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CASUISTIC PAPER

Secondary Fahr's syndrome mimicking meningoencephalitis

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ABSTRACT

Introduction and aim. Fahr's disease is a rare neurological disorder characterized by bilateral basal ganglia calcifications. The aim of this report is to highlight a case of Fahr's disease with atypical features such as neck rigidity and peripheral nerve involvement.

Description of the case. Here, we present the case of a South Asian patient with secondary Fahr's disease whose clinical presentation mimicked that of meningoencephalitis. The patient had neurological and neuropsychiatric symptoms along with abnormal body movements. She also had restricted neck mobility. Computed tomography of the head revealed bilateral dense calcifications in the basal ganglia suggestive of Fahr's syndrome. Investigations revealed severe hypocalcemia, hyperphosphatemia, and low parathyroid hormone levels, which led to the identification of hypoparathyroidism as the underlying cause. The presence of pre-existing epilepsy and neck rigidity made the diagnosis difficult. The relatively rapid development of symptoms along with the presence of peripheral nerve involvement made this case even more unique. Calcium levels were corrected, and there was a marked symptomatic improvement.

Conclusion. Neck rigidity and restricted neck mobility may be present in cases of Fahr's syndrome due to calcifications of the nuchal ligament or other spinal ligaments and thus must be differentiated from meningoencephalitis. Although the symptoms of Fahr's syndrome are generally limited to the central nervous system, there may be involvement of the peripheral nerves as well.

Keywords. calcinosis, calcium metabolism disorders, Fahr's disease, hypoparathyroidism, intracranial calcification

Introduction

The deposition of calcium in the brain tissue or its blood vessels is referred to as intracranial calcification, whose occurrence varies from 1% in younger people to as high as 20% in the elderly population.[1] Depending on the site of involvement and the size of the lesion, intracranial calcifications can lead to a wide array of clinical presentations. Basal ganglia calcifications may be found incidentally during neuroimaging in asymptomatic individuals or may result from various neurological and metabolic diseases.[2] One such pathological condition is Fahr's disease, a condition characterized by bilateral intracranial calcifications, particularly in parts of the brain that control movement (including the basal ganglia).[3]

It is a rare condition that generally presents with extrapyramidal symptoms, cerebellar symptoms, problems with speech, dementia, etc.[4] Here, we describe a case of Fahr's syndrome secondary to hypoparathyroidism, mimicking meningoencephalitis with neuropsychiatric manifestations.

Description of the case

History and examination

A 32-year-old lady presented with complaints of generalized weakness for two months, inability to take oral

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feeds, inability to sit or stand without support, loss of voluntary control over defecation for one week, and altered sensorium for the last five days. She also had on-and-off finger paresthesia over the course of the last couple of months. She had a history of significant weight loss of around ten kilograms in the past six months. She had one episode of fever five days ago, which was resolved by taking medication. The patient had a known case of epilepsy and had been controlled on anti-epileptic medications levetiracetam and valproate for the past 20 years. She was diagnosed with dilated cardiomyopathy (with an ejection fraction of 35%) at another hospital and was taking digoxin for it. There was no history of loss of consciousness, focal neurological weaknesses, or any history of trauma, radiation, or neck surgery.

Physical examination revealed the presence of pallor, a blood pressure of 90/60 mmHg, and a normal body temperature. Bilateral coarse crepitations were noted on auscultation of the chest. The cardiovascular examination findings were unremarkable. A neurological examination was then conducted: higher mental functions could not be assessed owing to her poor sensorium; examination of the cranial nerves was unremarkable; motor examination showed a normal tone of all major muscle groups, but the power could not be assessed properly due to the poor sensorium and abnormal body movements; sensory examination could not be performed; all deep tendon reflexes were 1+, revealing global hyporeflexia; and signs of meningeal irritation were present in the form of neck rigidity and restricted side-to-side neck movements, while Kernig's sign and Brudzinski's sign were negative. She had continuous abnormal movements involving the entire body, mimicking generalized seizures, which were exaggerated on initiation of any voluntary motor activity but were present even at rest. The psychiatric evaluation revealed that the patient had emotional lability and echolalia.

Investigations

Her hemogram showed hemoglobin levels of 7 grams per deciliter and a leukocyte count of 18,000 cells/μL. Urine analysis showed no presence of pus cells, nitrite, or leukocyte esterase positivity. Both blood and urine cultures yielded sterile results, and the chest X-ray appeared normal. Kidney function tests revealed very low serum calcium levels of 3.5 milligrams per deciliter (mg/dL), hyperphosphatemia (9.1 mg/dL), and hypokalemia (3.2 mg/dL).

In view of the hypocalcemia, serum vitamin D and parathyroid hormone (PTH) levels were investigated, and it was seen that vitamin D levels were normal while serum PTH levels were low, indicating primary hypoparathyroidism. Computed tomography (CT) of the head and neck revealed the presence of bilateral symmetrical dense calcifications involving the basal ganglia and caudate lobes, suggestive of Fahr's syndrome and calcifications of the nuchal ligament (Fig. 1).

