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Case Report

Findings of Fahr's Syndrome in A Patient Suspected With Subarachnoid Hemorrhage: An Evidence-Based Case Report

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ABSTRACT

Fahr's syndrome is an entity where there is symmetrical bilateral calcification of basal ganglia with parkinsonian and psychiatric symptoms. However, due to its rarity, clinicians tend not to include Fahr's syndrome in their differential diagnosis. This article aims to raise awareness about the diagnosis of Fahr's Syndrome through its unique presentation in this patient. Data was obtained primarily and secondarily. In this case, a 32 years old male was referred to our clinic with chief complaints of headache since a week prior and a seizure 5 days ago. A head CT and a CT angiography (CTA) of the circulus willisi were done and a bilateral and symmetrical calcification of the corona radiata, basal ganglia, thalamus, and nucleus dentatus were found. There is also hypocalcemia and low Parathyroid Hormone (PTH). Fahr's Syndrome may manifest unusually and hence clinicians have to be aware of diagnosing this entity.

Keywords: Fahr's Disease, Fahr's Syndrome

ABSTRAK

Sindroma Fahr's merupakan sebuah penyakit yang ditandai dengan kalsifikasi bilateral sietris dari basal ganglia dengan gejala psikatri dan parkinsonisme. Namun, akibat jarangnya ditemukan penyakit ini, klinisi cenderung tidak memikirkan sindroma Fahr's sebagai salah satu diagnosis banding. Artikel ini bertujuan untuk meningkatkan kewaspadaan terhadap diagnosis Sindroma Fahr's melalui presentasi unik pada pasien ini. Data diambil secara primer dan sekunder. Pada kasus ini, seorang laki-laki berusia 32 tahun dirujuk dengan keluhan utama sakit kepala sejak satu minggu dan kejang 5 hari sebelum masuk rumah sakit. Computed Tomography (CT) scan kepala dan Computed Tomography Angiography (CTA) dari sirkulus willisi dilakukan dan ditemukan adanya kalsifikasi bilateral simetris pada korona radiata, basal ganglia, talamus dan nukleus dentatus. Pada pemeriksaan laboratorium ditemukan adanya hipokalsemia dan hormon paratiroid (PTH) yang rendah. Sindroma Fahr's dapat datang dengan presentasi yang tidak khas sehingga para klinisi harus lebih tajam dalam mendiagnosis kasus ini.

Kata kunci: Penyakit Fahr's, Sindroma Fahr's

INTRODUCTION

Fahr's syndrome is a syndrome that is rarely encountered that is characterized by symmetrical bilateral calcification in basal ganglia with a prevalence of <1 in 1,000,000 people.[1] There is a limited amount of studies about Fahr's syndrome where epidemiologic studies show a wide range of Fahr's syndrome according to computed tomography (CT) findings, ranging from 0.49% to 10.02%.[2]

Main diagnostic criteria for Fahr's syndrome is symmetricaland bilateral calcification in basal ganglia. Fahr's syndrome is accompanied by neurologic

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dysfunction such as involuntary movements and or neuropsychiatric manifestations with an onset from 4th to 5th decade, no biochemical abnormalities or somatic features suggestive of metabolic, mitochondrial or other systemic diseases, no infectious, toxic or traumatic causes and no family history that is consistent with genetically inherited autosomal dominant disease.[2,3]

Fahr's disease must be differentiated from Fahr's sydrome. Patients with Fahr's disease usually suffer from the disease at the age of 40-60 years while in patients with Fahr's syndrome usually has an onset at the age of 30-40 years. Fahr's disease is genetically related while Fahr's syndrome is not genetic. Calcification of Fahr's syndrome occurs suddenly but occurs slowly in patients with Fahr's disease. Fahr's syndrome can also be misdiagnosed with a stroke due to motor impairment.[2]

This evidence-based case report will discuss about clinical and radiological manifestations of Fahr's syndrome with unique presentation and how to differentiate it with other clinical entities.

