Differential diagnosis between Alzheimer's disease and hypothyroidism in adults with Down syndrome

V. P. Prasher

Lecturer in Psychiatry
The University of Birmingham,
U.K.

The differential diagnosis between Alzheimer's disease and hypothyroidism in adults with Down syndrome who begin to show clinical deterioration needs to be emphasised. This study investigated clinical features which could be used to differentiate between the two conditions. Memory loss, mood and personality change, speech and gait deterioration, and slowing down were significantly associated with dementia but not with hypothyroidism. It is recommended that specific questions should be asked to elicit the presence of these features particularly in those individuals in whom assessment of biochemical thyroid status is not possible.

Down Syndrome Research and Practice
1995, **3** (1) 15-18

Introduction

An association between Alzheimer's disease and Down syndrome (Oliver & Holland, 1986; Prasher & Krishnan, 1993) and between thyroid dysfunction and Down's syndrome (Dinani & Carpenter, 1990; Prasher, 1994) have been well established. Both Alzheimer's disease and thyroid dysfunction occur more commonly in older individuals with Down syndrome and both disorders can present with decline in cognitive skills, physical deterioration and loss of adaptive skills. Differentiation between the two disorders can, therefore, be difficult.

Although assessment for biochemical thyroid status should be undertaken in all individuals who present with clinical deterioration, performing blood tests in people with Down syndrome, especially in older individuals, can at times be difficult (Prasher, 1994). It is, therefore, important to establish whether hypothyroidism can be differentiated from changes indicative of dementia on clinical grounds alone. Although studies have reported clinical changes of Alzheimer's disease in adults with Down syndrome (Oliver and Holland, 1986), and other studies have reported thyroid dysfunction changes in people with Down syndrome (Mani, 1988, Prasher, 1995), no study to date has investigated the clinical differentiation between Alzheimer's disease and hypothyroidism in people with Down syndrome. This study reports findings for 74 subjects.

Methodology

As part of the West Midlands Ageing Study individuals with Down syndrome were being investigated for thyroid dysfunction and changes of Alzheimer's disease. This study had a large sample size, a wide age range (16-75 years) and institutionalised and community residents. The sample was relatively representative of adults with Down syndrome in the region. All individuals were, where possible, assessed cytogenetically to determine the presence of Down syndrome.

For the study reported here a number of individuals with biochemical hypothyroidism and mild or moderate Alzheimer's disease according to DCR-10 criteria (WHO,1993) were identified. To exclude effects of institutionalisation only community residents were investigated. Persons with no evidence of hypothyroidism, dementia or any other significant psychiatric disorder were used as controls.

Subjects in all three groups were assessed for a number of symptoms and signs used to diagnose clinical hypothyroidism (Mani, 1988) and symptoms and signs used to diagnose dementia (Evenhuis, 1990). Primary carers were interviewed and individuals examined to elicit presence of such symptoms and signs.

Biochemical hypothyroidism was diagnosed when free thyroxine values were below 12 pmol/l (normal range 12-26 pmol/l) and thyroid stimulating hormone levels were over 4.0 microIU/ml (normal range 0.3-4.0 microIU/ml). For the dementia group, only individuals with mild or moderate dementia according to ICD-10 criteria (WHO, 1992) were used as a comparative group. People with severe Alzheimer's disease were not assessed as differentiation of severe dementia from hypothyroidism should not be difficult.

Table 1. Demographic details of hypothyroid, dementia and control groups.

Feature		Dementia Group (N=17)	Hypothyroid Group (N=12)	Control Group (N=44)	Findings
Age	Mean (SD)	50.9 Years (6.9)	42.9 Years (13.2)	38.9 Years (9.1)	Dementia Group sig older (ANOVA; p<0.5)
	Range	39-72 Years	25-62 Years	20-62 Years	
Sex	Male	47%	42%	57%	No sig difference at 5% level
	Female	53%	58%	43%	
Residence	Family Home	47%	67%	52%	No sig difference at 5% level
	Community Home	53%	33%	48%	
Severity of Learning Disability	Mild	18%	25%	23%	No sig difference at 5% level
	Moderate	76%	67%	73%	
	Severe	6%	8%	2%	
	Unknown			2%	
History of Hypothyroidism		4	1	4	

sig = significant.
SD = standard deviation.

