Original

Dementia Symptoms in Down Syndrome

Bessy Benejam[1]
[1]Down Medical Centre, Fundació Catalana Síndrome de Down
C/Comte Borrell 201-203, entresuelo
08029 Barcelona. Spain
Correspondence: neuropsicologia@fcsd.org

Abstract

It has been demonstrated that persons with Down syndrome (DS) develop neuropathological characteristics of Alzheimer's disease (AD) after the age of 40. Surprisingly, not all these patients will show clinical symptoms of dementia. This article is a review of the criteria currently used for diagnosis and includes a description of how dementia symptoms manifest in individuals with DS.

Keywords: Alzheimer's disease. Dementia. Down syndrome. Aging. Neuropsychology

Introduction

The observation of a clear-cut association between the genes on chromosome 21 and the development of Alzheimer's disease (AD) has led to increasing interest in age-related changes in patients with Down syndrome (DS). Postmortem studies have shown that all persons with DS over 40 develop the neuropathological lesions characteristic of AD although, surprisingly, not all of them will show the clinical features of dementia (1, 2). It has been estimated that dementia can be clinically diagnosed in 9% of adults with DS between the ages of 45 and 49 and in approximately 32% between 55 and 59, but no increase in prevalence has been shown over the age of 60 (3).

Until recently there have been very few studies on the cognitive decline associated with AD in patients with DS because of their short life expectancy; these patients rarely reached an age when they would be at risk of developing the disease. Medical advances, however, have made it possible for individuals with intellectual disability (ID) to live longer, and more persons with DS now live beyond the age of 50. Consequently, there has been increased interest in carrying out prospective studies to describe the first signs of decline in cognitive functions attributable to normal aging and to the development of dementia (4, 5).

Diagnosis of dementia in DS

It is difficult to diagnose dementia in persons with DS, especially in the initial stages of the disease. The cognitive skills of most individuals with DS are below the population average even before dementia develops, and the tools used for neuropsychological screening or evaluation in the normal population are ill-suited to this group. In these cases it is preferable to use tools specially designed to evaluate lower cognitive performance levels and avoid the floor effect.

It is important to diagnose dementia early for several reasons, particularly to be able to distinguish between patients who will present progressive, irreversible dementia (such as AD) and those who will show cognitive impairment caused by treatable conditions or diseases. Early detection of dementia will also make it possible to administer medications that may not cure the disease but will slow its course.

Before describing the diagnostic criteria for dementia, it is important to look at a number of points. Given that a person with ID starts out in a situation that does not correspond to «normalcy», such a person must present a change relative to his/her own baseline level of activity rather than a

difference compared to normal functioning before dementia can be considered. Longitudinal testing is therefore important because this will make it possible to determine the prior level of cognitive function in the individual with ID in order to see whether there is a progression in deficits before making a diagnosis of dementia. Furthermore, any decline in cognitive evaluation tests should also be accompanied by a change in the individual's social and/or occupational functioning or degree of independence in activities of daily living (ADL).

The way in which this decline manifests will depend on the DS individual's premorbid intellectual functioning and the degree of independence in ADL. The decline in persons with mild mental retardation will be similar to that of the general population, whereas in individuals with more severe ID it will be very different.

Diagnostic criteria in dementia

Since cognitive impairment in patients with ID often starts with changes in emotional control, motivation, or social behavior, the diagnostic criteria contained in ICD-10 (International Classification of Mental and Behavioral Disorders) were considered more appropriate than those in DSM-IV (Diagnostic and Statistical Manual of Mental Disorders), since the latter places greater emphasis on deficits in multiple cognitive areas and not so much on behavioral changes (6). The ICD-10 criteria make it possible to establish a diagnosis of dementia independently of its etiology and, secondly, to distinguish AD from other forms of dementia.

The table below summarizes the criteria for diagnosing dementia according to ICD-10 (Table 1).

Once dementia is diagnosed, it is important to rule out all possible causes of cognitive impairment before labeling the condition as AD. There are other conditions, such as hypothyroidism, sensory loss, depression, lack of sleep or drug poisoning that can give rise to a decline in cognitive functions.

When other causes of dementia have been excluded, a diagnosis of AD requires that the impairment of memory and other cognitive skills must be progressive. These criteria are consistent with those of the NINCDS-ADRDA for likely AD diagnosis (7). A definitive diagnosis of AD requires histopathological confirmation.

