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Meeting on Ataxia

Friedreich's ataxia : long-term therapy with idebenone. G. M. Buyse[1], L. Mertens[2], J. Ganame[3], W. Goossens[4], N. Goemans[1] (Departments of [1]Pediatric Neurology, [2]Pediatric Cardiology, [3]Cardiology, and [4]Laboratory Medicine, University Hospitals, Leuven, Belgium).

Friedreich's ataxia (FA) is a progressive neurodegenerative disorder associated with hypertrophic cardiomyopathy. Despite causative gene and protein identification, there is no curative treatment available for this disease that is associated with significant morbidity and early mortality. Frataxin deficiency causes iron-induced oxidative stress, with secondary deficiency of mitochondrial Fe-S cluster-containing enzymes and respiratory chain dysfunction.
Based on pathophysiology, idebenone (a potent free-radical scavenger) had been suggested as a therapy, and reduction of cardiac hypertrophy after 4-9 months of idebenone therapy in 3 patients with FA was reported in 1999. We have started treating our FA patients with idebenone in 2000. We decided to introduce novel cardiac imaging techniques (strain/strain rate imaging) as well as the use of an ataxia rating scale (Cooperative Ataxia Group Rating Scale) in the assessment protocol. In addition, we have been measuring erythrocyte protoporphyrin IX levels as a potential (therapeutic) marker in this disease. Our data showed for the first time that the structural improvements (reduction of cardiac hypertrophy) are preceded by an improvement of myocardial function. Interestingly, strain/strain rate imaging allowed early detection of response to antioxidant treatment and early discrimination of responders versus non-responders. In contrast, 1 year idebenone therapy did not prevent progression of ataxia in FA. Finally, although protoporphyrin IX levels were elevated at baseline and decreased with therapy, changes were not uniform and did not well correlate with the cardiac effect of idebenone. Our experience with idebenone in FA is now extended to long-term (3 years) treatment.

POLG mutations in neurodegenerative disorders with ataxia but no muscle involvement. G. Van Goethem[1,2,4], A. Löfgren[2,4], J. J. Martin[1,3,4], R. Mercelis[1], P. De Jonghe [1,2,4], B. Udd[5], C. Van Broeckhoven[2,4] ([1]Division of Neurology and the Neuromuscular Reference Center, University Hospital Antwerpen (UZA) ; [2]Department of Molecular Genetics, Flanders Interuniversity Institute for Biotechnology (VIB8) ; [3]Department of Neuropathology and [4]Born-Bunge Foundation (BBS), University of Antwerp (UA), Belgium ; [5]Department of Neurology, Vaasa Central Hospital, Vaasa and Tampere University Hospital, Tampere, Finland).

Abstract : Mutations in the polymerase gamma gene (POLG) are a frequent cause of autosomal dominant and autosomal recessive progressive external ophthalmoplegia (PEO), which is characterized by multiple deletions of mitochondrial DNA (mtDNA) in muscle. In several familial and isolated cases, PEO was accompanied by associated features including sensory ataxia due to axonal sensory neuropathy. We now report eight patients from five unrelated families with recessive mutations in POLG. All patients presented with juvenile or adult onset sensory ataxia, accompanied by associated CNS features. The latter included thalamic and cerebellar white matter lesions on MRI, myoclonus, epilepsy, cognitive decline, nystagmus and dysarthria. Two patients had not contracted PEO when they died in the fourth decade. Our data expand the clinical spectrum of mutations in POLG. All POLG mutations were recessive and occurred in homozygous state. In muscle, typical findings such as ragged red fibers and Southern blot mtDNA abnormalities were absent. However, a more sensitive PCR assay demonstrated multiple deletions of mtDNA in muscle.

Order where disorder is required : a common pathway leading to ataxia ? L. Servais[1,2], B. Dan[2] and G. Cheron[1] ([1]Unité d'électrophysiologie, Université de Mons Hainaut, Belgium ; [2]Service de neurologie pédiatrique, Hôpital Universitaire des Enfants Reine Fabiola, Belgium).