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METHOD

Primary data is collected by means of direct clinical examination and secondary data is coollected by means of medical records.

RESULT AND DISCUSSION

A 32-year-old male is referred to our hospital with subarachnoid bleeding as his diagnosis due to aneurysm rupture with headache as his primary complaints for one week before admission. He also complained of seizure 5 days before admission. No abnormalities were found in physical examination except severe pain with a visual analogue scalescore of 8. CT angiography (CTA) ofcircle of willis was done to exclude subarachnoid bleed and the result was normal hence a brain CT scan without contrast was done and symmetrical and bilateral calcification was found in corona radiata, basal ganglia, thalamus anddentate nucleus (figure 1). Laboratory findings found that there is a minimal elevation of SGOT and SGPT, low PTH (10.1 pg/mL) and hypocalcemia (1.21 mmol/L).Immunologic test was positive for anti-histone and EUROline scan was strongly positive. Serologic test for herpes, toxoplasmosis and HIV were negative. The patient was treated with calcium carbonate two times daily, tizanidine 2 mg three times daily and cavit-D3 three times daily.

Authors searched Pubmed and Google Scholar with keywords such as "*fahr [All Fields] AND ("syndrome"[MeSH Terms] OR "syndrome"[All Fields]*)"and the search is done on 4thAgustus 2019 (figure 2).

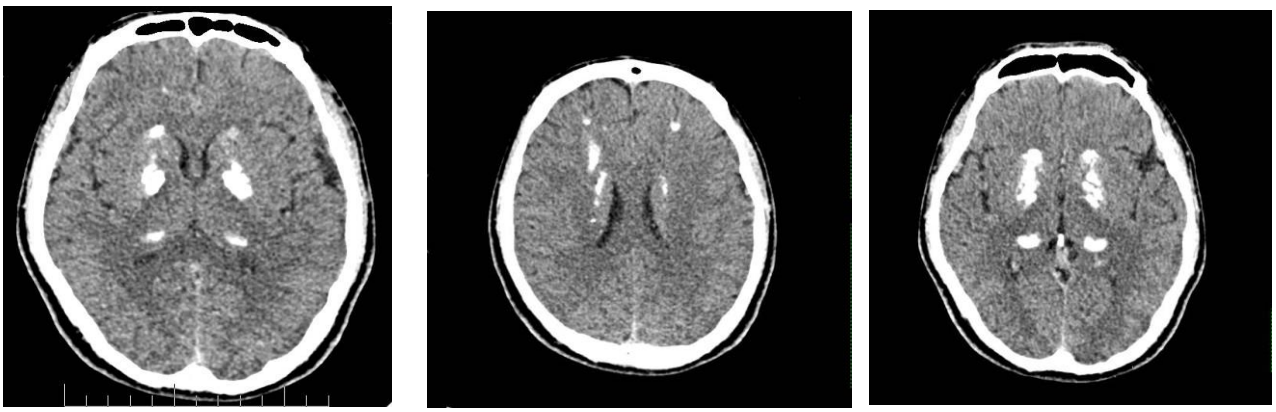

Figure 1. Basal ganglia and dentate nucleus calcification (left), bilateral corona radiata calcification (middle) and thalamus (right)