Table 1.
General criteria for dementia according to ICD-10

Memory impairment Evident especially for learning new information, although recall of previously learned information may also be affected in the most severe cases. The disruption involves verbal as well as non-verbal material.
Impairment of other cognitive skills Characterized by impaired judgment and thinking, such as planning and organization, and in general information processing. The impairment should be verified in relation to a previous higher level of functioning.
Awareness of environment Consciousness must remain clear for a sufficient length of time to be able to demonstrate the impairment of memory and other cognitive functions.
Impaired emotional control or motivation or changes in social behavior Changes will be manifested by at least one of the following: 1) emotional lability, 2) irritability, 3) apathy, 4) stultified social behavior.
Duration In order to make a definite diagnosis, the impairment of memory and other cognitive skills must be present for at least 6 months.

How does this decline manifest in persons with DS?

1) Memory impairment:

Memory loss tends to be one the the most evident symptoms in the early stages of dementia. The initial symptoms are usually related to the inability to recall recent events, while more remote memory is preserved in early stages. In persons with DS this usually manifests as a decline in the ability to recall recent information such as, for example, where one has left an object, taking medication, what day of the week it is or the names of acquaintances or important birthdays. Individuals may have difficulties in describing what they have done during the day or what they have eaten, or in following instructions given by the family, especially in cases in which more than one instruction is given at a time. There may also be problems in following a conversation or recognizing specific locations in the patient's own neighborhood. It is not uncommon for persons with DS to show episodes of spatial disorientation in the early stages of dementia, even on roads or routes well known to them (5). In the most severe cases of memory loss the person with DS may even forget what steps to take in carrying out previously learned tasks.

2) Impairment of other cognitive skills:

Many adults with DS may show language and speech impairments such as, for example, greater difficulty in starting a sentence or finding the right words (anomia), greater difficulty in verbal comprehension, or loss of intonation in speech (aprosodia). The language of an adult with DS and dementia may become unintelligible.

In cases of mild mental retardation, there may be greater difficulty in skills related to judgment, thinking, planning, and organization. The decline in judgment skills is evidenced when the person with DS loses, for example, the ability to choose appropriate clothing for weather conditions. Problems in planning and organization may become evident in non-routine tasks, such as going shopping or preparing breakfast.

In the most severe cases of mental retardation, it may be very difficult to detect a decline in these areas, since such persons may never have been able to perform non-routine tasks. In these patients, the first symptoms of cognitive impairment will be expressed as apraxia (inability to get dressed, brush their teeth or use cutlery at meals) or aphasia (greater difficulty in expressing themselves). Such patients may also have difficulty in recognizing objects visually (agnosia) and may confuse one object with another. When the mental retardation is more severe, the decline in cognitive functions will present mainly in the form of general slowing in all areas (slower when walking, eating, dressing, speaking, etc.), greater difficulty with attention or impaired temporal or spatial orientation (for example, diminished ability to distinguish between day and night, between a working day and a weekend; or moving around at home, confusing one room with another).

Problems such as agraphia (writing difficulties), alexia (reading difficulty) and acalculia (trouble with calculation skills) will manifest only in those individuals who have acquired such skills previously.

3) Emotional control, motivation and changes in social behavior:

It is known that many persons with DS and dementia present a wide range of psychiatric and behavioral symptoms similar to those observed in individuals with dementia in the general population. There may be sleep disorders (sleepwalking, problems with getting to sleep, restlessness, etc.), increased social withdrawal, loss of interest, loss of self-confidence (manifesting as a constant search for company, increased worrying, low self-esteem, restlessness, etc.), obsessive symptoms (repetitive behavior and movements, such as watching the same film over and over or going in and out of the bathroom several times), emotional incontinence (emotional lability, irritability and enhanced aggressiveness), hallucinations (commonly visual), physical complaints (related to hypochondriac behavior), personality changes, etc.

Given the high incidence of psychiatric disorders in persons with DS, the appearance of additional symptoms is often attributed to intellectual disability and not to the onset of dementia.

4) Activities of daily living:

It is also common for adults with DS who develop dementia to lose certain skills in performing basic activities that are instrumental in daily living. This loss of skill may manifest as requiring more help when getting dressed, bathing or brushing teeth. Other examples include loss of skill in using the DVD player, going shopping or using the telephone.

The initial symptoms of dementia

Studies of AD in the general population (i.e., without intellectual disability) have shown that the earliest cognitive deficit in the initial stages of dementia is usually progressive loss of recent memory (8). These results are consistent with other studies which have shown that neuropathological changes associated with AD occur first in the medial temporal regions, which are involved in memory formation. In patients with DS there is greater disparity in results. Holland et al. observed that the first symptoms of impairment in 71% of the subjects in their sample were changes in character and personality rather than a decline in mnesic functions. Among the behavioral changes observed, apathy and increased mental inflexibility were the most common (9). In the general population these behavioral symptoms tend to appear in later stages of dementia.