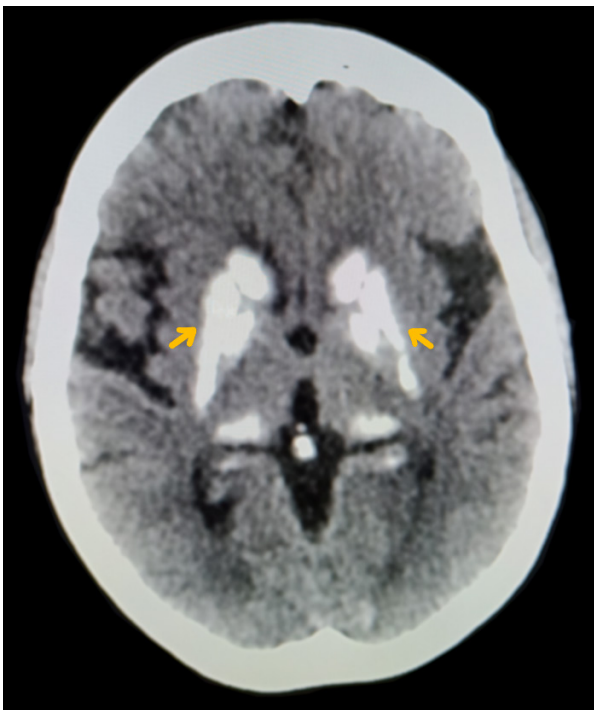

Fig. 1. Computed tomography (CT) of the head with arrows pointing to bilateral dense calcifications in the basal ganglia suggestive of Fahr's syndrome

Thus, a diagnosis of Fahr's syndrome secondary to primary hypoparathyroidism was established.

Differential diagnoses

Initially, meningoencephalitis with neuropsychiatric manifestations was suspected because of her altered mental status, abnormal body movements, neck rigidity, and elevated leukocyte count. A sample of the cerebrospinal fluid (CSF) was sent for biochemical, pathological, and microbiological analysis, but the results were unremarkable, which made meningoencephalitis unlikely. Digoxin toxicity was another differential to be considered as the patient had marked hypokalemia as a predisposing factor along with gastrointestinal disturbances and confusion, but a thorough medication history did not support this diagnosis.

Treatment

The patient was treated using intravenous calcium gluconate; five ampoules (50 milliliters) of 10% calcium gluconate were mixed in 100 milliliters of a 5% dextrose solution and infused slowly over an hour, three times a day. Intravenous magnesium sulfate, 2 grams, three times per day, was added as well. Her serum calcium levels improved from 3.5 mg/dL to 6 mg/dL, following which she was started on active vitamin D3 and hydrochlorothiazide. The calcium gradually reached

normal levels. Therapy with amantadine was started, and trihexyphenidyl was added later to avoid the extrapyramidal side effects. Transthoracic echocardiography revealed an ejection fraction of 57%, and digoxin was stopped. The patient was found to have subclinical hypothyroidism with a thyroid stimulating hormone (TSH) level of 20 micro-international units per milliliter (mIU/mL) and was started on low-dose levothyroxine.

Outcome and follow-up

The abnormal movements markedly decreased in intensity after her calcium levels were corrected but were still persisting, and thus, lamotrigine was prescribed in place of valproate as motor side effects are a known complication of it. There was a significant symptomatic improvement in the patient during her stay at the hospital. Her psychiatric symptoms also subsided gradually. She has been planned for teriparatide supplementation if her calcium levels continue to be on the lower side in the subsequent follow-up visits.

Discussion

Fahr's disease, named after Karl Theodore Fahr, is a disease characterized by bilateral calcifications in the brain, particularly involving the basal ganglia, and is thus also known as bilateral striopallidodentate calcinosis.[5] It is a rare neurological disorder that is classified as either primary or secondary based on the underlying etiology. It typically emerges in individuals aged between 40 and 50. The exact prevalence of the disease remains uncertain due to limited studies on the family members of affected patients.[6]

Secondary forms of the disorder are caused by an underlying systemic or metabolic disease. The etiologies that have been reported so far are calcium and phosphorus abnormalities like hypervitaminosis D, hypoparathyroidism, infections (including toxoplasmosis, tuberculosis, brucellosis, acquired immunodeficiency syndrome, and TORCH complex), toxic exposures (lead and carbon monoxide), astrocytoma, and immune disorders like systemic lupus erythematosus.[7] Hypoparathyroidism has been associated most frequently with Fahr's syndrome, even though it is not clinically common.[4] Thus, cases of basal ganglia calcifications with neurological signs and symptoms should be investigated for calcium and phosphate metabolic errors.

