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Short report

Dementia in a woman with Prader–Willi syndrome

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ABSTRACT

We report on a 58-year-old woman with Prader–Willi syndrome (PWS) and dementia.

This case report illustrates a new research area in older adults with PWS. Dementia might be associated with PWS. In the case of dementia, more clinical studies are warranted to observe whether premature Alzheimer changes or indications of other dementia forms indeed occur more prevalent in people with PWS.

1. Introduction

Prader–Willi syndrome (PWS) is a genetic disorder and results from the absence of the paternal part of the chromosome 15q11-q13 region. Several mechanisms can cause this absence. About 75% of the people with PWS have a deletion in the paternally derived 15q11-q13 region, the remaining subjects have a maternal uniparental disomy (UPD; 20–25%) or an imprinting defect (1%) [6,17].

The ageing process in people with intellectual disabilities has been topic of interest in the recent years. Compared to people without intellectual disabilities ageing specific conditions occur more often and, in general, they appear earlier in life [20,23,26,34,36,37]. Dementia is one of these ageing specific conditions. Persons with Down syndrome are known to have an increased risk to develop dementia of Alzheimer's type [4,30,34,35,40]. Less attention has been paid, however, to the risk of dementia in other specific genetic syndromes associated with ID like PWS.

We report on a case of an older woman with PWS who presented with findings highly suggestive of dementia.

2. Clinical report

The 58-year-old woman had a genetically confirmed diagnosis of PWS due to a uniparental disomy of chromosome 15. She has moderate intellectual disabilities. She used to have good verbal capacities and even had writing and reading skills. Although she already had an obsession for food as a child, she had a normal weight in her youth because the food access was closely supervised. She became obese from the age of 17. At that time she had a first psychosis and after hospitalization for 2 years, because of these psychiatric problems, she went to a residential home. Severe mood fluctuations and psychotic episodes were present all her further life, for which she used several sorts of psychiatric medication: antipsychotics, antidepressants and mood stabilizing agents.

Psychotic episodes during her adult life were characterized by optic and acoustic hallucinations, delusions (related to insufficiency, religion and fear), aggression, increase of obsessive behaviour, increase of food obsession, motor agitation. She was also diagnosed with a bipolar disorder. She suffered from mood swings. On the one hand she could be good-tempered, adorable, humoristic, interested in other people. On the other hand, in bad times, she could be depressed, compelling, fierce and accusatory.

From the age of 40 physical and mental deterioration seemed to start. Her movements became slower and she had less energy during the days. At the age of 50, both of her parents and an older sister died within a couple of months. At that time her ageing process accelerated. She started dragging her left leg and walking

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more slowly. More and more she needed help in her ADL (Activities of Daily Living). Her interest in food became less obvious and she showed less compulsive behaviour. From the age of 56, she became almost completely dependent of professional support. She became urinary and fecal incontinent and lost the ability to walk. She developed contractures of her fingers. She was restless during nights and sleepy during the day. She showed periods of maladaptive behaviour like screaming, irritability and aggression.

At present (early 2009) she is wheelchair bound and sleeps frequently during the day. Her behaviour calmed down. She only uses single words when speaking. Most of the time she is unresponsive to her environment.

3. Methods and results

Diagnosis of dementia in people with intellectual disabilities is complex. Evidence of progressive deterioration in an individual's level of functioning is needed in order to diagnose dementia [1]. Thereby, other treatable explanations for changes in functioning, like sensory impairments, depression, intoxications and delirium, have to be excluded.

3.1. Medical evaluation

A thorough medical evaluation was performed in order to find possible treatable causes for her decline. Visus controls revealed a high myopia and mild cataract. Her glasses seemed to be sufficient. She is known to have mild hearing loss on both sides. Hypothyroidia, diabetes mellitus and dehydration were excluded by laboratory testing. A CT-scan of the brain revealed no abnormalities. All psychiatric medication has been phased out at present, except for a low dosage of pipamperone (Dipiperon®) a day, without restart of the psychotic episodes. Neurological and psychiatric consultations did not reveal new diagnoses to explain her decline in functioning like depression or delirium.

3.2. Decline in functioning was measured on the following scales

3.2.1. SRZ

The Social Functioning Scale for ID, (SRZ) [22] is a validated Dutch scale for the level of social functioning. The SRZ consists of 31 items, divided into four subscales: Self Help, Communication, Persistence, and Social Skills. Possible SRZ-standard scores are 3−, 3, 4, 5, 6, 7, 8, 9, 9+, indicating poor to good social functioning.

Table 1 shows gradual decline on all SRZ subscales between the ages 47 and 58 years.

3.2.2. VABS

The Vineland Adaptive Behaviour Scales (VABS) [31] was used to measure adaptive behaviour. The subscales include Communication, Daily living skills, Socialisation and Motor.

