Intracranial Calcinosis: Fahr's Syndrome

Sir,

A 42-year-old male presented with a history of four episodes of generalised tonic-clonic seizures in the last 24 hours. He had been suffering from a similar type of seizure episode for the last 2 years, for which he was taking phenytoin tablets. Despite this treatment, he frequently had repeated attacks of seizures. He had no relevant family history. He denied fever, headache, vomiting, visual diminution, chronic diarrhoea or history of surgery, irradiation, trauma, or substance abuse. On examination, the patient was actively convulsing and had vital parameters such as a pulse rate of 110 beats per min, blood pressure of 120/86 mmHg, a respiratory rate of 20 breaths per minute and a temperature of 99.30f. There was no facial dysmorphism or any other musculoskeletal abnormality. Chovstek's sign and Trousseau's sign were present. After the postictal period, his neurological examination showed no abnormality in sensorial, cognition, sensory, motor, cranial nerve and cerebellar systems. Other systemic examinations were unremarkable.

Initial, laboratory tests, including hemogram, blood sugar, renal function, liver function and arterial blood gas analysis, were within the normal range. The notable results included low serum calcium (3.1 mg/dL) and high serum phosphorus (6.64 mg/dL). In the meantime, seizures were controlled with intravenous calcium gluconate, midazolam and antiepileptics. On further evaluation, intact serum parathyroid hormone was <2.9 pg/ml (reference value 18.5-88) and serum vitamin D was 25.9 ng/ml (sufficiency 30–100 ng/ml). The thyroid function test, serum cortisol and adrenocorticotropic hormones were normal. A computed tomography scan of the brain showed a bilaterally symmetrical area of calcification in the periventricular white matter, bilateral basal ganglia, thalami and both cerebellar lobes [Figure 1a-c]. The presence of severe hypocalcaemia, elevated phosphorus level, normal renal functions and inappropriately low parathormone level confirmed the diagnosis of primary hypoparathyroidism. Electroencephalography, two-dimensional echocardiography, chest x-ray and abdominal ultrasonography did not reveal any pathology. The patient was discharged on levetiracetam 500 mg twice a day, calcitriol 0.5 µg/day and elemental calcium 1 gm/day. At the follow up of 6 months, he was seizure free and taking only calcium and vitamin d tablets.

Basal ganglia calcification is a neurodegenerative disorder. Fahr's disease is a primary form of idiopathic basal ganglia calcification. On the other hand, Fahr's syndrome term is used for the acquired condition of basal ganglia calcification as a result of secondary causes.[1] Parathyroid gland-related disorders are most commonly associated with Fahr's syndrome [Table 1]. Other less common causes are metabolic and post-infectious.[1,2] The common manifestation of basal ganglia calcification ranges from increased irritability to lethargy, psychiatric and sensory symptoms, tetany, seizure, spasticity, altered mental status, impaired cognitions, movement, gait and speech disorders to coma and intracranial haemorrhage.[3]

The decreased calcium-phosphorus ratio and altered calcium homeostasis in primary hypoparathyroidism lead to microscopic colloid deposition and perivascular calcification in cerebral vessels, predominantly in the basal ganglia, and then spread to adjacent tissues. Basal ganglia calcification is directly correlated with the duration and severity of hypocalcaemia, the presence of choroid plexus calcification and cataract.[3,4]

Fahr's disease is an idiopathic condition also known as bilateral strio-pallido-dentate calcinosis and a diagnosis of exclusion. Fahr's disease is predominantly inherited as an autosomal dominant trait. Family history, a slightly later age at onset of symptoms with progressive neuro-psychiatric symptoms and coarse bilateral symmetrical basal ganglia calcification favours Fahr's disease. The management of a seizure in Fahr's disease requires antiepileptics with supportive treatment, while a seizure in Fahr's syndrome due to idiopathic hypoparathyroidism or pseudo-hypoparathyroidism requires calcium, calcitriol and vitamin D therapy.[1,5,6]

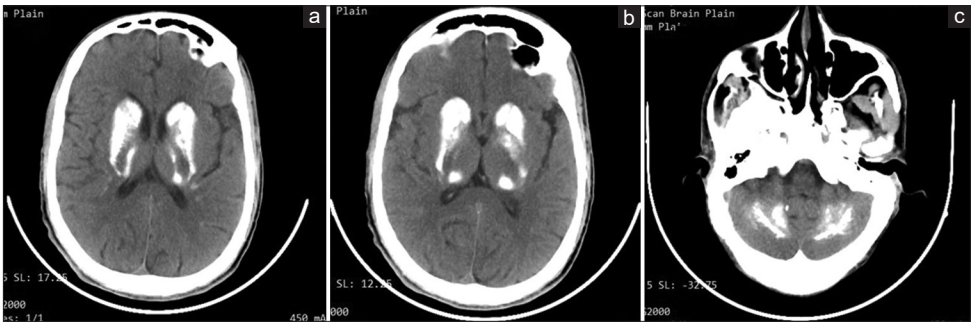

Figure 1: (a-c). Brain non-contrast computed tomography (CT) showed bilateral symmetrical calcification in the basal ganglia, thalamus and cerebellar hemispheres

Table 1: Causes of basal ganglia calcification[1-5]

Physiological: Normal aging finding (0.3-1.5% of CT brain)
Primary form - Fahr's disease - (Genes SLC20A2 on 8p11.21, PDGFRB on 5q32, PDGFB on 22q13.1, XPR1 on 1q25.3 and MYORG on 9p13.3
Secondary form –Fahar's syndrome
Endocrine: Parathyroid gland related disorders
Idiopathic hypoparathyroidism
Secondary hypoparathyroidism
Pseudo-hypoparathyroidism
Pseudo-pseudo-hypoparathyroidism
Hyperparathyroidism.
Post infectious. Toxoplasmosis, Herpes, AIDS, Brucellosis, TORCH complex
Toxin exposure: lead, carbon monoxide
Disimmunopathies: SLE
Other conditions
Aicardi-Gouteres syndrome
Tuberous sclerosis complex
Cockayne syndrome I and II
Mitochondrial diseases (MELAS, MERRF)
Coat's disease
Kenny Caffey syndrome type 1
Mitochondrial myopathy
Neurodegeneration with brain iron accumulation disease, Neuroferritinopathy,
Polycystic Lipomembranous Osteodysplasia with Sclerosing Leukoencepalopathy

SLC20A2, solute carrier family 20 member 2; PDGFB, platelet-derived growth factor beta; PDGFRB, platelet-derived growth factor receptor beta; XPR1, Xenotropic and Polytropic Retrovirus Receptor 1; MYORG, Myogenic Regulating Glycosilase; AIDS, acquired immune deficiency syndrome; TOTCH, toxoplasmosis, rubella, cytomegalovirus, or herpes simplex viruses; SLE, Systemic lupus erythematosus; MELAS, mitochondrial encephalopathy, lactic acidosis, and stsroke-like episodes; MERRF, myoclonic epilepsy with ragged red fibers

We conclude that Fahr's syndrome should be suspected if any patient presents with a seizure or altered mental status and has symmetrical and abnormal intracranial calcification. Early diagnosis with an endocrine workup for hypoparathyroidism and brain imaging is of the utmost importance. Early and proper treatment with calcium and Vitamin D, besides regular monitoring of serum calcium and phosphate levels, should be done for the prevention of neurological complications in patients with hypoparathyroidism.

Consent

Informed consent was obtained.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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