Introduction : Cerebellar ataxia is a common manifestation of various aetiology. In many cases, the link between the primary insult or gene defect and the cerebellar symptoms remains unknown. Insights into the pathophysiological pathways leading to ataxia may be gained by studying Purkinje cell firing behaviour, as these cells constitute the only output of the cerebellar cortex, integrating the different cerebellar inputs. This is reflected in a distinctive pattern of irregular firing.
Method : We studied the spontaneous firing behaviour of Purkinje cells recorded in different models of ataxic mice, such as mice deficient in calcium binding proteins (calretinin, calbindin and parvalbumin deficient mice), a murine model of Angelman syndrome (with a maternally-inherited Ube3a deficiency) and mice acutely intoxicated by pentobarbitone and ketamine.
Results : The only common distinctive point in the firing behaviour of Purkinje cells in these different models contrasting with control mice was the emergence of abnormal stable rhythmicity in spike firing. Rhythm index of spike firing significantly increased in every model, whether the spike firing rate increased (mutant mice) or decreased (intoxicated mice). This feature considerably reduced the possibility for Purkinje cells to modulate their spike firing according to cerebellar inputs.
Discussion : Based on these findings and to previous reports of Purkinje cells rhythmic firing in dystonic rats and in acutely ethanol or phenytoine-intoxicated mice, we propose a comprehensive model resulting in constraining Purkinje cells in highly rhythmic firing rather than their physiological irregular firing through increased parallel fibre entry, membrane hyperpolarisation or modification of dynamics in calcium change.

Episodic Ataxia type 2. M. Boel (Revalidatie- en Epilepsiecentrum, Pulderbos, and University Hospitals, Leuven, Belgium).

Abstract : Three families with episodic ataxia type 2 are reported. The heterogeneity of the phenotype and the need of an individual approach for treatment are illustrated by the clinical history of four patients.
Introduction : Episodic ataxia type 2 has an autosomal dominant mode of inheritance. The disease is caused by mutations in the calcium channel gene CACNL1A, though it is not enough to screen some hot spots in the gene (Ophoff 1996, Jen 2004). Typical patients manifest periodic ataxia with dysarthria, vertigo, nystagmus and nausea. The first episodes are usually noted during the first and the second decade of life, they are mostly provoked by emotional stress. Acetazolamide abolishes all attacks in most of the typical patients (Griggs 1978). The clinical spectrum is broader then reported earlier. Some patients have residual symptoms, others overlap with SCA6 ; some families have many epileptic patients others have more migraine symptoms.
The first family with EA2 described here seemed to be a very benign form, in the second family the propositus did not respond to acetazolamide completely and in the third family two female patients illustrate the overlap with epileptic disorders and the link with possible more progressive subtypes of EA2 or SCA6.

Unusual association of Ponto-Cerebellar Hypoplasia and periventricular heteropias : report of two cases. M.-C. Nassogne[1], Ch. Saint-Martin[2], L.Van Maldergem[3], F. Christiaens[1] ([1]Service de Neurologie Pédiatrique, [2]Service de Radiologie Pédiatrique, Cliniques universitaires Saint-Luc, Bruxelles, Belgium, [3]Institut de Pathologie et de Génétique, Loverval, Belgium ; E-mail : marie-cecile.nassogne@nepe.ucl.ac.be).

Ponto-cerebellar hypoplasia are rare conditions including several subtypes : PCH1 with spinal muscular atrophy, PCH2 with dyskinesia, PCH 3 without dyskinesia and other syndromes associated with metabolic disorders like congenital defects of glycosylation (Parini and Dobyns, 2003). We report two children with ponto-cerebellar hypoplasia associated with periventricular heterotopias. The first child was addressed at the age of 2 years for unstable walking. This female patient was the first child of healthy and unrelated Belgian parents. She was born at 39 weeks after normal pregnancy. She walked at 18 months. General examination was normal, except for some dysmorphic signs. Head circumference was at percentile 50. Neurological evaluation showed ataxia and tremor. Brain MRI showed a severe ponto-cerebellar hypoplasia with a small left cerebellum hemisphere. At the supratentorial level, periventricular heterotopias around the occipital horns were visualised. Nerve conduction velocities and electromyography were normal. EEG was normal. The second girl was referred for motor problem at the age of two years. Clinical exam revealed a mild right hemiparesis. Brain MRI showed a moderate ponto-cerebellar hypoplasia and periventricular heterotopias around the occipital horns. EEG was normal. Metabolic investigations plasma amino acids, urinary organic acids, very long chain fatty acids and isoelectric focusing of serum sialotransferrin, were negative for both children. Chromosomal analysis, including

subtelomeric rearrangements were negative. Mutations in the filamin gene were not found. Brain MRI's of both parents were normal. These two children presented with the unusual association of ponto-cerebellar hypoplasia and periventricular heterotopias suggesting a specific entity.

