Objective: To report a case initially fulfilling the clinical criteria for probable Alzheimer disease, although later clinical features suggested dementia with Lewy bodies. Oxygen 15–labeled positron emission tomograms revealed a pattern of hypometabolism characteristic of Alzheimer disease. At postmortem, there was no evidence of the pathological features of Alzheimer disease, but diffuse cortical Lewy bodies were seen in the pigmented brainstem nuclei and cerebral cortex.

Design: A case report.

Setting: Tertiary referral center.

Patient: A 65-year-old white man presented with a 3-year history of memory loss and language difficulties.

Results: Oxygen 15–labeled positron emission tomograms revealed hypometabolism in the frontal, temporal, and parietal lobes, more severe on the left than right. Metabolism in the left caudate was just outside the 95% reference range. Occipital metabolism was normal.

Conclusions: Positron emission tomographic studies have been reported to show occipital hypometabolism in dementia with Lewy bodies, in addition to the characteristic posterior bitemporal biparietal pattern of Alzheimer disease. We suggest that although this finding may favor a diagnosis of dementia with Lewy bodies, it is not necessary for diagnosis.

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Although criteria for clinical diagnosis may aid the distinction between Alzheimer disease (AD) (International Classification of Diseases, 10th Revision, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, and National Institute Neurological Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association) and dementia with Lewy bodies (DLBs),1,2 diagnosis may be difficult, particularly early in the course of the disease. Thus, although a parkinsonian syndrome is one distinguishing feature of DLBs, a proportion of patients with dementia of the Alzheimer type may also have extrapyramidal signs in the absence of Lewy bodies that are attributable to extranigral factors.3,4

Neuroimaging may contribute to the differential diagnosis. Alzheimer disease is characterized by atrophy of medial temporal lobe structures on magnetic resonance images or computed tomograms, but this atrophy is also seen to a lesser extent in patients with DLBs.5-7 It is therefore suggested that it is the absence of medial temporal atrophy that is highly suggestive of DLBs. [123I]-2β-carbomethoxy-3β-(4-iodophenyl)-N-(3-fluoropropyl)nortropane (a dopaminergic presynaptic ligand) and single photon emission computed tomography can be used to assess nigrostriatal pathway integrity in vivo.8 Preliminary results, though inconclusive, suggest that it may be possible to distinguish DLBs and AD by the absence of nigrostiatal degeneration in the latter. Positron emission tomographic studies have shown occipital hypometabolism in DLBs in addition to the characteristic posterior bitemporal biparietal pattern of AD,9-12 but thus far have not contributed to establishing the differential diagnosis of DLBs and AD. Elderly patients with late-life depression may have a widespread, nonfocal pattern of reduction in glucose metabolism similar to that seen in patients with AD,13 a finding that may further complicate the diagnosis.

Report of a Case

A 65-year-old retired businessman presented in May 1988 with a 3-year history of memory loss and language difficulties. He stated that he had trouble finding both spoken and written words, as well as difficulty with reading, comprehension, and
Intelligence Scale-Revised and obtained a verbal IQ of 80. He was able to copy complex gestures.

Statistically significant areas of hypometabolism included the frontal, temporal (predominantly left and posteriorly), and parietal lobes (predominantly left). Metabolism in the left caudate was just below the 95% reference range. The occipital and cerebellar rates of metabolism were normal. A diagnosis of probable AD with extrapyramidal features was made.

Over the following year, there was a progressive deterioration in the patient’s mental status: his verbal and performance IQ scores had declined to 73 and 71, respectively. There was a further decline in his memory functions. Naming and perceptual skills remained relatively preserved. He was gradually slowing up; his walk was slow and quite widespread, with little attenuation throughout, predominantly anteriorly, which were sometimes independent but more often were present as a generalized disturbance. A computed tomographic scan of the brain revealed no abnormalities.

An oxygen 15–labeled PET scan was performed (CTI 931-08/12 camera; Computed Technology and Imaging Inc, Knoxville, Tenn) at the Medical Research Council Cyclotron Unit (Hammersmith Hospital, London, England). The performance characteristics of this scanner and the practical procedure have been previously described. An oxygen 15–labeled steady-state inhalational technique was used with calculation of the regional cerebral metabolic rate for oxygen (CMRO2 ). A series of parametric images of CMRO2 were computed. Anatomically correct regions of interest were placed by transforming standard anatomical coordinates (from an anatomical atlas) to functional imaging coordinates. The technique involved estimating the position of the intercommissural line (AC-PC line) directly from the PET image and orientating the PET image about this line. The PET slices were then directly comparable with atlas slices. Regions placed on the PET image allowed regional values of CMRO2 to be obtained. The results were compared with those from a group of 9 normal subjects (women older than childbearing age and men older than 30 years [mean age, 59.9 years]). These subjects were asymptomatic, with normal results on clinical examinations, scoring at least 29/30 on the Mini-Mental State Examination. The mean±SD CMRO2 value for each cortical region (left and right hemispheres) is shown in the Table. Individual values are given for each region, and those outside the 95% reference range of the normal data differ significantly from normal at a level of P<.05.

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and a trial of carbidopa-levodopa therapy was initiated. There was minimal improvement, and as the dosage was increased, adverse effects were experienced. The therapy was discontinued, without clinical deterioration. The patient died 5 years after his initial presentation.

The brain weighed 1323 g, and the brainstem, with the cerebellum, 162 g. There was mild cerebral atrophy affecting mainly the frontoparietal region, while the temporal lobes, with the hippocampi, were preserved. The pigmented nuclei of the brainstem were paler than usual.

