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CASE REPORT

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Idiopathic basal ganglia calcification (Fahr's disease) in a 9-year-old Nigerian child

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Abstract: Fahr's disease is a rare neurodegenerative disorder characterized by deposition of calcium on the walls of blood vessels of the Basal ganglia and Dentate nuclei of the Cerebellum. Patient can present with diverse array of symptoms including but not limited to seizure, extrapyramidal symptoms and mental retardation. We report a case of a 9-year-old female child with history of recurrent seizure. Brain CT showed symmetrical calcification in the basal ganglia.

Key words: Fahr's syndrome, intracranial calcification, seizure

Introduction

Fahr's disease or Fahr's syndrome also known as idiopathic basal ganglia calcification is a rare inherited or sporadic neurological disorder that was first described by a German neurologist, Karl Theodor Fahr in 1930.[1] It is often characterized by abnormal deposition of calcium in the areas of the brain that control movements such as the basal ganglia, thalamus, dentate nucleus, cerebral cortex, cerebellum, subcortical white matter and hippocampus.[2] The mineral deposit tends to select small capillaries and small vessels of the white matter unlike in atherosclerosis.[3-7]

The disease could be inherited as either autosomal dominance or autosomal recessive and can also occur sporadically. Attempts made at localizing the locus, suggested locus 14q48[8]though no gene was identified [7] however, a second and third loci have been located on chromosome 8 and chromosome 2 respectively.[9] These different locations thus suggest a genetic heterogeneity.
Fahr's disease usually affects individuals in the 3rd and 6th decades of lives with a prevalence of <1/1,000,000 amongst adults[1,8] however a few cases have been reported in children with nodocumented prevalence rate globally or in sub-saharan Africa.[10] Fahr's disease is not commonly associated with any metabolic derangement or underlying medical conditions.[11]
The disease is characterized by abnormal deposition of calcium in areas of the brain that control movements including basal ganglia, thalamus, dentate nucleus, cerebral cortex, cerebellum, subcortical white matter, and hippocampus.[5,12] Most cases present with extra pyramidal symptoms initially. Additionally, they may present with cerebellar dysfunction, speech difficulty, dementia and neuropsychiatric symptoms.[13,14] In affected children, the disease is often characterized by inhibition of mental development and early mortality. Such children typically present with motor deficits though 40% have primarily cognitive and other psychiatric symptoms.[13,14]
Pathological features are similar in both adults and infants and which result from calcification developing within the vessel wall and in the perivascular space and ultimately extending to the neuron.[14] It is also thought to result from a defect in iron transport and free radical production, resulting in tissue damage which leads to initiation of calcification occurring secondary to presence of a Nidus comprising Mucopolysaccharide and related substances.[13-15] Progressive basal ganglia mineralization tends to compress the vessel lumen, thus initiating a cycle of impaired blood flow, neural tissue injury and mineral deposition.[13-15]

The diagnostic criteria for Fahr's disease include, bilateral calcification of the basal ganglia visualized on neuroimaging especially CT scans, progressive neurological dysfunction which includes movement disorder and/neuropsychiatric manifestations.
Others include absence of biochemical abnormalities and somatic features suggestive of a mitochondrial or metabolic disease or other systemic disorder. It is also suggestive in the absence of infectious (eg Toxoplasmosis, Tuberculosis), toxin, or traumatic cause, and family history consistent with autosomal dominant inheritance.[16-19] Normal levels of calcium, phosphorus, alkaline phosphate, parathyroid hormone help to differentiate Fahr's disease from common endocrine disorders such as hyperparathyroidism, pseudo-hypoparathyroidism and pseudo-pseudo hypoparathyroidism.[20]

Treatment is often aimed at addressing the symptoms and as well as improving quality of life.

There are few reports of Fahr's syndrome in African children making this one the first to be reported in a Nigerian Child. The aim is to encourage high index of suspicion amongst physicians. Children with recurrent a febrile seizures of unknown cause, with no postive history of the disease and who exhibit other features that resemble Fahr's syndrome should undergo neuro-imaging.

Case report

A 9-year-old female child presented to the children emergency room of Federal Medical Center, Asaba, Nigeria with symptoms of recurrent seizure and loss of consciousness. Seizures were generalized tonic-clonic, each episode lasting about 10-15 minutes associated with eventual loss of consciousness. There was no antecedent fever, head trauma, ingestion of any toxic substance, abnormal movement or gait.
Past medical history revealed previous history of recurrent seizure which started at the age of 7 years. Perinatal, natal, post-natal and milestone developmental history were significantly normal. She is presently in Primary 6, doing well academically and is the last of 4 children of the parents and the family has no history of seizure disorder.

Clinical examination revealed an unconscious child with Glasgow Coma Score of 5/15, afebrile, in no respiratory distress, with no signs of meningeal irritation. Pupils were of normal size and reacted normally to light, there was hypotonia with hyporeflexia however, other systems were grossly normal. A provisional diagnosis of recurrent seizure of unknown cause was made and some lab investiagtions requested for. The results of the Laboratory investigations as shown in Table 1 were normal and Blood culture result yielded no bacterial growth.
Further tests to rule out other possible causes of recurrent seizures were carried out including chest radiograph and abdominal ultra sound scan which showed normal results. However, the only abnormality noted was in the Cranial CT which revealed extensive symmetrical calcification foci involving the basal ganglia, thalamus and sub-cortical white matter region.

