ASSOCIATION OF FAHR DISEASE WITH RHABDOMYOLYSIS AND HYPOPARATHYROIDISM

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ABSTRACT

Fahr syndrome is an idiopathic deposition of calcium in the basal ganglia (most commonly in the Globus pallidus) of the brain; other most common sites may include striatum pallidum. It can have a wide variety of presentations like progressive psychosis, dementia, movement disorders, gait disturbances or it can also be asymptomatic.

Department of Neuro-medicine Hyderabad admitted this 28 year old male first. And then was referred to us in the department of Neuro-medicine JPMC Karachi. He is a known case of epilepsy for 8 years, who now presented with the complaint of fever, fits, and altered sensorium for 3 days. The CT scan of his brain showed hyperdense areas, bilateral symmetrical extensive basal and cerebral calcifications. CSF examination of the patient showed unremarkable results. On further examinations, it was found he also had Rhabdomyolysis and Hypoparathyroidism.
It is unusual to have an association of Fahr syndrome with Rhabdomyolysis and Hypoparathyroidism. Our case report describes the unique behavior of this syndrome.

INTRODUCTION: Fahr syndrome, as the name indicates, was discovered by Fahr in 1930 in a patient 55-year-old who died after a series of tetanic seizures. It is also known as idiopathic calcification of basal ganglia or bilateral striatopallidodentate calcinosis. Because there are calcium deposits in the brain particularly in areas like basal ganglia, cerebellar dentate nuclei, and white matter, with later atrophy. But the process of calcium deposits in basal ganglia only was defined by Delacour in 1850 [1-2.]

It is a rare inherited or sporadic neurological disorder with prevalence of <1/1,000,000 3-5. Fewer than 200 cases have been reported till today. It is more common in men (male: female ratio 2:1) 6. It is further divided into two types:

Primary: familial brain calcification, with no any cause other than genetic. It has been reported commonly related to chromosome 14q (IBGC1) while other loci are identified to be on chromosomes 2 nd 8 [3-8-9.]

Secondary: Brain calcification due to any metabolic, infective, autoimmune, and other causes.

Besides Fahr syndrome, there is also another condition called Fahr disease. Table 01 shows the diagnostic checklist and difference between the Fahr disease and Fahr syndrome[10]

A diagnosis of either Fahr's disease or Fahr's syndrome should be considered if some or all of the following symptoms are present:

- Basal ganglia movement disorder
- Pyramidal signs
- Cognitive impairment
- Gait disorder
- Cerebellar abnormalities
- Speech dysfunction
- Psychiatric presentations
- Sensory changes.

Consider a diagnosis of Fahr's disease if

- Age of onset 40 to 60 years
- Evidence of coarse, progressive, bilateral, symmetrical basal ganglia calcification
- Presence of genetic autosomal dominant or recessive trait

Consider a diagnosis of Fahr's syndrome if

- Age of onset 30-40 years
- Evidence of symmetrical, bilateral intracranial calcification

and

Presence of any of the following endocrinopathies:

- idiopathic hypoparathyroidism
- secondary hypoparathyroidism
- pseudohypoparathyroidism
- pseudopseudohypoparathyroidism
- hyperparathyroidism

or

Presence of any of the following:

- brucellosis infection, intrauterine or perinatal
- neuroferritinopathy
- polycystic lipomembranous osteodysplasia with sclerosing leucoencephaloathy
- Cockayne syndrome
- Aicardi-Gouteres syndrome
- tuberous sclerosis
- mitochondrial myopathy
- lipoizd proteinosis

Treatment

If Fahr's disease—

- No specific remediation; only symptomatic therapies.

If Fahr's syndrome—

- Treatment should be directed at the specific pathology, with symptomatic therapy adjunctively.

Table 01

Clinical presentation:

A person with Fahr syndrome can present in many ways. However initially, it is asymptomatic. But later in life, between 3rd and 6th decade, it can become symptomatic due to any trigger and can present with:

- Seizures often with urinary incontinence,
- Gait disturbances,
- Endocrinopathies,
- Psychosis,
- Cognitive impairment,
- Dementia,
- Basal ganglia movement disorders and
- Sensory changes etc.

Diagnosis:

Although the medical imaging techniques, like computed tomography (CT) and magnetic resonance imaging (MRI), are enough to see the calcifications, but these are not enough to diagnose a case of Fahr's syndrome. So a diagnostic criteria has been established.

Diagnostic criteria:

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 [11].