Table 1
Standard scores of the client on SZR subscales at consecutive ages.

Age at testing/SRZ-standard scores SRZ subscale	47 years	52 years	53 years	55 years	56 years	57 years	58 years
Self help	7	6	5	3−	3	3−	3
Communication	9	7	7	6	7	5	5
Persistence	6	5	4	3	3	3	3
Social skills	7	6	5	3	3	4	3
Total	8	6	5	4	4	3	3

The VABS scores (Table 2) show that the woman deteriorated substantially on Communication skills, Daily living skills, Socialisation and Motor skills between the age of 53 and 58.

3.3. Signs of dementia was rated on the following scale

3.3.1. DSDS

The Dutch revision of the Dementia Scale for Down Syndrome of Gedye [15], was used [25]. Validity and reliability of this scale are sufficient. The DSDS consists of 60 items, and is a diagnostic instrument for dementia in persons with ID. The scores indicate absence or presence of dementia, and gives qualitative indications for the four stages of dementia (early, middle, late, very late). It also focuses on differential diagnoses of dementia e.g. depression, hypothyroidism, visual and hearing impairment.

Dementia is likely if the number of present features in questions of dementia stage 1 is $\geq$8, or score on dementia stage 1 and 2 is $\geq$10. Indicative for early dementia is a score of $\geq$17 on dementia stage 1 and 2 domains. Indicative for middle stage dementia is a score of $\geq$7 on dementia stage 3 domain. Indicative for late stage dementia is a score of 3 items on dementia stage on dementia stage 4 domain.

The scores of the woman on the DSDS also indicate dementia (Table 3). In conclusion functional deterioration on all domains of the SRZ and VABS was assessed. Scores on the DSDS were indicative for the presence of dementia in the very late stage. Possible differential diagnoses were excluded.

4. Discussion

We report on a case of an older woman with PWS who presented with findings highly suggestive of dementia.

4.1. Ageing in persons with ID

Life expectancy of persons with ID has increased substantially during the last decades due to improvements in medical care and living circumstances. This results in increasing numbers of elderly adults with intellectual disabilities [27,29]. Ageing is related to age-related problems like sensory impairments, heart and vascular diseases, joint problems and dementia.

4.2. Dementia

Dementia is a clinical state characterized by loss of function in multiple cognitive domains. The most commonly used criteria for diagnoses of dementia is the DSM-IV-TR [12] and the ICD-10 [18]. Diagnostic features include: memory impairment and at least one of the following: aphasia, apraxia, agnosia, disturbances in executive functioning. In addition, the cognitive impairments must be severe enough to cause impairment in social and occupational functioning. Importantly, the deterioration must represent a decline from a previously higher level of functioning. Finally, the diagnosis of dementia should not be made if the cognitive deficits occur exclusively during the course of a delirium. There are many different types of dementia. Some of the major disorders causing

Table 2
VABS scores of the client at consecutive ages.

Age at testing/VABS-scores VABS subscale	53 years	58 years
Communication	4; 10 years	1; 9 years
Daily living skills	1; 6 years	0; 8 years
Socialisation	4; 7 years	1; 4 years
Motor	1; 2 years	0; 8 years

Table 3
Scores on DSDS of the client at age 58.

DSDS stages (number of items)	Number of positive scores
Dementia stage 1 (20 items)	12
Dementia stage 2 (20 items)	11
Dementia stage 3 (15 items)	7
Dementia stage 4 (5 items)	3
Total (60 items)	33

dementia are: degenerative diseases (e.g. Alzheimer's Disease, Pick's Disease), vascular dementia, anoxic dementia, traumatic dementia, infectious dementia (e.g. Creutzfeldt–Jakob Disease), toxic dementia.

In the general European population 6.4% of the people suffer from dementia. The prevalence of dementia increases with age (0.8% in the group age 65–69 years and 28.5% at age 90 years and older). Alzheimer's disease is the most prevalent cause of dementia [24]. Risk factors for developing dementia include age, positive family history and risk factors associated with cardiovascular diseases like hypertension, atherosclerosis, type II diabetes mellitus and smoking.

4.3. Dementia in persons with ID

In persons with ID, dementia is as prevalent as it is in the general population [19] but presentation can be very different.

Information on dementia in specific syndromes is scarce [34]. In people with Down's syndrome dementia is more prevalent and presents at a relatively young age. At obduction the neuropathological changes of Alzheimer's disease are present in almost 100% of the older (40+) persons with Down syndrome. However, only about 17% of the people with Down syndrome above the age of 45 show signs of Alzheimer dementia in daily life [8].

