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Gait Disorder In Children Revealing Neurodegeneration Due To Pantothenate Kinase Deficiency

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Abstract:
Background*: Pantothenate Kinase deficiency leads to neurodegeneration with overload cerebral iron expressed clinically by extrapyramidal dysfunction progressive: dystonia, rigidity, choreoathetosis, gait disorder.*
Clinical case report: ***Conclusion:*** *Child aged 5 years with a history of delayed psychomotor development without any concept of fetal or neonatal suffering, hospitalized for gait disorder (impaired gait and falls). Neurological examination reveals the presence of generalized dystonia. Brain MRI makes it possible to highlight neurodegeneration due to Pantothenate Kinase deficiency.*
Key Words*: Pantothenate Kinase deficiency, Gait disorders, Dystonia, Trihexyphenidyl.*

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I. Introduction

In typical form of neurodegeneration due to Pantothenate Kinase deficiency (or Pantothenate Kinase-Associated Neurodegeneration PKAN) the onset of disorders begins before the age of 6 years, but there is great variability in the age of presentation (6 months to 12 years). The majority of children initially present with gait or posture disorders secondary to dystonia[1]. Dystonia is reported in 87% of individuals (the most frequently reported extrapyramidal characteristic). Oromandibular dystonia is observed[2]. a syndrome pyramidal with hyperreflexia and Babinski's sign. retinitis pigmentosa, which can cause significant loss of vision[3]. Cataracts can develop as a result of retinitis pigmentosa. cognition declines with disease progression.[4].the classic picture is one of progressive decline, with periods of clinical stability interspersed with periods of neurological disturbance. The majority of affected individuals are unable to move within 15 years of diagnosis[3,2]. Later complications include dysphagia (leading to feeding difficulties), gastroesophageal reflux and constipation. Death is generally secondary to cardiorespiratory complications (pulmonary infections, aspiration pneumonia), secondary deleterious effects of malnutrition and, rarely, a dystonic state. The atypical form of PKAN generally occurs in the second or third decade. The Initial symptoms are often slurred speech and/or behavioral problems.Typical motor signs of the disease may not appear until later in the disease, most patients with dystonia, parkinsonism and spasticity of variable intensity. Extrapyramidal motor symptoms in atypical PKAN are correlated with the age of onset, adolescents presenting more dystonic symptoms than parkinsonian syndrome, while the opposite pattern is observed in patients starting illness after 20 years. The progression of atypical PKAN is much slower than that of classic form, generally with a rapid decline at the beginning of the disease then stabilization symptoms. Intellectual functions may be disrupted in PKAN, but cognitive disorders do not are not constant. Intellectual deficits are more common in forms with early onset,and their severity is all the greater the earlier the age of onset of the disease is [4].

II. Clinical Case

Child aged 5 years with a history of delayed psychomotor development without any concept of fetal or neonatal suffering, hospitalized for gait disorder (impaired gait and falls). Neurological examination reveals the presence of generalized dystonia (axial and segmental). Brain MRI reveals hyper-intensity in the region central surrounded by a ring of hypo-intensity on coronal and transverse T2 images of the globus pallidus. Improvement of walking disorders under Trihexyphenidyl.

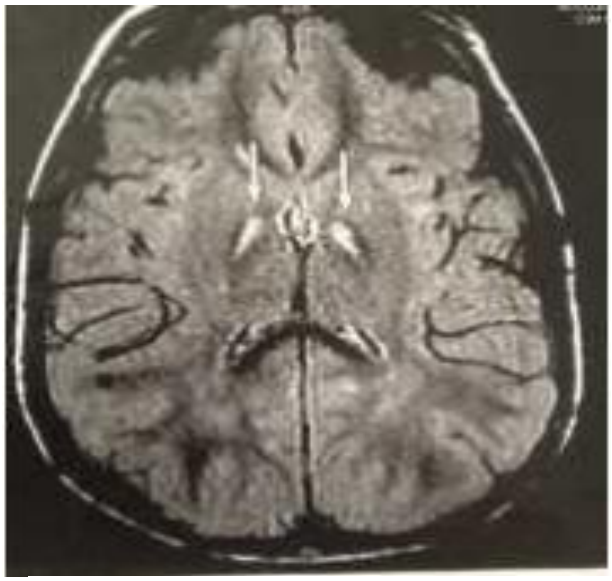

Figure 1. Brain MRI, bipallidal hypersignal with hyposignal halo, FLAIR sequence.

