FAHR'S SYNDROME SECONDARY TO HYPOPARATHYROIDSM MIMICKING AS PARKINSON'S DISEASE: A CASE REPORT

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April 20, 2024

INTRODUCTION:

Fahr's disease or Fahr's syndrome is characterized by the calcification of basal ganglia and cerebral cortex, which is usually transmitted in an autosomal dominant manner. It is a rare neurological condition and most of the patients with the disease condition present with movement disorders, tremors, dyskinesia, and sometimes gait disturbances, cognitive impairment, speech disturbances, psychiatric changes such as mania, sensory changes or even pain [1-3]. Fahr's disease should be differentiated from Fahr's syndrome, which is usually secondary to underlying systemic pathology, this could be differentiated with blood tests for serum calcium, iPTH, along with other routine blood investigations. Moreover, basal ganglia calcification seen in CT scans could radiologically mimic the disease condition, thus clinical correlation with radiological investigations are the key in the diagnosis of Fahr's disease [2, 4, 5]. Here, we present a case of a 65-year-old male, with Fahr's syndrome secondary to hyperparathyroidism which initially mimicked as Parkinson's disease and later improved after starting the patient on vitamin D and calcium carbonate therapy.

CASE REPORT:

CASE HISTORY:

A 65-year-old male, with no previously known co-morbidities presented to the Neurology department with the complaint of tremors, slowness of movements and occasional postural instability for the last 1 year. According to the patient the symptoms were gradual on progression and was increasing in intensity for the last 1-1.5 months. Moreover, the patient also had a recent newly developed history of headache, generalized with no any relevant aggravating or relieving factor, along with recurrent falls for the last 3 days. There was no history of seizure-like activities, loss of consciousness, nausea, vomiting, paralysis/paresis. The patient had no significant past history nor any similar family history. The vitals were normal during the arrival to the clinic. On clinical examination, there a positive Chvostek sign was seen. Moreover, rigidity and narrow based gait was noted. The power, bulk and tone were normal in all 4 limbs. There was no sensory deficit and plantar reflex was down going.

METHODS:

A series of laboratory investigations were sent which showed a decreased serum calcium level of 7 mg/dL (reference range, 8.6 – 10.2 mg/dL), decreased serum phosphate level of 1.9 mg/dL (reference range, 3 –

4.5 mg/dL), and a decreased parathrome level of 6.6 pg/mL (reference range, 15 – 65 pg/mL). Detailed laboratory workup is given in Table 1.

Table 1: Blood investigation reports

Investigations	**Value**	**Reference Range**
Hemoglobin	12.4 gm%	(13-18 gm%)
Total Leucocyte Count	8600 /cumm	(4000-11000 /cumm)
Sodium/Potassium	136/4.3	(135-145 / 3.5-5.2)
BUN/Creatinine	14/0.9 (mg/dL)	(7-18 / 0.8-1.3 mg/dL)
S. Calcium	**7 mg/dL**	8.6-10.2 mg/dL
S. Phosphate	**1.9 mg/dL**	3-4.5 mg/dL
Parathormone levels	**6.6 pg/mL**	15-65 pg/mL
S. Albumin	**3.1 mg/dL**	3.8-4.9 mg/dL
Thyroid function test fT3/fT4/TSH	3.01/1.31/0.755	(2.77-5.27 pg/mL | 0.78-2.19 ng/dL | 0.465-4.68 mIU/L)
Serology HIV 1&2 Ag/AntiHCV Ab/HBsAg/VDRL (RPR)	NON REACTIVE	NON REACTIVE

The patient was then subjected to radiological investigations. Non-contrast CT of Head was done which showed symmetrical coarse calcifications involving bilateral centrum semiovale, corona radiate, basal ganglia (caudate nucleus and globus pallidi), pulvinar of thalami, dentate nuclei and cerebellum (Figure 1). MRI was done which showed changes in bilateral caudate nucleus and globus pallidi (Figure 2).

CONCLUSION AND RESULTS:

A diagnosis of Fahr's syndrome secondary to hypoparathyroidism was made. The patient was then started on intravenous calcium gluconate therapy followed by oral vitamin D and calcium carbonate therapy. He was advised to follow up in 3 months. Upon follow up on 3 months, the patient's symptoms were clinically improving and thus the oral medications were continued.

