Pantothenate Kinase Associated Neurodegeneration: A Case Report

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Abstract

Pantothenate kinase-associated neurodegeneration (PKAN) is a form of neurodegeneration with brain iron accumulation (NBIA), formerly called Hallervorden-Spatz syndrome. PKAN is the first described inborn error of coenzyme A metabolism. PKAN encompasses two clinical subtypes, classic and atypical. We here report an eight year girl diagnosed as classic PKAN. We also review the literature about PKAN.

Key words: Eye of tiger sign, NBIA, Neuroregeneration, Iron Accumulation, Hallervorden Spatz Syndrome

Introduction

Pantothenate kinase-associated neurodegeneration (PKAN) is autosomal recessive neurodegenerative disorder. It is the first described inborn error of coenzyme A metabolism. In the absence of genetic diagnostic testing clinical examination and typical MRI finding help in diagnosis of PKAN.

The Case

An eight year old girl product of third degree consanguineous couple, 2nd in birth order presented with progressive increase in falls while walking and abnormal posturing of limbs for last two years. There was no diurnal variation in symptoms. She also had progressive cognitive decline and decrease in speech output. There was history of decreased vision in dark for past 1 year. Her one elder brother died of similar illness at eleven years of age, whose illness started at the age of eight years. On clinical examination her weight was 15 kg, OFC 51 cm. On clinical examination her vitals were stable, no neurocutaneous markers, no organomegaly. Nervous system examination revealed extrapyramidal dysarthria, decreased speech output, generalized dystonia, spasticity and extensor toe sign. On fundus examination there were bilateral retinal pigmented changes (Figure 1). Magnetic resonance imaging of brain revealed “eye of tiger” sign (Figure 2.1, 2.2) on T2 weighted images.

Discussion

On the basis of clinical and radiological findings diagnosis of classical form of pantothenate kinase associated neurodegeneration was made. PANK2 mutation could not be done due to financial constraints. Child was started on trihexyphenidyl, baclofen, physiotherapy, occupational therapy and advised regular follow up.
characterized by progressive dystonia and basal ganglia and substantia nigra iron deposition with onset that usually occurs before age of ten years. Commonly associated features include dysarthria, rigidity, and pigmentary retinopathy. Some of these children (approximately 8%) have associated acanthocytosis in their peripheral blood smears. Most of these patients develop difficulties between 5 and 8 years of age. About 25% of affected individuals have a 'atypical' presentation with later onset (age >10 years), prominent speech defects, psychiatric disturbances, and more gradual progression of disease.

Brain magnetic resonance imaging is standard in the diagnostic evaluation of all forms of PKAN. The 'eye of the tiger' sign, a central region of hyperintensity surrounded by a rim of hypointensity on coronal or axial T2-weighted images of the globus pallidus, is highly correlated with the presence of a PANK2 mutation in classic cases.

The hypointense signals on T2 weighted image is due to iron deposition in iron rich brain tissue and the central hyperintensity is due to the glioses and spongioses due to cell death due to cysteine containing neurotoxic substrates. Areas of the globus pallidus and the pars reticulata of the substantia nigra have proportionately increased iron content in normal individuals; however, in PKAN, iron-containing pigment accumulates to an extraordinary degree in these areas. In classic PKAN, two-thirds of affected individuals demonstrate pigmentary retinopathy.

The eye-of-tiger-sign can sometimes be seen in other NBIA or non NBIA conditions.

In few cases of neuroferritinopathy, corticobasalganglia degeneration and progressive supranuclear palsy especially in elderly people with carbon monoxide poisoning eye-of-tiger-sign is seen. However the clinical features like age of onset differentiate these from PKAN. In neuroferritinopathy, MRI reveals involvement of caudate, putamen, thalamus and cerebral cortex. Another condition, where the 'eye of tiger' like appearance is seen, is dihydropteridine reductase deficiency in which there will be associated features like cortical calcifications and cysts. Even the clinical presentation varies with microcephaly, parkinsonism, oculogyric crisis and disturbed psychomotor development.

There is no specific treatment for PKAN. Treatment requires multidisciplinary approach including neurologist, ophthalmologist, physiotherapist, occupational therapist, geneticist and speech therapist. Dystonia is among the most common associated movement abnormalities. Dystonia and spasticity can be managed with Trihexyphenidyl and baclofen. Intrathecal baclofen may be considered if oral treatment fails. Laryngeal dystonia may require tracheotomy if respiration is impaired. Deep brain stimulation (DBS) of globus pallidus may be a effective strategy in PKAN. If there is difficulty in swallowing and nutrition is impaired, gastrostomy placement may prove necessary. Oral glycopyrrolate and hyoscine patch may be useful for drooling. As PKAN is autosomal recessive in inheritance, at each conception sibling of proband has 25% chance of being affected. Prenatal diagnosis may be possible if facilities of genetic testing are available.

References


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