was diagnosed with dementia at the age of 78 years.

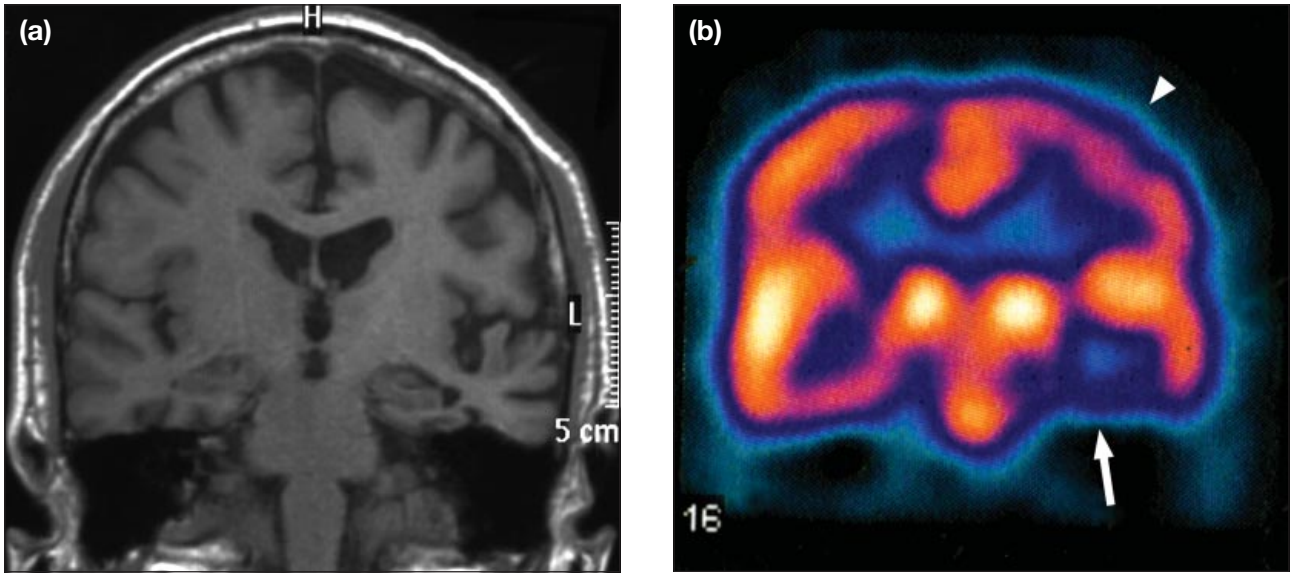

Figure 1. Imaging for patient 1. (a) Coronal T1-weighted magnetic resonance image showing unilateral left frontotemporal atrophy; and (b) coronal single photon emission computed tomography image showing left frontal lobe (arrowhead) and left temporal lobe (arrow) hypoperfusion.

Physical examination was unremarkable, with no evidence of neurological deficit. Magnetic resonance imaging (MRI) showed unilateral left frontotemporal atrophy (Figure 1a). MRS was done by a single voxel (2 x 2 x 2 cm) placed on a midsagittal T1-weighted image covering the right and left posterior cingulate gyri, using the point-resolved spectroscopic sequence with a repetition time of 2000 ms, echo time of 30 ms, a single water-suppressed spectrum, pre-scan automated parameter optimisation consisting of frequency and receiver gain adjustment, and shimming and gradient tuning (Gyroscan Intera 1.5T; Philips, Best, The Netherlands). Data were acquired at a spectral bandwidth of 1000 Hz and 64 signals were averaged for each water-suppressed spectrum. The averaged signals were exported and processed on an off-line computer and analysed by LCModel. MRS showed depressed NAA/Cr (1.304 [normal ratio, 1.53±0.13]) and raised MI/Cr (1.379 [normal ratio, 0.65±0.08]), compatible with either AD or FTD.[1] Cere-bral perfusion SPECT using 25 mCi injection of technetium-99m ethyl cysteinate dimer was done 45 minutes post-injection by a dual-headed gamma camera (Infinia Hawkeye; General Electric, Milwaukee, USA) equipped with a fan beam collimator. Images were acquired in 120 projections over a 360° arc using the step-and-shoot mode with an acquisition time of 20 seconds per projection. Transverse slices were created by filtered back-projection using a Butterworth filter with a cut-off frequency of 0.38 and an order of 8.00. The transverse slices were corrected for attenuation and were re-angulated, yielding orbitomeatal parallel slices. SPECT showed asymmetrical left frontotemporal hypoperfusion, consistent with the MRI findings (Figure 1b).