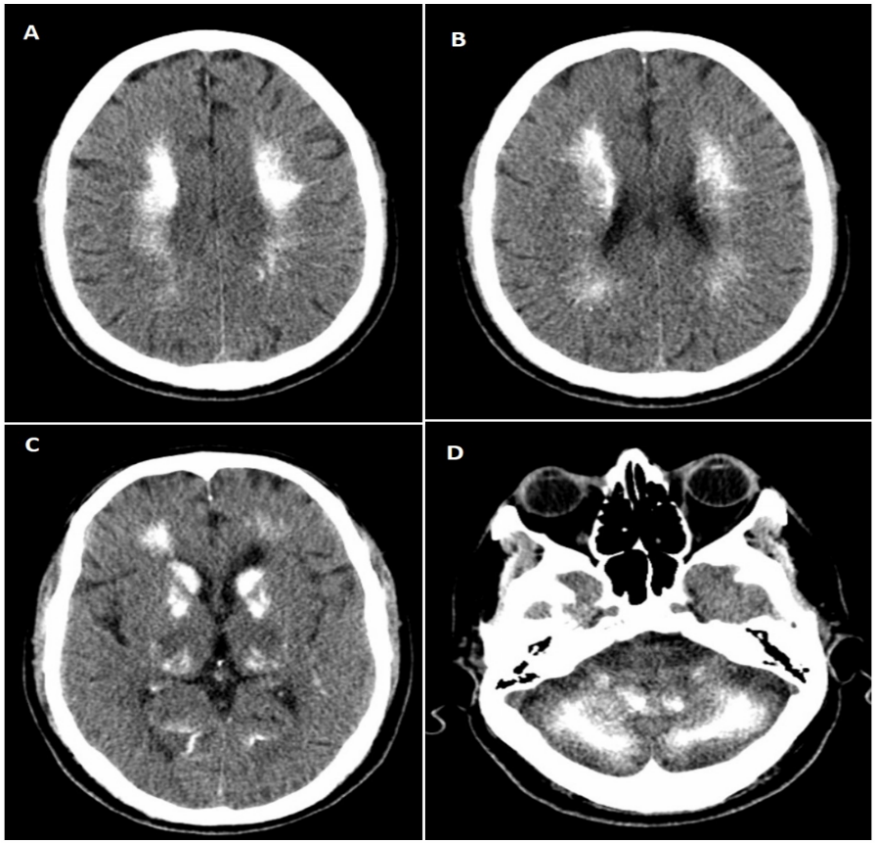

Figure 1: Axial sections of NCCT Head showing symmetric coarse calcifications involving bilateral centrum semiovale (A), corona radiate (B), basal ganglia (caudate nucleus and globus pallidi) and pulvinar of thalami (C), dentate nuclei and cerebellum (D)

DISCUSSION:

Fahr's syndrome is usually a bilateral and symmetrical intra-cranial calcification with a predilection for basal ganglia and dentate nucleus. Moreover, primary hyperparathyroidism has been closely described in relation with the bilateral calcific nature of Fahr's syndrome[2, 5]. However other causes such as lupus, tuberous sclerosis, Alzheimer's, muscular dystrophy and mitochondrial diseases have also been described to be the underlying condition predisposing Fahr's syndrome [5, 6]. The exact prevalence of Fahr's syndrome is unknown, however it has been incidentally detected in around 0.3-1.2% of NCCT head examinations[5]. Moreover, the pathophysiology behind Fahr's syndrome is poorly understood however anatomical and morphological changes were seen in small vessels, perivascular regions, neuroglia and neurons [7]. It should be understood that Fahr's disease exhibit clinical heterogeneity, therefore the diagnosis should be made on the basis of neurological evidence with no alternative explanation for symmetrical bilateral basal ganglia calcification[7].

The common clinical features include headaches, seizures, and movement disorders. Gait disturbances, dystonia, paresis, speech alterations, dementia, tremors, chorea are other specific features seen in Fahr's syndrome [2, 5]. This combination of neuropsychiatric features along with striopallidodentate calcinosis is known as Fahr's syndrome [5]. Similarly, the available epidemiological data suggest higher prevalence of disease in men with clinical features occurring around the 5^{th}decade of life. Severe forms of the disease leads to severe neuropsychiatric manifestations accounting to the degrading quality of life [7]. Batla et al. in their review article pointed psychiatric features, movement disorders and cognitive impairment to be the major manifestations of Fahr's syndrome[8]. Moreover, Batla et al. have also found that the evidence of

basal ganglia calcification in NCCT head could be as high as 20%, which shall thus be differentiated with the primary condition of Fahr's syndrome [2, 4, 5, 8]. Laboratory examinations should also aim for blood calcium, iPTH, and other routine blood tests which helps in differentiation of idiopathic Fahr's disease with Fahr's syndrome [5]. Though CT scans have been found to be of great importance, the role of MRI over CT has not been well demonstrated [5]. Though, MRI provides a better anatomical detail than CT scan, it is less specific in detecting calcifications. Kozic et al reported 3 individuals with calcifications in the brain which was falsely interpreted in MRI[10]. Similarly, a molecular genetic pattern testing also helps in the diagnosis of primary and secondary Fahr's disease/syndrome; the multigene panel including *PDGFB, PDGFRB, SLC20A2, XPR1* and various other genes of interest[1, 8, 10, 13].