Table 2. Clinical findings for hypothyroid, dementia and control groups.

Feature	Dementia Group % (N=17)	Hypothyroid Group % (N=12)	Control Group% (N=44)	Findings for significance between hypothyroid and dementia groups*
Memory Loss	100	17	2	Z=4.6 p<0.01
Personality Change	53	17	2	Z=2.0 p<0.5
Mood Change	76	25	2	Z=2.7 p<0.01
Behavioural Deterioration	29	8	4	Z=1.4 NS
Slowing Down	88	33	11	Z=3.0 p<0.01
Speech Deterioration	71	17	2	Z=2.8 p<0.01
Gait Deterioration	76	25	0	Z=2.7 p<0.01
Onset Urinary Incontinence	35	17	0	Z=1.1 NS
Onset Seizures	30	17	0	Z=0.1 NS
Increased Muscle Tone	24	17	0	Z=0.4 NS
Hair Loss	24	17	18	Z=0.4 NS
Dry Skin	47	58	34	Z=0.7 NS
Reduced Appetite	24	0	0	Z=1.7 NS
Disturbed Sleep Pattern	30	8	2	Z=1.4 NS
Weight Change	2	8	2	Z=0.3 NS

* = Non-parametric analysis. Mann-Whitney test.
NS = Not significant.

Table 3. Adaptive behaviour scale scores for hypothyroidism, dementia and control groups.

Domain		Dementia Group Mean (SD)	Hypothyroid Group Mean (SD)	Control Group Mean (SD)
Part I	Independant Functioning	53.24 (19.53)	54.25 (21.61)	74.77 (12.48)
	Physical Development	16.24 (5.04)	15.92 (5.48)	20.25 (2.74)
	Economic Activity	1.35 (2.00)	1.83 (2.41)	3.80 (3.17)
	Language Development	12.47 (5.81)	14.50 (8.17)	18.98 (6.81)
	Numbers and Time	2.47 (2.60)	3.08 (3.82)	4.77 (3.24)
	Domestic Activity	4.24 (4.51)	5.00 (5.34)	9.18 (4.18)
	Vocational Activity	1.29 (2.89)	1.50 (3.53)	4.27 (4.76)
	Self Direction	8.53 (3.73)	9.08 (3.99)	13.50 (4.31)
	Responsibility	1.53 (1.55)	2.17 (1.85)	3.34 (1.83)
	Socialization	11.82 (4.81)	14.67 (6.85)	17.70 (4.22)
Part I Overall Score		113.18 (41.42)	122.00 (52.41)	170.37 (37.93)
Part II	Violent and Destructive Behaviour	5.53 (4.12)	2.17 (2.48)	0.61 (1.30)
	Antisocial Behaviour	3.71 (9.90)	2.42 (2.71)	0.82 (1.45)
	Rebellious Behaviour	5.35 (8.94)	0.67 (1.23)	0.57 (1.15)
	Untrustworthy behaviour	1.35 (3.84)	1.75 (2.83)	0.50 (1.28)
	Withdrawal	5.65 (6.17)	2.58 (4.21)	1.64 (3.21)
	Stereotyped Behaviour	0.82 (1.42)	0.58 (1.16)	0.30 (0.76)
	Inappropriate Interpersonal Manners	0.82 (2.43)	0.42 (0.79)	0.27 (0.66)
	Unacceptable Vocal Habits	1.35 (2.37)	0.67 (1.61)	0.27 (0.62)
	Unacceptable or Eccentric Habits	2.47 (4.11)	0.83 (1.85)	1.23 (2.33)
	Self-abusive Habits	0.35 (0.70)	0.25 (0.62)	0.23 (0.64)
	Hyperactive Tendencies	0.29 (0.85)	0.00 (0.00)	0.00 (0.00)
	Sexually Aberrant Behaviour	1.00 (2.67)	0.25 (0.62)	0.27 (0.90)
	Psychological Disturbances	4.29 (9.27)	1.92 (0.62)	1.30 (2.36)
Part II Overall Score		30.00 (44.90)	14.50 (10.77)	8.00 (9.86)

No statistically significant difference for domain and total scores between hypothyroid and dementia groups.

