The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 3, 2025

EARLY-ONSET FAHR SYNDROME: A RARE PRESENTATION WITH PRIMARY HYPOPARATHYROIDISM AND EPILEPTIC SEIZURES

Dr Sahrish Bhutto[*1], Dr. Asna Shabbir[2], Dr. Maryum Anwar[3], Dr. Arshika Faisal[4], Dr Tayyaba Anwar[5], Dr Heena Rais[6]

[*1]*Pediatric Resident, Ziauddin Hospital Karachi*
[2,3,4]*House Officer, Ziauddin Hospital Karachi*
[5]*Assistant Professor Pediatric Medicine, Ziauddin Hospital Karachi*
[6]*Consultant Pediatric Medicine, Ziauddin Hospital Karachi*

[*1]sahrmail@hotmail.com, [2]asnashabbir123@gmail.com, [3]maryumanwar09gmail.com, [4]arshikafaisal@gmail.com, [5]tayyaba.anwar@zu.edu.pk, [6]heena.rais@zu.edu.pk

DOI: https://doi.org/10.5281/zenodo.14974192

Keywords
Fahr's syndrome, paediatric, hypoparathyroidism, hypothyroidism, basal ganglia, calcification

Article History
Received on 26 January 2025
Accepted on 26 February 2025
Published on 05 March 2025

Corresponding Author: *

Abstract

Fahr syndrome is a rare neurodegenerative disorder characterized by abnormal calcium deposition in the basal ganglia and other parts of the brain, clinically manifesting with neurological and neuropsychiatric symptoms. The disease most commonly affects the middle-aged population, with the paediatric population being rarely affected.

Here, we report a rare case of Fahr syndrome in a 7-year-old female with concurrent meningoencephalitis. She is a known case of congenital heart disease, who presented with a history of fever, cough, shortness of breath, and tonic-clonic seizures. On investigation, her magnetic resonance imaging (MRI) with contrast revealed bilateral calcifications in cerebral hemispheres involving the basal ganglia and subcortical white matter of frontoparietal lobes, while laboratory investigations showed hypocalcemia, hypothyroidism, and hypoparathyroidism.

CT scan, at the moment, is the most reliable imaging modality to establish the diagnosis of Fahr's syndrome. Currently, there is no definitive treatment for the disease and the management is primarily symptomatic.

INTRODUCTION

Fahr's syndrome refers to bilateral symmetric calcium deposits that accumulate in the brain, usually in the cerebellar region and basal ganglia. These deposits cause neurological and psychiatric symptoms [1]. Fahr's syndrome is inherited autosomally dominantly, with a prevalence of less than 1 in 1,000,000 cases and an age preference between 40 and 50 years of age in both familial and non-familial cases. The disease manifests clinically in a variety of symptoms including differential paresthesia, neuropsychiatric symptoms, parkinsonism, convulsive seizures, and cerebellar symptoms [2].

CASE REPORT

A 7-year-old unvaccinated female child presented to the emergency department with a history of fever, productive cough, and shortness of breath for the past two weeks along with a history of multiple episodes of generalized tonic and clonic seizures since one week. She's a known case of Tetralogy of Fallot for which palliative surgery (Blalock Taussig shunt) at the age of 2 years. The patient has had multiple episodes of seizures, since the 3rd day of life for which lamotrigine was prescribed but the patient was non-compliant. Furthermore, family history

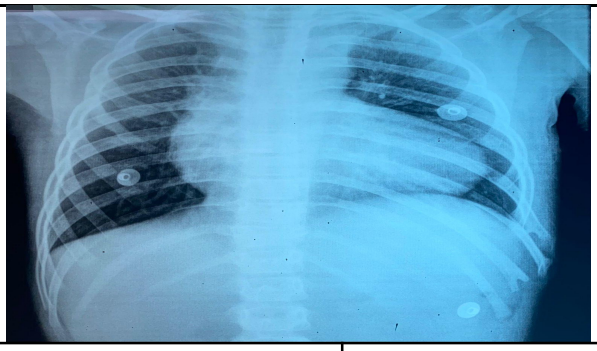
reveals the death of one sibling at the age of 11 months. He was a case of congenital heart disease and also had history of generalized tonic, clonic seizures but the exact cause of death remain undetermined.

