Bangladesh Crit Care J September 2024; 12 (2): 160-162

Case Report

An Elderly Lady with Tetany and Brain Calcification

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DOI: https://doi.org/10.3329/bccj.v12i2.76462

Abstract:

We present the case of a 59-year-old Bangladeshi lady who presented in Intensive Care Unit with tetany and altered level of consciousness. Tetany resolved after giving IV calcium injection. Initial laboratory investigations showed hypocalcemia. Non-contrast CT brain showed irregular bilateral symmetrical calcifications in basal ganglia, thalami, cerebellum and corona radiata. Subsequent laboratory test revealed low parathyroid hormone level. So, she was diagnosed as Fahr's syndrome due to secondary hypoparathyroidism. This is a rare neurological disorder characterized by metabolic, biochemical, neuroradiological and neuropsychiatric abnormalities due to symmetrical and bilateral intracranial calcifications.

Key words: *Basal ganglia calcification, Fahr's syndrome, Hypocalcemia, Hypoparathyroidism, Tetany.*

Introduction:

Fahr's syndrome/disease is defined as bilateral striato-pallido-dentate calcinosis, as found in neuroimaging.[1] Patients present with a wide range of neuropsychiatric symptoms and extrapyramidal disorders. Clinical correlation with radiological and biochemical findings, especially calcium metabolism, is crucial in diagnosis and differentiating between Fahr's syndrome and Fahr's disease. Here we describe a case who presented with tetany. After proper evaluation, she was ultimately diagnosed as Fahr's syndrome.

Case Report:

A 59-year-old hypertensive female presented with abnormal movement of limbs for 10 days in in-patient unit of a private hospital in Dhaka city. Immediate after admission, tetany was observed & patient had decreased level of consciousness. So, she was transferred to Intensive Care Unit (ICU) in another tertiary care hospital. She had no history of fever prior to this illness. Patient had thyroidectomy surgery 15 years back. No other members of her family had such type of illness. On admission in ICU, her GCS was 13/15 (E4M5V4), pulse 110/min, BP 130/90 mm Hg, respiratory rate 18 breaths/min, SpO_2 97% with 2L O_2 via nasal prong and arterial blood gas (ABG) analysis showed respiratory alkalosis (pH:7.47, PaO_2: 70, $PaCO_2$: 33, HCO_3: 25). Bilateral cataracts and tetany were observed during examination. Chvostek's sign and Trousseau's sign were positive. There was neither any signs of focal neurological deficits nor any signs of meningeal irritation.

Introduction:

Laboratory tests showed severe hypocalcemia (3.4 mg/dl, normal range: 8-10.5 mg/dl), and hypokalemia (3 mg/dl, normal range: 3.5-5.1 mg/dl). Other serum electrolytes, serum phosphate (PO_4), complete blood count, blood urea, serum creatinine, liver enzymes, urine R/M/E, Chest X-ray, ECG

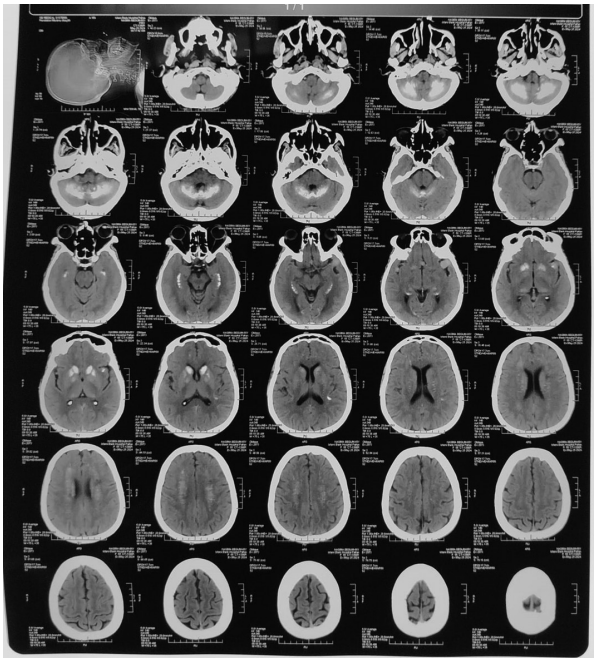

Figure 1: Axial view of Brain CT showing irregular bilateral symmetrical calcifications in basal ganglia, thalami, cerebellum and corona radiata

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Received : August 14, 2024; Accepted : August 31, 2024

and Echocardiography were normal. Non-contrast computed tomography (CT) brain was done which showed irregular bilateral symmetrical calcifications in basal ganglia, thalami, cerebellum and corona radiata (fig 1and 2). Based on clinical features, hypocalcemia and CT scan findings, Fahr's syndrome/disease was suspected. Parathyroid hormone (PTH) level was sent and it was found to be low (6 pg/ml, normal range: 9-80pg/ml). The patient was then diagnosed as Fahr's syndrome due to secondary hypoparathyroidism.

