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Case Report

Hallervorden Spatz Disease: A Rare Case with Classical Disease Presentation in a 9 Year Old Girl

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Abstract

Hallervorden-spatz disease, now known as pantothenate kinase-associated neurodegeneration PKAN disease comes under the umbrella of new term neurodegeneration with brain iron accumulation (NBIA). Classically it affects children in adolescent age. Clinical features range from severe extrapyramidal effects like dystonia and athetosis to psychiatric disturbances. Some patients may develop eye involvement in the form of retinitis pigmentosa. Diagnosis is usually clinical and supported by MRI findings of tiger-eyes appearance of basal ganglia. Available treatment is only symptomatic not curative. In this report we have discussed the classical presentation of hallervorden spatz disease in a 9 year old girl who was diagnosed on the basis of clinical findings, eye changes along with MRI findings.

Keywords: Hallervorden-spatz disease, neurodegenerative brain disease, Dystonia, Extrapyramidal syndrome

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Hallervorden-spatz disease is a rare neurodegenerative disorder characterized by iron accumulation in the brain. It may be familial, inherited as autosomal recessive disorder, or can occur sporadically[1]. Clinical features may be highly variable, including dystonia, parkinsonism, ataxia, spasticity, psychiatric symptoms, intellectual impairment and regression of milestones.[2] The classical disease presents in late childhood to early adolescence, between ages 7 and 15 years. However, the cases with infantile and adult onset have also been recorded.[3] It has worldwide prevalence of around 1-2 per million.[4]

Case Report

A 9 year old girl presented in the out-patient department of Mayo hospital Lahore with complaints of frequent falls, regression of milestones and increased tone in all limbs. She had achieved her developmental milestones normally until the age of 3 years. Afterwards parents noticed that she developed difficulty in walking associated with frequents falls and progressively became unable to sit and open her mouth over the period of 6 years. Parents also reported episodes of aggressive behavior. There was no history of preceding febrile illness, drug intake, jaundice, urinary or fecal incontinence, fits or any focal deficit. She had visited multiple doctors and had been treated with benzodiazepines with no significant improvement. She is 4th in number among 6 siblings born to consanguineous parents. She was born at term via spontaneous vaginal delivery and is vaccinated according to EPI. All siblings are alive and healthy. Moreover, there is no history of similar illness in the family. On examination her weight was 20kg, height was 110cm and head circumference was 50cm. She had generalized dystonia involving masseter muscles as well along with generalized hyper-reflexia and up going planters. Fundoscopic eye examination showed retinitis pigmentosa.

MRI brain showed bilateral symmetrical basal ganglia hypointensities along-with central area of hyperintensity, labelled as the "eye of the tiger' appearance, characteristically present in patients suffering Hallervorden Spatz disease.

The patient was put on benzodiazepines along with oral baclofen. Due to severe trismus, nasogastric feeding tube was placed. There was some improvement in dystonia. Parents were counselled about the progressive nature of disease. A neurologist was involved and follow up plan was prepared.

Table 1: *Laboratory Values of Different Biochemical Parameters*

Sr. No.	Labs	Results	Reference range
1.	Serum ceruloplasmin level	0.22g/L	(n= 0.22-0.5g/L)
2.	24 urinary cooper	131microg/day	(wilson > 200)
3.	ANA	Negative	Negative
4.	Anti dsDNA	Negative	Negative
5.	Serum Ferritin level	100 microgram/l	11-307 microgram/l