Patient 2

Patient 1's younger brother was 48 years old when he presented in 2006 with recent memory loss. In view of his strong family history of dementia, MRI and MRS were initially performed to detect any early changes that may suggest an increased risk for dementia. MRI of the brain was unremarkable, with no evidence of cortical atrophy or cerebral infarction (Figures 2a and b).

MRS of the posterior cingulate gyri showed depressed NAA/Cr (1.121) and elevated MI/Cr (0.934). The right temporal lobe showed a similar MRS pattern to that in the posterior cingulate gyri, while both frontal lobes showed elevated MI/Cr (1.069 on the right side and 1.055 on the left side), with normal NAA/Cr (1.560 on the right side and 1.573 on the left side). The MRS results indicated that the patient was at high risk for dementia. Brain SPECT was then performed to further differentiate the type of dementia. SPECT showed right inferior frontal lobe hypoperfusion, and right medial temporal lobe and left inferior temporal lobe hypoperfusion. There was also an incidental finding of a right occipital lobe focal perfusion defect with no corresponding MRI lesion. The SPECT perfusion deficits were suggestive of FTD with bilateral asymmetrical involvement and the parietal lobes were normal in perfusion, which is not compatible with AD[3] (Figures 2c and d).

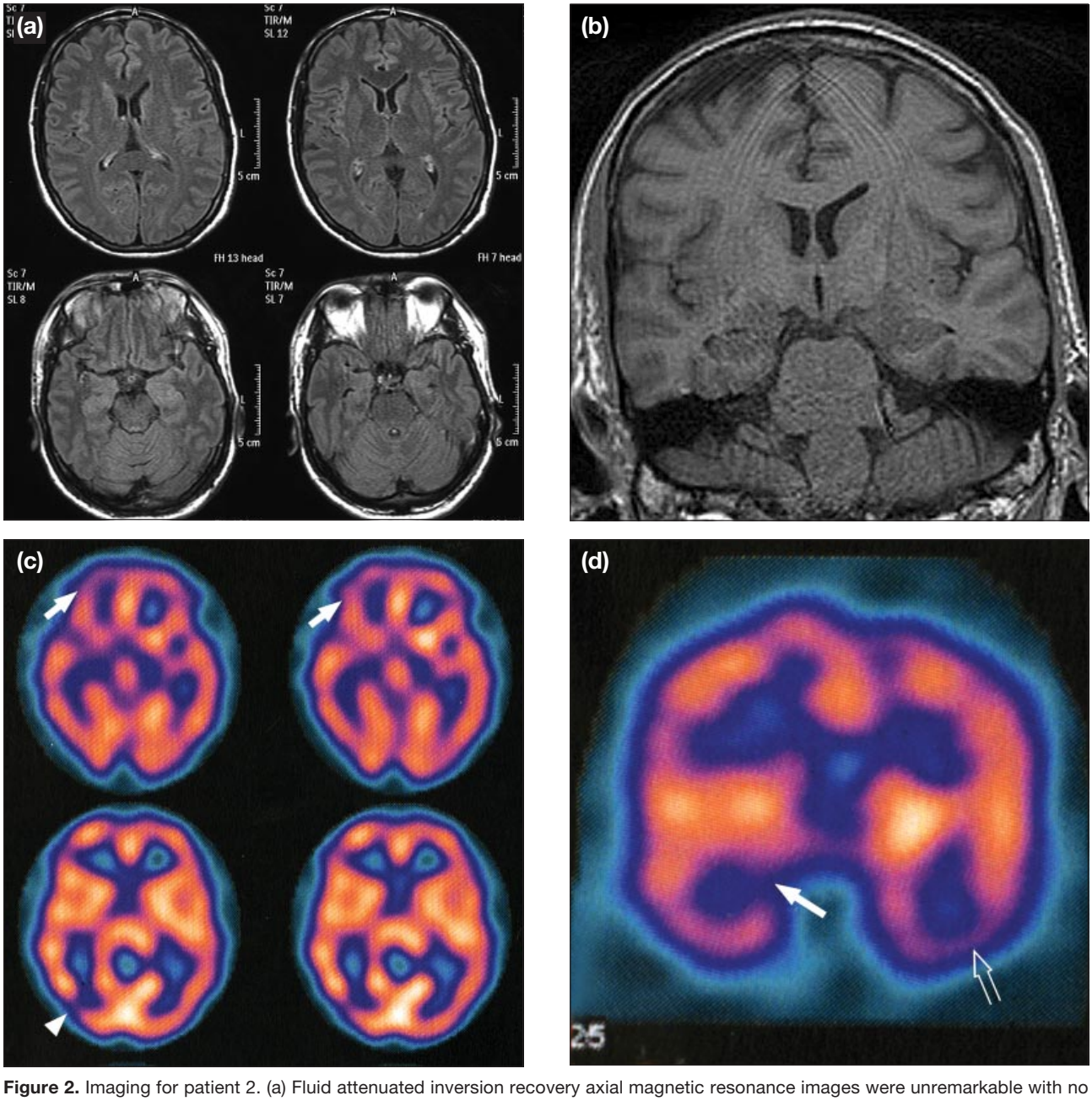

Figure 2. Imaging for patient 2. (a) Fluid attenuated inversion recovery axial magnetic resonance images were unremarkable with no evidence of infarction, white matter degenerative change, or cortical atrophy; (b) coronal T1-weighted magnetic resonance image of the brain was unremarkable; (c) axial single photon emission computed tomography showing right frontal lobe hypoperfusion (arrows) and right occipital lobe perfusion defect (arrowhead); and (d) coronal single photon emission computed tomography showing bilateral asymmetrical temporal lobe hypoperfusion.

Subsequent clinical follow-up showed early presentation of FTD clinical features.

DISCUSSION

The most common form of dementia is AD, which is characterised by amnesia, visuospatial disorientation, apraxia, and aphasia, reflecting the affinity of the pathological process for the limbic system and parietotemporal association cortex. However, the spectrum of disorders of primary degenerative brain disease may not conform to this typical neuro-psycho-pathological profile. The best recognised of these clinical syndromes is FTD.