Ataxia with Vitamin E Deficiency : clinical signs and effect of vitamin E supplementation. M. D'HOOGHE[1,2], I. DEHAENE[2], M. VAN ZANDIJCKE[2] ([1]child neurologist and [2]neurologists, Algemeen Ziekenhuis Sint-Jan, Brugge, Belgium).

AVED is an autosomal recessive disorder caused by mutations of the α-tocopherol transfer protein (α-TTP) gene. The α-TTP is a liver-specific protein for secretion of vitamin E in nascent very-low-density lipoproteins (VLDLs). The patients absorb vitamin E normally but their plasma pool of vitamin E is rapidly eliminated due to impaired secretion into VLDLs resulting in poor conservation (2, 7). The age of onset in most patients is ± 20 years (2).
We report a case of a young female (°1972) who consulted us in '95 for coordination problems. She is the child of consanguineous parents (first cousins). Since'87 she had periods of tiredness, improving after the intake of multivitamins. From +/-'92 on she developed coordination problems. There was no dysarthria. She had an obvious dysgraphia. She showed limb and truncal ataxia with very unsteady gait. There was a severe loss of proprioceptive sensations and a less marked diminution of exteroceptive sensations. The muscle stretch reflexes were diminished, the Babinski sign was negative. The ocular fundus was normal. Motor and somatosensory evoked potential studies showed a prolonged central conduction time.
A vitamin E deficiency was found : vitamin E 0,1 mg/dl (N 0,5-2,0) ; vitamin E / serum lipids 0,162 (N >0,6) ; peroxide-induced in-vitro haemolysis of red cells 58% (N <10%). The faetal fat excretion was normal. DNA-analysis (M.Koenig, IGBMC Strasbourg, France) revealed a homozygote mutation A120T in the α-TTP gene on chromosome 8q13 (this case is reported in the study of Cavalier et al, Am. J. Hum. Genet .1998 (2)).
The diagnosis of ataxia with (isolated) vitamin E deficiency was made. In AVED patients daily administration of high doses of vitamin E (2 × 800 mg of RRR-α-tocopherol) stops worsening and may ameliorate some neurologic abnormalities.
Without vitamin E supplementation patients become wheelchair bound after a mean disease duration of 13 years (3, 4). Our patient was treated with daily high doses of vitamin E in oil suspension. The serum vitamin E levels normalized. Within a few months there was a significant reduction of the ataxia. In addition to the persistent severe loss of proprioceptive sensations our patient presents an obvious diminution of exteroceptive sensations, which is unusual in AVED patients. Temporary subjective worsening of symptoms occurs during various minor illnesses. The patient also presents a peculiar impaired dual task performance ('stops walking when talking'), as is described in elderly people with frequent falls, Alzheimer's disease, Parkinson's disease, and vestibular disorders (1, 5, 6, 8).

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Follow-up of infants with Cerebellar Infarction and born with history of severe prematurity. E. SCALAIS, A. FRANÇOIS, R. STEVENS, C. NUTTIN, L. WITHOFS, O. BATTISTI, P. KALENGA, J. P. LANGHENDRIES, P. MATON (Luxembourg and Rocourt, Belgium).

Cerebellar infarction in severe preterm infants have been reported previously. However, limited information is currently available on the follow-up of those children with this lesions. Therefore magnetic resonance imaging (MRI) performed

