

Hemianopsia in Dementia With Lewy Bodies

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Objective: To describe the pathologic changes that caused a left homonymous hemianopsia in a patient with dementia with Lewy bodies.

Design: Report of a case and postmortem studies.

Main Outcome and Results: A 66-year-old woman experienced parkinsonism and left homonymous hemianopsia early in the course of a rapidly progressive dementia that culminated in death only 21 months after the onset of her symptoms. Postmortem examination re-

vealed pathologic features consistent with the diagnosis of dementia with Lewy bodies. The only apparent explanation for her visual field deficit was a disproportionately large number of neurofibrillary tangles in the right striate, peristriate, and inferotemporal cortices.

Conclusion: A clinically obvious homonymous hemianopsia can result from the occipital and inferotemporal cortical degeneration in dementia with Lewy bodies.

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DEMENTIA WITH Lewy bodies has an uncertain nosology and a varied clinical terminology, which includes diffuse Lewy body disease, Lewy body dementia, dementia with cortical Lewy bodies, senile dementia of Lewy body type, and Lewy body variant of Alzheimer disease.¹⁻⁸ The term *dementia with Lewy bodies* (DLB) was recently proposed by the Consortium on Dementia with Lewy Bodies⁷ and is used in this article. Most patients exhibit a combination of dementia, parkinsonism, and psychiatric symptoms, but striking deviations from this symptom complex are common, leading to a variety of incorrect clinical diagnoses.¹⁻⁸ Herein we report a unique patient with DLB who initially complained of heaviness in the right upper extremity and subsequently developed a dense left homonymous hemianopsia during the course of a rapidly progressive dementia.

REPORT OF A CASE

A previously healthy 66-year-old right-handed woman was hospitalized with a 5-day history of heaviness in her right upper extremity and a flulike illness, associated with malaise, nausea, vomiting, and diarrhea. She attributed her right

upper extremity symptoms to an unusual amount of writing done while completing her income tax returns. Her internist suspected a stroke and performed a computed tomographic scan of the head, which revealed a 6-mm lucency in the deep left frontal white matter. Magnetic resonance imaging revealed a 6-mm subcortical focus of increased T₂ signal in the same location. A neurologist (R.J.E.) found that she was a cooperative historian who scored 26 of 30 on the Folstein Mini-Mental State Examination.⁹ She remembered 0 of 3 words at 1 minute and did a very poor job of copying intersecting pentagons. She had difficulty spelling the word "world" backward, but she corrected herself and eventually accomplished this task. She was able to pantomime simple motor tasks. There was no aphasia. Cranial nerves were normal, including voluntary eye movements and optokinetic nystagmus. She exhibited mild facial masking, hypophonia, micrographia, and cogwheel rigidity in both upper extremities, greatest in the right. She had no tremor or weakness, and muscle stretch reflexes, plantar responses, and sensory examination were normal. Arm swing while walking was diminished bilaterally, greatest on the right, and her steps were slightly short and cautious but not shuffling. Postural stability was nor-

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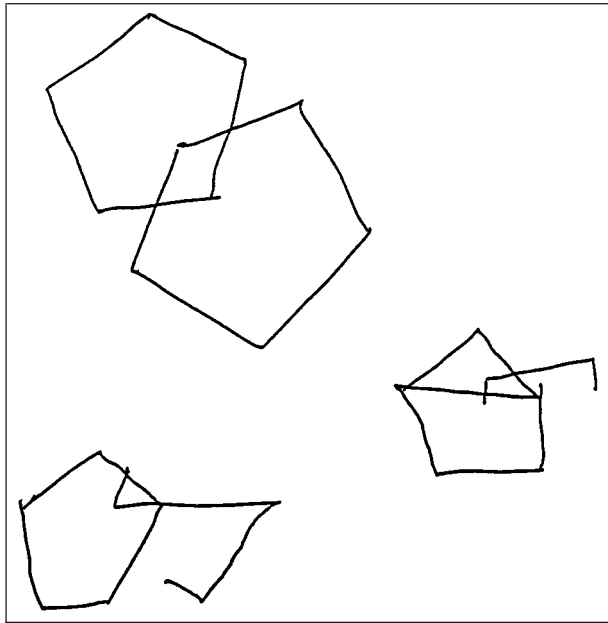


Figure 1. Two of the patient's errant attempts at drawing intersecting pentagons are displayed with a drawing by one of us (R.J.E.). These intersecting pentagons were drawn when her Mini-Mental State Examination score was 29.

mal. An outpatient neurologic examination 4 weeks later revealed the same motor signs but an improved Mini-Mental State Examination score of 29. She lost 1 point because of her persistent inability to draw intersecting pentagons (**Figure 1**).