Based on the positive or abnormal brain CT findings, history, clinical features, normal blood chemistry and absence of any other underlying pathology, the diagnosis of Fahr's disease was made. The child was admitted, and based on the history of not having eaten many hours prior to the seizure and loss of consciousness was commenced on 5% dextrose-saline. She regained consciousness 6 hours later . She was further commenced onlevetiracetam 14mg/kg in 2 divided doses (7mg/kg 12 hourly) for control of seizures, was stabilized after 3 days on admission, discharged and followed up on outpatient basis.

Cranial CT showing symmetric basal ganglia calcification

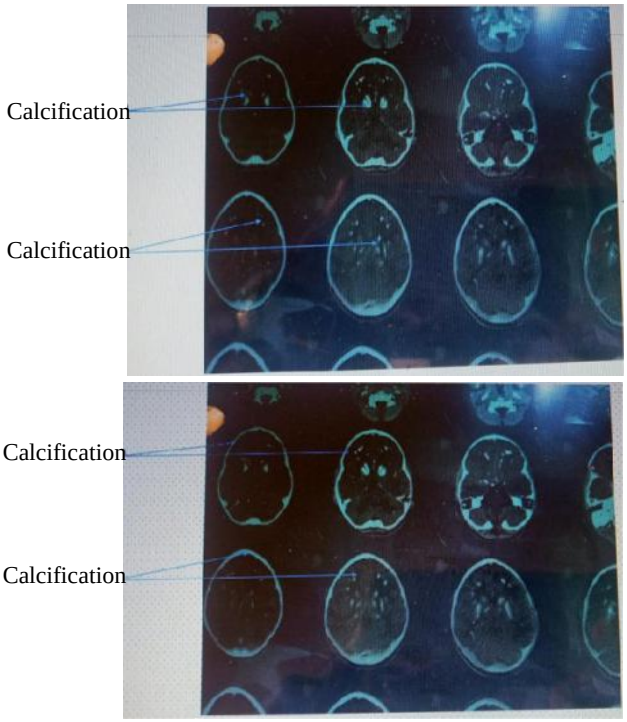

Table 1: Laboratory investigation results

Parameters	Patient's result	Normal ranges
Random Blood glucose	96mg/dl	< 200 mg/dl
CSF analysis		
CSF Protein	18mg/dl	45mg/dl
CSF Glucose	2.9mmol/l	2.5 - 4.4 mmol/l
Complete blood count		
Total WBC	5.6	4.0 -11.0 x 10^{9}/ L
PCV	46.6	36 - 48 %
Red Cell Count	5.05	4.0 - 5.2 x 10^{12} / L
Platelet count	350	150 - 450 x 10^{9}/ L
Thyroid Function Test		
T3	122 ng/dl	100 - 200ng/dl
T4	6.7 µg/dl	4.6 - 12.0
TSH	3.2 IU/L	0.4 - 4.0 IU/L
Parathyroid hormone (PTH)	38pg /ml	10 - 55
Liver function test		
Alkaline Phosphate(ALP)	13 µmol/ L	9 - 35
Alanine transaminase(ALT)	5.6 µmol / L	≤12
AspartateTransaminase (AST)	3.0 µ mol /L	≤12
Electrolyte profile		
Sodium	131 mmol/l	120-146 mmol/l
Potassium	3.7 mmol/l	3.3 - 5.0 mmol/l
Bicarbonate	24 mmol/l	20-32 mmol/l
Urea	1.2 mmol/l	1.7 -8.0 mmol/l
Creatinine	80 mmol/l	72- 127 mmol/l
Ionized Calcium	2.4 mmol/l	2.25 - 2.75 mmol/l
Inorganic Phosphorus	1.0 mmol/l	0.8 - 1.5 mmol/l
Blood culture	Yielded no bacterial growth	

Discussion

Fahr's disease is commonly found in patients in their 3rd and 6th decade of life [12,18] but this is contrary to the age of our patient who was 8 years at the time of diagnosis. The only clinical symptom this patient presented with

was recurrent seizure. Though seizure was reported by Manyan et al[12] but the most frequent presentation is neuropsychiatric and motor disorder.[12,13]

In the index patient, seizure was thought to due to neuronal damage caused by calcification as documented by Thillaigovindan and colleagues.[13] Though our patient demonstrated absence of neuropsychiatric symptoms, a diagnosis of Fahr's disease was made having met the criteria for diagnosis which included presence of symmetrical intracranial calcification in the CT Scan of the basal ganglia, normal calcium/phosphate levels, absence of other metabolic disorder underlying disease that could cause derangement in calcium/phosphate metabolism, normal levels of thyroid, parathyroid hormones and alkaline phosphatase. Intra-cerebral calcification has been suggested to be due to defective iron transport and free radical production, genetic mutation causing loss of blood brain barrier and accumulation of calcium phosphate in the brain, and abnormal lipid deposition and demyelination of the basal ganglia.[11,13-15]

Though our patient had no neuropsychiatric symptoms, symptoms of Fahr's disease have been found to vary from patient to patient and evolve as the disease evolves.[12] It may not be surprising if the index patient develops neuropsychiatric and Parkinson-like disease as the calcification progressively worsens.

Though the exact disease causing gene is not known, it has been documented that the disease locus is on chromosome 14,[7]for our patient, there was no member of the family with similar illness, so the disease is likely to be sporadic.

Treatment of fahr's disease is symptomatic and improvement in quality of life as there is no known cure for now. Our patient is currently seizure free being on treatment with levetiracetam and doing well in school in terms of academic performance.

Conclusion

Though Fahr's disease is a rare neuro-degenerative disease, more cases may be identified with increasing high index of suspicion and neuroimaging with CT scan/ MRI. Cranial CT/MRI should continue to be a standard of care for all patients with seizures.

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