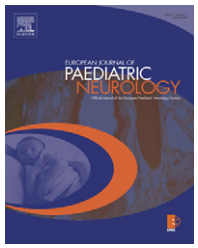
EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY 12 (2008) 97–101

Official Journal of the European Paediatric Neurology Society



Original article

Infantile onset progressive cerebellar atrophy and anterior horn cell degeneration—A late onset variant of PCH-1?

Dorit Lev[a,b], *Marina Michelson-Kerman*[a,b], *Chana Vinkler*[a,b], *Lubov Blumkin*[a,c], *Stavit A. Shalev*[d], *Tally Lerman-Sagie*[a,c,*]

[a]*Metabolic Neurogenetic Service, Wolfson Medical Center, Holon, affiliated to Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel*
[b]*Institute of Medical Genetics, Wolfson Medical Center, Holon, affiliated to Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel*
[c]*Pediatric Neurology Unit, Wolfson Medical Center, Holon, affiliated to Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel*
[d]*Genetic Institute, Ha'Emek Medical Center, Afula, Israel*

ARTICLE INFO

Article history:
Received 11 October 2006
Received in revised form
3 June 2007
Accepted 22 June 2007

Keywords:
Pontocerebellar hypoplasia
Cerebellar atrophy
Mental retardation
Anterior horn cell degeneration
Spinal muscular atrophy

ABSTRACT

Despite major recent advances in our understanding of developmental cerebellar disorders, classification and delineation of these disorders remains difficult. The term pontocerebellar hypoplasia is used when there is a structural defect, originating in utero of both pons and cerebellar hemispheres. The term olivopontocerebellar atrophy is used when the disorder starts later in life and the process is a primary degeneration of cerebellar neurons.

Pontocerebellar hypoplasia type 1 is associated with spinal anterior horn cell degeneration, congenital contractures, microcephaly, polyhydramnion and respiratory insufficiency leading to early death. However, anterior horn cell degeneration has also been described in cases with later onset pontocerebellar atrophy and recently the spectrum has even been further extended to include the association of anterior horn cell degeneration and cerebellar atrophy without pontine involvement.

We describe two siblings from a consanguineous Moslem Arabic family who presented with progressive degeneration of both the cerebellum and the anterior horn cells. The patients presented after 1 year of age with a slow neurodegenerative course that included both cognitive and motor functions. There is considerable phenotypic variability; the sister shows a much milder course. Both children are still alive at 6 and 9 years. The sister could still crawl and speak two word sentences at the age of 3 years while the brother was bedridden and only uttered guttural sounds at the same age.

Our cases further extend the phenotype of the cerebellar syndromes with anterior horn cell involvement to include a childhood onset and protracted course and further prove that this neurodegenerative disorder may start in utero or later in life.

*Corresponding author. Pediatric Neurology Unit, Wolfson Medical Center, Holon 58100, Israel. Tel.: +972 35028458; fax: +972 35028141.
E-mail address: asagie@post.tau.ac.il (T. Lerman-Sagie).
1090-3798/$ - see front matter © 2007 European Paediatric Neurology Society. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejpn.2007.06.005

1. Introduction

The classification schemes of congenital disorders of the cerebellum have limitations.[1–3] The classifications are either based on neuroradiological findings[1,4] or on the embryological derivation of the involved structures.[2]

In a recent article, Sztriha and Johansen challenged the previous classifications by demonstrating four groups of hindbrain malformations in 25 patients from a cohort of children with a high parental consanguinity rate. This classification system has already enabled successful genetic linkage studies.[5]

Among the four depicted groups, one group consisted of 5 patients who had pontocerebellar or cerebellar hypoplasia with anterior horn cell involvement. One of the patients had pontocerebellar hypoplasia with anterior horn cell disease consistent with Barth's definition of pontocerebellar hypoplasia type 1,[6] while four patients only showed cerebellar hypoplasia with anterior horn cell involvement. The onset of the clinical manifestations was somewhat later and the clinical course longer in the patients who had cerebellar hypoplasia without visible involvement of the brainstem on MRI.[5] Rudnik-Schoneborn et al. described the clinical and neuroradiological findings in nine patients out of six siblingships with evidence of cerebellar defects and early onset spinal muscular atrophy (SMA); they called their paper: extended phenotype of pontocerebellar hypoplasia with infantile SMA, but the MRI's of most of the patient's that are shown demonstrate cerebellar atrophy and not pontocerebellar hypoplasia. Rudnik-Schoneborn et al.,[6] and Sztriha and Johansen[5] demonstrate the spectrum of clinical variability and thus the overlap between the late onset syndrome of olivopontocerebellar atrophy (OPCA) and pontocerebellar hypoplasia.