Eight months later, she returned to the neurologist with the complaint of reduced vision in her left eye. This developed insidiously, and she was unsure of its duration. Examination revealed an obvious left homonymous hemianopsia to finger counting and gross hand waving. This visual deficit was present in both eyes and was particularly dense in the inferior quadrant. Her neurologic examination and Mini-Mental State Examination score were otherwise unchanged. An ophthalmologist found no significant ocular pathologic conditions (retina, optic disc, and anterior chamber). Humphrey automated perimetry was somewhat limited by her poor attention, but the results were consistent with a left homonymous hemianopsia (**Figure 2**). Another magnetic resonance imaging scan performed with and without contrast was unchanged since the initial study.

A gradual severe deterioration in cognitive and motor function occurred during the next 12 months. She had periods of severe confusion, agitation, depression, and visual hallucinations of animals and unfamiliar people in her home. In desperation, she was taken to several other physicians and was treated unsuccessfully with selegiline hydrochloride, a combination product of carbidopa and levodopa, vitamin E, thioridazine, alprazolam, fluoxetine hydrochloride, thiothixene, benzotropine mesylate, trazodone hydrochloride, lorazepam, and electroconvulsive therapy. The trial of electroconvulsive therapy was aborted after 1 treatment because of severe delirium. Administration of thioridazine (50 mg/d) and thiothixene (5 mg/d) each produced a disabling increase in her parkinsonism. Selegiline hydrochloride (5 mg) administered twice daily and a combination prod-

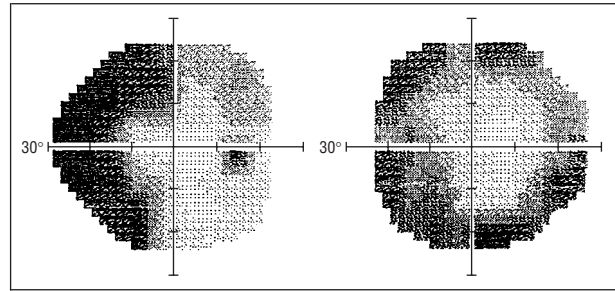


Figure 2. The Humphrey perimetric examination was consistent with a left homonymous hemianopsia.

uct of carbidopa and levodopa (25 and 100 mg, respectively) administered 3 times daily produced no appreciable improvement in her bradykinesia or rigidity, and use of both drugs increased her confusion and hallucinations. Twenty months after her initial hospitalization, she was dependent in all activities of daily living, and her Mini-Mental State Examination score was 0. Language comprehension and expression were limited to simple sentences. She had a persistent left homonymous hemianopsia to static objects and to gross hand and arm movement, and this visual field deficit was superimposed on severe simultanagnosia in all visual fields. She exhibited marked facial masking and generalized severe rigidity, paratonia, and bradykinesia but no tremor. Her posture and gait were markedly parkinsonian, and she had occasional myoclonic jerks of the torso and extremities. A single-photon emission computed tomographic scan with technetium Tc 99m hexamethylpropyleneamine oxime revealed a large area of right parietal-occipital and inferior temporal hypoperfusion. An electroencephalogram revealed diffuse medium amplitude polymorphic theta and delta slowing and no alpha rhythm. Cerebrospinal fluid examination was normal. Apo-E genotyping was not performed. She died while sleeping 21 months after her initial symptoms, by which time she was bedridden and mute.

There was no history of dementia in the patient's immediate family. Her mother and father died of coronary artery disease at ages 60 and 70 years, respectively. The patient had 1 brother, aged 65 years, and 1 sister, aged 63 years, who enjoyed good health.