FTD commonly presents between the ages of 45 and 65 years, affecting both sexes equally. A history of a similar disorder in a first-degree relative occurs in approximately 50% of patients. The behavioural characteristics of patients with FTD are disinhibition, overactivity, and restlessness or, alternatively, inertia in the frontal and temporal variants.[4] All patients with

FDT have emotional shallowness with loss of sympathy and empathy for others. Perceptual, spatial, and praxic skills remain strikingly well preserved throughout the illness. A recent study has shown variations in regional SPECT hypoperfusion related to clinical features of FTD.[5] Frontal lobe involvement is associated with apathy, whereas temporal lobe involvement is associated with hypomania-like behaviour. In addition, right frontal lobe hypoperfusion is associated with loss of insight, environmental dependency, and stereotyped behaviours, whereas left frontal lobe hypoperfusion is associated with decline in personal hygiene, and left temporal lobe hypoperfusion with compulsion and mental rigidity. Patient 1 demonstrated the clinical features of the temporal variant form of FTD.

Kantarci et al conducted a large-scale study to determine the MRS findings and intergroup differences of common dementias.[1] These researchers demonstrated that MRS is extremely sensitive for early diagnosis of dementing illnesses before any convincing structural change occurs at MRI. However, the MRS patterns of AD and FTD are similar and diagnostic differentiation is therefore less specific, especially in the presence of mild cognitive impairment. However, cerebral perfusion SPECT has demonstrated the unique ability to differentiate FTD from AD by their characteristic perfusion deficit patterns,[6] making SPECT an invaluable tool for the early clinical diagnosis and differentiation of mild cognitive impairment.

The characteristic features of MRI, MRS, and cerebral perfusion SPECT in advanced FTD were well demonstrated in patient 1, whereas cerebral perfusion SPECT offered a preclinical diagnosis of FTD for patient 2, with the use of MRS as a screening tool. Since focal lobar cerebral atrophy is a known feature of advanced FTD, patient 2's neurological progress will continue to be monitored by MRI and MRS.

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