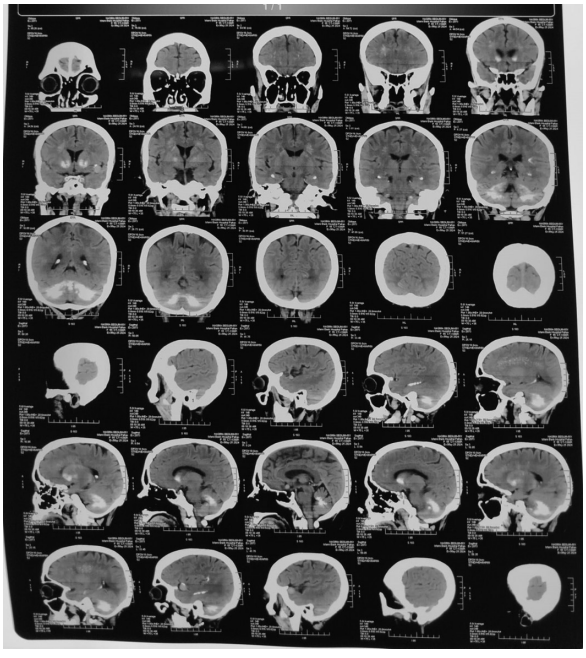

Figure 2: Coronal and Sagittal section of brain CT scan of patient showing calcifications in basal ganglia, thalami, cerebellum and corona radiata

As she had tetany on admission, so intravenous (IV) 10% calcium gluconate was given immediately. Her condition was improved and she was kept on oral calcium supplementation and vitamin D. Later she was transferred under Endocrinologist for further evaluation and management.

Discussion:

Fahr's syndrome is characterized by various neurological disorders due to abnormal intracranial calcium deposits in various areas, especially in basal ganglia, dentate nucleus and cerebral cortex. German neurologist Karl Theodor Fahr first described this condition in 1930.[2]It is also called Bilateral Striopallido Dentate Calcinosis (BSPDC) or Idiopathic Basal Ganglia Calcification (IBGC). It is a rare neuro-degenrative disorder having prevalence of <1/1,000,000.[3]

Though initially Fahr's syndrome and Fahr's disease were considered as same entity, now-a-days they are encountered as different entity. Fahr's syndrome is caused by secondary factors; on the other hand, Fahr's disease arises from a primary hereditary condition.[4] The syndrome usually affects individuals in the 3rd and 4th decades. Fahr's disease is commonly transmitted as an Autosomal Dominant trait. It may also passed as Recessive trait, or may occur sporadically.[4] It affects individuals aged 40-60 years. Though our patient was an elderly lady, but she had underlying disorder of parathyroid gland; so diagnosed as Fahr's syndrome.

There are several aetiological factors for Fahr's syndrome (table I). Among them, Endocrine disorders, especially parathyroid problems, are the most common. Production of PTH is reduced in hypoparathyroidism which causes hypocalcemia and hyperphosphatemia, and ultimately this leads to ectopic calcifications. Idiopathic hypoparathyroidism is characterized by absence, atrophy or fatty replacement of the parathyroid glands. Secondary hypoparathyroidism occur as a complication of post-thyroidectomy surgery. It usually takes around 8-10 years to cause basal ganglia calcification from hypoparathyroidism alone.[2] As vitamin D plays important role in calcium metabolism, disturbance in its homeostasis has implications in Fahr's syndrome. Intrauterine or perinatal infection by Toxoplasma, Rubella, Cytomegalovirus (CMV), and Herpes may cause calcification in basal ganglia and dentate nuclei.[4] Intracranial calcification may worsen with advancing age and unregulated calcium serum level.[5] In Fahr's disease, the calcification occur from genetic mutation (SLC20A2 and XPR1).[6]

Table I: Underlying causes of Fahr's syndrome [4]

Aetiologies	
Endocrine disorders	Idiopathic hypoparathyroidism Secondary hypoparathyroidism Pseudohypoparathyroidism Pseudo-pseudo hypoparathyroidism Hyperparathyroidism
Adult onset neuro-degenerative conditions	Neurodegeneration with brain iron accumulation disease Neuroferritonopathy Polycystic lipomembranousosteodysplasia with sclerosingleukoencephalopathy
Infectious disease	Intrauterine and perinatal infections Cockayne syndrome type 1 Cockayne syndrome type 2
Inherited or early onset syndrome	Aicardi-Gouteres syndrome Tuberous sclerosis complex Brucellosis Coat's disease

