Case Report: Hallervorden–Spatz Syndrome with Seizures

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ABSTRACT

Hallervorden-Spatz syndrome is a disorder characterized by dystonia, parkinsonism, and iron accumulation in the brain. The disease is caused by mutations in gene encoding pantothenate kinase 2 (PANK2) and patients have pantothenate kinase-associated neurodegeneration. We present an 8-year-old boy with progressive muscle dystonia, neuroregression, frequent fall and multiple injury marks of different stages. Seizures are rare with PANK2. This child had seizure onset at 4 years of age and seizure free on valproate and levetricetam. The CT scan showed tiger eye appearance and mutations on PANK2 gene.

1. Introduction

Hallervorden-Spatz syndrome is an autosomal recessive disorder characterized by dystonia, parkinsonism, and iron accumulation in brain. Patients have pantothenate kinase-associated progressive neurodegeneration and regression of milestones (Jankovic, Kirkpatrick, Blomquist, Langlais, & Bird, 1985).

2. Case Report

We present an 8-year-old boy who had frequent falls, not gaining milestones, progressive muscle dystonia, neuroregression, and multiple injury marks of different stages. Child was delivered to second degree consanguineous parents and was the third birth order. The first male baby was affected with the same illness while another male baby had normal intelligence but had coloboma and retinitis pigmentosa. The youngest baby was female and normal. This child had seizures since 4 years of age and seizure free on valproate and levetricetam. Child had neuroregression and unable to sit and stand. He was unable to speak even bisyllables words. However, he could understand and follow simple commands. His evaluation for ophthalmological abnormality revealed retinitis pigmentosa. He had bilateral orbital cellulitis which required intravenous antibiotics. With possibility of Hallervorden-Spatz syndrome, CT scan of brain was done which revealed tiger eye appearance. A mutation analysis by PCR sequencing was utilized to identify *PANK2* mutations, which revealed two mutations: one in exon 3 (Leu385CysfsX13) and one in exon 4 (Arg440Pro) of the gene. Parents were also heterozygous for the same mutations; however the elder sibling

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was not evaluated because of financial reasons. Child was medicated on iron chelation, pantothenate, coenzyme Q, multivitamins, and rehabilitation measures.

3. Discussion

Hallervorden-Spatz syndrome refers to a spectrum of autosomal recessive disorders that share the common features of neurodegeneration and iron accumulation in the brain. Its prevalence was estimated to be around 1-3 per 1000000 individuals. Heterozygous individuals may not display characteristics suggestive of the disorder; however there have been reported cases in which heterozygous individuals develop features of classic form of disease (Rossi et al., 2012).

The disorder is caused by a mutation in *PANK2* gene located at the chromosomal locus 20p13-p12.3 (Tanfani, et al., 1987). PKAN was first described by Hallervorden and Spatz (1922). PANK2 codes for the protein pantothenate kinase 2, which is responsible for stifling the accumulation of N-pantothenoyl-cysteine and pantetheine. When this accumulation is not suppressed, direct cell toxicity or free radical damage will occur. Mutant *PANK2* gene coded proteins are often caused by null or missense mutations most notably a 7bp deletion in the *PANK2* gene coding sequence. This child had also shown the novel mutation for *PAKN2*, while parents were heterozygous. This disorder has been reported in specific communities based on intra-community marriages.

One of the communities reported is Agrawal community mainly based in Northern Part of India. Our case was also from north India; however the family was not Agarwal. Signs and symptoms typically begin in early childhood and are progressive, often resulting in death by early adulthood. Symptoms include dystonia, dysphagia and dysarthria, rigidity/stiffness of limbs, tremor, writhing movements, dementia, spasticity, rigidity, weakness, seizures (rare) and toe walking (Taylor et al., 1996). Pigmentary degeneration of the retina and iron deposition in the basal ganglia may accompany this form of the disease. This child had seizures apart from common features. Seizure onset was at 4 years of age and controlled with two antiepileptic drugs. Around 25% of individuals have an atypical form of PKAN that develops post-10 years of age and follows a slower, more gradual pace of deterioration (Zhang et al., 2005). These individuals face significant speech deficits, extrapyramidal defects, later psychiatric, and behavioral disturbances.

MRIs are very useful in making a sound diagnosis (Zhou, et al., 2001). MRI (T2w GRASE sequence) usually shows iron deposits in the basal ganglia the so called eye of the tiger sign. Genetic tests can confirm an abnormal gene causing the disease. Microscopic features of PKAN include iron granules, spheroid bodies, and Lewy bodies within neurons.

Pharmacologic treatment of PKAN is mainly based on iron chelation. Pantothenate, coenzyme Q, and other anti-oxidants vitamins are believed to be beneficial. Treatment of immobility, skin injuries, respiratory infections and bleedings is usually supportive. Physiotherapy, speech therapy, and occupational therapy are useful too. Prognosis is usually poor. Death usually occurs 10 years after the onset of the disease.

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