

Case Report

Is there an association between Fahr's disease and cardiac conduction system disease?: A case report

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Abstract

BACKGROUND: Fahr's disease is a rare neurodegenerative disorder of unknown cause characterized by idiopathic basal ganglia calcification that is associated with neuropsychiatric and cognitive impairment. No case of Fahr's disease with associated cardiac conduction disease has been described in the literature to date. The objective of this case report was to describe a young female with various cardiac conduction system abnormalities and bilateral basal ganglia calcification suggestive of Fahr's disease.

CASE REPORT: A 19-year-old female was transferred to our hospital for a pacemaker insertion. Her past medical history included cognitive impairment and asymptomatic congenital complete heart block since birth. Her manifestations included cognitive impairment, tremors, rigidity, ataxia, bilateral basal ganglia calcification without clinical manifestations of mitochondrial cytopathy. She also had right bundle branch block, left anterior fascicular block, intermittent complete heart block, atrial arrhythmias with advanced atrioventricular blocks and ventricular asystole manifested by Stokes-Adams seizures, which was diagnosed as epilepsy.

CONCLUSIONS: According to our knowledge, this was the first case report of a suspected association between Fahr's disease and isolated cardiac conduction system disease. In addition, this case illustrated that in patients with heart blocks and seizures, a diagnosis of epilepsy needs to be made with caution and such patients need further evaluations by a cardiologist or electrophysiologist to consider pacing and prevent future catastrophic events.

KEYWORDS: Fahr's Disease, Basal Ganglia Calcification, Cardiac Conduction Defect, Congenital Heart Block, Epilepsy.

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Fahr's disease (FD) is a rare neurodegenerative disorder of unknown cause characterized by sporadic or familial idiopathic basal ganglia calcification that is associated with neuropsychiatric and cognitive impairment.¹ The true prevalence of FD is unknown, but Tedrus et al. reported an incidence of 0.68% among 3,662 cranial computed tomography (CT) scans analyzed.² Generally, the majority of basal ganglia calcification is idiopathic in nature and other causes include metabolic diseases (hyper or hypoparathyroidism), mitochondrial cytopathy, lupus, tuberous sclerosis, and infectious diseases such as brucella, toxoplasmosis, tuberculosis and acquired

immunodeficiency syndrome. The calcifications seen in all these conditions are usually asymmetric and not restricted to basal ganglia.¹ In FD, a symmetric calcification with cloudy and/or thin linear pattern located in the basal ganglia can be found.¹

The onset of FD is insidious, usually in middle-aged patients. Clinically, FD manifests as Parkinsonism (55%), often in association with dementia, ataxia, or other hyperkinetic movements including chorea, tremor, and dystonia.³ FD is predominantly an autosomal dominant disease with mutations in genes located on the long arm of chromosome 14.¹ No case of FD with associated cardiac conduction

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disease has been described in the literature to date. The objective of this case report was to describe a young female with various cardiac conduction system abnormalities, as well as bilateral basal ganglia calcification suggestive of FD.

Case Report

A 19-year-old Arab female patient was referred to Royal Hospital, Muscat, Oman in July 2011 from a regional hospital for pacemaker insertion. Her past medical history included cognitive impairment and asymptomatic congenital complete heart block (CHB) since birth. She had referred to the regional hospital with one month history of recurrent fainting attacks lasting for a few minutes, sometimes associated with generalized tonic-clonic seizures. She was diagnosed with epilepsy. Her treatment started with sodium valproate. There was no history of fever, rash, head trauma or any drug abuse. Her brain CT scan had shown bilateral basal ganglia calcification which was not present previously. Her family history was negative for any cardiac or neurological disorders. She was born of consanguineous parents and had three siblings who were normal. Her echocardiogram was normal and her baseline ECG showed incomplete right bundle branch block with left anterior fascicular block, normal PR/QT interval (Figure 1) with intermittent narrow QRS CHB and a ventricular rate of 40 beats per minute (bpm) (Figure 2).