We describe late onset (after the first year of life) progressive cerebellar atrophy and anterior horn cell degeneration without pontine involvement in two siblings of Moslem Arabic consanguineous origin. The brother's condition deteriorated rapidly losing most acquired milestones after 1 year of age but he is still alive at the age of 9 years while the sister's course is slower and she was still able to crawl and speak in two word sentences at the age of 3 years. Our family further extends the phenotype, demonstrating phenotypic variability in the same family and prolonged survival. It also proves that when the cerebellar atrophy starts postnatally there is preservation of the pons.

2. Case histories

2.1. *Patient 1*

The first child, a 9-year-old boy, was the product of a normal pregnancy and delivery. The parents are healthy first-degree double cousins, from Moslem Arabic origin. Birth weight was 3.5 kg and head circumference was normal. He developed normally until the age of 1 year: reached out for toys at 4 months, sat at 7 months and crawled at 9 months. At that age the parents noticed a regression in his motor and cognitive development. He did not start walking; he could no longer sit without support and became unstable. He did not develop language. He was referred for evaluation at the local child development center, which included normal urine organic acids and normal serum amino acids levels. Thyroid function tests, blood lactate, and karyotype were normal. EEG and brain stem auditory evoked responses were normal. He had normal repeated ophthalmoscopic examinations with normal fundi. Nerve conduction and electromyography EMG was normal. Brain MRI showed reduced size of the vermis and cerebellar hemispheres, normal brainstem and an enlarged fourth ventricle and cisterna magna. The ventricular system, myelination and gray matter structures; basal ganglia and thalamus were normal (Fig. 1).

Over the following years he did not make any significant developmental progress and his condition deteriorated slowly.

The patient was first seen at the neurogenetic clinic at the age of 5 years. He lay almost motionless in a supine, frog position. He could sit with support and eat with a spoon. He smiled but made poor eye contact. Horizontal nystagmus was prominent. He was mildly dysmorphic with hypertelorism, long eyelashes, hypertrichosis and prominent ears. Head circumference was 52 cm (50th percentile). Moderate kyphosis was noted. He recognized his family members and understood simple commands. There was no speech and he communicated by making guttural sounds. Neurological examination demonstrated axial hypotonia but increased appendicular tone with brisk tendon reflexes, clonus and positive Babinski sign. He had no tongue fasciculations nor tremor and the leg muscles were atrophic. There was no withdrawal to painful stimuli. He had arm dysmetria with athetoid movements. An examination at the age of 7 years revealed progressive deterioration; he could no longer sit with support, he still recognized his family but he could not communicate.

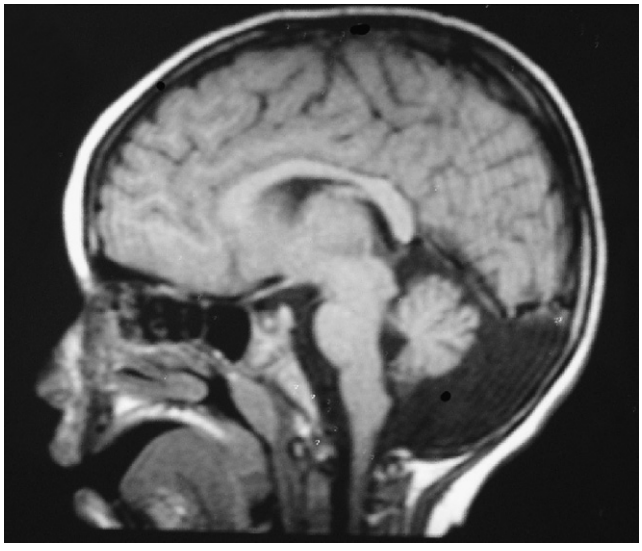


Fig. 1 – Brain MRI of patient 1, at the age of 2 years: T1 midsagittal image demonstrates enlarged cisterna magna with atrophic vermis. The pons is preserved.