A Case of Sporadic Pick Disease With Onset at 27 Years

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Background: Pick disease is an uncommon cause of dementia in middle age, and young-onset cases have rarely been reported.

Setting: A specialist hospital.

Patient: Patient with onset of cognitive impairment at the age of 27 years whose cerebral biopsy specimen demonstrated Pick cells and tau-positive Pick bodies.

Conclusion: Pick disease should be considered in the differential diagnosis of dementia in young adults.

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Pick disease is characterized macroscopically by focal atrophy of frontal and temporal cerebral cortex and microscopically by swollen achromatic cells (Pick cells) and argentophilic tau-positive inclusions (Pick bodies). However, the term has also been used more widely to encompass cases with focal neuropsychological deficits and focal atrophy in the absence of Pick cells and Pick bodies.1,2 Such cases may show nonspecific histological features of neuronal loss and/or gliosis. The cause remains obscure; rarely there is evidence for autosomal dominant inheritance3 but most cases appear to arise sporadically. Behavioral disturbance and speech and language impairment are early features. Most cases occur in the fifth and sixth decades, but earlier cases have been described.4,5

We describe a biopsy-proven case of sporadic Pick disease with onset at 27 years.

REPORT OF A CASE

A 29-year-old white woman was referred for further investigation of personality change and cognitive decline. Her perinatal history and early development were normal apart from enuresis until the age of 10 years. Her premorbid personality was described as extrovert. There was no family history of dementia or psychiatric disorder.

At the age of 27 years, she became withdrawn and apathetic. Her performance at work declined, and she eventually lost her job as a secretary 8 months after the onset of her illness. Impairment of speech with slurring developed at this time, and she admitted to feeling depressed although she had not manifested any biological features of depression. In the last year she had fallen several times, become incontinent of urine, and had difficulties with basic activities of daily living such as brushing her teeth, dressing, and using cutlery. In addition, she developed a voracious appetite.

Initial assessment after 18 months revealed normal findings on general neurological examination and routine serum biochemistry, hematology, autoimmune profile, electroencephalogram, and cerebrospinal fluid studies. A magnetic resonance imaging scan of the brain showed a few areas of abnormal signal in the cerebral white matter, the significance of which was unclear.

Her continued intellectual decline led to a further assessment, and when seen in a specialist clinic 22 months after the onset, there was virtually no spontaneous speech and her answers were monosyllabic. Her speech lacked cadence and was slurred and slow. She had difficulty performing the full range of eye movements. Bilateral grasp reflexes were present, and deep tendon reflexes were generally brisk. The plantar responses were flexor, tone and power were normal, and there was no tremor. On cognitive assessment, she was able to describe briefly how she got to the...
hospital. Comprehension and short- and long-term memory were preserved. She had great difficulty with complex motor movements and bimanual tasks and with rapidly alternating movements. She was unable to mime a simple activity such as combing her hair. She scored 22 (of 30) on the Mini-Mental State Examination.

She was admitted for further investigation 2 months later. Neurological examination revealed utilization behavior. A snout reflex and bilateral grasp reflexes were present. Tongue movements were slow. Tone was increased in the left arm, and both plantar responses were extensor. Cognitive reassessment demonstrated a further decline. She now scored 9 on the Mini-Mental State Examination. Her extreme restlessness and distractibility made detailed assessment impossible, but her responses were perseverative and new visual perceptual difficulties emerged.

The following laboratory tests were normal or negative: full blood cell count, erythrocyte sedimentation rate, red cell folate, vitamin B₁₂, urea and electrolytes, thyroid function tests, serum angiotensin converting enzyme, random glucose, serum protein electrophoresis, copper and ceruloplasmin, serum amino acids, very long chain fatty acids and white cell enzymes, syphilis serology, human immunodeficiency virus types 1 and 2 serology, antineutrophil cytoplasmic antibody, lupus anticoagulant, and antiphospholipid antibodies. An isolated abnormality on liver function tests was an elevated alanine aminotransferase level of 146 U/L (reference range, 7-56 U/L). Repeated testing 2 months later showed an alanine aminotransferase level of 109 U/L. Serological test results for viral hepatitis were negative.

An abdominal ultrasound scan showed a normal liver and spleen. Results of electroencephalography and cerebrospinal fluid examination were normal. A magnetic resonance imaging scan of the brain demonstrated enlarged sulci and ventricles consistent with generalized cerebral atrophy rather than the asymmetric frontotemporal atrophy more commonly associated with Pick disease.

Results of bone marrow, muscle, and axillary skin biopsies were normal. Results of a liver biopsy to exclude Wilson disease were also normal. In view of the young age and diagnostic uncertainty, a biopsy of the right frontal lobe was performed, and a specimen containing cerebral neocortex with overlying leptomeninges and a narrow ribbon of subcortical white matter was submitted for histological examination. The histological slides showed preservation of the cortical architecture although there was moderate gliosis throughout cerebral cortex and subcortical white matter. Cortical spongiosis was absent in the tissue samples examined. Immunohistochemistry with an antibody to α-B-crystallin highlighted the presence of occasional swollen achromasic neurons (Pick cells) located primarily in the deeper cortical laminae (Figure 2, A). In addition, there were numerous typical Pick bodies found in the cytoplasm of small and medium-size cortical neurons in both superficial and deep cortical laminae. These inclusions were argyrophilic (Figure 2, B) and were tau (Figure 2, C) and ubiquitin immunoreactive. Immunohistochemistry with antibodies to Aβ-peptide and prion protein gave negative results.

The terminological confusion of Pick disease makes the analysis of age at onset reported in the published literature very difficult. The use of the terms Pick disease and Pick complex to describe a clinical syndrome of frontotemporal deficits with focal atrophy encompasses a variety of different diseases defined by their histological features. Some early ages at onset, for example, that described by Mowadat et al, were clinical diagnoses without histological confirmation. Moreover, even the early reported cases of Pick disease with Pick cells and Pick bodies were based on silver staining, and may not necessarily have been tau positive. However, a review of the published literature on argentophilic Pick bodies reveals some early-onset cases. For example, Lowenberg et al described a male patient with onset by age 25 and death at 27 years. His mother had been similarly affected. The cases of von Braunmuhl and Leonard of 2 sisters with onset at 29 years and 31 years, also with a family history. The patient described by Stewart et al also had a very early onset at the age of 27 years, with histopathological features of Pick bodies. These cases, together with our case, are the earliest-onset reported with histologically definite sporadic Pick disease.
A review of 50 cases of histologically confirmed Pick disease indicated onset of the disease earlier than that found with Alzheimer disease, being relatively uncommon after the age of 70 years, although this may in part reflect a sampling bias. Alzheimer disease very rarely occurs before the age of 40 years and, if so, usually occurs in association with presenilin 1 mutations and familial autosomal dominant disease. Pick disease with Pick inclusion bodies is only rarely reported to be familial. By contrast, some pedigrees with hereditary dementia with nonspecific histological features have been linked to mutations in the tau gene and can have an early age at onset. Onset of a degenerative dementia in the 20s is very rare and can lead to diagnostic confusion with psychiatric disorders. Pick disease needs to be considered in the differential diagnosis of behavioral and cognitive decline in young adults.

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Figure 2. A, Pick cell showing swollen ballooned cytoplasm (α-B-crystallin immunohistochemistry, ×900). B, Pick bodies (arrowhead) have a densely stained homogeneous appearance in silver-stained section (Bielschowsky silver impregnation, ×900) and, C, are positive for tau (arrowhead) (tau immunohistochemistry, original magnification ×300).