She was admitted during one of the fainting episodes. During the hospitalization period, she developed recurrent Stokes-Adams attacks with seizures and the monitor demonstrated intermittent advanced varying atrioventricular (AV) blocks with wide QRS escape rhythm suggesting infrahisian block (Figure 3). The atrial rate during these advanced AV blocks was 250-300 bpm indicating either atrial tachycardia or atrial flutter. This was followed by asystolic cardiac arrest with monitor indicating prolonged P-wave asystole (Figure 4). Immediate cardiopulmonary resuscitation was initiated and she was treated with intravenous adrenaline (total dose = 3 mg), atropine (total dose = 3 mg) followed by dopamine infusion (10 mcg/kg/min). She had been successfully resuscitated along with a brief ventilator support and transferred to our center on dopamine infusion, with a stable heart rate of 100 bpm. On examination at our hospital, she demonstrated cognitive impairment, mild rigidity, limb ataxia, and tremors with normal eye. She also underwent fundus, cranial nerve, and other neurological examinations. Her cardiac examination and transthoracic echocardiogram were normal. Brain CT scan in our hospital confirmed bilateral "cloudy" looking symmetric basal ganglia calcification (Figure 5). Secondary causes of the calcifications were excluded by laboratory testing. Serum concentration of calcium, phosphorus, magnesium, alkaline phosphatase, calcitonin, parathyroid

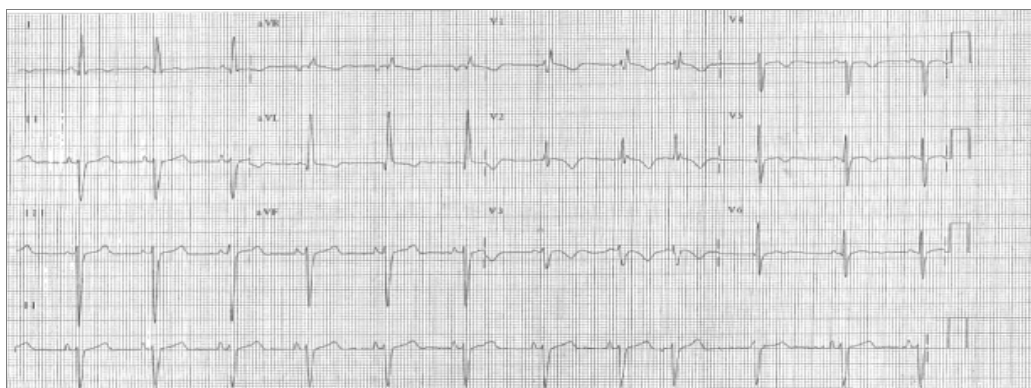


Figure 1. Electrocardiogram of a patient with Fahr's disease showing incomplete right bundle branch block with left anterior fascicular block, and normal PR interval during sinus rhythm