AUTOPSY EXAMINATION

The autopsy was limited to the brain, according to the husband's wishes. The brain weighed 1360 g. The cerebral hemispheres were symmetrical, and the temporal lobes were mildly atrophic. The cerebral vasculature contained minimal atheromatous changes. The only major abnormality on coronal sectioning was a marked pallor of the pigmented nuclei. The left frontal lobe focus found with computed tomography and magnetic resonance imaging corresponded to a small cluster of dilated veins without any destruction of neighboring tissues.

MICROSCOPIC EXAMINATION

Six-micrometer sections of formalin-fixed, paraffin-embedded tissue were stained with hematoxylin-eosin and

Cortical Densities of Neurofibrillary Tangles (NFT), Neuritic-Cored Plaques (NP), Diffuse Plaques (DP), and Lewy Bodies (LB)*

| Cortical Area | NFT/mm ² | | NP/mm ² | | DP/mm ² | | LB/mm ² | |
|---------------|---------------------|------|--------------------|------|--------------------|------|--------------------|------|
| | Right | Left | Right | Left | Right | Left | Right | Left |
| CA1/HIP | 13.2 | 18.7 | 1.5 | 10.2 | 0 | 8.2 | 0.24 | 0.94 |
| ERC | 26.9 | 23.0 | 10.3 | 6.1 | 14.9 | 5.5 | 0.30 | 0.08 |
| CING | 1.8 | 0.5 | 8.3 | 1.6 | 21.8 | 17.0 | 1.09 | 2.01 |
| FC | 0.7 | 0.8 | 10.6 | 5.3 | 28.9 | 29.2 | 0.04 | 0.02 |
| PC | 0.5 | 1.4 | 9.2 | 6.8 | 25.2 | 26.6 | 0.04 | 0.18 |
| STC | 6.1 | 0.5 | 5.8 | 7.2 | 24.2 | 17.8 | 0.09 | 0.61 |
| ITC | 26.4 | 3.8 | 9.0 | 11.4 | 23.2 | 25.6 | 0.33 | 0.80 |
| OCC-ST | 2.6 | 0 | 15.9 | 3.4 | 14.1 | 12.3 | 0 | 0.07 |
| OCC-PS | 10.0 | 3.5 | 12.5 | 17.5 | 20.6 | 17.5 | 0.34 | 0.14 |

*CA1-HIP indicates CA1-hippocampus; ERC, entorhinal cortex; CING, anterior cingulate cortex; FC, middle gyrus of the frontal cortex; PC, angular gyrus of the parietal cortex; STC, superior temporal cortex; ITC, inferior temporal cortex; OCC-ST, occipital striate cortex; and OCC-PS, occipital peristriate cortex.

with the Sevier-Munger and modified Bielschowsky silver stains. The cortical areas examined were the hippocampal, entorhinal, inferior temporal, superior temporal, middle frontal gyrus, anterior cingulate, parietal angular gyrus, striate occipital, and peristriate occipital cortices. Sparse to moderate neuronal loss, gliosis, neurofibrillary tangles, diffuse plaques, and neuritic-cored plaques were found in all these cortical areas. The hematoxylin-eosin and silver stains revealed 1 or more microscopic fields ($\times 200$; area, 0.096 mm²) with 1 to 3 Lewy bodies without halos in these same cortical areas. Roughly twice as many Lewy bodies were found in the same microscopic areas using an anti-ubiquitin immunohistochemical stain.

Neuronal loss, free neuromelanin, and multiple Lewy bodies with halos were found in the substantia nigra, locus ceruleus, and dorsal motor nucleus of the vagus. A few neurofibrillary tangles were present in the periaqueductal region. No pathologic changes existed in the thalamus, subthalamus, or globus pallidus. Mild to moderate rarefaction and gliosis were found in the deep cerebral white matter, most pronounced bilaterally in the periventricular occipital white matter, but there was no evidence of cerebral infarction. The optic nerves, chiasm, and tracts were normal.

