

# Two sisters with mental retardation, cataract, ataxia, progressive hearing loss, and polyneuropathy

J H Begeer, F A Scholte, A J van Essen

## Abstract

**Two sisters are described with a disorder characterised by mental retardation, congenital cataract, progressive spinocerebellar ataxia, sensorineural deafness, and signs of peripheral neuropathy. Progressive hearing loss, ataxia, and polyneuropathy became evident in the third decade. The differential diagnosis of this syndrome is discussed including the syndromes described by Berman *et al* and Koletzko *et al*.**

Ataxic syndromes combined with mental retardation have often been described<sup>1,2</sup> and sometimes these patients have other abnormal features.<sup>1-10</sup> Besides mental retardation and ataxia, our patients, two sisters, had congenital cataract, progressive hearing loss, and progressive polyneuropathy. We could find no similar combination of symptoms in published reports.

## Case reports

### CASE 1

This 59 year old woman has had mild mental retardation from birth. She has a congenital cataract for which she has been operated upon three times. Unfortunately, more detailed information about the pregnancy, neonatal period, and early development is not available. She has small stature (1.55 m, 10th

centile), her weight is 63.5 kg (above the 90th centile), and her head circumference is 53 cm (15th centile). In her third decade she developed a progressive sensorineural deafness, together with ataxia. Recent neurological evaluation showed slight hypertonia of the legs. The tendon reflexes were absent and there were flexor plantar responses in both feet. Truncal ataxia is present, but ataxic symptoms of the extremities are less pronounced. No sensory disturbance could be detected owing to lack of cooperation by the patient. However, a fracture of the ankle in 1985 and a burn on the right foot in 1990, which were not noticed by the patient herself, are evident signs of disturbed sensation. There is complete bilateral perceptive deafness and no cardiac pathology. Abnormalities of the irides with eccentric and asymmetrical pupils are probably the result of the cataract operations in the first year of life. There is a slight corneal macula on both sides. Both fundi are normal.

The following laboratory investigations were all normal: blood vitamin B1 and B6, blood and CSF protein electrophoresis, CSF protein and cell count, blood, urine, and CSF lactate and pyruvate, blood phytanic acid, blood and urine organic acids and amino acids, ceruloplasmin, lysosomal enzymes, and routine blood chemistry. Cytogenetic investigation showed a normal female karyotype (GTG banding at approximately the 450 band level). Reduced motor conduction velocities in the peroneal nerve and the posterior tibial nerve were found on both sides. The right and left median and ulnar nerves were normal. Sensory conduction velocities (retrograde) of the median and radial nerves could not be measured. There was no response to stimulation of the wrist and thumb with ring electrodes. The disorder is now more pronounced than in 1980. Biopsy of the sural nerve showed serious axonal atrophy. CT of the brain did not indicate any abnormalities.

### CASE 2

This woman is the 50 year old sister of case 1 and was also born with a congenital cataract for which she has been operated upon. She is mildly mentally retarded. Because of progressive hearing loss she has used a hearing aid since she was 40 years old. At

---

Department of Child Neurology, University Hospital, PO Box 30001, 9700 RB Groningen, The Netherlands.

J H Begeer

Mariëncamp, Institute for Mentally Retarded People, PO Box 8, 9450 AA Rolde, The Netherlands.  
F A Scholte

Department of Medical Genetics, University of Groningen, Antonius Deusinglaan 4, 9713 AW Groningen, The Netherlands.

A J van Essen

Correspondence to Dr Scholte.

---

Received for publication 26 November 1990.  
Revised version accepted for publication 3 April 1991.

## Differential diagnosis of syndromes with mental retardation, cataract, ataxia, progressive hearing loss, and polyneuropathy.