in infants with history of severe prematurity was reviewed retrospectively. Fifteen infants with cerebellar infarction were identified. The mean birth weigh was 950 g (range : 700 - 1260g) and the mean gestational age was 26.8 weeks (range : 25.0 – 29.0 weeks). All infants had supratentorial lesions (intraventricular hemorrhage : 14, periventricular leucomalacia : 12) diagnosed by ultrasound in the neonatal period. Infants were followed up for a mean of 6.5 years (range 3.5 -11 years). MRI was performed at the mean age of 33 months. Periventricular leucomalacia was observed at the supratentorial level in almost all infants. At the infratentorial level MRI showed lesions mainly in the territory of the inferior cerebellar arteries. Atrophy of cerebellar hemispheres was severe (> 50 % of cerebellum) in eight infants, moderate (10-50% of cerebellum) in six infants and mild (10% of cerebellum) in one infants. All infants presented with motor delays (mild 60 % ; moderate 26% ; severe : 6%). Cognitive deficit was more pronounced except in one infant (moderate : 40% ; severe : 53%) . Microcephaly was found in only three infants (20%). This study confirmed that in infants with extreme prematurity, cerebellar infarction may be associated with supratentorial lesions and may also contribute to the cognitive deficit.

Normal cognitive development in a girl with Rhombencephalosynapsis. N. Bockaert, H. Verhelst, R. Van Coster (Department of Pediatrics, Division of Child Neurology, Ghent University Hospital , Belgium).

The patient is the second child of healthy, unrelated parents. Hydrocephaly was noted at 34 weeks of gestation. Amniocentesis revealed a normal karyotype and normal alpha-phoetoprotein concentration. She was born at a gestational age of 39 weeks after normal delivery (breech presentation). Birth weight was 2700g, length 48cm and head circumference 36cm. Apgar score was 0 after 1 minute. She recovered after stimulation and balloon-oxygenation, and Apgar score after 10 minutes was 8. CT scan taken on the first days of life showed dilatation of both lateral ventricles and third ventricle. The fourth ventricle was normal. Because of a severe increase of head circumference (40cm at age 4 weeks), an MRI was performed that revealed rhombencephalosynapsis.
Rhombencephalosynapsis is a rare disorder characterised by dorsal fusion of both cerebellar hemispheres and agenesis or hypogenesis of the vermis. Fusion of dentate nuclei and superior cerebellar peduncles and hydrocephaly is not always present. The latter is due to aqueductal atresia. Clinical findings range from mild truncal ataxia and normal cognitive abilities to severe cerebral palsy and mental retardation. The origin of rhombencephalosynapsis is not known yet. Homeotic genes important for early differentiation of cerebellar territory are thought to play a major role.
At the age of three months, she received a ventriculo-atrial shunt. She was able to sit at the age of 10 months and walked unsupported at the age of 24 months. Speech development was normal except for some articulation difficulties. She is 5,5 years old now, and has a normal cognitive development. She has some problems with fine motor skills and equilibrium. Nevertheless she will start primary school shortly after her sixth birthday.

PMP 22 point mutation associated with early onset Charcot-Marie-Tooth disease type 1A with prominent ataxia. K. Keppens, N. Goemans (Department of Pediatric Neurology, University Hospitals, Leuven, Belgium, E-mail : k.keppens@skynet.be).

Charcot-Marie-Tooth disease (CMT), a hereditary motor and sensory neuropathy, is known to have a wide variation in clinical presentation and evolution.
Different mutations have been described in CMT patients. The commonest type is CMT 1A, mostly associated with a duplication of the gene encoding peripheral myelin protein 22. (PMP 22, gene map locus 17p11.2)
We present 2 patients with a point mutation on 17p11.2. Their phenotype is associated with an earlier onset and a more prominent ataxia than the classical phenotype in CMT 1A with 17p11.2 duplication. In contrast foot deformity and distal muscle weakness are less pronounced.

Eyes movements in two brothers with Ataxia Oculomotor Apraxia type 1. A. Aeby[1], Ch Van Nechel[2], M. Koenig[3], C. Christophe[4], B. Dan[5], F. Christiaens[6] ([1]Neuropédiatrie, Hopital Erasme, Belgium ; [2] Neuroophtalmologie, Hopital Brugmann et Erasme, Belgium ; [3] Institut de génétique, CNRS-INSERM, CU Strasbourg, France ; [4] Service de Radiologie, Hopital Universitaire des Enfants Reine Fabiola (H.U.D.E.R.F), Belgium ; [5] Service de Neurologie, Hopital Universitaire des Enfants Reine Fabiola (H.U.D.E.R.F) , Belgium ; [6] Neuropédiatrie, Hopital Saint-Luc, Belgium).

