Course of Alzheimer Disease in People with Down Syndrome

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Abstract:

INTRODUCTION

The neuropathologic changes associated with Alzheimer disease (AD) have long been known to occur in people with Down syndrome (DS) by about age 40. However, less is known about the clinical presentation of AD in people with DS. Clinical manifestations of dementia were reviewed in 31 individuals with DS who were diagnosed with AD.

METHODS

A retrospective chart review of 31 (18 men and 13 women) was performed on patients with DS who were evaluated at the Adult Down Syndrome Center with the diagnosis of AD and died during the period from January 1992 to December 2006.

RESULTS

The mean age of onset of symptoms was 52.3 years (range 39-69), the mean age of death was 55.9 years (45-71 years) and mean survival from onset of symptoms to death was 3.6 years (1-8 years). Symptoms reported included change in cognition (97%), memory impairment (97%), change in gait and/or unsteadiness (97%), personality and/or behavioral changes (90%), incontinence of urine and/or stool (87%), seizures (77%), sleep disturbance (74%), swallowing dysfunction (58%), change in speech (45%), reduced concentration (19%), and hallucinations (13%).

CONCLUSIONS

The clinical findings in people with DS who develop AD are described. Of particular interest are the earlier mean age of onset compared to people without DS (52.3 years vs 72.8 years); the shorter mean course from onset of symptoms to death (3.7 years vs 5.7-10.5 years in various studies); the higher association with seizures (77% vs 1.5%) and the lower report of hallucinations (13% vs 23%).

Introduction:

The finding that essentially all people with Down syndrome (DS) develop by 40 years of age the neuropathology (plaques and neurofibrillary tangles) seen in Alzheimer disease (AD) has been known for many years (Solitaire, 1966; Ropper and Williams, 1980; Cork, 1990). However, less is known why many people with DS don't develop AD or what the natural history is when people with DS do develop AD (Lott and Lai, 1982; Chicoine, et al, 1994). Lai (1992) reported an earlier onset of AD. Holland et al (2000) reported initial changes of AD in people with DS to be mood and personality changes. Temple and Konstantareas (2005) found that people with DS who developed AD had fewer hallucinations.

As our understanding of AD expands and improved treatments or even cures are discovered, a clear understanding of the symptoms and course of AD in people with DS will become even more important. A basic understanding of the natural history of AD in DS will be necessary to improve early diagnosis and assessing treatment effectiveness.

Methods/Subjects:

- A retrospective chart review of 31 patients
- Adult patients with Down Syndrome diagnosed with Alzheimer disease
- Expired during the period from January 1992 to December 2006
- Symptoms reported during the time from diagnosis until death were reviewed
- Descriptive statistics reported [mean; SD (range); number (percent)]

Results:

Outcomes / Symptoms	Results
Age of onset of symptoms (yrs)	52.3 ± 6.3 (36-69)
Age of death (yrs)	55.9 (45-71)
Survival from onset of symptoms to death (yrs)	3.6 (range 1-8)
Male Gender	18 (58%)
Change in cognition	30 (97%)
Memory impairment	30 (97%)
Change in gait or unsteadiness	30 (97%)
Personality and/or behavioral changes	28 (90%)
Incontinence of urine and/or stool	29 (87%)
Seizures	24 (77%)
Sleep disturbance	23 (74%)
Swallowing dysfunction	18 (58%)
Change in speech	14 (45%)
Reduced concentration	6 (19%)
Hallucinations	4 (13%)

Discussion:

The mean age at onset of AD in our sample was 52.2 ± 6.3 years. To determine if this differs from the literature, we compared our findings with the finding of Li's et al (2002), who reported on a population of adults with AD a mean onset time of 72.8 ± 6.8 years. Cohen's d was calculated using pooled standard deviation and the effect size was fairly large (d = 3.04). In other words, the average person in our sample is 3.04 standard deviations from the average person in Li's sample or more than 99% of our sample was younger at onset than the average person in Li's study.

A similar comparison was performed to determine if our mean reported time from onset to death was different than the literature (3.7 ± 1.9 years; and 5.9 ± 3.7 years, respectively; Ganguli et al, 2005) and the effect size was medium (d = 0.60). The average person in our sample was 0.60 standard deviations below the average person in Ganguli's sample and 73% of our sample had a shorter onset to death than in Ganguli's sample.

In this study, we reported that approximately 77% of our sample experienced seizures and approximately 13% were reported to experience hallucinations. Again, we found our sample differed from the literature at a statistically significant level (seizures: t = 8.518, p < 0.001; hallucinations: t = 7.358, p < .001). Scarmeas et al, (2009) stated seizure rates in their sample were approximately 2% and Bassiony et al, (2003) reported a hallucination rate of 23%.

Conclusions:

- The average age on onset of Alzheimer disease in people with DS is about 20 years earlier than in people without DS.
- The average time from onset of symptoms to death was shorter for people with DS by 2.2 years (3.7 years vs 5.9 years.
- A variety of symptoms associated with AD in people with DS were described.
- Seizures are much more common in AD in people with DS (77% vs 2%)
- Hallucinations were described less frequently in AD in people with DS (13% vs 23%)

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