Brief Report

Dementia and Down Syndrome

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Through deinstitutionalization, more adults with mental retardation are living in the community under the care of family physicians. Patients with Down syndrome are at high risk for early Alzheimer's disease. This case report describes a 43-year-old woman with Down syndrome whose progressive functional decline over 3 years was attributed to dementia of the Alzheimer type.

Key words. Dementia; Down syndrome; Alzheimer's disease; mental competency; adults.
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According to life expectancy data published by Baird and Sadovnick,[1] 60% of individuals born with Down syndrome will be alive at age 50 and 25% will be alive at age 65. Beyond the age of 40, individuals with Down syndrome are at increasing risk for the development of a dementia clinically and neuropathologically indistinguishable from dementia of the Alzheimer type. The following case report illustrates many of the typical features of dementia complicating Down syndrome.

Case Report

The patient in this case was born in 1952 with Down syndrome. She suffered no concomitant congenital heart disease or gastrointestinal tract anomalies and never required hospitalization or surgery. Until 3 years ago, she loved to swim, dine at restaurants with her father, and travel by airplane to the family condominium in Florida.

Three years ago, her behavior began to change. She refused to climb the several flights of stairs up to the family's Florida condominium. On a subsequent trip to Ohio, she refused to traverse the ramp to the aircraft, and the family was forced to drive her home by automobile. She quit swimming and eventually refused to leave her home.

About 1 year ago, she developed urinary incontinence. The parents hired a home health aide to assist in her care. The family could not locate a physician who would conduct home visits and her medical care was limited to emergency department visits by means of ambulance for such problems as fecal impaction and bronchitis. After telephoning Down syndrome organizations and reviewing medical books and articles, the patient's sister suspected that she was showing signs of Alzheimer's disease.

Three months before hospitalization, the patient suffered her first tonic-clonic seizure. By that time, she no longer recognized family members. Her parents and family had varied opinions regarding her present status and future needs. Her father, a retired military officer in his 80s, minimized the severity of his daughter's functional decline and desired that she remain in their home, irrespective of further deterioration. Her mother and two sisters believed that the emotional stress of continued home care was exceeding their capacity and that she required a move to an extended care facility.

Finally, the week prior to hospitalization, she could not be coaxed out of bed and refused to swallow any solid food and most liquids. When a home visit was conducted, she appeared dehydrated and delirious. She was admitted to the hospital for intravenous rehydration, evaluation of her sudden refusal to eat and to ambulate, and for evaluation of her progressive global functional deterioration.

Initial laboratory tests included a normal red blood count but with mild macrocytosis (mean corpuscular volume 102.2 fl [normal, 80 to 100 fl]); sodium was 153 mmol/L (normal, 141 to 150); thyroid-stimulating hor-

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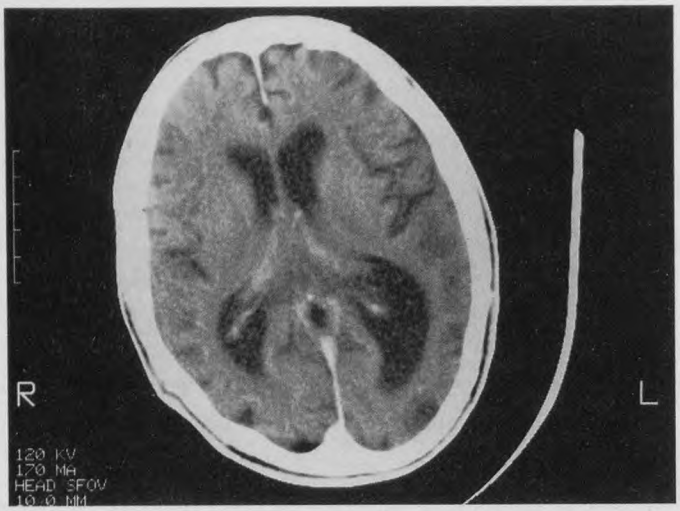

Figure. A cranial axial computerized tomographic image shows atrophic changes with associated ventriculomegaly.

mone (TSH) 35 mIU/L (normal, 0.4 to 5.0) with a normal free-thyroxine index; serum B_{12} level was 183 pmol/L (normal, 166 to 738); and folate was within normal limits. The admission chest radiograph was interpreted as normal, but computerized tomography (CT) of the abdomen 2 days later revealed bilateral lower lobe pulmonary infiltrates and cholelithiasis. A nuclear medicine biliary scan did not suggest cholecystitis. A CT scan of the brain was interpreted as indicating atrophic changes with associated ventriculomegaly without midline shift (Figure).

The patient was given intravenous fluids and antibiotics to treat the pneumonia suggested by infiltrates on CT scan. Thyroid supplementation was gradually introduced.

Because of her refusal to ambulate and her mild diffuse hyperreflexia, cervical spine films were obtained. They failed to suggest atlantoaxial instability and a neurosurgical consultant did not find evidence of cervical myelopathy. Consultation with a geropsychiatrist confirmed the family's suspicion that the patient was manifesting signs of Alzheimer's type dementia. A witnessed tonic-clonic seizure with prolonged postictal quadriplegia prompted daily anticonvulsant treatment. Modest doses of chlorpromazine (25 to 50 mg up to three times daily) seemed to diminish her fearful repetitive verbalizations; for example, "I want to go home," "Where's Sissy?" and "Shut up, you bastard." As her fear abated, the patient permitted the staff to improve her hygiene and to provide nursing care. Her appetite improved modestly, but she still refused to leave the bed. She was discharged to a nursing home with community hospice support for both the family and the nursing home staff.