Ataxia Oculomotor Apraxia (AOA) 1is the most frequent cause of recessive ataxia in Japan and Portugal. This neurodegenerative disease begins usually in the first decade of life with early onset ataxia and cerebellar atrophy, oculomotor apraxia, axonal motor neuropathy and decrease serum albumin levels. Recently, the causative gene, Aprataxin (APTX), has been identified and map to 9p13.3.

Oculomotor apraxia is characterized by impaired ability to generate saccades on command . A variety of disorders that cause saccadic palsy or slow saccades are characterized by the development of a strategy of head thrusting or blinking to shift gaze, that closely resembled to oculomotor apraxia.
We will describe two brothers with AOA type 1 with homozygote mutation in the aprataxin gene (585C_A, exon 5) without thrue oculomotor apraxia as described by Cogan but with slow saccades or saccadic palsy showing that oculomotor apraxia is not a necessary condition to the diagnosis of AOA type 1. We will also explain the slight differences between congenital and acquired oculomotor apraxia.

Cerebellotrigeminal-Dermal Dysplasia. F. ROELENS[1], M. DE RAMMELAERE[2], G. MORTIER[3] ([1]Child neurologist, Heilig Hartziekenhuis, Roeselare, Belgium ; [2]Dominiek Savio Instituut, Gits, Belgium ; [3]geneticist, Dept. Medical Genetics, Ghent University Hospital, Belgium).

Gomez-Lopez-Hernandez syndrome (cerebello-trigeminal-dermal dysplasia) (G-L-H syndrome) is a condition that includes abnormalities of the cerebellum (rhombencephalosynapsis), cranial nerves (trigeminal anesthesia), and scalp (temporal alopecia). The first patients were reported in 1979 by Gomez et al., and in 1982 by Lopez-Hernandez et al. So far, only 8 patients with this condition have been documented.
We describe a ninth patient, with rhombencephalosynapsis and trigeminal anesthesia as main symptoms. Mild temporal alopecia and turricephaly are also present, as are mental retardation, dysmetria and weak equilibrium. The prominent psychiatric problems and shaking or rolling head movements in our patient, have already been described in a few other patients with G-L-H syndrome.
Only sporadic cases are known of this rare syndrome. So far, no genetic cause has been found. Currently, microarray based comparative genomic hybridisation (‘array-CGH’) is going on to detect submicroscopic chromosomal rearrangements.

Pontocerebellar atrophy, microcephaly and chorea in a patient with Pontocerebellar Hypoplasia type 2 syndrome. R. VAN COSTER, H. VERHELST (Department of Pediatrics, Division of Child Neurology, Ghent University Hospital, Belgium).

The clinical features of the patient were dominated by severe developmental delay, secondary microcephaly (-4SD) and severe choreatic movements. He was born at term from non-consanguineous parents with birth weight 2960 g, length 47 cm and head circumference 33,2 cm. During the first days of life he presented with feeding problems necessitating temporarily gastric tube feeding. Cerebral MRI at the age of two months showed severe hypoplasia of the cerebellum and pons. MRI at the age of 12 years showed the same subtentorial abnormalities and, in addition, supratentorial cortical atrophy. Karyotype was normal, as well as the metabolic screening investigations. During the first decade of his life, mental and motor development remained severely retarded. He continued to suffer from continous choreatic movements which impaired seriously his every day quality of life. He also had gastro-intestinal dysfunction. After a meal he became tense and agitated, his face with a red blush and with excessive transpiration. He also suffered from generalized tonic seizures. Successive therapeutic trials with Orap,, Triapidal,, dopamine, Majeptil,, Artane, and Omeprazol, were unsuccesful. Slight clinical improvement was obtained by administration of clonazepam. Pontocerebellar atrophy, combined with microcephaly and chorea was first reported by Brun in early 1900, and later also described by P. Barth. The underlying molecular cause of this disease is not known yet (video recording of the patient is available).

Ataxia as first neurological sign of ADEM. H. VERHELST, R. VAN COSTER (Department of Pediatrics, Division of Child Neurology, University Hospital Ghent, Belgium).

