FAHR Disease-Review and Case Report.

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Abstract

Introduction: Fahr Disease is a rare neurodegenerative condition characterized by diffuse calcifications within brain. It is common in the fourth to sixth decade and few cases have been described in pediatric population. Diagnosis is based on the typical location of calcifications, age and family history of the disease. Treatment is symptomatic with anti epileptics, anti depressant and anti psychotic medications.

Case presentation: This case report describes a twelve year old boy with suspected Fahr Disease. The clinical presentation was seizure, ataxia, tremor. The patient was managed conservatively with anti seizure medication.

Conclusion: Fahr Disease is a rare neurodegenerative disease and can present in pediatric population as well.

Key words: Fahr Disease, Pediatric

Introduction

Fahr's disease is a rare, degenerative neurological condition. The disease was first described by a German neurologist, Karl Theodor Fahr in 1930.[1] The pathogenesis and clinical presentation of Fahr syndrome, known also as bilateral striatopallidodentate calcinosis (BSPDC) or Chavany-Brunhes syndrome, are partially understood, but there is still a lot to be discovered.[2] The calcifications are located within the globus pallidus, striatum, dentate nucleus, basal ganglia as well as within white and gray matter of the brain and cerebellum. Histologically the calcifications consist of non-atheromatic compounds embedded in a protein-polysaccharide complex.[2] The composition of deposits consist of calcium, zinc, iron, aluminum, magnesium, silicon, copper and phosphorus varying based upon the location as well as contact with blood vessel.[3] Majority of cases are sporadic. Familial forms have been described with autosomal inheritance, the genes involved being SLC20A2, PDGFRB, PDGFB and XPR14-8]. Metabolic causes such as hypoparathyroidism have been described.[6,9] Other proposed causes include impairment of cerebral blood flow (vascular theory), inflammation (meningitis, encephalitis), autoimmune condition like systemic lupus erythematosus, monoclonal gammopathy. Other association with brain tumors such as astrocytoma or pineal body gangliocytoma has also been described.[5]

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CLINICAL PRESENTATION

Fahr's syndrome slow and progressive course with most cases occurring in fourth to sixth decase. Few cases have been reported in the pediatric population.[6] Children present with mental retardation whereas adults present with dementia, psychiatric symptoms and movement disorders.[10] Common symptoms include dystonia, ataxia, chorea, seizure, cognitive impairment, psychotic features like delusion, anxiety, mania, depression. Children can have growth retardation, microcephaly and optic atrophy, recurrent loss of consciousness, urinary incontincence.9 But in most cases disease is asymptomatic.

DIAGNOSIS

Routine use of computed tomography has led to increased diagnosis of the condition. CT is more sensitive than magnetic resonance imaging for detecting calcifications which can easily be visualized in a non contrast scan.

The following diagnostic criteria were established:

1.Bilateral calcifications of the basal ganglia or other areas of brain on neuroimaging (may not apply to patients from families with Fahr's syndrome);

2.Progressive neurological dysfunction and/or psychiatric symptoms;

3.Onset between the ages of 40–50;

4.Absence of biochemical abnormalities and somatic states suggestive of a metabolic or mitochondrial disease;

5.Absence of toxic, infectious or traumatic causes of intracranial calcifications;

6.Positive family history of Fahr' syndrome and/or proved genetic background.

If a patient meets the last criterion, the diagnosis can be made without the presence of one of the first two criteria. In cases of a negative or unknown family history, other five criteria must be fulfilled.[8] Not all intracranial calcifications point towards Fahr's syndrome. Calcium deposits with a thin, linear or cloudy pattern have a high-specificity. On the other hand symmetric micronodular or asymmetric unilateral calcifications are not characteristic of this disease .[9]

TREATMENT

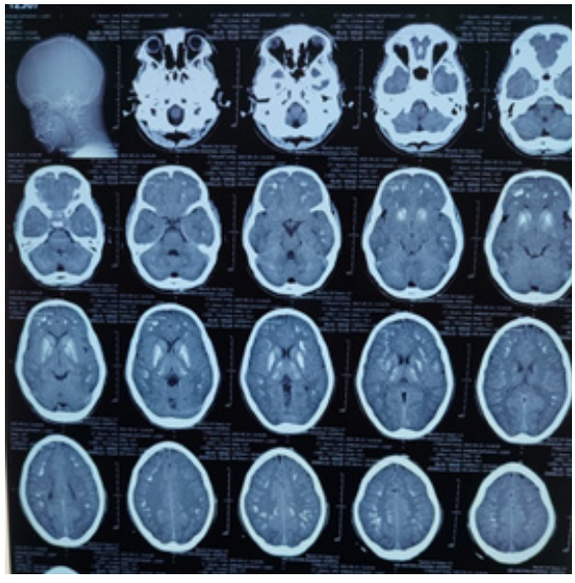
In most cases, treatment is symptomatic and includes antipsychotics, antidepressants, antiepileptic and procognitive drugs. A distinctive feature of parkinsonian syndromes with concomitant calcifications is an outstanding resistance to the therapy with levodopa. This disorder more likely results from insensitivity of postsynaptic striatal structures rather than presynaptic damage observed in the primary parkinsonism .[10]

CASE DESCRIPTION

12 year old boy from kalikot district, a remote region in karnali, nepal presented to the out patient clinic with loss of consciousness multiple episodes over a priod of two years. The seizure were associated with loss of consciousness. Patient used to fall to the ground with sudden loss of tone without any abnormal tonic/clonic movement of limbs, urinary /bowel incontinence, frothing, tongue bite, abnormal cry. Patient couldn't describe any pre seizure aura/behavioural changes. The seizure lasted around 15- 20 seconds and occurred three/four times in a week. There wasn't associated sensory symptoms. The patient had left school because of the seizure. There was no history of febrile seizure, family history of seizure. There was no postictal confusion/weakness.

