PICKS DISEASE

Background

1. Definition
   - Dementia secondary to focal degeneration of the frontal and/or temporal lobes
   - Progressive personality and behavioral changes
2. General Information
   - First described by Arnold Pick in 1892
   - Also known as: Frontotemporal dementia or degeneration, Frontal lobe dementia or degeneration, Pick Complex
   - Behavioral variant most common; may also present with language and motor impairments

Pathophysiology

1. Pathology of Disease
   - Degeneration and atrophy of frontal and/or temporal lobes with fibrous scarring due to astrocyte proliferation and neuronal loss[1]
   - Tau protein depositions (Pick bodies) found in some variants; more commonly in familial cases. Up to 50 Tau mutations have been found
   - Various other protein mutations have been found on autopsy
   - Serotonin binding decreased in frontal lobes[2]
2. Incidence, Prevalence
   - Exact prevalence unknown; estimates range from 10-20% of dementias
   - Relative frequency of 3-10% according to autopsies[2]
   - Mean age at onset - 57 years[3]
   - Rare before age 40 or after age 75
   - Possible male predominance[4]
   - Most cases have no family history of dementia; some variants are noted to have autosomal dominant inheritance
3. Morbidity / Mortality
   - Gradually progressive
   - Advanced disease predisposes patients to serious complications such as injuries and pneumonia

Diagnostics

1. History
   - Variable symptoms at presentation
   - Cognitive and visual-spatial abilities initially preserved[1]
   - Behavioral variant[1]
     - Personality changes: apathy, impulsivity, disinhibition, etc.
     - Lack of insight and loss of concern for self or others
     - Loss of social decorum
     - Ritualistic behaviors: hoarding, pacing, etc.
     - Emotional blunting
     - Difficulty adapting to change
     - Changes in attention ranging from distractible to perseverative
   - Language variants[5]

        - Progressive non-fluent aphasia characterized by difficulty naming objects and dysfluent speech
        - Semantic dementia characterized by fluent empty speech with loss of word meaning
    - Motor variants
        - Motor neuron disease resulting in atrophy, flaccidity, muscle fasciculations
        - Corticobasal degeneration characterized by rigidity and uncontrolled spontaneous movements
        - Progressive supranuclear palsy characterized by vertical gaze palsy, rigidity, bradykinesia, dystonia
2. Physical Examination
    - Primitive reflexes such as grasp, rooting, sucking noted as frontal lobe disease progresses[1]
    - Incontinence
    - Rigidity, tremor, akinesia
    - Low blood pressure
3. Diagnosis
    - Primarily clinical
    - Laboratory evaluation may be helpful to rule out other causes of delirium and dementia; no diagnostic labs specific to Picks disease
    - Diagnostic imaging
        - MRI required to rule out illness due to other structural cause
        - Atrophy of affected frontal and temporal lobes noted in later disease
    - Other studies
        - Neuropsychologic testing can help quantify impairment but not diagnostic
        - MMSE may be normal in early cases[5]
        - EEG remains normal despite dementia[1]
        - Definitive diagnosis by postmortem autopsy
4. Diagnostic Criteria[6]
    - Development of behavioral or cognitive deficits manifested by either
      1a: Early and progressive changes in personality; emotional blunting and/or loss of empathy; difficulty modulating behavior; often resulting in inappropriate responses or activities, or
      1b: Early and progressive change in language; problems with expression of language or severe naming difficulty; problems with word meaning
    - 1a or 1b deficits cause significant impairment in social or occupational functioning; represent significant decline from previous level of functioning
    - Course characterized by gradual onset and continuing functional decline
    - 1a or 1b deficits not due to other nervous system conditions (e.g., cerebrovascular disease), systemic conditions (e.g., hypothyroidism), or substance-induced conditions.
    - Deficits do not occur exclusively during delirium.
    - Disturbance not better accounted for by psychiatric diagnosis (e.g., depression).

Differential Diagnoses

1. Alzheimer disease
    - Often later age of onset; less behavioral feature; more prominent memory loss than frontotemporal dementia
    - Has more cholinergic deficits
    - Definitive diagnosis postmortem
2. Lewy body dementia
    - Visual hallucinations common, but not commonly seen in Picks disease
3. Psychiatric disorders (depression, OCD, Bipolar disorder, etc.)
    - Earlier age of onset
    - May have delusions or hallucinations; uncommon with Picks disease
    - Respond more favorably to pharmacologic treatment
4. Structural disease (tumor, infarct, trauma, abscess, etc.)
    - Seen on CT or MRI

Therapeutics

1. Supportive treatment
    - No pharmacologic treatment slows progression
    - Established routine and patterns may help avoid agitation
    - SSRIs may help with obsessive compulsive behaviors, disinhibition, depression, and carbohydrate craving[7]
    - Trazodone and antipsychotic medications tried with varying success
2. Long-Term Care
    - In-home nursing care or skilled nursing facility may be needed to provide cares and supervision as disease progresses

Prognosis

1. 50% mortality at 5 years from diagnosis, 80% at 8 years
2. Semantic deficits, word-finding problems, and language difficulties at the time of diagnosis give a worse prognosis[3]
3. Positive family history and age >64 years at onset also have a worse prognosis

Patient Education

1. Association for Frontotemporal Disorders, www.ftd-picks.org

References

1. The Lund and Manchester Groups. Clinical and neuropathologic criteria for frontotemporal dementia. J Neurol Neurosurg Psychiatry 1994; 57(4): 416-418.
2. Weder, N., Aziz, R., Wilkins, K., and Tampi, R. Frontotemporal Dementias: A Review. Ann Gen Psychiatry 2007, 6 (15)
3. Garcin, B., Lillo, P., Hornberger, M., Piguet, O., Dawson, K., Nestor, P.J., Hodges, J.R. Determinants of survival in behavioral variant frontotemporal dementia. Neurology 2009; 73: 1656-1661.
4. Johnson, J.K., Diehl, J., Mendez, M.F., Neuhaus, J., Shapira, J.S., Forman, M., Chute, D.J., Roberson, E.D., Pace-Savinsky, C., Neumann, M., Chow, T.W., Rosen, H.J., Forstl, H., Kurz, A., Miller, B.L. Frontotemporal lobar degeneration: Demographic characteristics of 353 patients. Arch Neurol 2005; 62: 925-930.

5. Kertesz, A. Pick Complex: An integrative approach to frontotemporal dementia. The Neurologist 2003; 9(6): 311-317.
6. McKhann, G., Trojanowski, J.Q., Grossman, M., Miller, B.L., Dickinson, D., & Albert, M. Clinical and pathological diagnosis of Frontotemporal dementia: Report of a work group on Frontotemporal dementia and Picks disease. Archives of Neurology 2001; 58: 1803-1809.
7. Swartz, J.R., Miller, B.L., Lesser, I.M., Darby, A.L. Frontotemporal dementia: Treatment response to serotonin reuptake inhibitors. J Clin Psychiatry 1997; 58(5): 212-216.
8. Zheng Chiu, W., Kaat, L.D., Seelaar, H., Rosso, S.M., Boon, A., Kamphorst, W., Van Swieten, J.C. Survival in progressive supranuclear palsy and frontotemporal dementia. J Neurol Neurosurg Psychiatry 2010; 81: 441-445.

Author: Tamara Kramer, MD, *Mercy Health System FMRP, WI*

Editor: Robert Marshall, MD, MPH, Capt MC USN *Puget Sound Family Medicine Residence, Naval Hospital, Bremerton, WA*