Acute disseminated encephalomyelitis (ADEM) is an inflammatory disease, following an antecedent infection or immunization, typically affecting the subcortical white matter. A wide range of neurological abnormalities characterizes the clinical course.
We report two patients with ADEM who presented initially with ataxia. The first patient, a boy 18 months old, developed ataxia one week after onset of a febrile illness. Clinical examination at that moment revealed no other neurological signs. One day later, however, he was found stuporous in his bed. The second one, a boy of 4 years, became stuporous and hypotonic two days after onset of ataxia and subfebrilitas. Again, at presentation, ataxia was the only neurological abnormality. In both cases the diagnosis of ADEM was made on MRI of the brain, showing hyperdense signals on T2-weighted images as typically seen in ADEM. Cerebellar involvement was prominent in both patients.

Ataxia is a know clinical feature of ADEM and is present in 30 to 65% of the patients. Moreover, ataxia can be the only presenting neurological manifestation as illustrated by the two presented cases. Early correct diagnosis is important for adequate therapy.
In conclusion : Ataxia can be the first and only neurological sign of ADEM. ADEM should be included in the differential diagnose of acute ands subacute ataxia, especially when occurring after infection or immunization.

Mild cerebellar and cognitive dysfunction in two siblings with Joubert syndrome. R. VAN COSTER[1], R. CRAEN[2], H. VERHELST[1] (Department of Pediatrics, [1]Division of Child Neurology, and [2]Division of Endocrinology, Ghent University Hospital, Belgium).

Two siblings presented with mild cerebellar signs and cognitive impariment. The youngest one started walking at the age of 28 months. Clinical examination at 12 years of age showed an abnormal gait (“awkward gait”), equilibrium problems, fine motor disturbances and unability to run. Speech was slow. Mild dysmorphic facial features were present including a large, broad based nose and midfacial hypoplasia. There was a decline in length curve. A growth hormone deficiency was detected at the age of four years and she was treated succesfully with growth hormone. Her IQ was 69. She went to a school for mildly retarded children (type 8) and also received additional training in a specialized revalidation center for children. Social abilities were estimated as poor. Cranial MRI revealed abnormal architecture of the cerebellum and a molar tooth sign. Supratentorial findings were normal. Pituitary gland was present but ectopic. The older brother presented with the same features as his sister. He had been able to sit without support at the age of one year and walked from the age of 22 months. Fine motor and gross motor problems as well as problems with equilibrium were noticed. His speech was slow and scanded. Mild facial dysmorphic features including a broad nasal base were present. His body length followed the third percentile until the age of 14 years. A growth hormone stimulation test demonstrated a deficient response. Cranial MRI showed the same cerebellar abnormalities as seen in his sister. Both siblings were diagnosed as Joubert syndrome. DNA analysis in candidate genes for Joubert syndrome has been performed but was negative until now (video recording of both siblings available).

Cerebellar hemiatrophy in a patient with Becker Dystrophy. J. VERHAEGHE, H. VERHELST, R. VAN COSTER (Department of Pediatrics, Division of Child Neurology, Ghent University Hospital, Belgium).

Significant volume loss in one cerebellar hemisphere is a rare finding in children. Usually it is seen in the context of ischemia, or as a consequence of a lesion in the contralateral cerebral hemisphere (“crossed cerebrocerebellar atrophy”). The presence of a cerebellar hemiatrophy in a patient with Becker muscular dystrophy might be a coincidental finding. However, a causal relationship is not excluded. It is know that in Purkinje cells normally a full length dystrophin isoform is expressed (Dp 427p, MW = 427kDa). In the patient presented here a deletion of exons 45-47 was found which knocks out not only Dp 427p but also two smaller dystrophin isoforms (Dp 260 and Dp 140). The latter is expressed in brain. Dystrophins in the brain are selectively localized in postsynaptic neurons in cerebral cortex, hippocampus and cerebellum and co-localize with GABAA receptor subunit clusters in these regions. Dystrophin may play an important role in the clustering or stabilisation of GABAA receptors in a subset of central inhibitory synapses. Lack of dystrophins can cause loss of function in specific area's of the brain. FDG-PET scan in Duchenne muscular dystrophy patients showed regional differences in brain glucose metabolism, including asymmetrical involvement of the cerebellum. In the right cerebellar hemisphere a significant decrease was seen at area VIIIB, while in the left cerebellar hemisphere a decrease was detected more in the crus. For these reasons, it seems not impossible that the right cerebellar atrophy in the presented patient is not a coincidental finding.
The propositus is now 15 years old. During pregnancy the mother was treated with Strumazol because of hyperthyreoidy. Initial motor development was slightly retarded. He walked at the age of 22 months. At the age of 6 years he was referred to the hospital with suspicion of myopathy. Besides motor problems he also suffered from equilibrium problems and slight mental retardation. CK in blood varied between 8630 and 11 500U/L. Echocardiography showed no cardiomyopathy. Cerebral CT and MRI scan revealed a cerebellar hemiatrophy at the right. A 120 kb long deletion corresponding to exons 45-47 of the dystrophin gene was detected in DNA extracted from white blood cells.

