Published in final edited form as:
Neurology. 2011 February 15; 76(7 0 2): S61–S63. doi:10.1212/WNL.0b013e31820c34ca.

Acalculia in Autopsy-Proven Corticobasal Degeneration

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Keywords

corticobasal; acalculia; parietal

INTRODUCTION

Corticobasal degeneration (CBD) is a neurodegenerative condition presenting with an asymmetric extrapyramidal disorder, cortical sensory loss, and apraxia. While the original case descriptions mentioned acalculia(1), few studies have investigated this(2, 3) and reports of acalculia in autopsy-proven CBD are very rare. We detail two autopsy-defined CBD cases with acalculia to emphasize that CBD compromises cognitive functioning due to disease that includes parietal cortex.

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Disclosure

Dr. Pantelyat reports no disclosures.
Mr. Dreyfuss reports no disclosures.
Dr. Moore reports no disclosures.
Dr. Gross has received research fellow/trainee support from the American Academy of Neurology Foundation.
Ms. Schuck receives research support from the NIH (NIA, NINDS) and from Marian S. Ware Drug Discovery.
Dr. Irwin has received research fellow/trainee support from the NIH/NIA.
Dr. Trojanowski has received funding for travel and honoraria from Takeda Pharmaceutical Company Ltd.; has received speaker honoraria from Pfizer Inc; serves as an Associate Editor of *Alzheimer's & Dementia*; may accrue revenue on patents re: Modified Avidin-Biotin Technique, Method of Stabilizing Microtubules to Treat Alzheimer's Disease, Method of Detecting Abnormally Phosphorylated Tau, Method of Screening for Alzheimer's Disease or Disease Associated with the Accumulation of Paired Helical Filaments, Compositions and Methods for Producing and Using Homogeneous Neuronal Cell Transplants, Rat Comprising Straight Filaments in Its Brain, Compositions and Methods for Producing and Using Homogeneous Neuronal Cell Transplants to Treat Neurodegenerative Disorders and Brain and Spinal Cord Injuries, Diagnostic Methods for Alzheimer's Disease by Detection of Multiple MRNAs, Methods and Compositions for Determining Lipid Peroxidation Levels in Oxidant Stress Syndromes and Diseases, Compositions and Methods for Producing and Using Homogenous Neuronal Cell Transplants, Method of Identifying, Diagnosing and Treating Alpha-synuclein Positive Neurodegenerative Disorders, Mutation-specific Functional Impairments in Distinct Tau Isoforms of Hereditary Frontotemporal Dementia and Parkinsonism Linked to Chromosome-17: Genotype Predicts Phenotype, Microtubule Stabilizing Therapies for Neurodegenerative Disorders; and Treatment of Alzheimer's and Related Diseases with an Antibody; and receives research support from the NIH/NIA and from the Marian S. Ware Alzheimer Program.
Dr. Grossman serves on a scientific advisory board for Allon Therapeutics Inc.; serves as Editor of *Cognitive and Behavioral Neurology*; has served as a consultant for Pfizer Inc and Forest Laboratories, Inc.; and receives research support from the NIH.

CASE REPORTS

CASE 1

A 72-year-old right-handed schoolteacher with hypertension and hypothyroidism was evaluated for progressive cognitive and motor difficulties over 3 years. She first noted writing difficulty. Her right hand began performing involuntary, semi-purposeful movements. She required increasing assistance dressing and cutting food. She misjudged spatial relationships while driving and cooking. She had several falls. Examination revealed MMSE = 27. She had ideomotor apraxia, slowed writing, and difficulty copying geometric designs. Number knowledge was impaired, including miscounting "X" marks on a paper and erring during oral and written calculations (e.g. given "9 + 12," she responded "20"). Memory, digit span, reading, comprehension and speech were intact. She had axial rigidity and decreased right arm swing, but no other involuntary movements. Neuropsychological evaluation (z-scores relative to 25 demographically-matched controls) revealed deficits on spatial tasks (e.g. geometric figure copy z = −7.74), mild executive dysfunction (e.g. animal category naming fluency z = −1.90), and preserved language (e.g. Boston Naming test z = −0.86) and memory (delayed-recall of a 10-word list z = 0.02). MRI showed parietal atrophy. Over the next 18 months, ideomotor apraxia worsened, and she developed apractic agraphia and spatial alexia. Number knowledge declined, including miscounting small arrays of objects and erring with single-digit calculations (2+3 = 7; 3+4 = 6). She developed an "alien hand" on the right, complaining "it'll fight you," cortical sensory loss, and increasing axial rigidity. The patient died 5 years after symptom onset. Autopsy revealed gross symmetric parietal atrophy (Figure, Panel A). Microscopic examination showed severe neuronal dropout and gliosis in the superficial cortical layers (Figure, Panel B), with tau-positive neuronal (Figure, Panel C) and glial (Figure, Panel D) inclusions bilaterally in the parietal lobe and throughout the cerebrum, basal ganglia, thalamus and midbrain, consistent with the pathologic diagnosis of CBD.

CASE 2

A 60-year old right-handed engineer with a history of treated B12 deficiency presented with worsening drawing and writing over two years that interfered with work. He could not locate the sink in his home or park his car. Cutlery was difficult to use, and he noticed difficulty with calculations and word-finding. Examination revealed MMSE = 22. He had spatial deficits copying a geometric design. There was ideomotor apraxia, apractic agraphia, left-right discrimination difficulty, finger agnosia, and mild anomia. Simple oral calculations were impaired, including single-digit oral and written addition errors (50% correct) and poor object counting. Memory was intact. Tone was more rigid in right than left limbs, with axial rigidity but no other involuntary movements. There was a cortical sensory deficit. Neuropsychological evaluation revealed impaired spatial (e.g. geometric figure copy z = −5.89) and executive (animal category naming fluency z = −2.66) functioning, with intact memory (delayed-recognition of a 10-word list z = −1.01) and language (Boston Naming test z = −0.86). MRI demonstrated symmetric bilateral parietal-occipital atrophy (Figure, Panel E). Over the next year, there was worsening apraxia, writing, naming and walking. At autopsy three years following presentation, histopathologic examination revealed neuronal loss and gliosis as well as tau-positive changes consistent with CBD.

DISCUSSION

Corticobasal syndrome (CBS), the clinical diagnosis of these two cases, is a disorder characterized by lateralized motor features, including dystonia, rigidity, gait impairment, and alien limb phenomena(4, 5). Cognitive deficits are common, including apraxia, spatial difficulties, executive limitations, effortful speech, distorted handwriting, and altered

personality. Cortical sensory loss is typical, but memory difficulty is modest(6). While CBD often initially presents in a lateralized manner, contralateral features invariably emerge longitudinally. CBD, a frequent neuropathological correlate of CBS, affects frontal and parietal cortical and white matter regions and the basal ganglia most profoundly, but temporal and hippocampal regions tend to be less compromised(6).

In 15 patients with autopsy-proven CBD that included the two cases detailed here, acalculia was noted in 28.6%, although this was thought to be an underestimation since calculations were not often examined(6). Acalculia is caused by disease in either hemisphere. CBS patients have significant impairments estimating and comparing quantities, performing calculations with small numerosities, and using quantity knowledge to support word meaning(2, 3, 7). These deficits, evident for both Arabic numerals and non-verbal dot arrays, underline their degraded mental representation of quantity and number knowledge. MRI in CBS regularly shows parietal atrophy, including areas associated with number knowledge(3).

Cognitive difficulties are common in extrapyramidal disorders. They are often related to disruption of a frontal-striatal loop that compromises executive resources. These CBD cases emphasize that cognitive abnormalities in extrapyramidal disorders may also involve degeneration of parietal regions.

Acknowledgments

Study Funding: Supported in part by the NIH (NS44266, AG17586, AG15116, NS53488, AG32953).

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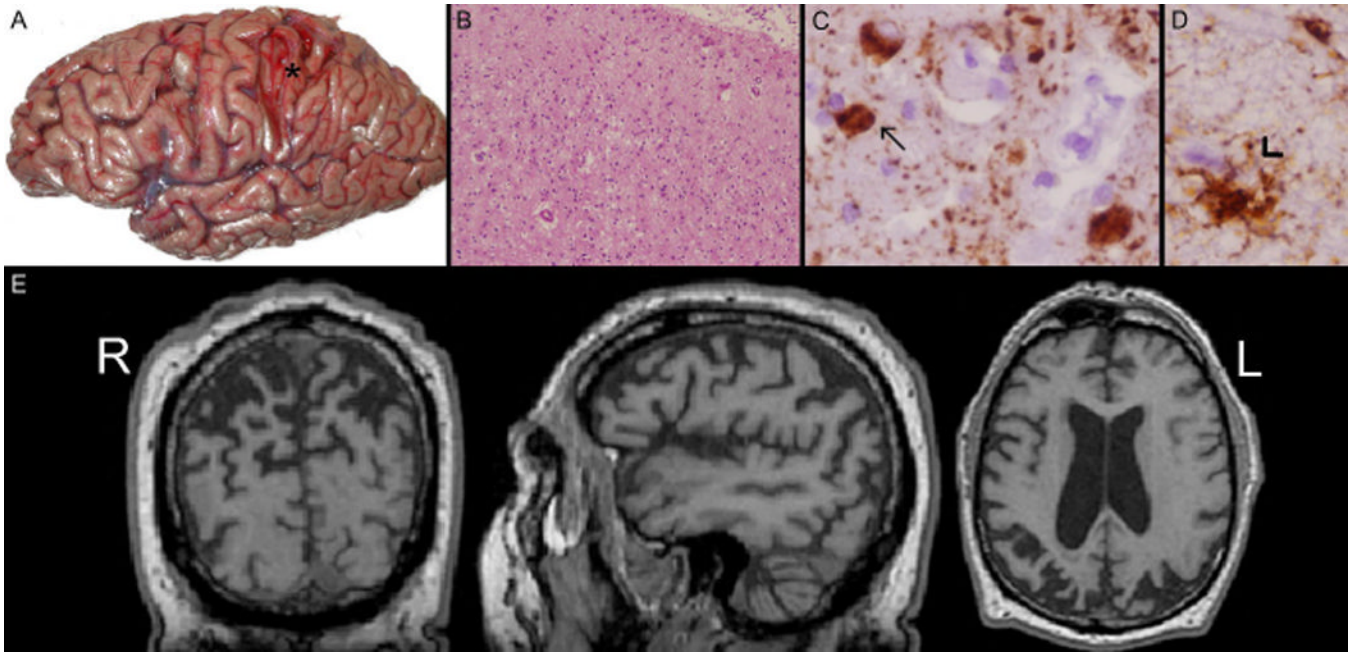

FIGURE. IMAGING AND PATHOLOGICAL FEATURES OF CORTICOBASAL DEGENERATION

Panel A: Gross atrophy in parietal lobe (asterisk) of Case 1; Panel B: H & E preparation of the angular gyrus of Case 1 at 10X magnification showing significant neuronal dropout and gliosis in the superficial cortical layers; Panel C: PHF stain for tau in the cortex of the angular gyrus of Case 1 at 60X magnification showing balloon cells (arrow); Panel D: PHF stain for tau in the white matter of the angular gyrus of Case 1 at 60X magnification showing an astrocytic plaque (arrowhead); Panel E: T1 MPRAGE MRI sequence showing bilateral parietal-occipital atrophy in coronal (y = −60), sagittal (left hemisphere) (x = −47), and axial (z = +14) views of Case 2.