A variety of neurological features are associated with Fahr's syndrome. Extent and side of brain calcification have an effect on clinical manifestations. Common clinical features are loss of consciousness, seizures and tetany. Chorea, tremors, myoclonus, dystonia, spasticity, gait disorder, dementia, parkinsonism and speech disorder are other common signs. Dementia and extra-pyramidal symptoms become worse with extensive calcifications.[4] Neuropsychiatric symptoms include difficulty with concentration and memory, changes in personality or behaviors, psychosis and dementia.

Some hematological and biochemical tests are done in Fahr's syndrome. Serum Calcium, Magnesium, Phosphorus, Alkaline phosphatase, Calcitonin, PTH and 1,25 hydroxy vitamin D3 should be checked. Analysis of CSF is done to assess for infectious aetiology and autoimmune disease. Blood and urinary analysis may be done to detect disorders of calcium metabolism and heavy metal intoxication. If no other primary cause for brain calcification is detected or if the family history is suggestive of autosomal dominant inheritance, then molecular genetic testing should be considered.[4] Calcificationsappear as clusters of punctuate densities which are distributed symmetrically above Sella Turcica and lateral to the midline in skull X-ray. Subcortical and cerebellar calcifications appear wavy in radiograph. [4]CT scan of brain is the preferable diagnostic tool to detect Fahr's disease and syndrome. Brain calcification is progressive and gradual. Lenticular nucleus, especially the internal globus pallidus, cerebellar gyri, brain stem, centrum semiovale and subcortical white matter are the frequently affected area.[4] Though basal ganglia calcification is an incidental finding in about 0.3%-1.5% of brain CT scans in elderly people, they do not have associated clinical findings and considered as physiological calcification.[7] Age related basal ganglia calcifications are usually small, asymmetric and limited to globus pallidus.[8] Other sites for physiological intra-cranial calcification are pineal gland (most common), choroid plexus (second common site), habenula, falx cerebri, and cerebellar tentorium.[2] Fahr's syndrome can be detected by magnetic resonance imaging (MRI) also. Calcified areas appear as low intensity area on both T2 and T2 images.[4] There may be prolongation of QT interval in ECG. Arrhythmias can be found in patients with severe hypocalcemia (Ca<5 mg/dl).[2]

Treatment for Fahr's syndrome is tailored to the underlying condition. Symptomatic treatment is needed in most patients. Anti-epileptic is given for seizure, Atypical anti-psychotic for depression and mood related disorders, Clonazepam for dystonia, and Anti-parkinsonian for Parkinsonism.[1,9] It should be remembered that exacerbation of extra-pyramidal symptoms may occur with use of anti-psychotic in patients with features of psychosis, irritability and other behavioral disorders. Some anti-epileptics, like phenytoin, phenobarbital and carbamazepine, may cause vitamin D deficiency and thus worsen hypocalcemia. So, anti-epileptics without any adverse effects on calcium and vitamin D metabolism, like levetiracetam, should be used in patients with seizure.[2] Management goal for hypoparathyroidism is to maintain serum calcium level within the low-normal range, and serum phosphorus level in the high-normal range. Target is to reduce symptoms of hypocalcemia, minimize the risk of kidney stones and prevent ectopic calcification deposition in tissues. As genetic mutation is the main pathology in Fahr's disease, there is no specific therapy till date. Some authors suggested that vitamin D may be potential treatment in these patients.[2,6] Vitamin D may reduce intracranial calcification by binding to SLC20A2 gene, the gene-mutation responsible for Fahr's disease.[6] This mechanism may inhibit the progression of disease.

Asymptomatic family members (age >18 years) of patient of Fahr's disease may do brain CT scan, but it cannot predict age of onset, type of symptoms or rate of progression. At risk individuals younger than 18 years should not be tested because of psychological impact and social stigmata.[4] Asymptomatic individuals older than 18 years should do test while making decisions regarding conception and career planning. Those with positive test result need long term follow-up and evaluations.

Conclusion:

Presence of symmetric, bilateral and multiple calcifications in head CT scan, especially in basal ganglia, should always raise consideration of Fahr's syndrome or disease. Distinguishing physiological calcification from pathological calcification is of utmost importance. Both Fahr's syndrome and disease can cause various neuropsychiatric manifestations. Identification of underlying disorder is crucial for preventing progression of Fahr's syndrome. Future research is needed to develop new treatment modalities as currently there is lack of specific treatment.

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