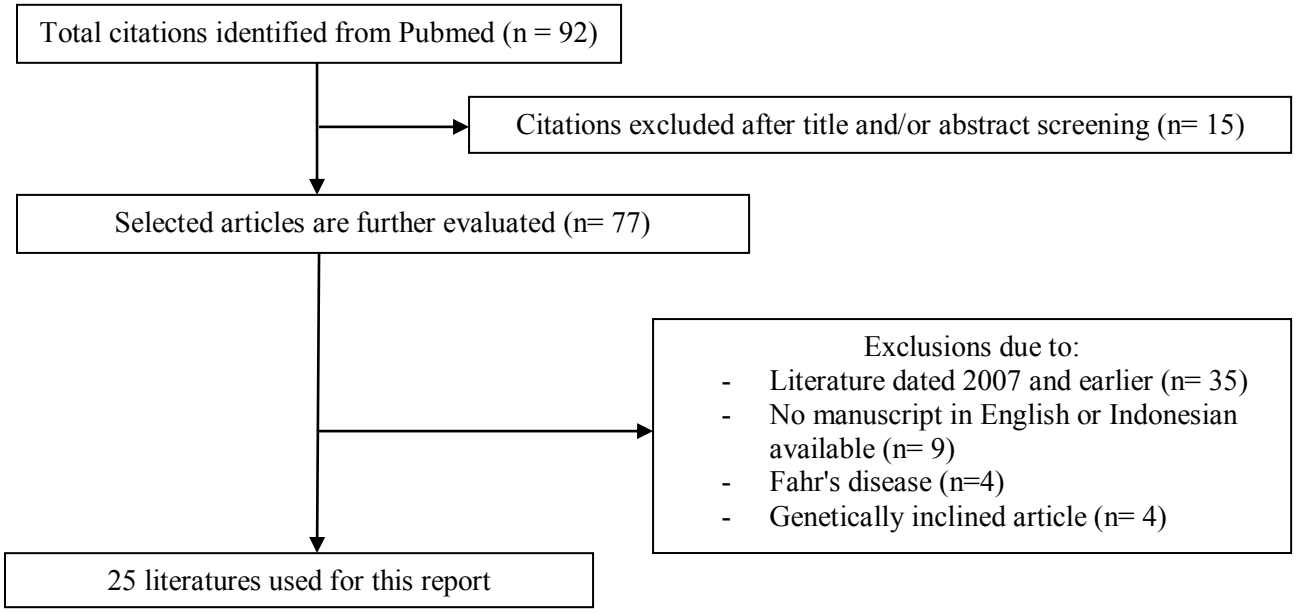

Figure 2. Algorithm of literature search and selection

Fahr's disease was discovered by Karl Theodor Fahr in 1930 when he diagnosed a 55-year-old male patient with dementia, hypothyroidism, immobility without paralysis and basal ganglia calcification with Fahr's disease.[4,5] The diagnostic criteria for Fahr's disease is quite uniform, unlike diagnostic criteria for Fahr's syndrome which varied in each study (table 1). Fahr's syndrome is defined as the presence of striatiopallidal symmetrical bilateral calcifications on the base of cranium.[11] There are more than 50 clinical conditions associated with Fahr's syndrome (table 2) and parathyroid disease is one of the most common causes. [2,12,13] Clinical manifestations of Fahr's syndrome vary from neurological to cardiological (table 3). The diagnosis of Fahr's syndrome requires a CT scan that shows bilateral symmetrical calcifications involving the striatum, pallidum with or without deposits in the nucleus dentatus, thalamus and white matter.[5] Magnetic resonance imaging (MRI) cannot be used as the main radiological modality in diagnosing Fahr's syndrome due to varying signal intensities and depending on the proton density of calcium, other mineral ions, concentrations of binding proteins and mucopolysaccharides in various stages of the disease or varying metabolic stages.[16,17] Management for Fahr's syndrome is targeted to the underlying conditions of Fahr's syndrome with symptomatic treatment as adjuvants.[10] Anticonvulsants can be given to overcome seizures and movement disorders caused by PTH. Calcium supplementation and alpha hydroxyl vitamin D3 can correct serum calcium and phosphate.[18] Fahr's syndrome has infrequent complications such as Morbus Fahr and overactive bladder.[19,20] In this patient, the diagnosis of Fahr's syndrome is delayed due to a referral diagnosis in the form of subarachnoid hemorrhage. The diagnosis of Fahr's syndrome is made using head CT scan with symmetrical bilateral calcification findings on the corona radiata, basal ganglia, thalamus and dentatus nucleus. The discovery of PTH and low calcium and 32 years of age support the diagnosis of Fahr's syndrome.