At the time of admission, the patient was sick-looking with an altered level of consciousness, GCS of 10/15. CRT *(capillary refill time)* was *4 seconds*. The physical assessment revealed a heart rate of *89 beats per minute*. Respiratory rate of *22 breaths per minute* and Blood Pressure of *145/90mmHg* . The oxygen saturation *84% in room air* .Central cyanosis and *grade 2 clubbing* were present. Oral thrush was present. On systemic examination, central nervous system examination revealed brisk reflexes with upgoing planters. Respiratory examination showed bilateral equal air entry with diffuse crepitations. Cardiovascular and abdominal examinations were unremarkable.

Admission laboratory studies were notable for the initial blood profile with significantly elevated levels of hemoglobin *(Hb)*, hematocrit *(hct)*, total WBC count, and neutrophils, Significantly demote levels of lymphocytes *(table no. 1)*. Followed by serum electrolytes *(table no.2)* revealing elevated levels of sodium along with borderline increased levels of chloride and creatinine. There were significant low levels of serum calcium.

Table no 1	***Case Values***	***Reference Ranges***
Haemoglobin	16.8 g/dL	11.5-15.5 g/dL
Hematocrit	56%	35%-45%
Total WBC	18.9 x 10x9/L	4.5-14.5 x 10x9/L
Neutrophils	80%	40%-60%
Lymphocytes	14%	20%-40%
Platelets	314 x 10x9/L	180-450 x 10x9/L

Table no 2	***Case Values***	***Reference Ranges***
Sodium	155 mEq/L	136-149 mEq/L
Chloride	2.0 mEq/L	98-109 mEq/L
Potassium	112 mEq/L	3.8-5.2 mEq/L
Bicarbonate	21 mEq/L	22-29 mEq/L
Urea	36 mg/dL	10-50 mg/dL
Creatinine	1.6 mg/dL	0.6-1.5 mg/dL
Calcium	7.2	8.8- 10.8 mg/dL



(Figure no.1)

The chest x-rays (*Figure no.1)* revealed cardiomegaly , uplifted apex (boot-shaped appearance) with oligemic lung fields. Sharp costo phrenic angles. The lung fields and included bones are otherwise unremarkable.

The Lumber puncture was performed under sterile measures, and CSF was sent for detailed analysis, revealing the following results (*table no. 3).*

Table no 3	***Case values***	***Normal ranges***
Volume	02ml	-
Colour	colourless	-
Appearance	clear	-
Coagulum	absent	-
Glucose	103 mg/dL	60% of the plasma glucose
Protein	57 mg/dL	20 to 40 mg/dL
RBC	01 cell/mm3	0 cells/mm3 (Nil)
WBC	02 cell/mm3	0 to 5 cells/mm3

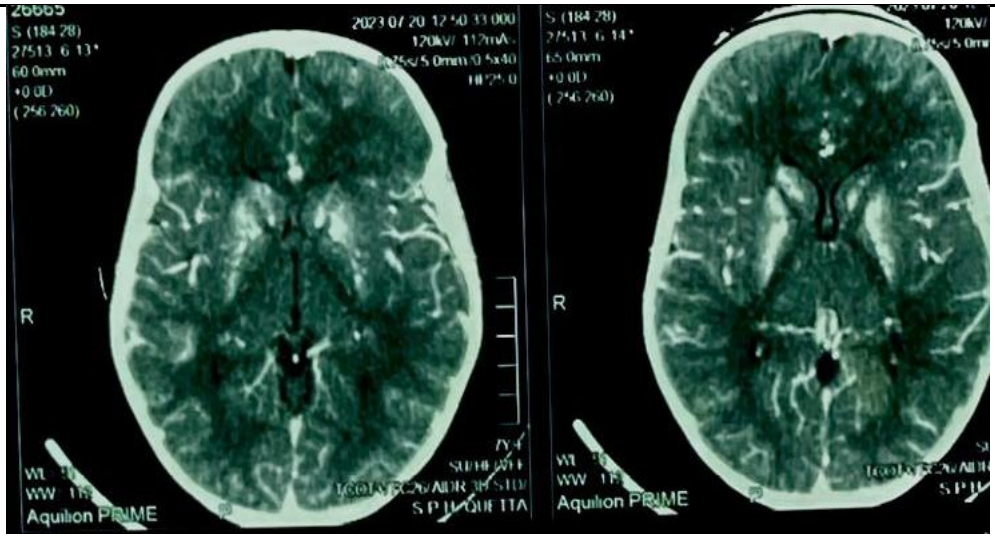
Arterial blood gases *(table no. 4)* are indicative of hypoxemia and low oxygen saturation.