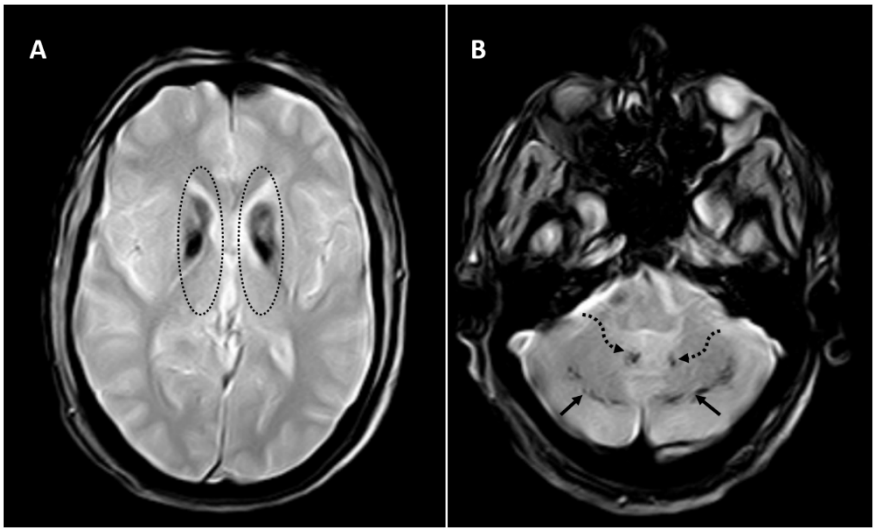

Figure 2: Axial sections of SWI sequence of MRI brain showing susceptibility changes in bilateral caudate nucleus and globus pallidi (dotted circles, A), dentate nuclei (curved dotted arrows, B) and cerebellum (black, arrows, B)

Fahr's syndrome usually follows secondary to underlying pathologies such as hypocalcemia, hypoparathyroidism, autoimmune conditions, infections, mitochondrial diseases, infections, toxic exposures, and can be associated with other conditions such as Cockayne syndrome, and Aicardi-Goutieres syndrome [9]. The primary form is a group of primary familial brain calcification (PFBC) and a heterogenic pathological variant has been identified in more than half of the cases. Moreover, studies have found the chance of inheritance to be as high as 50% from parents to the offsprings [9, 10].

Management should be primarily focused in the treatment of the underlying condition. Seizure, secondary to hypoparathyroidism could be the primary manifestation in patients with Fahr's syndrome, yet clinical trials have shown antiepileptic therapies have not been beneficial in treatment in patients with such conditions [11]. These symptoms that are related to the Fahr's syndrome, can be treated with vitamin D3 and steroids as well. Atypical antipsychotics are also proven beneficial [1]. Moreover, there are ongoing trials studying the effects of bisphosphonates on Fahr's disease and syndrome [12].

CONCLUSION:

This case highlights the importance of considering Fahr's syndrome, when the patient presents with symptoms suggestive of Parkinson's disease, and in the presence of basal ganglia calcifications on neuroimaging. Moreover, the diagnosis of Fahr's syndrome also highlights the importance of blood investigations, including serum calcium and parathyroid hormone. Early recognition and appropriate management are crucial to prevent misdiagnosis and ensure optimal patient outcomes. The case also underscores the necessity for a

multidisciplinary approach involving neurologists, endocrinologists, radiologists to accurately diagnose and manage the disease condition.

AUTHORSHIP:

Name	Contribution
Shritik Devkota	Conceptualization, Formal analysis, Methodology, Reviewing and editing, Resources, Investigations
Samiksha Lamichhane	Conceptualization, Formal analysis, Project Administration, Writing-Review and editing, Visualiza
Prajjwal Pokharel	Resources, Data Curation, Writing – original draft, Writing – Review and Editing, Software, Visua
Silvia Maharjan	Writing-Review and Editing, Formal analysis, Data Curation, Software
Kesha Meghashyam	Supervision, Validation, Investigatons, Writing-Review and Editing

PROTECTION OF HUMANS AND ANIMALS:

The authors declare that the procedures were followed according to the regulations established by Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA AVAILABILITY STATEMENT:

The datasets analyzed during the current study are available from the corresponding author upon reasonable request. Additionally, comprehensive literature sources used for the literature review are cited appropriately, within the manuscript.