	Marinesco-Sjögren <sup>5,6</sup>	Jeune <i>et al</i> <sup>7</sup>	Lichtenstein and Knorr <sup>8</sup>	Flynn and Aird <sup>9</sup>	Koletzko <i>et al</i> <sup>4</sup>	Berman <i>et al</i> <sup>3</sup>	Strömrgren <i>et al</i> <sup>10</sup>	Our study
Mental retardation	+	+	-	-	+	+	Dementia	+
Cataract	+	-	-	-	+	-	+	+
								(Present at birth)
Ataxia	+	+	+	+	+	+	+	+
Progressive hearing loss	-	+	+	+	+	+	+	+
Polyneuropathy	-	+	+	+	+	+	-	+
Growth deficiency	+	+	-	-	-	±	?	±
Inheritance	AR	AR	AR	AD	AR	AR	AD	AR

present there is a loss of 60 dB below 1000 Hz and of 100 dB above 1000 Hz. She has increasing difficulty in walking owing to progressive ataxia. Her height is 1.52 m (3rd centile), her weight is 50 kg (60th centile), and her head circumference is 53 cm (15th centile).

Her visual acuity is severely impaired with an amblyopic right eye and a vision of 0,2 with correction of S + 16 in the left eye. There is nystagmus in both eyes. The fundi are normal. The gait is wide based owing to truncal ataxia, tandem walk is disturbed, and the Romberg sign is positive. Dysdiadochokinesis is present with otherwise no intention tremor on purposeful movement. The tendon reflexes are absent and there are plantar flexor responses in both feet. Sensory disturbances are present in the distal parts of the legs. Electromyographic investigation showed reduced motor conduction velocities of the right peroneal and median nerves. Normal values were found on the left side. Sensory nerve conduction velocities were not determined.

The ataxic symptoms in both sisters are mainly caused by impairment of the proprioceptive system, although a cerebellar component is also contributory.

### Family history

Our patients are the second and the youngest of six children of non-consanguineous parents. The third child also had a congenital cataract. She died at 4 years of pneumonia. The parents and the other children are in good health. The paternal grandfather of our patients and his mother both have a brother with children with Sjögren-Larsson syndrome. Another brother of the paternal grandfather had a child with Duchenne muscular dystrophy.

### Discussion

The combination of symptoms in our patients has not been previously reported. The syndromes with the most similar features to our patients are shown in the table. The patients of Berman *et al*<sup>3</sup> (three male sibs) and of Koletzko *et al*<sup>4</sup> (three daughters of consanguineous parents) had clinical features very much the same as our patients, only without cataracts. However, the progressive hearing disorder and the ataxia started in infancy in the patients of both Berman *et al*<sup>3</sup> and Koletzko *et al*<sup>4</sup>. We feel that the syndrome in our patients does not really match one of these syndromes and, especially, the congenital cataract is only seen in our patients. Inheritance is presumably autosomal recessive.

- Harding AE. *The hereditary ataxias and related disorders*. Edinburgh: Churchill Livingstone, 1984.
- Baraitser M. *The genetics of neurological disorders*. Oxford: Oxford University Press, 1982.
- Berman W, Haslan RHA, Koningsmark BW, Capute AJ, Migeon CJ. A new familial syndrome with ataxia, hearing loss, and mental retardation. *Arch Neurol* 1973;29:258-61.
- Koletzko S, Koletzko B, Lamprecht A, Lenard HG. Ataxia-deafness-retardation syndrome in three sisters. *Neuropediatrics* 1987;18:18-21.
- Marinesco G, Draganesco S, Vasiliu D. Nouvelle maladie familiale caractérisée par une cataracte congénitale et un arrêt du développement somato-neuro-psychique. *L'Encéphale* 1931;26:97-110.
- Sjögren T. Hereditary congenital spinocerebellar ataxia accompanied by congenital cataract and oligophrenia. *Confin Neurol* 1950;10:293-308.
- Jeune M, Tommassi M, Freycon F, Nivelon JL. Syndrome familial associant ataxie, surdité et oligophrénie. Sclérose myocardique d'évolution fatale chez l'un des enfants. *Soc Fr Pédiatr* 1963;18:984-7.
- Lichtenstein H, Knorr A. Über einige Fälle von vortschreitender Schwerhörigkeit bei hereditärer Ataxie. *Deutsche Z Nervenheilk* 1930;114:1-28.
- Flynn P, Aird RB. A neuroectodermal syndrome of dominant inheritance. *J Neurol Sci* 1965;2:161-82.
- Strömrgren E, Dalby MA, Ranheim B. Cataract, deafness, cerebellar ataxia, psychosis and dementia - a new syndrome. *Acta Neurol Scand Suppl* 1970;43:261-2.