Ataxia Oculomotor Apraxia 1. J. LEROY[1], F. ROELENS[2], M. DE RAMMELAERE[3], R. VAN COSTER[4], J. DE BLEECKER ([1]Baylor College of Medicine, Dept. Molecular and Human Genetics, Houston, Texas, USA ; [2]Child neurologist, Heilig Hartziekenhuis, Roeselare, Belgium ; [3]Dominiek Savio Instituut, Gits, Belgium ; [4]Child neurologist and 5Neurologist, Ghent University Hospital, Belgium).

Over 30 years ago cerebellar ataxia was diagnosed in a dozen children in a special school for the physically handicapped in Western Belgium. In at least half of them physical and neurological examination, recurrent pulmonary infections, analysis of serum markers and a steadily progressive course with fatal outcome before or during adolescence, supported the diagnosis of ataxia telangiectasia, which at the time could not yet be confirmed by demonstration of mutations in the ATM gene. In two of the longer surviving unrelated patients, preadolescent onset Friedreich ataxia was recognized on clinical grounds and later confirmed by showing homozygosity for the GAA trinucleotide expansion in intron 1 of the FRDA gene encoding frataxin.
Two male siblings, children of consanguineous parents also belonging to the original group, had from admission prominent ocular motor apraxia associated with truncal and appendicular ataxia, severe slurring of speech and nearly absent DTRs. Unlike the AT patients they have not suffered from recurrent grave infections and they maintained aided ambulation until about the 30th birthday. Subsequently they became wheelchair-bound due in part to peripheral neuropathy. MRI showed cerebellar atrophy, but normal supratentorial anatomy. Normal intelligence has remained unaltered. Albuminaemia was low but still within the control range. Also the cholesterolaemia was within normal limits. No values from the early stages of the disorder were available
In both patients the homozygous transition 837G>A was found in exon 6 of the aprataxin gene, located on chromosome 9p13 resulting in the non-sense mutation W279X and in a premature translation stop of the HIT/Zn-finger protein, aprataxin.
This result was obtained in the laboratory which has characterized the AOA1 gene [Moreira et al (2001) Nat Genet 29 : 189] and has since reported on the AOA2 gene located on 9q34 [Moreira et al (2004) Nat Genet 36 : 225] associated with a second type of Ataxia ocular motor Apraxia syndrome with later clinical onset. Clinical and molecular sorting of childhood ataxia syndromes will occur much earlier in the future, challenged only by the genetic heterogeneity bound to be more extensive than hitherto realized.

Atypical myoclonus, deafness, gait and posture disorders : an unusual syndrome. A.-L. POIRRIER, J.-P. MISSON (Department of Neuropediatrics, CHR-Citadelle, University of Liege, Liege, Belgium).

Determining the aetiology of movement disorders is an increasing challenge for paediatricians. Myoclonus is the most common involuntary movement disorder meaning a sudden disabling muscle jerk, occurring in a number of diseases of heterogeneous origin.
Case Report
A healthy born girl develops at 2 months a bilateral perception deafness. At 2 years, she walks with light ataxia. At 3 years, tremors of the four extremities and the face are present. She quickly develops myoclonus of variable intensity involving the four limbs, global hypotonia and dysarthria. At 8 years, the walk is deteriorated, and a rolling armchair is needed at 10. No familial history is recorded except a deep bilateral deafness of her eldest brother. She has an unremarkable physical examination, a normal consciousness and alertness without dysmorphy. The social, familial and school life is very affected. Medical imagery, electrophysiology, blood and urinary analyses, genetic research and molecular biology have been done. No precise diagnosis can be established. The patient benefits as pharmacological treatment of levetiracetam and piracetam. The management targets improvements of the gait and the posture, learning of autonomy, physiotherapeutic care, speech therapy and social integration.