FUNDING INFORMATION:

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CONSENT:

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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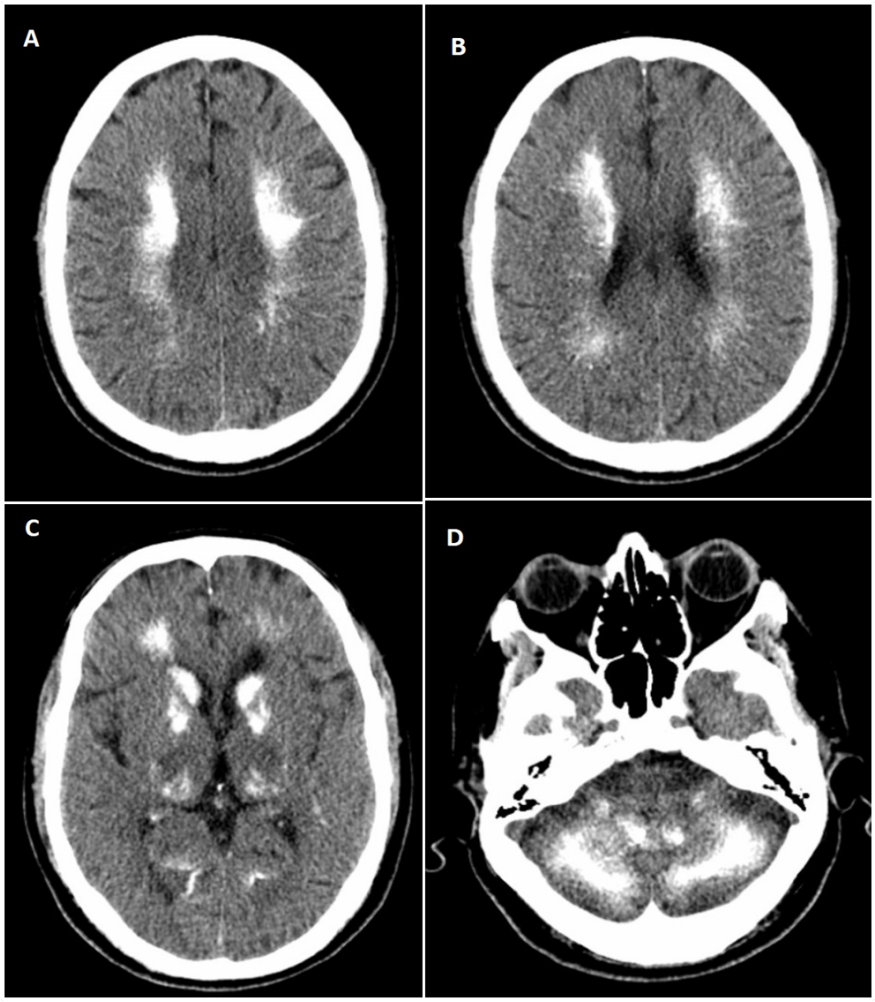

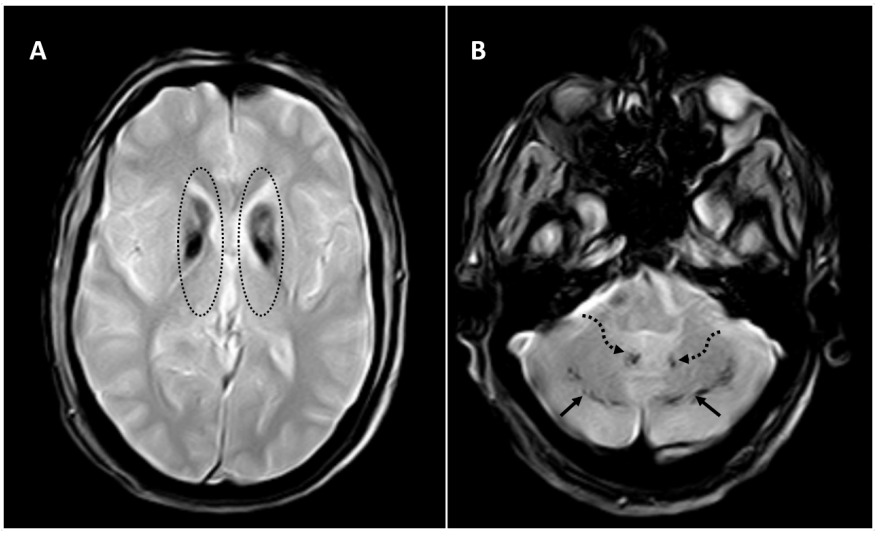

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Table 1.docx available at https://authorea.com/users/772287/articles/857082-fahr-s-syndrome-secondary-to-hypoparathyroidsm-mimicking-as-parkinson-s-disease-a-case-report