Table no 4	***Case values***	***Normal range***
pH	7.404	7.35 to 7.45
paCo2	35.3	35 to 45mmHg
Pao2	49.0	80 to 100 mmHg
HCO3	21	22 to 26 mmHg
Base excess	-2.5	-2.0 mml/L
Saturation o2	84.2	95% to 100%

Abnormally low levels of serum TSH, T3, and T4 are indicative of hypothyroidism *(serum TSH 0.005 IU/L, T3 0.27ug/ml, T4 4.24ug/ml).*

The Parathyroid hormone levels were tested which came out to be significantly low, *< 3.00 pg/ml (reference range: 10 - 65 pg/ml)*

Albumin levels of *(3.03g/dL; reference value of 3.50 to 5.20 gm/dL)*



Assessment using a Head MRI scan ***(Figure no.2)***

The *MRI with contrast images (Figure no.2)* of the brain was reviewed that showed symmetrical areas of calcifications in bilateral cerebral hemispheres involving the head of caudate nuclei, globus pallidus, and subcortical white matter of frontoparietal lobes suggesting Fahr Disease.

Imaging results and the patient's clinical presentation raised the possibility of Fahr's illness. *Fahr's syndrome* was identified after all metabolic reasons, electrolyte imbalances, infections, and toxic or traumatic etiologies were ruled out. The results of the biochemical tests, MRI scans, and clinical features all supported this diagnosis. The co-existence of hypothyroidism and hypoparathyroidism further reinforced Fahr's syndrome diagnosis.

TREATMENT COURSE

Fahr's disease has an early onset type in which patients usually acquire psychiatric symptoms first, followed by mobility abnormalities, among those under 40 years of age. This syndrome does not currently have a recognized treatment. However, given there is no known cure for the calcifications brought on by Fahr's illness, only symptomatic treatment is offered for psychological and mobility issues.

The patient was initially treated with a focus on suspected meningoencephalitis/brain abscesses. The child had undergone surgery and was a known case of Tetralogy of Fallot. At the time of presentation to our hospital, the patient was in a state of shock. The patient was kept on oxygen support and Inotropes.

The course of treatment began with an intravenous injection of ceftriaxone, vancomycin, and metronidazole along with iv phenytoin . Due to continuous episodes of seizure, second-line anti-epileptics was added i.e. IV levetiracetam. And because of low serum calcium intravenous injection of calcium gluconate started. Injection Acyclovir was added to the treatment after the cerebrospinal fluid analysis report. After 72 hours of treatment, the condition of the patient was not improving, therefore the intravenous antibiotic was switched from injection ceftriaxone to injection meropenem, while the remainder of the treatment was continued. Fresh frozen plasma was transfused once due to deranged levels of PT/INR/APTT *(PT- 18 secs; normal range 11 seconds. INR - 16; normal range 2.0- 4.5. APTT- 34 secs; normal range 29 seconds).* Strict neuroprotective measures were implemented.

Thyroxine was added to the regimen, and the antibiotic was switched to an intravenous injection of piperacillin and tazobactam. Polymyxin E injection was also administered, along with an antifungal cover. Treatment for hypoparathyroidism was started with calcitriol and calcium drops. Despite receiving triple inotropic support, the patient's condition deteriorated daily while she remained in the hospital. On the 12th day of admission, she expired due to sudden collapse and cardiopulmonary arrest.

DISCUSSION

Idiopathic Basal Ganglia Calcification (IBGC) or Fahr's syndrome is a neurodegenerative disorder presenting with neurological and neuropsychiatric symptoms characterized by calcifications in the basal ganglia and other regions of the brain. Fahr's syndrome is relatively rare and affects individuals between 40 years and 60 years [1]. Men present at twice the prevalence rate of women, with a mean age of symptom onset of 40 years [8]. This case report portrays a rare case of a 7-year-old female child who presented with an altered level of consciousness, generalized tonic-clonic seizures, fever, cough, and shortness of breath with a family history of the death of one sibling previously.

The literature only contains a handful of case reports of the disease involving the paediatric age group. A case of two male and female siblings affected by Fahr disease, in China, was reported by Wang H et al. whose initial manifestation was extrapyramidal movement disorder in early childhood and teenage [9]. Another case of a 9-year-old Nigerian child was documented by Muoneke et al who presented with a history of recurrent seizures [10].