There are indications that dementia presentation may differ in those with and without Down Syndrome (DS) [7]. Therefore it is important to consider the population with and without DS separately. In a UK study, 26 non-DS dementia cases were reported by caregivers [33]. The most common presenting symptoms were general deterioration in functioning (50%), followed by behavioural or emotional change (15%). Deterioration in memory and other cognitive functions were less prominent in the early stages of the disorder. Other signs include symptoms of depression such as lack of energy, low mood and disturbed sleep, persecutory delusions and auditory hallucinations, or delirium; while late stage symptoms such as urinary incontinence, difficulty in walking and faecal incontinence were common [7,14].

4.4. Diagnostic evaluations

In practice, the first evidence of decline in persons with ID is usually noticed by the caregivers [2]. In general, caregivers provide most of the information for the detailed diagnostic assessment. Ideally information from multiple caregivers from a variety of situations (e.g. living, working) should be gathered for a complete overview of the person's functioning.

Diagnosis of dementia in adults with ID requires changes of baseline functioning, which exceeds that of normal ageing. Normative ageing results in certain sensory, physical and behavioural changes. To understand pathological changes it is important to know the differences between these normative changes in person with ID and changes that result from disease or other pathological processes [21]. The clinical presentation of dementia may be confused with other conditions such as visual and hearing problems, hypothyroidia, medicine intoxications, delirium, depression, normal pressure hydrocephalus and internal diseases like feeding deficiencies, diabetes mellitus and dehydration. These reasons for decline might be treatable and reversible [21]. Significant life events such as bereavement or changes in living or work circumstances may also result in cognitive or behaviour changes that could be wrongly attributed to dementia. Diagnostic evaluation should therefore include a medical, cognitive and functional assessment.

In our patient we should also distinguishing the clinical characteristics of dementia from chronic psychosis. Our patient suffered from psychiatric problems during adult age (bipolar disorder and psychosis). Symptoms of these psychiatric episodes differed from the clinical picture of decline from the age of 50. During psychoses she showed, besides the typical hallucinations and delusions, an increased interest in food and increased obsessive–compulsive behaviour. During the decline from the age of 50 her interest in food became less obvious and she showed less obsessive–compulsive behaviour. The main characteristic of this process was her functional decline in ADL and physical well-being (e.g. losing continence and ability to walk). She became more and more dependent of professional support. Besides, during recent years almost all psychiatric medication has been faded out, without a restart of psychotic symptoms like hallucinations, delusions, aggression and increase of obsessive behaviour which she showed before. The functional decline continued continuously. In our opinion this underlines the diagnosis of dementia instead of chronic psychosis.

To get insight in the possible causes of changes in behaviour, it is necessary to compare the present and previous level of functioning. A baseline screening, including cognitive, health and functional assessment, is advisable. International guidelines advice to start screening in persons with ID beginning at age 40 in individuals at increased risk for premature ageing (i.e. Down syndrome, severe/profound ID), and beginning at age 50 in others. Longitudinal follow-up of these assessments (at least yearly) are important to monitor the ageing process or the stage of dementia [21].

4.5. Ageing in Prader–Willi syndrome

The knowledge regarding PWS and age-related characteristics is mainly focused on child- and young adulthood. PWS is characterized by severe hypotonia and feeding problems in early infancy. In later childhood and adolescence this is followed by hyperphagia and, without any dietary instructions, extreme obesity [17]. In general, individuals have mild to moderate intellectual disabilities [9]. Adolescence and adulthood are dominated by health problems secondary to obesity, including diabetes mellitus, respiratory problems, obstructive sleep apnoea, hypertension and cardiovascular problems [5,6,28]. Individuals with PWS can show significant maladaptive behaviour and emotional characteristics including temper tantrums, inappropriate social behaviour, automutilation (skin picking), stubbornness, mood lability, impulsivity, depression, anxiety, obsessive–compulsive symptoms and autism spectrum disorder [6,11,16,38]. About 10% of the adult subjects develop major psychiatric problems, ranging from depression to obsessive–compulsive and psychotic episodes [3,11,32,39].

Young adults in their twenties show the highest levels of maladaptive and compulsive behaviour [13]. Subjects in their thirties however, seem to 'mellow' behaviourally and show much less destructive, food-seeking, impulsive behaviour than younger adults, and they also have higher rates of under activity, fatigue and withdrawal [10,13]. So far, not much is known about characteristics of older adults with PWS and the ageing process. Dementia in PWS has not been reported in literature.

4.6. Future recommendations

The presently reported woman illustrates a new research area in older adults with PWS. In order to get a better understanding of the ageing process, possible premature ageing and the prevalence of dementia in persons with PWS, more studies are necessary. The association between PWS and dementia could of course be coincidental. However, nowadays some persons with PWS will reach their fifties, sixties or even seventies. We hypothesize deterioration in many elderly from the age of about 40.

Yearly dementia screening in the PWS population is advisable and should start at latest from the age of 50. In the case of dementia, study of brain material is warranted to observe whether premature Alzheimer changes or indications of other dementia forms indeed occur more prevalent in people with PWS.

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