Hypoparathyroidism is a rare endocrine disorder caused by either a defect in the secretion or the effect of PTH.[8] It has a variety of clinical presentations, but neuromuscular irritability is one of the most common symptoms that occurs due to low blood calcium levels. The exact mechanism that leads to the calcification of the basal ganglia in hypoparathyroidism is not known, but a number of theories have been postulated to explain it. One potential explanation has been attributed to hyperphosphatemia, wherein the activation of the inorganic phosphate transporter (PiT1) due to elevated serum phosphate levels is thought to increase the expression of osteogenic molecules in the gray matter and the caudate nucleus.[9] Some studies also implicate the local destruction of the blood-brain barrier in abnormal calcification.[10] It is also postulated that metabolic dysfunctions cause an aberrant calcium/phosphorus ratio, which causes colloids to precipitate in cerebral arteries and lead to the formation of the calcified deposits.[11]

When it comes to clinical presentation, most individuals with intracranial calcifications are asymptomatic, and the discovery of these calcifications is often incidental, with no significant clinical consequences.[12] Even most cases of diagnosed Fahr's disease have minimal to no symptoms.[13] Among the relatively few cases of symptomatic Fahr's disease reported so far, the clinical manifestations are quite diverse and include neurological problems (like seizures, myoclonus, spasticity, gait disorder, speech impairment, dementia, coma, etc.), movement disorders (like unsteady gait, clumsiness, involuntary movements, muscle cramping, and fatigability), and neuropsychiatric symptoms (like psychosis, depression, deterioration of intelligence, inability to make decisions, etc.).[4] All three categories of symptoms were present in this case.

This patient was particularly unique because the history of epileptic disorder obscured some of the symptoms arising due to Fahr's syndrome, and it is difficult to point out from history alone which symptoms may have predated the onset of the calcifications. Another interesting finding was the presence of signs of meningeal irritation and the development of altered sensorium, coupled with the history of an episode of fever, which led to the initial impression of meningoencephalitis. Even though the CSF analysis ruled out that diagnosis, the findings of neck rigidity and restricted neck mobility are noteworthy. The neck rigidity could have been due to calcifications of the nuchal ligament or other ligaments around the vertebral column, which have been previously reported in a few cases of hypoparathyroidism.[14] This, along with the neuropsychiatric symptoms, were the reasons for this patient's clinical presentation mimicking meningoencephalitis.

Another important feature is that the clinical findings are generally limited to the central nervous system (CNS) in Fahr's disease,[15] but in this case, there was involvement of the peripheral nerves as well in the form of finger paresthesia, which was most probably caused by hypocalcemia. We found it intriguing that the patient's symptoms manifested in a relatively short amount of time and were quite severe, considering that Fahr's syndrome is typically a paucisymptomatic disorder that develops slowly and indolently, as previous reports have indicated.[16]

For the management of Fahr's disease, there have been various suggestions put forward that rely on limited clinical experience. The treatment of Fahr's syndrome is primarily symptomatic and focused on treating the underlying etiology of the secondary disease. It has been recommended that appropriate antiepileptic drugs be used for seizures, and patients who develop psychiatric symptoms should be treated with mood stabilizers or antipsychotic drugs.[7] Atypical antipsychotics may be preferred because of the presence of extrapyramidal symptoms in many cases of Fahr's disease.[17] Among the anti-epileptics, newer agents like levetiracetam and lamotrigine have been recommended, as the earlier anti-epileptic drugs such as phenytoin, carbamazepine, and valproate can impede the absorption of calcium and metabolism of vitamin D, resulting in a detrimental impact on calcium balance.[13]

For secondary forms of the disease, early diagnosis and treatment of the underlying cause may help stop the progression of the calcification and even reverse it in a few cases.[4] In this case, correction of the electrolyte imbalance arising due to hypoparathyroidism was our primary goal. Hypoparathyroidism is one of the very few hormone deficiency syndromes where the primary treatment is not simply the replacement of the hormone. Calcium and vitamin D supplementation, along with the use of thiazide diuretics, remain the mainstays for the long-term management of hypoparathyroidism, but maintaining the eucalcemic state while avoiding complications like hypercalciuria is a challenge.[8] The correction of the calcium and phosphate levels led to a significant improvement in the abnormal body movements in our patient, similar to the cases reported by Maghraoui et al. and Abe et al. who found that correcting the serum levels of these electrolytes led to an improvement in seizures and movement disorders.[18,19]

Conclusion

Cases of basal ganglia calcification with neurological signs and symptoms should be investigated for calcium and phosphate metabolic errors. Neck rigidity and restricted neck mobility may be present in cases of Fahr's syndrome due to calcifications of the nuchal ligament or other spinal ligaments and thus must be differentiated from meningoencephalitis. Although the symptoms of Fahr's syndrome are generally limited to the CNS, there may be involvement of the peripheral nerves as well. The management of Fahr's syndrome is generally aimed at providing symptomatic relief and treating the underlying cause.

Declarations

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Author contributions

Conceptualization, K.V. and V.K.; Methodology & Patient Care, K.V., V.K., A.V.H., R.B., and V.S.O.; Investigation, K.V. and A.V.H.; Resources, V.K.; Data Curation, K.V., A.V.H., R.B., and V.S.O.; Writing – Original Draft Preparation, R.B.; Writing – Review & Editing, K.V. and V.S.O.; Visualization, R.B., V.S.O.; Supervision, V.K.

Conflicts of interest

The authors declare no competing interests.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Ethics approval

Written informed consent was taken from the patient.

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