Fahr's syndrome is thought to be a calcification of the brain's basal ganglia based on findings from brain imaging studies of patients with neurological or psychiatric symptoms like dyskinesia, depression, dementia, and seizures. Several conditions are associated with this condition, such as astrocytoma, cytomegalovirus infection, tuberculosis, hyperparathyroidism, hypoparathyroidism, and hypervitaminosis D [3]. While the definitive cause of Fahr's syndrome is still unknown, abnormalities in the parathyroid gland's regulation of calcium and phosphorus levels have been linked to the condition. A case of hypoparathyroidism-related movement disorder in a patient with Fahr's syndrome was documented by Mahmood et al. Another Fahr's syndrome case involving primary hypoparathyroidism and movement disorders was reported by Zhou et al [1].

Similarly, our 7-year-old patient has Fahr's syndrome with primary hypoparathyroidism which is rarely documented in the literature. The fact that hypoparathyroidism sometimes exists along with the occurrence of Fahr's syndrome may be partially explained by the role parathyroid hormone (PTH) plays in maintaining calcium levels in the cerebrospinal fluid and preventing phosphorus accumulation in the periventricular regions [2]. Increased calcinosis can result from hypoparathyroidism, and it's thought that calcium deposits in the vessel wall before moving on to the neuron. Due to poor local circulation brought on by this basal ganglia deposition, there is further neuronal damage and hence more calcium deposition [7].

Moreover, Fahr syndrome is also known to be significantly associated with genetics, most commonly presenting in an autosomal dominant pattern of inheritance. Numerous mutations including SLC20A2 on chromosome 8p11.2 and PDGFRB on chromosome 5q32, PDGFB on chromosome 22q13.1, and XPR1 on chromosome 1q25 are linked to the disease [12].

Presentation of Fahr's syndrome can be highly variable, ranging from asymptomatic to a combination of severe motor, neuropsychiatric, and Parkinsonian symptoms. According to a study that evaluated the involvement of symptoms in 99 cases of Fahr's disease, 33% of the cases reported to be symptomatic [8].

Asokan et al. documented a case of Fahr's syndrome in which speech difficulties were the primary symptom [1].

According to the Fahr's Disease Registry, approximately 55% of cases have movement disorders as their most common presentation. Out of them, 57% of the cases had Parkinsonism, 19% had chorea, 8% had tremor, 8% had dystonia, 5% had athetosis, and 3% had orofacial dyskinesia. Additional neurological symptoms include cognitive decline, speech problems, pyramidal signs, cerebellar signs, gait abnormalities, psychiatric features, and sensory abnormalities [4].

Fahr's syndrome diagnostic criteria have been revised and derived from Moskowitz et al. 1971, Ellie et al. 1989, and Manyam 2005. They are as follows:

1. Neuroimaging reveals bilateral basal ganglia calcification. Other areas of the brain might also be seen.
2. Progressive neurologic dysfunction is usually accompanied by neuropsychiatric symptoms and/or a movement disorder. While it can also appear in childhood, this disorder

usually occurs initially in the fourth or fifth decade of life.
3. The absence of somatic symptoms and biochemical abnormalities that might be related to a metabolic, mitochondrial, or other systemic illness.
4. Absence of trauma, toxin, or infectious cause.
5. Family history in line with dominant autosomal inheritance [5].

In the presence of family history, the diagnosis can be made even if the first 2 criteria are not met. If there is no family history, the diagnosis of Fahr's disease can be made based on the presence of the first 5 criteria, provided the calcifications are typical of Fahr's disease [8].

Ruling out other causes of intracranial calcifications is essential to establish a diagnosis of Fahr's syndrome, including infectious, metabolic, congenital, and vascular [7].

In recent times, CT has replaced magnetic resonance imaging (MRI) as the gold standard method of diagnosis. On CT, calcified regions appear as hyperdense lesions, which is considered essential for confirming the diagnosis [2]. Most frequently, calcifications are observed in the globus pallidus. Some other areas that have been documented to exhibit calcification include the putamen, internal capsule, dentate nucleus, thalamus, cerebellum, and cerebral white matter [8]. MRI images of the brain, in our case, showed symmetrical areas of calcifications in bilateral cerebral hemispheres involving the head of caudate nuclei, globus pallidus, and subcortical white matter of frontoparietal lobes suggesting Fahr Disease.

Laboratory investigations may be carried out including serum levels of calcium, calcitonin, parathyroid hormone, alkaline phosphatase, infectious markers, and heavy metal concentrations [7]. In our case, the patient's reports revealed decreased serum calcium, thyroid, and parathyroid hormone levels.