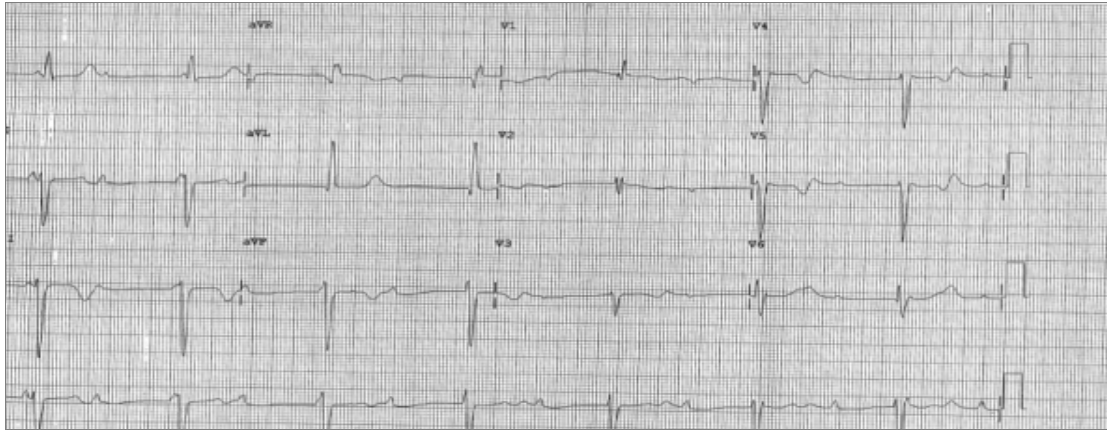


Figure 2. Electrocardiogram of a patient with Fahr's disease showing intermittent narrow QRS complete heart block with a ventricular rate of 40 beats per minute

hormone, sodium valproate level and autoantibodies were normal. The electroencephalography (EEG) showed generalized theta slowing suggesting developmental delay without any epileptic focus. The neurological manifestations along with basal ganglia calcification suggested FD. Genetic testing was refused by the family. She underwent single chamber permanent pacemaker (VVI) implantation with ventricular rate set at 70 bpm. She did not experience any recurrence of arrhythmias or fainting attacks/seizures. At six-month follow-up, she was 80% pacemaker dependent with no recurrence of seizures.

Discussion

This patient met all the criteria for the diagnosis of FD, except the family history. The criteria described in the literature are: 1) bilateral calcification of the basal ganglia; 2) progressive neurological dysfunction and/or neuropsychiatric manifestation; 3) age of onset typically in the fourth or fifth decade (may also present earlier in life); 4) absence of biochemical abnormalities and somatic features suggestive of a mitochondrial or metabolic disease or other systemic disorders; 5) absence of an infectious, toxic, or traumatic cause; and 6) family history consistent with autosomal dominant

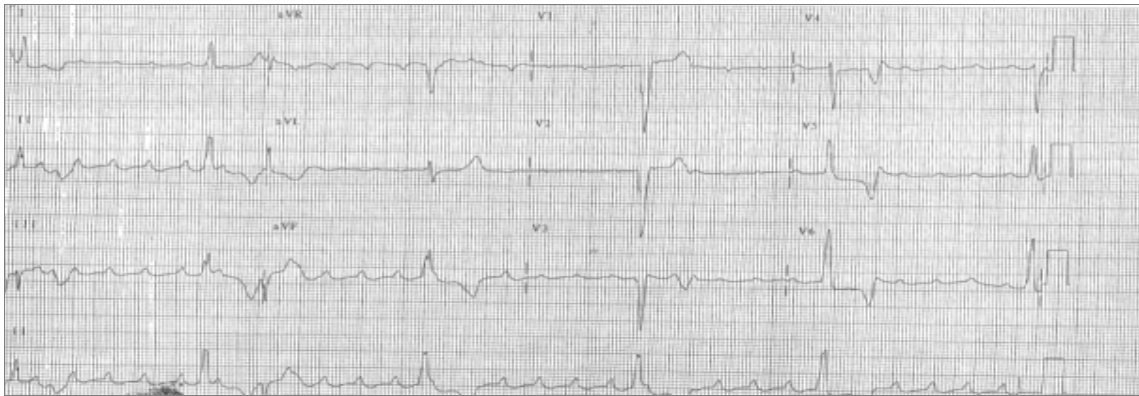


Figure 3. Electrocardiogram of a patient with Fahr's disease showing intermittent advanced varying atrioventricular blocks



Figure 4. Monitor rhythm strip of a patient with Fahr's disease showing prolonged ventricular (P-wave) asystole with occasional ventricular escape beats (The atrial rate during these advanced AV blocks was 250-300 bpm indicating either atrial tachycardia or atrial flutter)

inheritance.^{1,3} In presence of family history, the diagnosis can be established in the absence of one of the first two criteria.^{1,3} When the family history is negative, the presence of the first five criteria is sufficient for a positive diagnosis of FD, only if the calcifications are typical of FD, as in this patient.^{1,3} Early adult onset of FD, in 20-40-year-old patients has been reported with either recessive inheritance or sporadic without any positive family history.¹ Kearns-Sayre syndrome, a mitochondrial disorder can have bilateral basal ganglia calcification on CT as well as CHB, but other major clinical manife-

stations like progressive external ophthalmoplegia, ptosis, pigmentary retinopathy were absent in this patient.