Case report

Our case report is about a 28-year-old male, known case of epilepsy for 8 years. He presented with the complaint of fever for 1 week and seizure followed by unconsciousness for 6 days. He had tonic colonic seizures associated with tongue bite, urinary incontinence and mouth froth followed by the loss of consciousness. The average time duration of his seizures was about 15-20 minutes. He developed fever in one day, which was sudden in onset, low-grade, continuous, and associated with rigors and chills, irrespective of time of occurrence. The patient also had a history of fracture of his right femur, secondary to a road traffic accident. He was diagnosed with epilepsy 8 years ago in a local clinic with no any solid reports or documentation but was started on carbamazepine 200mg OD. The patient had no history of addictions or allergies or blood transfusions. His family history is

significant, his elder brother is epileptic for 5 years and his mother is a known diabetic for an unknown period of time. On examination, we found that he was vitally stable but he had clubbing (grade one), he looked mildly anemic. He had positive meningeal irritation signs i-e neck rigidity and kerning's sign. His pupils were normal and reactive to light bilaterally. His Cardio-respiratory systems were unremarkable.

On Investigations, that we performed, we found that his Hb level was decreased to 7.9 g/dl with White cell count increasing to 14.5*10 9, neutrophils 87% and lymphocytes 10%. His serum Urea Creatinine and Electrolytes levels showed a decrease in potassium levels to 2.7mEq/L, with the marked increase in urea 145 and creatinine 6.98, suggesting acute kidney Injury. His CPK levels were increased to 9520 U/L, suggesting the diagnosis of Rhabdomyolysis, which may also have played role in his Acute Kidney Injury. His CSF examination was unremarkable. His plain CT scan of the brain was performed on 25 slice Toshiba Activion 16 CT scanner with 5.0 mm slice thickness that showed Bilateral Basal Ganglia calcification, as arrows seen in figure 1. So his clinical history, examination, and investigations led us to the diagnosis of Bilateral Basal Ganglia Calcification due to Fahr syndrome. His alkaline phosphatase levels were in normal range but his Calcium levels were decreased to 6.99 with an increase in phosphate levels to 8.40 and with serum Parathyroid Hormone levels decreased to 0.8, suggesting Hypocalcaemia due to Hypoparathyroidism. The cause of Hypoparathyroidism was not found.

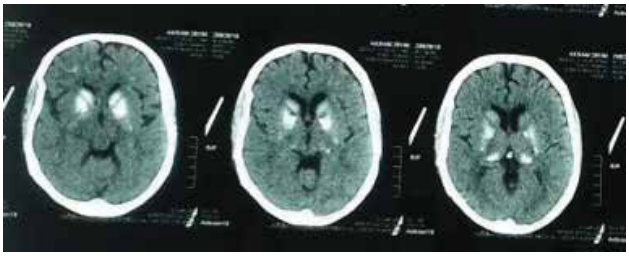

Figure.1 Plain CT scans of the brain

Discussion

Fahr syndrome, a rare case of bilateral basal ganglia calcification. Which may present with neurological clinical features like seizures, gait disturbances, dementia, psychosis, moment disorders, and sensory changes etc. Bilateral basal ganglia calcification can be differentiated into Fahr's disease and Fahr's syndrome, as stated above.

Our case is diagnosed as Fahr syndrome in a 28-year-old male known case of epilepsy for 8 years. He presented with the complaint of tonic colonic seizures and fever for 1 week, loss of consciousness for 6 days. On history, examinations and investigations of the patient we found bilateral calcification of basal ganglia on his CT scan, giving rise to diagnosis of Fahr syndrome. On further evaluating the labs of the patient we found CPK levels raised to 9520 U/L suggesting Rhabdomyolysis. And we also found serum calcium decreased to 6.99, serum phosphate of 8.40 with normal alkaline phosphatase levels, but decreased parathyroid hormone levels t 0.8 U/L suggesting strong diagnosis of Hypocalcaemia secondary to Hypoparathyroidism. The lab results also showed increased urea and creatinine levels.

As in a case report, Hypoparathyroidism, Hypothyroidism and Thrombocytopenia: Rare Constellation of Fahr's Syndrome, published in journal of endocrinology and metabolism 12. It was stated that Fahr's syndrome is associated with Hypoparathyroidism. In another study, as mentioned above, it was stated that Fahr's syndrome is associated with multiple endocrinopathies. Our case report also suggests that Fahr's syndrome is also associated with Rhabdomyolysis. The cause of Hypoparathyroidism and Rhabdomyolysis in our patient was not found.

Conclusion

We have concluded that Fahr's syndrome is associated with Rhabdomyolysis and Hypoparathyroidism. But since Fahr syndrome is a rare inherited disease it is possible to have assumption of association of Rhabdomyolysis and Hypoparathyroidism with Fahr syndrome. And thus it requires a full genetic work up to knowing its associations with other diseases and to know its treatment so that we could decrease mortality and morbidity in young patients like ours.

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