Short report

Familial cerebellar ataxia and diabetes insipidus

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SUMMARY Two sisters are reported who both developed partial cranial diabetes insipidus in their 4th decade, followed by progressive cerebellar ataxia. This appears to be the first report of cerebellar ataxia and diabetes insipidus occurring together as a genetic entity.

Numerous inherited disorders have been identified in which cerebellar ataxia occurs either alone or in association with other clinical abnormalities which may extend beyond the central nervous system.¹ We report sisters, both of whom have shown evidence of late onset cerebellar ataxia and mild cranial diabetes insipidus.

Case reports

The sisters were the second and third children of four siblings, born to healthy unrelated parents. Their father died aged 47 years of carcinoma of the bronchus; their mother died aged 90 years of "old age". Neither parent, nor anyone else in the extended family had a history of cerebellar or pituitary disease.

Case 1: The elder sister first presented at age 66 years with a 2 year history of clumsiness, deterioration in handwriting and difficulty in walking. Prior to this she had been treated for 5 years with pitressin injections during her fourth decade for mild diabetes insipidus. Subsequently she showed slowly progressive deterioration of neurological status with normal intellectual skills. Recent examination revealed mild dysarthria, ataxic limb movements with an intention tremor, unsteady gait and brisk lower limb reflexes. The plantar responses were extensor. Romberg's test was negative and sensation was normal.

Investigations which were normal included routine haematological and biochemical screens, thyroid function tests, cerebrospinal fluid examination, visual evoked responses and lateral skull radiography. Cranial CT showed marked cerebellar atrophy with mild generalised cerebral atrophy. The water deprivation test results are indicated in the table. This showed a high normal initial serum osmolality of 290

mosm/kg (normal 285 ± 4.4 mosm/kg) with inappropriately low urine osmolality and very poor urinary concentration after 6 hours of water deprivation. The marked response to desmopressin indicated that the diabetes insipidus was cranial rather than renal in origin.

Case 2: The younger sister presented at age 46 years with a 2 month history of polydipsia and polyuria. A water deprivation test showed a urine specific gravity of only 1009 after 7 hours deprivation, consistent with diabetes insipidus. At age 61 years her pitressin was withdrawn and she lost 7 lbs in weight within one week. Her serum and urine osmolalities were 297 mosm/kg and 126 mosm/kg respectively. Neurological symptoms started at age 56 years and consisted of slurred speech and impaired co-ordination. Examination showed limb ataxia, nystagmus and dysarthria. She deteriorated slowly over the next 5 years with complete loss of mobility and died at age 61 years. Postmortem examination was not undertaken.

Discussion

The late onset cerebellar ataxia was much more slowly progressive in Case 1. Comparable intrafamilial variation in rate of progression has been previously noted.² In addition both sisters presented in middle age with cranial diabetes insipidus, again less severe in Case 1.

Table Results of water deprivation test in Case 1

Time	Urine Osmolality (mosm/kg)	Serum Osmolality (mosm/kg)	Weight (kg)
10.00	215	290	41.0
11.00	269	289	
12.00	294	295	
13.00	291	292	
14.00	341	289	39.25
15.00	422	291	
16.00	433	287	
17.00	426	289	

Water deprivation from 07.00 to 13.00.
Desmopressin 2 µgm IM given at 13.00.

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Several families showing autosomal recessive inheritance of cerebellar ataxia and hypogonadotrophic hypogonadism have been reported.^{3,4} Also ataxia has been described in the autosomal recessive DIDMOAD or Wolfram syndrome,⁵ but neither of our patients exhibited diabetes mellitus, optic atrophy or neurosensory deafness. We are unaware of any description of cerebellar ataxia and diabetes insipidus, cranial or nephrogenic, occurring together as a genetic entity.

Most forms of familial late onset cerebellar ataxia show autosomal dominant inheritance,¹ as does familial cranial diabetes insipidus.⁶ This family's pedigree is consistent with either autosomal recessive or dominant inheritance, since it is possible that the father might have manifested signs or symptoms had he not died at the young age of 47 years. An alternative explanation of two inherited disorders occurring in both sisters as a chance occurrence, seems very improbable.

References

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