There are various causes for AV blocks in adults and children including ischemic, sclerodegenerative, metabolic, infective, infiltrative, familial cardiomyopathy with or without post-surgery and drug induced dystrophy and congenital heart diseases. Isolated congenital heart blocks in childhood without structural heart disease are of two types, namely antibody positive and antibody negative.⁴⁻⁶ Isolated congenital heart block, with an incidence of 1 in

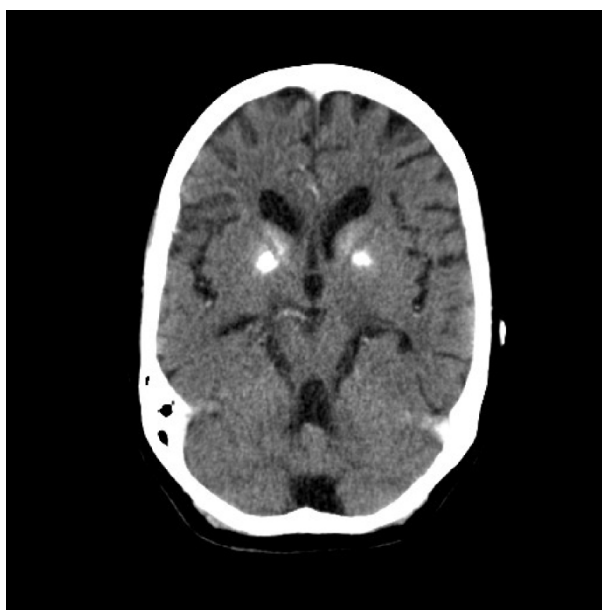


Figure 5. Brain CT scan demonstrating bilateral symmetric basal ganglia calcification in a patient with Fahr's disease and isolated cardiac conduction system disease

17,000 live births, is generally associated with presence of maternal autoantibodies, specifically in children with maternal lupus.⁵ However, in a study, Villain et al. reported that 50% of congenital heart blocks detected before the age of 15 years were anti-Ro/La-negative.⁶ In the antibody positive group, maternal antibodies cross the placenta and damage the conduction system resulting in heart block in fetal life. In less than 10% of patients, congenital AV block is first or second degree at birth, and in half of these cases, it progresses to a third-degree block after birth.⁵ The antibody negative complications present at a later age and the conduction disease is progressive, as noted in this patient.⁴ Many children with isolated congenital heart block are asymptomatic. Pacing is indicated for symptomatic patients, but there is a risk of sudden death even in asymptomatic patients due to sudden progression.⁴ Isolated sclerodegenerative disease of the conduction system (Lenegre's disease) can rarely occur at a young age, but not at birth and it should be clinically suspected in middle-aged or slightly older people.⁷ In this patient, congenital CHB had

been noted since birth and there was a long period of stable conduction abnormalities including intermittent CHB. However, she progressed rapidly to advanced AV block, atrial arrhythmias and ventricular asystole leading to Stokes-Adams attacks with seizures. It seems like all her previous manifestations of fainting attacks with seizures may have been secondary to asystole that was misdiagnosed as epilepsy.

Conclusion

We presented a patient with clinical and imaging features suggestive of FD in association with isolated cardiac conduction disease that has not been reported previously. The intriguing question of whether there is a really genetic association or just coincidence between FD and cardiac conduction system disease needs further studies. In addition, this case indicated that in patients with congenital AV blocks, a diagnosis of epilepsy needs to be made with caution and such patients need further evaluations by a cardiologist or electrophysiologist to consider pacing and prevent future catastrophic events.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

PP and KS were involved in the diagnosis and management of the patient. PP drafted the manuscript, and collected and prepared the images. KS critically reviewed the manuscript and provided the references.

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