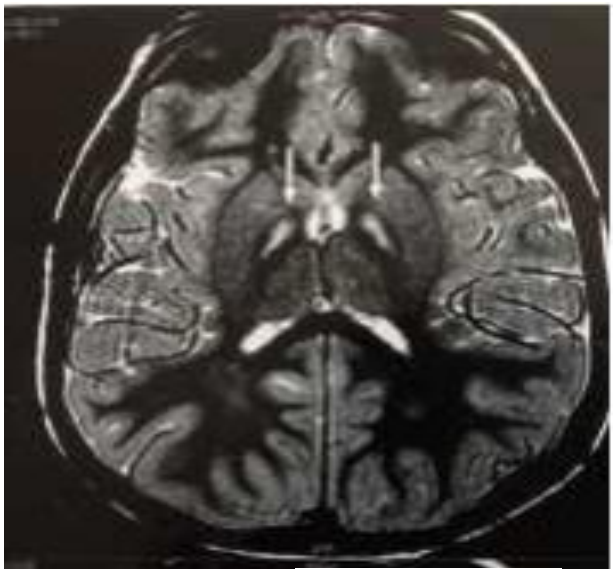

Figure 2. Brain MRI ,The eye of the tiger sign.

III. Discussion

The differential diagnosis includes Wilson's disease, excluded by the presence of concentration normal plasma ceruloplasmin and normal copper metabolism. The diagnosis of neurodegeneration due to Pantothenate Kinase deficiency is suggested on brain MRI (sign of the eye of the tiger).

Wilson's disease is a genetic disorder resulting from a disorder of metabolism of the copper. The brain MRI can resemble that of a neurodegeneration due to Pantothenate Kinase deficiency patient, we find on it hyperintensities on T2 weighting in the basal ganglia, particularly the striatum, the brainstem and cerebellum. Subcortical atrophy is often visible. The copper balance sheet shows reduced total copper, increased 24-hour copper, and ceruloplasminemia lowered. Calcifications of the basal ganglia, or Fahr's disease, can also be taken to wrong for neurodegeneration due to Pantothenate Kinase deficiency. Calcium appears hypointense on T2, and is differentiated from iron on CT, where it appears hyperdense. Manganese transport anomalies may also be responsible for deposits on the basal ganglia, they are hyperintense in T1 and isointense in T2. Mitochondrial cytopathies such as Leigh syndrome can cause abnormalities signal at the level of the basal ganglia. These are mainly T2 hyperintensities which exceed the putamen. Colliculi involvement is highly specific for diseases mitochondrial. Finally, leukodystrophies above and/or below are frequently associated with tentorial. MRI spectroscopy also frequently finds a lactate peak.

Brain MRI are generally quasi-pathognomonic. Centered T2 sequences on the basal ganglia show hypointense globus pallidi, with a region central and anterior hyperintensity, producing the so-called (Tiger's eye sign).

Brain MRI is generally the key test revealing intracerebral iron overload, whichputs on the diagnostic track.The quality of the brain imaging performed, in particular the power of the magnetic field MRI and the thickness of the sections, allows precise identification of pathological deposits of iron in the brain.Iron appears isointense on T1 sequence and hypointense on T2, as does calcium.However, CT scans make it possible to differentiate calcium from iron, the first appearing hyperdense and the second isodense. Iron-sensitive MRI sequences, such as SWI (Susceptibility Weighted Images), GRE (Gradient Echo Sequences) and T2* are the fundamental sequences for allow the diagnosis of PKAN to be made (1). Iron overload can be quantified using T2* mapping and quantitative QSM (Quantitative Susceptibility Mapping) sequences.These sequences show relatively symmetrical iron deposits in the globus pallidi

The usual treatments for dystonia such as benzodiazepines or baclofen can be useful. Trihexyphenidyl, if cognitive state permits, can also be tried. The indication of botulinum toxin in cases of focal dystonia (e.g. cervical dystonia, knee flexum, equinus foot position, jaw dystonia) should be asked by an expert in the management of abnormal movements. In case of effectiveness and good tolerance, it could be repeated regularly.

Bilateral deep brain stimulation of the internal globus pallidus can also be discussed in an expert center, after having tried the treatments mentioned above. Its effectiveness has been demonstrated in patients with PKAN, when performed early in the progression of the disease, before the dystonia becomes too disabling and the deformations orthopedics present [5].

IV. Conclusion

Gait disorders in children with neurodegeneration due to panthothenate Kinase deficiency are most often due to dystonia. The tiger's eye sign suggests the diagnosis on brain MRI. Treatment with Trihexyphenidyl aims to improve walking by acting on dystonia. (L-Dopa has no effects).

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