Deb et al. carried out a qualitative study from the carer's perspective on the initial dementia symptoms in persons with DS. They obtained results very similar to those found in the general population, i.e., marked loss of memory of recent events alongside the relative preservation of memory of more remote events (5). Other early symptoms were confusion, general slowing, speech and language problems, sleep disorders (such as waking up early and sleepwalking), and loss of skills. In the behavioral aspect, they and other authors observed greater problems in socializing (social withdrawal), loss of self-confidence (causing nervousness, low self-esteem, constantly seeking attention and excessive worrying), loss of interest, obsessive symptoms (such as repetitive movements or behaviors), emotional incontinence, delirium and hallucinations, hypochondriac behavior and personality changes (enhanced aggressiveness) (5, 10, 11).

Symptoms like social withdrawal, lowered initiative, repetitive behavior, emotional incontinence, and marked psychomotor slowing are characteristic of dysfunction of the frontal lobe or the executive system. Authors who have observed these same symptoms have suggested that they are the result of interaction between the neuropathology characteristic of AD and the structural disruption in the brains of patients with DS (12, 13), rather than the result of dementia with an etiology other than AD. It is known that persons with DS show structural abnormalities in the frontal and temporal lobes, which makes these areas highly vulnerable to acquired brain damage.

There is another explanation for the early onset of these behavioral symptoms in persons with DS who

develop dementia. It is often impossible to diagnose dementia in the early stages in a person with intellectual disability, especially in the most severe cases of mental retardation, in which it is not possible to administer neurocognitive tests. Dementia is therefore usually diagnosed when the disease has progressed into later stages (5).

Symptoms often detected in the more advanced stages of dementia are more severe intellectual impairment, more marked personality and mood changes, loss of sphincter control, epileptic attacks, loss of mobility and increased muscle tone (10).

Conclusions

From the neuropathological standpoint, it has been shown that there is a relation between Down syndrome and Alzheimer's disease. Since the cognitive skills of persons with Down syndrome are below those of the average population, diagnosing dementia in this population is complicated. The scales used for the general population are seldom suited to detecting the changes that may take place in the cognitive functions of persons with intellectual disability who develop a neurodegenerative disease. This study has described the criteria currently in use to diagnose dementia in persons with DS and includes several examples of how the symptoms manifest in this population.

Bibliography

1. Mann D.M. (1988) Alzheimer's disease and Down's syndrome. Histopathology 13, 125-37.
2. Deb S., de Silva P.N., Gemmell H.G., Besson J.A., Smith F.W., Ebmeier K.P. Alzheimer's disease in adults with Down's syndrome: the relationship between regional cerebral blood flow equivalents and dementia. Acta Psychiatr Scand 1992;86:340-5.
3. Coppus A., Evenhuis H., Verberne G.J., Visser F., van Gool P., Eikelenboom P., van Duijin C. Dementia and mortality in persons with Down's syndrome. J Intellect Disabil Res 2006;50:768-77.
4. Devenny D.A., Krinsky-McHale S.J., Sersen G., Silverman W.P. Sequence of cognitive decline in dementia in adults with Down's syndrome. J Intellect Disabil Res 2000;44: 654-65.
5. Deb S., Hare M., Prior L. Symptoms of dementia among adults with Down's syndrome: a qualitative study. J Intellect Disabil Res 2007;51:726-39.
6. Aylward E.H., Burt D.B., Thorpe L.U., Lai F., Dalton A. Diagnosis of dementia in individuals with intellectual disability. J Intellect Disabil Res 1997;41: 152-64.
7. McKhann G., Drachman D., Folstein M., Katzman R., Price D., Stadlan E.M. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984;34: 939-44.
8. Linn R.T., Wolf P.A., Bachman D.L., Knoefel J.E., Cobb J.L., Belanger A.J., Kaplan E.F., D'Agostino R.B. The 'preclinical phase' of probable Alzheimer's disease. A 13-year prospective study of the Framingham cohort. Arch Neurol 1995;52: 485-90.
9. Holland A.J., Hon J., Huppert F.A., Stevens F. Incidence and course of dementia in people with Down's syndrome: findings from a population-based study. J Intellect Disabil Res 2000;44:138-46.
10. Prasher V.P., Filer A. Behavioural disturbance in people with Down's syndrome and dementia. J Intellect Disabil Res 1995;39:432-6.
11. Evenhuis H.M. The natural history of dementia in Down's syndrome. Arch Neurol 1990;47:263-7.
12. Holland A.J., Hon J., Huppert F.A., Stevens F., Watson P. Population-based study of the prevalence and presentation of dementia in adults with Down's syndrome. Br J Psychiatry 1998;172:493-8.
13. Ball S.L., Holland A.J., Hon J., Huppert F.A., Treppner P., Watson P.C. Personality and behaviour changes mark the early stages of Alzheimer's disease in adults with Down's syndrome: findings from a prospective population-based study. Int J Geriatr Psychiatry 2006;21:661-73.