Currently, there is no definitive treatment of Fahr's syndrome except for symptomatic management to improve the neuropsychiatric symptoms. Neuropsychiatric improvement has resulted from treating underlying aetiologies such as hypoparathyroidism but, there is currently no specific treatment to restrict or reverse the progression of calcification in the basal ganglia in Fahr's syndrome [11].

The standard treatment for hypoparathyroidism involves calcium and vitamin D supplements. The therapeutic principle is based on the idea that PTH deficiency or dysfunction may result in less 1-25 (OH), an active metabolite of vitamin D, being produced, which in turn may result in less intestinal calcium uptake. The most widely used calcium agent is calcium carbonate, which makes up 40% of elemental calcium [6].

Conclusion

The majority of the reported cases of Fahr syndrome that have been documented in the literature are present in the middle-aged population. In our case, however, a 7-year-old female presented with the disease secondary to hypothyroidism and hypoparathyroidism. Moreover, the disease can clinically present with a wide range of symptoms, from profound motor, neuropsychiatric, and Parkinsonian symptoms combined to virtually no symptoms at all. Currently, the only effective treatment for Fahr's syndrome is symptomatic management aimed at alleviating the neuropsychiatric symptoms with no standard course of treatment. Fahr's syndrome has a variable and frequently dire prognosis.

REFERENCES

Khan ZR, Waheed W, Mabood J, Ali A, Burki G. A unique presentation of Fahr's syndrome secondary to hypoparathyroidism. Cureus. 2021 June 30;13(6).

Shah SY, Hadi FA, Idrees M, Levin-Carrion Y, Pande H, Oorloff MD, Khan QA, Nadella A. Fahr's Syndrome Secondary to Primary Hypoparathyroidism Presenting With Seizures and the Role of Steroid Therapy. Clinical Medicine Insights: Case Reports. 2023 May;16:11795476231178119.

Lee YJ, Park S, Kim YW, Park KM, Kim IH, Park JH, Park BS. A case of seizure revealing Fahr's syndrome with primary hypoparathyroidism. The American journal of case reports. 2018;19:1430.

Asokan AG, D'souza S, Jeganathan J, Pai S. Fahr's syndrome-an interesting case presentation. Journal of Clinical and Diagnostic Research: JCDR. 2013 Mar;7(3):532.

Saleem S, Aslam HM, Anwar M, Anwar S, Saleem M, Saleem A, Rehmani MA. Fahr's syndrome: a literature review of current evidence. Orphanet journal of rare diseases. 2013 Dec;8(1):1-9.

Zhou YY, Yang Y, Qiu HM. Hypoparathyroidism with Fahr's syndrome: A case report and review of the literature. World Journal of Clinical Cases. 2019 Nov 11;7(21):3662.

Schupper AJ, Chen MM. A unique presentation of Fahr syndrome secondary to chronic hypoparathyroidism: A case report. Imaging Med. 2018;10(5):129-31.

Manyam BV, Walters AS, Narla KR. Bilateral striopallidodentate calcinosis: clinical characteristics of patients seen in a registry. Mov. Disord. 16, 258 (2001).

Wang H, Shao B, Wang L, Ye Q. Fahr's disease in two siblings in a family: A case report. Exp Ther Med. 2015 May;9(5):1931-1933. doi: 10.3892/etm.2015.2356. Epub 2015 Mar 16. PMID: 26136916; PMCID: PMC4471777.

Okike, C. O., Ajaegbu, O. C., Origbo, L., & Muoneke, U. V. (2021). Idiopathic basal ganglia calcification (fahr's disease) in a 9-year-old Nigerian child. Nigerian Journal of Paediatrics, 48(1), 46–49. https://doi.org/10.4314/njp.v48i1.9

Mufaddel AA, Al-Hassani GA. Familial idiopathic basal ganglia calcification (Fahr`s disease). Neurosciences (Riyadh). 2014 Jul;19(3):171-7. PMID: 24983277; PMCID: PMC4727649.

Beneki E, Papazarkadas X, Karras A, Kalantzis K, Tsatiris K. A Rare Case of Fahr's Syndrome in a Patient with Secondary Hypoparathyroidism and Neuropsychiatric Symptoms. Innov Clin Neurosci. 2021 Apr-Jun;18(4-6):11-14. PMID: 34980977; PMCID: PMC8667711.