Further to the checklist of symptoms, comparison of adaptive function was also undertaken. The Adaptive Behaviour Scale (ABS) (Nihira, 1974) was used. This is a widely used and well established instrument for assessment of adaptive function. Domain and total scores for Part I and Part II were used. Part I assessed independent functioning and Part II maladaptive behaviours. Domain 14 of Part I 'use of medication' was excluded. Comparative analysis for the three groups was undertaken.

Results

Seventy-three individuals were assessed. Demographic details are given in Table 1 (page 16). The dementia group was found to be significantly older. The mean thyroxine level for the hypothyroid group was 8.58 (SD 2.74) with a mean thyroid stimulating hormone value of 28.58 (SD 33.67).

Findings for frequency of symptoms and signs are given in Table 2 (page 16). Several features were found to occur in both dementia and hypothyroidism groups. However, memory loss, emotional change, slowing down, personality change, speech and gait deterioration were found to be statistically significantly associated with dementia but not with hypothyroidism. Increased dry skin and weight change were more frequent in the hypothyroid group but not at the 5% significant level.

Both the dementia and hypothyroid groups scored significantly lower on Part I of the ABS than the control group (Table 3, page 17). The dementia group scored lower than the hypothyroid group for virtually all domains and total Part I scores but this was not statistically significant at the 5% level. Both groups scored higher on the Part II (maladaptive behaviours) than the control group, with the dementia group scoring the highest. No particular ABS domain could be used to differentiate dementia from hypothyroidism.

Discussion

This study demonstrates that there are clinical differences in the presentation of mild/moderate Alzheimer's disease and hypothyroidism in adults with Down syndrome. Deterioration in memory, changes in mood and personality, deterioration in speech and gait and bradykinesia are strong indicators of Alzheimer's disease rather than hypothyroidism. Ultimately, biochemical analysis for thyroid status would clarify the position, although such tests would be better supported and be more cost effective if there was greater suspicion on clinical grounds.

Glossary

Bradykinesia: Difficulty in initiating and executing movements.
Cytogenerically: Related to genetic structure of the cell.
Hypothyroidism: Subnormal activity of the thyroid gland.
Thyroxine: Thyroid hormone.

References

Dinani,S. & Carpenter,S. (1990). Down's syndrome and thyroid disorder. *Journal of Mental Deficiency Research,* 34, 187-193.
Evenhuis,H.M. (1990). The natural history of dementia in Down's syndrome. *Archives of Neurology,* 47, 263-267.
Mani,C. (1988). Hypothyroidism in Down's syndrome. *British Journal of Psychiatry,* 153, 102-104.
Nihira,K., Foster,R, Shellhaas,M. and Leyland,H. (1974). *AAMD Adaptive Behaviour Scale,* 1974 Revision, Washington, D.C.: American Association on Mental Deficiency.
Oliver,C. and Holland,A.J. (1986). Down's syndrome and Alzheimer's disease: a review. *Psychological Medicine* 16, 307-322.
Prasher,V.P. and Krishnan,V.H.R. (1993). Age of onset and duration of dementia in people with Down syndrome. A study of 98 reported cases. *International Journal of Geriatric Psychiatry,* 8, 915-922.
Prasher,V.P. (1994). Prevalence of thyroid dysfunction and autoimmunity in adults with Down syndrome. *Down's Syndrome Research and Practice,* 2, 67-70.
Prasher,V.P (1995). Reliability of diagnosing clinical hypothyroidism in adults with Down syndrome. *Australia and New Zealand Journal of Developmental Disabilities* (In Press).
World Health Organisation (1992). *The ICD-10 Classification of Mental and Behavioural Disorders. Clinical Descriptions and Diagnostic Guidelines*. Geneva: WHO.
World Health Organisation (1993). *The ICD-10 Classification of Mental and Behavioural Disorders. Diagnostic criteria for research.* Geneva: WHO.

Address for correspondence:

Dr. V.P. Prasher, MMedSc, MRCPsych, MD
Department of Psychiatry
The University of Birmingham
Queen Elizabeth Psychiatric Hospital
Mindelsohn Way
Birmingham, B15 2QZ
U.K.