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RESEARCH ARTICLE

INFANTIL NEUROAXONAL DYSTROPHY: A CASE REPORT

S.El Moudden, K. Mkadem, S. Chaouki and M. Hida
Pediatric Neurology Unit, Pediatric Department, Chu Hassan Ii, Fes, Morocco.

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Abstract

Infantile neuroaxonal dystrophy is a rare, hereditary neurodegenerative disease that begins before the end of the second year of life, after an interval of normal psychomotor development; caused by Biallelic mutations in the PLA2G6 gene in the most of cases. It is characterized by progressive motor and cognitive deterioration leading to a bedridden state and death before the end of the first decade. We report the case of a two and a half year patient who showed psychomotor regression with ophthalmological damage, truck hypotonia and impaired visual contact as the main neurological signs. Infantile neuroaxonal dystrophy is a rare and serious disease in children with a risk of generally fatal complications, but it remains a preventable disease thanks to genetic counselling.

Introduction:-

Infantile neuroaxonal dystrophy (INAD) is a neurodegenerative disorder of early age, which can lead to early death. It is due to Biallelic mutations in the PLA2G6 gene in the most of cases of INAD.

The most important clinical manifestations are progressive, the disorder is starting at the end of the first or beginning of the second year of life, between 6 months and 3 years of age, before the beginning of the first symptoms the infant development is normal. Then a progressive disorder is starting to appear, the early symptoms are regression in developmental and gross motor milstones, truncalhypotonia, nystagmus and strabismus.

The progression of infantile neuroaxonal dystrophy (INAD) in the most of the cases is rapid and can be fatal; the patients present a cognitive decline, spastic tetra paresis, pyramidal manifestations, strabismus, nystagmus, optic atrophy and bulbar dysfunction. Seizures may accrue in a minority of patients.

We report the case of a 2 year and 6 month old female patient, who presented psychomotor and milstone regression with ophthalmological involvement, low muscle tone and impaired eye contact as the main neurological signs in whom infantile neuroaxonal dystrophy was confirmed by genetic study.

DNAI is a rare and serious disease in children, with a risk of complications that are generally fatal, but it remains a preventable disease thanks to genetic counseling.

Case report:

The present case report is a Moroccan child aged 2 years 6 months, 2nd of two siblings, from non-consanguineous parents; there are no similar cases in the family. Pregnancy and delivery were unremarkable. Who presents since the

Corresponding Author:- Dr. Sanae El Moudden
Address:-Pediatric Neurology Unit, Pediatric Department, Chu Hassan II, Fes, Morocco.

age of 18 months a behavioral disorder followed by a psychomotor regression and delayed milstones (gross motor delay / speech delay) which gradually progressed. On clinical examination, there was truck and peripheral hypotonia, reduction of muscle strength, therefore the deep tendon reflexes were present, the eye contact was also present, and there were no cerebellar signs. Examination of the cranial pairs revealed no nerve paralysis, but ophthalmological examination showed temporal papillary pallor, more marked on the right, without atrophy.

Because of the presence of the psychomotor regression and the ophthalmological involvement, hereditary affections were suspected first: DNAI, following the electromyography (EMG): an axonal sensitive neuropathy was found, we completed the exploration with the genetic study whom revealed a homozygous mutation of PLA2G6: C1556G>C. the MRI of the brain showed cerebellar atrophy with increased T2 and flair of the white matter , which indicate that iron accumulation seems to become more appreciable later in the disease course.

The treatment was symptomatic, As regards the patient's evolution; she is alive, with persistence of tetra-paresis without spasticity.

Discussion:-

Infantile neuroaxonal dystrophy is part of a research group called NBIA (Neurodegeneration with brain iron accumulation). This is a heterogeneous group of rare inherited neurodegenerative diseases characterized by high levels of iron in the brain.The most common form is pantothenate kinase associated with neurodegeneration (PKAN) accounting for 35% of the affected population. It is due to mutations in the PANK2 gene. The second form is Infantile neuroaxonal Dystrophy (DNAI) [1].witch is an autosomal recessive genetic disease caused by mutations in the PLA2G6 gene. It is located on chromosome 22q13.1 and contains 17 exons spanning more than 70 kb [2]. The prevalence of neuroaxonal dystrophy is unknown, but over 150 cases have been reported worldwide [3]. It is a disease of early childhood; the average age of patients at diagnosis is 15 months [4].Symptoms of DNAI generally begin before the end of the second year of life, after an interval of normal psychomotor, milstone and cognitive development. Regression of development is the first manifestation of the disease.The initial symptom is usually delayed psychomotor development or milestone regression, with loss of head holding, sitting, walking and language. This Regression is not specific to DNAI and occurs in many other neurodegenerative diseases. The symptoms of INAD often begin before the child can walk independently If they have learned to walk, frequent falls or unusual gait are noticeable [5]. The disease is progressive, leading to spastic or hypotonic tetra paresis with areflexia and distal traction. Vision is usually affected quite early in the course of INAD;the child may develop pendularnystagmus, strabismus or even decreased visual acuity due to optic atrophy. These are common at an early stage of the disease, or may be presenting and early symptoms [4].

Epilepsy with partial or generalized seizures is occasional and usually occurs during the course of the disease, generally controlled by antiepileptic drugs. In our case, the patient was seizure-free. As the disease progressed (over months and years), the clinical picture worsened, with the appearance of a bulbar syndrome characterized by swallowing disorders and laryngeal congestion.

Psychiatric symptoms such as incessant crying, attention deficit hyperactivity disorder (ADHD) and aggressive behavior has been reported in INAD [5].because of neurodegeneration, there is intellectual regression, this intellectual deterioration occurs during childhood, evolving into full-blown dementia [4].

At the EEG (electroencephalography), a characteristic rapid activity of large amplitude is usually present after the age of 2. However, it seems that this EEG finding is not visible in very early or late stages of the disease; EMG (electromyography) may reveal signs of chronic denervation with normal nerve conduction velocities (NCV). A normal EMG does not exclude the diagnosis [6], but axonal sensory and/or motor polyneuropathy may be present; in our case report, the EMG revealed axonal sensory polyneuropathy.

On the other hand, the main neuroradiological findings reported in the literature are marked cerebellar atrophy and diffuse T2 signal hyperintensity in the cerebellar cortex, probably related to extensive gliosis and iron accumulation. The diffuse, progressive cerebellar atrophy that is detected at a very early age mainly involves the lower part of the vermis. This is the only MRI finding in almost all PLA2G6 mutation-positive patients reported in the literature [7].Moreover; Cerebellarhyperintensity becomes increasingly evident with disease progression on the second and the third MRI. Our patient’s MRI showed cerebellar atrophy with white matter hyper signaling. [8].

Genetic studies are still the reference diagnostic method for DNAI [3]. PLA2G6-associated neurodegeneration (PLAN) is a complex group of neurodegenerative diseases resulting from mutations in a gene known as PLA2G6.

Finally, Treatment is currently symptomatic: psychomotor, physcaltherapy, ergotherapy, anti-epileptic drugs.

Conclusion:-

DNAI is an inexorably progressive disease, and death generally occurs between the ages of 5 and 10, often because of loss of bulbar function leading to pneumonia. The average age of death according to the literature is 9 years [4].in our case, the patient is still alive.

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