Blocks of tissue were taken from the frontal, temporal (with the hippocampus), parietal, and occipital lobes; basal ganglia (to include the caudate nucleus, lentiform nucleus, and nucleus basalis of Meynert); amygdala; midbrain; pons; medulla oblongata; and cerebellar vermis and hemisphere. Sections were stained with hematoxylin-eosin and the modified Bielshowsky technique and immunostained for α-synuclein, β-protein, β-amyloid, and ubiquitin.

Histologically, the substantia nigra and the locus ceruleus showed neuronal loss, extraneuronal pigment, many Lewy bodies, several pale bodies, Marineigo bodies, an occasional neurofibrillary tangle, and astrocytosis. Immunostaining for α-synuclein revealed additional abnormal positively stained neurites. Lewy bodies were also seen in the cerebral cortex, including the transentorhinal, insular, insular, temporal, frontal, and parietal cortices. Many Lewy bodies were also noted in the nucleus basalis of Meynert and amygdala. A network of abnormal neurites was demonstrated in the CA2-CA3 area of the hippocampus, by both α-synuclein and ubiquitin. Alzheimer-type changes of neuritic plaques and neurofibrillary tangles were extremely rare in the neocortex and hippocampus (Figure). Immunohistochemical studies for β-amyloid showed no significant deposits in the cerebral parenchyma. Applying the Newcastle Consensus Criteria, the diagnosis of DLBs (neocortical type) was made.

**COMMENT**

The hypometabolic pattern associated with AD using both oxygen 15- and fludeoxyglucose 18-labeled PET (FDG-PET) is characterized by posterior biparietal and bitemporal hypometabolism with a variable reduction in metabolism in the frontal association cortices. However, metabolic patterns in individual patients are heterogeneous and can be related to cognitive and behavioral profiles and to the regional severity of histopathological changes. This pattern of hypometabolism is in contrast to that of the caudate and thalamus, for example, which have been shown to be relatively preserved in AD. Thus, these areas are now used as reference tissues in image analysis.

Albin et al described FDG-PET studies in 6 patients: 3 with a pathological diagnosis of DLBs and 3 with both AD and DLBs. All cases showed a marked reduction in parietal, temporal, and frontal association cortex and posterior cingulate cortex metabolism, similar to that seen in patients with AD. In addition, however, both

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A. Cortical Lewy bodies in the temporal lobe (α-synuclein, original magnification ×480). B. Abnormal Lewy neurites in the CA2 and CA3 region of the hippocampus (α-synuclein, original magnification ×280). C. Positively stained inclusions and neurites in the nucleus basalis of Meynert (α-synuclein, original magnification ×480). D. Lewy bodies, neuronal loss, extraneuronal pigment, and astrocytosis in the substantia nigra (ubiquitin, original magnification ×280). All parts of the figure were stained using the avidin-biotin complex method.
groups of patients showed marked hypometabolism in the occipital association and primary visual cortices. These areas of hypometabolism did not correlate pathologically with areas of high density of Lewy bodies.

A similar pattern was reported by Imamura et al.\textsuperscript{10} who studied 19 patients with probable DLBs and 19 with probable AD using FDG-PET. When the regional cerebral metabolic rate for glucose in the DLB disease group was compared with that in the AD group, significant decreases were seen bilaterally in the temporo-parieto-occipital association cortices (including the occipital lobes, except medial), and the cerebellar hemispheres. The patients with AD, in contrast, showed more marked decreases in the middle cingulate gyrus and the medial temporal areas. The recurrent visual hallucinations of DLBs have been attributed to occipital cholinergic deficits, and Imamura and colleagues suggest that degeneration in neurons projecting from the basal nucleus of Meynert to the occipital lobe may lead to occipital hypometabolism.

The results of 2 other series comparing FDG-PET in patients with AD and DLBs add support to these early findings. Ishii et al.\textsuperscript{11} reported that the occipital cerebral metabolic rate for glucose (normalized to the sensorimotor cerebral metabolic rate for glucose) is useful in the differential diagnosis of AD and DLBs, with a sensitivity and specificity of 92%. Similarly, Higuchi et al.\textsuperscript{12} showed that hypometabolism was most pronounced in the visual association cortex and that by calculating a metabolic ratio cutoff level in this region, AD and DLBs could be distinguished with 86% sensitivity and 91% specificity.

Direct comparison with our case is difficult because of our use of oxygen 15-labeled PET (rather than FDG-PET) and because of the traditional regions-of-interest method that was used at the time the patient presented, whereby regional CMRO\textsubscript{2} values are directly compared with mean regional control levels. However, both clinical and PET features are clearly moderately atypical in this case. The predominantly left temporal lobe, left parietal lobe, and frontal hypometabolism that were seen in our patient and DLB cases demonstrate that although occipital cholinergic deficits, and Higuchi et al.\textsuperscript{12} showed that hypometabolism was most pronounced in the visual association cortex and that by calculating a metabolic ratio cutoff level in this region, AD and DLBs could be distinguished with 86% sensitivity and 91% specificity.

This case provides further information on PET in autopsy-confirmed DLBs. It emphasizes the clinical heterogeneity that can be observed within the degenerative dementias and demonstrates that although occipital hypometabolism on functional imaging may favor a diagnosis of DLBs, it is not necessary for diagnosis.

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Corresponding author and reprints: Martin N. Rossor, MD, FRCP, Dementia Research Group, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, England (e-mail mrossor@dementia.ion.ucl.ac.uk).

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