Quantitative analysis of senile plaques and neurofibrillary tangles was performed bilaterally on paraffin-embedded 10- μ m sections stained with the modified Bielschowsky stain. Areas of 5 to 12 mm² were quantified in the hippocampus (CA1), entorhinal, inferior temporal, superior temporal, middle frontal gyrus, anterior cingulate gyrus, parietal (angular gyrus), and occipital (striate and peristriate) cortices. Similarly, quantitative analysis of cortical Lewy bodies was performed bilaterally on paraffin-embedded 10- μ m sections stained with an anti-ubiquitin stain, and areas of 4 (CA1) to 79 mm² (parietal cortex) were quantified in the same cortical regions used in the quantification of plaques and tangles. Quantification was performed with a computer software (Neurolucida, MicroBright Field Inc, Colchester, Vt) that combines a live image of the slide with an operator-generated overlay. The position of each neurofibrillary tangle, neuritic-cored plaque, diffuse plaque, and Lewy body was marked on the overlay. Diffuse plaques were identified as having no neurites or amyloid core. The le-

sion densities are summarized in the **Table**. Neuritic-cored plaques and diffuse plaques had a roughly even neocortical distribution. However, the right superior and inferior temporal cortices and the right striate and peristriate occipital cortices contained far more neurofibrillary tangles than did other neocortical areas.

COMMENT

Our patient exhibited progressive cognitive decline, parkinsonism, visual hallucinations, and fluctuating agitation, confusion, and depression. She therefore fulfilled all the consensus criteria for the clinical diagnosis of probable DLB.^{7,8} Dementia with Lewy bodies was our initial diagnosis, but the rapid progression with myoclonus and the left homonymous hemianopsia were cause for continued diagnostic uncertainty. Initially, the asymmetric motor signs and visual field deficit led to an unproductive search for cerebral vascular disease. The erroneous clinical diagnoses that were considered over the course of this patient's 21-month illness included stroke, Parkinson disease, vascular dementia, Binswanger disease, major depression, Alzheimer disease, and Creutzfeldt-Jakob disease. Such diagnostic uncertainty is common in individuals with DLB because of its varied clinical picture and course.¹⁻⁷

The neuropathologic findings in our patient fulfilled the diagnostic criteria for DLB, proposed by the Consortium on Dementia with Lewy Bodies.^{7,8} The pathology in our patient was similar to that in other patients with DLB,^{1-5,7,8} except our patient exhibited a striking predominance of neurofibrillary tangles in the right inferotemporal and occipital cortices. Alzheimer pathologic manifestations occur in most cases of DLB, but neocortical tangles are seen in a minority of patients with DLB.⁷ The high density of tangles in the right occipital and inferotemporal cortex was the only apparent explanation for our patient's early constructional apraxia and symptomatic left homonymous hemianopsia.

Did our patient have both Alzheimer disease and DLB? This question is unanswerable because the distinguishing clinical and neuropathologic criteria are still being defined.⁷ The Consortium on Dementia with Lewy Bodies⁷ acknowledged that Alzheimer pathologic features are common occurrences in DLB, and our patient

illustrates the difficulty in separating Alzheimer disease from DLB. Her relatively young age makes age-associated Alzheimer features an unlikely explanation for the Alzheimer pathologic changes in her brain.

An inferotemporal-occipital predominance of tangles is not characteristic of Alzheimer disease or DLB, but such pathologic changes are found in patients with Alzheimer disease with unusually severe visual impairment.¹⁰⁻¹⁵ The visual deficits in these patients with Alzheimer disease include Balint syndrome, constricted peripheral visual fields, visual agnosia, quadrantanopsia, and hemianopsia.¹⁰⁻¹⁵ Quadrantanopsia and hemianopsia are rare in individuals with Alzheimer disease¹²⁻¹⁴ and have not been reported previously in individuals with DLB. Furthermore, we know of no other case in which quantitative neuropathologic examination was performed to explain the hemianopsia. Previous patients with Alzheimer disease with quadrantanopsia and hemianopsia had coexistent simultanagnosia, but the hemianopsia preceded the simultanagnosia in our patient, consistent with her markedly asymmetric inferotemporal-occipital pathology.

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