History of tremor involving bilateral hands, more pronounced during writing causing deterioration in handwriting but can hold objects and perform other daily activities. Tremor started one year back and slowly progressing. Perinatal history unremarkable, completed extended program on immunization. Patient was in grade 2 before he left school. Patient has one elder brother who is in good health. They hadn't sought any medical care due to unavailability of specialist doctors. Patients systemic examination was normal.

On higher mental function examination speech was slow, muffled. Fluency was present. Comprehension to speech was present. Patient could understand spoken and written nepali language. There was no issue with short and long term memory. Horizontal nystagmus was present. Gait ataxia was present pronounced during standing and walking. Dysdiadochokinesia and past pointing were positive. Bulk, tone, power, reflex examination was within normal limits. Sensory examination was unremarkable. Fundoscopy was normal. No signs of meningeal irritation. Back examination was normal. Metabolic profile couldn't be done due to financial issues of the patient's family. Non contrast computed tomography of head was done which showed bilateral symmetric dense calcification in dentate nuclei, basal ganglia, thalami, and corona radiata. Electroencephalogram was done which showed abnormal spikes. Patient received levetiracetam for seizure control.



Discussion

Bilateral Striopallido Dentate Calcinosis (BSPDC), which is otherwise known as idiopathic Basal ganglia calcification, is a neurodegenerative disorder which is popularly known as Fahr's Syndrome. A bilateral, symmetrical, intra cranial calcification characterizes Fahr's disease with a predilection for the basal ganglia and the dentate nuclei. Because of the symmetrical involvement of these nuclei, the descriptive terminology, BSPDC, has been put forth 5 Our patient had calcification involving the basal ganglia, dentate nuclei and cerebral cortex.

This is a very rare disease of unknown prevalence. The typical age at the onset of the symptoms is 40-60 years. Our patient was only twelve years old. Few cases have been described in pediatric population. This is among the few inherited neurological conditions that lead to progressive dystonia Parkinsonism and neuropsychiatric manifestations.

The most common presentations as per the Fahr's Disease Registry are movement disorders, which account for about 55% of the cases. Among these, Parkinsonism was seen in 57% cases, chorea was seen in 19% cases, tremor was seen in 8% cases, dystonia was seen in 8% cases, athetosis was seen in 5% cases and orofacial dyskinesia was seen in 3% cases. The other neurological manifestations include a cognitive impairment, cerebellar signs, speech disorders, pyramidal signs, psychiatric features, gait disorders and sensory changes.[6]The clinical diagnosis of Fahr's disease is based on the combination of clinical features, brain imaging and on an exclusion of other causes of the intracranial calcification.[7] Our patient's main clinical features were seizure, hand tremor, gait ataxia, muffled speech.

The imaging findings of the symmetric and extensive calcification are usually typical, as was seen in our case. The disorders of calcium metabolism may occur in association with the intracerebral calcification. Hypoparathyroidism,ps eudohypoparathyroidism and hyperparathyroidism may be

associated with the intracerebral calcification. Other causes of the intracranial calcification include infectious diseases like Toxoplasmosis and Syphilis and inflammatory illnesses like SLE. But Fahr's disease represents a heterogeneous group of disorders that are not associated with any known disorder of the calcium metabolism.8

Genetic studies have shown an autosomal dominant inheritance in the familial cases. A genetic heterogeneity and an anticipatory effect also have been observed. One multigenerational family with a linkage to the IBGC1 of chromosome 14 has been identified, but the causal gene is still unknown. The genetic studies which were done on other families did not replicate the result.[9]

Benke et al., studied brain metabolism by using brain positron emission tomography with flurodeoxyglucose in a person with Fahr's disease, who presented with a predominant frontal lobe syndrome and dementia. There was a massive reduction of the glucose metabolism in both the basal ganglia and the frontal lobes, which included the orbitofrontal and the anterior cingulate areas, which correlated with the clinical picture of disinhibition and a personality change .[10]

Computed tomography scan remains the most effective screening tool. No prenatal or genetic tests are available for genetic counselling. The minimum age at which a negative CT scan can suggest the exclusion of the disease has not been established as yet. To clarify whether the disease is sporadic or familial, doing the imaging scan of the parents and other kindred is more reliable than their clinical screening.[7] Our patient was diagnosed using CT scan.

The treatment targets include symptomatic support. The response to levodopa in those with Parkinsonian features is reportedly poor. Atypical antipsychotics are preferred for the psychiatric symptoms because of the coexistence of the extra pyramidal syndrome in these group of patients. [4-6] The National Institute of Neurological Disorders and Stroke (NINDS) supports and conducts research on neurogenetic disorders such as Fahr's disease. The goals of this research are to locate and understand the actions of the genes which are involved in this disorder. Finding these genes could lead to an effective method of treating and preventing Fahr's syndrome.[5-8]

Our patient was a pediatric case with early onset symptoms. He was managed symptomatically with anti epileptic medication levetiracetam. Besides propranolol was prescribed for tremor. The parents were thoroughly explained about the diagnosis and the incurability of the condition.

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COMPETING INTEREST

The author reports no competing interest for publishing this case report.

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