Since admission to the nursing home, the patient has continued to deteriorate. Her tonic-clonic seizures have increased in frequency, requiring gradual increases in her carbamazepine therapy, and myoclonic features have emerged. Thyroid hormone supplementation and parenteral vitamin B_{12} supplementation did not improve her cognitive or behavioral function, macrocytosis, or constipation. She lost an additional 10 pounds in the 7 months following her discharge from the hospital. Though still unable to recognize family or friends, she is less fearful and her chlorpromazine has been discontinued.

Discussion

Nearly all persons with Down syndrome over the age of 40 manifest *neuropathologic* changes characteristic of Alzheimer's disease, including neurofibrillary tangles, neuritic plaques, and neuron cell loss.[2] This contrasts with the findings of several prospective, longitudinal studies which suggest that the average onset of *clinical* dementia is in patients in their early 50s.[3–5]

The specific clinical features of dementia are determined in part by the individual's premorbid functional status. Lai and Williams[4] followed 96 individuals with Down syndrome and nontreatable dementia for 8 years. They identified three phases of clinical deterioration. The initial phase of dementia manifested as memory impairment, temporal disorientation, and reduced verbal output in higher functioning individuals, while low-functioning individuals demonstrated apathy, inattention, and decreased social interaction. In the middle phase of dementia, decline in activities of daily living (ADLs), deterioration of workshop performance, and a slowed shuffling gait were noted. Seizures, mostly tonic-clonic, emerged in 84% of the patients with dementia and Down syndrome. In the final phase, these patients were nonambulatory and incontinent, with death typically due to infection. The dementia associated with Down syndrome generally follows a rapidly progressive course: death typically occurs within 3 to 5 years of the onset of dementia.

In patients without Down syndrome, Alzheimer's disease is characterized by a later age of onset and a slower course of decline. Jost and Grossberg[6] reported a retrospective review of the medical records of 100 randomly selected, autopsy-confirmed Alzheimer's disease patients enrolled in a university-based Alzheimer's association brain bank. In this sample, the average age at diagnosis was age 75 years, 32 months after symptom onset, and the average total disease duration was 5 to 8 years.

Chicoine et al,[7] reporting their experience with an adult Down syndrome clinic, cautioned against prematurely attributing functional decline in patients with Down syndrome to Alzheimer's disease. Of 48 patients presenting with diminished skills, 34 (71%) were diag-

nosed with depression, 13 (27%) with adjustment reaction, 12 (25%) with hypothyroidism, 2 (4%) with anxiety, and just 2 (4%) with dementia. Notably, the average age of patients seen at this clinic was 34 years. In adults with Down syndrome, other common conditions that can cause functional decline or worsen the impact of Alzheimer's disease include: hearing and visual impairment,[8] obstructive sleep disorders, vitamin B_{12} or folate deficiencies, and medication toxicities, especially anticonvulsants.

Vieregge et al[9] reported that hypothyroidism was present in 59% of their study group of persons with both Down syndrome and dementia, compared with 33% of a nondemented group with Down syndrome alone. The increased frequency of thyroid dysfunction among children and adults with Down syndrome, and the difficulty in distinguishing clinical features of hypothyroidism from those of Down syndrome underlies the recommendation for annual TSH and T_4 screening for all ages.[10] It is, however, unclear whether individuals with elevated TSH but normal T_4 levels, such as the patient in our case, benefit from treatment.

Since non-neurologic conditions can affect behavior and function in adults with Down syndrome, a brief review of preventive health care in this population is relevant. Adults with mental retardation manifesting functional decline require thorough medical, psychiatric, and environmental assessment. The history should routinely include questions regarding ADLs, instrumental activities of daily living, behavior and personality changes, and signs and symptoms of sleep disorders. During the physical examination, the physician needs to observe for the following conditions: cerumen impaction, serous otitis, sinusitis, tonsillar hypertrophy, and mitral valve prolapse. Ophthalmologic screening for cataracts and keratoconus and auditory testing for conductive and sensorineural deficits is recommended every 2 years. As indicated above, annual TSH and T_4 screening is suggested. In individuals who have never undergone cardiac studies, echocardiography should be strongly considered because of the high prevalence of asymptomatic mitral valve prolapse and other valvular abnormalities in adult patients with Down syndrome.[11] If significant valvular disease is confirmed, then subacute bacterial endocarditis prophylaxis is needed. The Ohio/Western Pennsylvania Down Syndrome Network publishes a preventive medical checklist that summarizes expert opinion regarding health care screening for these patients.[12]

As with our patient, many individuals with Down syndrome who develop Alzheimer's disease reside with aging parents who may be frail and at risk for dementia themselves. Educating and supporting family members and professional caregivers is essential. They benefit most from practical, concrete advice on the management of specific problem behaviors, such as anger, aggression, wandering, and sleep disturbance. Published materials by Alzheimer's Disease and Related Disorders Association[13] are helpful to patients and physicians in dealing with these issues. Concurrent psychiatric disorders, most commonly depression, psychosis and anxiety, may respond to pharmacotherapy. Patients with Down syndrome and dementia also require close surveillance for concurrent medical disorders such as hypothyroidism, infection (exemplified by our patient's occult pneumonia), seizures, and anemia. Published clinical experience of specialty clinics, such as the Lutheran General Adult Down Syndrome Clinic[6] and the Down Syndrome Aging Clinic,[14] provides valuable information about the evaluation and management of persons with Down syndrome and dementia.

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