Table 1. Comparison in criteria used to diagnose Fahr's Syndrome

Author(Year)	Diagnostic Criteria	Study type
Lowenthal et al (1986)[6]	(1) Calcification with a characteristic distribution or at least affects globus pallidus with or without cerebellum calcification; (2) Obvious calcification seen in CT scan; (3) Calcification should be big enough to be detected in macroscopic examination	Literature Review
Saleem et al (2013)[2]; Modified from Moskowitz et al (1971)[7], Ellie et al. (1989)[8], Manyam (2005)[9]	1) Bilateral calcification in basal ganglia or other regions in radiologic examination; 2) Progressive neurologic dysfunction that involves motoric dysfunction and or neuropsychiatric manifestations. Onset begins at 40-50 years old even though it may manifest during childhood. 3) No biochemical and somatic etiologies that are suggestive for mitochondrial, metabolic or systemic dysfunctions. 4) No infectious, toxic or traumatic causes.	Literature Review
Malathi et al (2016)[10]	Consider Fahr's syndrome if: a) Onset starts from 30–40years b) Evidence of bilateral and symmetrical intracranial calcification AND Presence of endocrinopathies such as: a) Idiopathic hypoparathyroidism b) Secondary hypoparathyroidism c) Pseudohypoparathyroidism d) Pseudopseudohypoparathyroidism e) Hyperhypoparathyroidism OR Presence of one or more comorbids below: a) Intrauterine or perinatal brucellosis b) Neuroferritinopathy c) Polycystic lipomembranous osteodisplasia with sclerosing leukoencephalopathy d) Cockayne syndrome e) Aicardi-Gouteres syndrome f) Tuberous sclerosis g) Myopathy mitochondrial h) Lipoid proteinosis	Descriptive Study

Table 2. Classification of diseases associated with Fahr's syndrome

Author (Year)	Clinical Condition		Study Type
	Categories	Example	
Anca et al (2013)[14]	Inflammation	Cytomegalovirus, HIV, tuberculosis	Case Report
	Tumor	Astrocytoma	
	Hypoxia and vascular	Arteriovenous malformation, ischemic encephalopathy	
	Endocrine	Hypoparathyroidism, pseudohypoparathyroidism, hyperparathyroidism	
	Toxic	Carbon monoxide and lead intoxication, hypervitaminosis D, radiotheraphy	
	Metabolic and degenerative	Mitochondrial encephalopathy, leucodystrophic disease, familial idiopathic disease	
	Others	Malabsorption, Down syndrome, lupus, tuberous sclerosis	
Saleem et al (2013)[2]	Endocrine	Idiopathic hypoparathyroidism,secondary hypoparathyroidism, pseudohypoparathyroidism,pseudopseudohypoparathyroidism,hyperhypoparathyroidism	Literature Review
	Adult onset neurodegenerative disorder	Neurodegeneration with iron deposits in brain, neuroferritinopathy	
	Infection	Intrauterine and perinatal infection Cockayne syndrome type 1 and 2	

	Inherited or early onset syndrome	Aicardi- Gouteres syndrome Tuberous sclerosis Brucellosis	
Baba et al (2005)[15]	Sporadic conditions with metabolism abnormalities from calcium, phosphor and PTH	Idiopathic hypoparathyroidism, post-operative hypoparathyroidismhypoparathyroidism due to external radiation, hyperparathyroidism	Literature Review
	Sporadic conditions withou metabolic abnormalities without from calcium, phosphor and PTH but with systemic involvement	Down syndrome, systemic lupus erythematosus,acute lymphocytic, toxoplasmosis, HIV, cytomegalovirus	
	Sporadic conditions withou metabolic abnormalities without from calcium, phosphor and PTH as well as systemic involvement	Calsification with diffuse neurofibrillary tangles neurofibril difus, