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Posterior Cortical Atrophy: Unique Features

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Abstract

Posterior cortical atrophy (PCA) is a visual-cognitive syndrome caused by Creutzfeldt-Jakob disease (CJD), Alzheimer's disease (AD), or subcortical gliosis. We report a case of posterior cortical atrophy unique in (1) comprehensive documentation of clinical, radiologic, electroencephalographic, metabolic and histopathologic findings, (2) repeated clinical and laboratory assessment, and (3) establishment of unique occipital subcortical gliosis in a patient with AD. Clinical manifestations of PCA caused by AD included visual agnosia, cortical blindness, optic apraxia, delusions, hallucinations, agitation, depression, amnesic deficit, Wernicke's aphasia, acalculia, and left/right disorientation. Posterior cortical atrophy produced by AD can be demonstrated on magnetic resonance imaging, positron emission tomography, and electroencephalography; determination of the etiology requires tissue examination. Autopsy-diagnosed cases in the literature document PCA due to CJD and AD with equal frequency.

Introduction

Posterior cortical atrophy (PCA) is a visual-cognitive syndrome described in patients with Alzheimer's disease (AD), Creutzfeldt-Jakob disease (CJD), or subcortical gliosis; Clinical manifestations of PCA may include: visual agnosia, environmental agnosia, alexia, ocular apraxia, Balint's syndrome, and a marked discrepancy between low performance IQ and normal to high verbal IQ scores (Cogan, 1985; Benson, 1988). Less frequently, anxiety, prosopagnosia, hemiachromatopsia, and Gerstmann's syndrome accompany PCA (Benson, 1988; Freedman and Costa, 1992). Visual cognitive deficits may be more prominent than memory abnormalities. Freedman (1991), Levine (1993), and Wakai (1994) report patients whose judgment, personality, insight, awareness, and language ability remained intact even in the later stages of illness, indicating that this disease remained confined to posterior hemispheric structures until late in the illness.

Although many of the autopsy-diagnosed PCA cases reported in the early literature were caused by the Heidenhain variant of CJD, AD is an alternate and possibly more frequent cause. We report a case of PCA due to AD, unique in the comprehensive longitudinal documentation of clinical, radiologic, electroencephalographic, metabolic and

histopathologic findings, and in the degree of white matter gliosis accompanying the atrophic changes.

Case report

A 63-year-old right-handed man with a high school education and professional musical training first experienced memory problems in his 6th decade. He began losing items as early as age 49. He could compensate for his deficits with lists, notes, and support from friends, but at age 56, his friends noted a marked decrease in his ability to find his way in familiar environments. At age 57, his occasional fasting seemed to bring on a more rapid deterioration in visuospatial function.

Onset of extreme panic attacks 5 years into his illness at age 61 prompted a neurologic work-up. The patient endorsed exaggeration of his pre-existent phobias toward heights, water, driving, and physicians. At the time, he was found to have poor short term memory; defective constructions (clock was drawn as a mirror-image); deficits in category naming; components of a Gerstmann syndrome (acalculia, right/left disorientation, finger agnosia); alexia; astereognosis, and extinction to double simultaneous stimulation on the right for auditory and on the left for visual stimuli. An evaluation revealed diffuse slowing on electroencephalogram (EEG); minimal diffuse cerebral atrophy with computerized tomography (CT); and generalized cerebral cortical atrophy and mild age-related periventricular white matter changes on magnetic resonance imaging (MRI). Neuropsychologic testing documented a performance IQ of 0 (he could not perform any of the tasks) in the context of a verbal IQ of 91. A low vitamin B₁₂ level of 63 indicated possible B₁₂ deficiency, presumed secondary to his selective dietary habits, after which the patient regularly received i.m. cyanocobalamin supplements. Cyanocobalamin treatments had no effect on his course. The patient was treated with cognitive-enhancing, antidepressant, anxiolytic and neuroleptic medications; most produced temporary but not sustained improvement in his agitation.

At age 63, the patient spoke incoherently. He lost the ability to recognize objects visually (visual agnosia), could not recognize familiar faces (prosopagnosia), was able to read letter by letter but could not recognize entire words (alexia/ventral simultanagnosia), and could not look to his extreme left (ocular apraxia). He retired from work as a percussionist yet remained socially active. In the following year the patient progressed to cortical blindness and marked, nearly continuous agitated behavior. Although he seemed to excuse his visuospatial deficits as poor corrective lenses (Anton's syndrome) at first, he later acknowledged his conical blindness. Visual acuity tiling revealed no evidence of visual perception including large or small stimuli, moving light, or colors. Pupillary reflexes remained intact. He manifested rare periods of clear mentation but was apraxic and required assistance with activities of daily living.

On presentation at age 67 years, the patient had no delusions or hallucinations and was concerned about his health and treatment. Mental status testing showed marked impairment in all other areas. In addition to his previous deficits, the patient was agraphic, unable even to sign his name. He continued with frequent agitation.

Neurological examination revealed full spontaneous extraocular movements despite ocular apraxia, gegenhalten in all four extremities, and positive grasp reflexes. Motor strength and primary sensation were intact. Serum vitamin B₁₂ was within normal limits on continued cyanocobalamin injections; thyroid stimulating hormone, anti-neuronal antibody titer, vitamin E and ceruloplasmin levels, and protein electrophoresis were within normal limits; he had a non-reactive serum rapid protein reagent, negative capillary gas chromatography for fatty acid disorders, and homozygous ApoE 3/3 genotype.

MRI (see Fig. 1a, b) showed diffuse sulcal widening, marked regional atrophy in both occipital lobes, and markedly increased white matter signal intensity in the posterior regions on T₂-weighted images. A leukoencephalopathy was suspected. MRI 7 and 8 years into the illness did not show progression of structural changes.

Quantitative EEG (QEEG) at age 67 demonstrated loss of the posterior dominant rhythm and development of excessive symmetrical slowing when compared with QEEG from the previous year. The slow wave power was most prominent in the fronto-central regions, with slightly more prominent slowing over the left hemisphere. The patient showed bilateral temporoparietal dysfunction and relative sparing of the central cortex over the motor strip.

Fluoro-deoxyglucose positron emission tomography (FDG-PET) at age 66 (see Fig. 2a) revealed global cortical thinning, more pronounced in the occipital lobes, and markedly abnormal cerebral glucose metabolism diffusely with relative sparing of the primary sensory and motor cortices. Repeat FDG-PET at age 67 demonstrated progression of hypometabolism in the temporal lobes (see Fig. 2b).

Right frontal lobe biopsy at age 67 revealed nuclear pyknosis, conspicuous lipofuscin accumulation, neuritic plaques staining with ubiquitin, and neurofibrillary tangles, consistent with the diagnosis of AD.

The patient eventually succumbed to respiratory failure at age 69. Post-mortem brain pathology included classic findings for AD, as well as preferential atrophy in the parieto-occipital regions, poorly delineated subcortical myelin loss in the white matter, and associated astrocytic gliosis confined to the occipital lobes. As in the brain biopsy specimen, no Lewy bodies were found with ubiquitin staining. The number of senile plaques and neurofibrillary tangles had advanced substantially between biopsy and autopsy.

Discussion

Over a 12-year period, the patient described here manifested a course atypical for AD. His cognitive deficits included memory, language, visuospatial function and behavioral disturbances, but eventually ocular apraxia, ventral simultanagnosia (described below), visual agnosia, environmental agnosia, prosopagnosia, and Anton's syndrome featured more prominently: Diagnostic studies consistently showed severe posterior cortical atrophy and MRI revealed increased signal intensity that was symmetric, confluent, and progressive in the occipital regions. In addition, autopsy revealed white matter gliosis, which is not commonly observed in AD pathology.

Of 37 pathologically studied cases found in the literature and presenting with PCA, equal numbers (18) had AD (Morel, 1945; Cogan, 1985; Kobayashi *et al.*, 1987; Hof *et al.*, 1990, Berthier *et al.*, 1991; Levine *et al.*, 1993; Victoroff *et al.*, 1994; Ala and Frey, 1996; Rogelet *et al.*, 1996) and CJD (Kirschbaum, 1968; Morita *et al.*, 1975; Okiyama *et al.*, 1989; Victoroff *et al.*, 1994). One case had progressive subcortical gliosis (Victoroff *et al.*, 1994). CJD presenting with visual cognitive deficits related to predominantly occipital lobe involvement has been termed the 'Heidenhain variant.' Kirschbaum (1968) reported 16 such patients.

Patients with PCA due to AD usually exhibit onset of symptoms in the sixth decade (Black, 1996). The patient described here had symmetrical posterior cortical atrophy. Asymmetric cases of posterior cortical atrophy reported by Freedman (Freedman *et al.*, 1991, Freedman and Costa, 1992) manifested their asymmetric left-predominant atrophy with Gerstmann's syndrome or right hemi-achromatopsia and prosopagnosia. A musician described as having asymmetric PCA, worse on the right, manifested spatial agraphia, visual apraxia, severe expressive music deficits but intact rhythm repetition and fluent, intelligible language. No pathologic diagnosis was given, although the clinical diagnosis was AD (Polk and Kertesz, 1993).