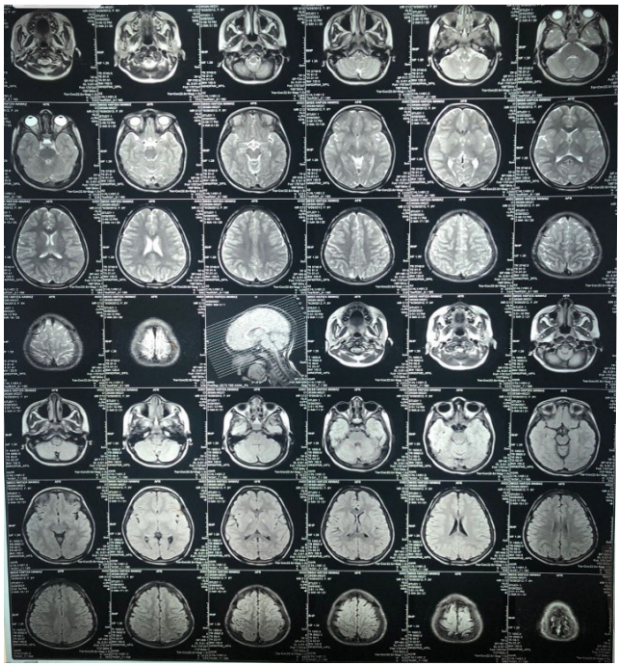

Figure I: *MRI Brain of patient T2 Image*

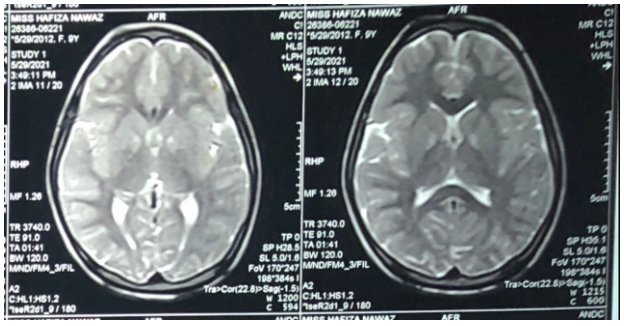

Figure II: *MRI Brain T2 Image showing Typical "Eye of Tiger" Appearance*

Discussion

Hallervorden spatz disease, an autosomal recessive disorder was narrated for the first time in literature by Hallervorden and Spatz in 1922. The PKAN2 gene responsible for this disease has been identified on chromosome 20 which encodes for pantothenate kinase, that is needed in the formation of coenzyme A from pantothenate, and fundamental to synthesis of fatty acid and energy metabolism. It can result in accumulation of cysteine followed by iron in the basal ganglia. The cysteine-iron complex results in tissue damage by enhancing oxidative stress, as in few other neurodegenerative diseases, so it is better to use the term 'Pantothenate Kinase-Associated Neurodegeneration' as elaborated by Zhou.[5,6] Gregory et al have described that the salient clinical features range from progressive dystonia and dysarthria, spasticity, Parkinsonism to neuropsychiatric and cognitive abnormalities, and optic atrophy or retinitis pigmentosa. Unfortunately our patient had developed all of these features progressively over past 6 years.[7] Moreover our patient had onset of symptoms at very young age (3 years) while most of reported cases are more than 5 years old at the time of onset of disease.[3,8,10] Initial symptoms may be marked behavioural disturbance as reported by Abrar et al, a case of 9 years old boy having onset of behavioral disturbances like hyperphagia, generalized hyper-excitibility and impulsiveness, disinhibited irrelevant talk, self-muttering and seldom episodes of aggressiveness and self harm, followed by abnormal posturing and movements in the lower limb[8]. For diagnostic purpose, MRI brain is considered as standard that shows peculiar radiologic sign called "eye of the tiger" , referring to symmetric abnormal low signal on T2-weighted MRI (due to accumulation of iron) in globus pallidus bilaterally with central high signal (due to gliosis and spongiosis) in patients with PKAN2 disease. Our patient was also diagnosed on the basis of this characteristic MRI finding. Iodine-123-tropane-SPECT scanning and (IBZM)-SPECT scanning may be helpful in diagnostic workup for Hellervorden Spatz disease.[8] Treatment of this disease is usually symptomatic not curative. Dopamine agonist and anticholinergic agent have been used traditionally for managing rigidity and spasticity. Baclofen (oral/ intrathecal) helps in improving spasms and stiffness hence, reducing dystonia. Our patient showed a slight reduction in dystonia after starting oral Baclofen. Botulinum toxin injected intramuscularly has been used for the management of hypertonicity. In our patient we planned for this option because of severe trismus and inability to open mouth but parents refused at the moment, so we kept our patient on feeding via nasogastric tube. Benzodiazepines have been used for choreoathetosis and in this regard Nitrazepam which we started in our patient proved to be of some help. Other drugs which we started in our patient were vitamin B12 and folic acid. Other treatment options in trial phase are use of coenzyme A and high dose of pantothenate, while Iron chelation has been attempted without major benefit.[8,9] In literature we could find very few reported cases of Hallervordan spatz disease in pediatric age group, in Pakistan, our's will

be a beneficial addition to available knowledge regarding this rare disease.[8,10]

Conflict of Interest: None

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