The patient described here manifested cognitive deficits consistent with bilateral hemispheric dysfunction (components of Gerstmann's syndrome, aphasia, visual apraxia, poor visuospatial constructions), but the outstanding clinical features related to visual processing. Farah (1990) delineates two forms of simultanagnosia: dorsal and ventral. Both dorsal and ventral forms of simultanagnosia include the failure to identify more than one object in a scene at once, but the neuroanatomic lesions and therefore visual processing deficits differ. Dorsal simultanagnosia, caused by bilateral occipital or parieto-occipital injury, represents a visual attention deficit. The patient can attend only to one whole object at a time. By contrast, ventral simultanagnosia is caused by a left inferior occipito-temporal lesion, manifesting as an impairment of visual short-term memory. Given sufficient time, dorsal simultanagnosic patients can piece together a scene because they can recall the different components. The ventral simultanagnosic patient cannot synthesize the individual components of the scene. The current patient's ability to read letters but not to remember the sequence of letters in order to read the word itself might represent a ventral simultanagnosia.

Anton's syndrome appeared transiently as PCA worsened in the patient described here. AD does not usually affect primary sensory cortices, although Crystal *et al.* 1982 reported right parietal lobe atrophy that caused left body posturing and cortical sensory loss. Vermersch's (Vermersch *et al.*, 1992) biochemical mapping based on detection of Tau 55, 64, and 69 reported sparing of primary sensory and striate cortices relative to sensory association areas in AD. The patient reported here is among the very few in the literature with pathologic involvement of the primary visual cortex.

The MRI of the patient described here clearly demonstrated posterior cortical atrophy. Not all cases show such dramatic regional atrophy. CT may appear normal despite such marked debilitation that the patient cannot participate meaningfully in neuropsychological testing (Benson *et al.*, 1988). Some patients, whether with AD or CJD, develop noticeable posterior

cortical atrophy only late in the course of the illness (Benson *et al.*, 1988; Wakai *et al.*, 1994). Only 3 months after initial onset of dementia and having a normal CT, a patient with the Haidenhain type of CJD showed bilateral occipital atrophy on MRI. By the end of her illness (20 months), the patient had diffuse atrophy (Wakai *et al.*, 1994). The MRI of the patient described here revealed marked posterior atrophy with dilatation of the occipital ventricular horns and confluent posterior white matter signal hyperintensities. Autopsy confirmed that this represented gliosis. There was no progression in the degree of atrophy detectable by MRI between years 8 and 9 of his illness.

The patient's PET studies showed bilateral posterior hypometabolism along with more mild diffuse changes that worsened in the temporal lobes between years 8 and 9 of his illness. Kiyosawa *et al.* 1989 found similar hypometabolism in visual association cortex and inferior parietal cortex bilaterally in patients with AD and visual agnosia. Wakai (1994) reported dorsal, as opposed to posterior hypometabolism, and Freedman (1991) found asymmetry of hypometabolism consistent with the asymmetry of cerebral atrophy seen on MRI. The PET studies described here showed sparing of primary somatosensory and motor cortices, which supports the regional immunohistochemical detection of neurofibrillary tangles in AD patients. Posterior hypometabolism is not unique to AD. PET scans of patients with dementia with Lewy bodies (DLB) show occipital hypometabolism. DLB might be considered in the differential diagnosis for PCA, when visual hallucinations and extrapyramidal signs accompany the visual-cognitive syndrome (Albin *et al.*, 1996).

Post-mortem pathology in the patient described here revealed classic findings for AD, as well as marked atrophy in the parieto-occipital regions, poorly delineated sub-cortical myelin loss in the white matter, and associated astrocytic gliosis confined to the occipital lobes. This gliotic change has not been reported previously as an autopsy finding in PCA. Hof (1990) reported eight AD patients with Balint's syndrome who had significantly higher neurofibrillary tangle counts in Brodmann areas 17 and 18 and the superior colliculus, as well as higher senile plaque counts in occipital cortex when compared with pathology from patients with more typical AD histories.

In conclusion, this case provides more complete documentation of the natural history of PCA caused by AD as seen in clinical evaluations, electroencephalography, neuro-imaging, PET, and histopathology. AD should be considered in the differential diagnosis of PCA, even when atypical features are present. The patient reported here extends the spectrum of AD to include PCA with white matter changes in the occipital region. Clinically, simultanagnosia and cortical blindness must be included among the unusual manifestations of AD.

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Fig. 1.

(a) T1-weighted transaxial MRI with gadolinium enhancement at age 67 years, showing diffuse sulcal widening, ventriculomegaly specific to the occipital horns, and disproportionate atrophy in occipital lobes bilaterally. (b) T2-weighted transaxial MRI at age 67 years, showing increased white matter signal intensity in the posterior regions.

Fig. 2. FDG-PET scans of brain at (a) age 66 years and (b) age 67 years show progression of global cortical thinning which is more pronounced in the occipital lobes. There is markedly abnormal cerebral glucose metabolism diffusely with relative sparing of the primary sensorimotor cortices.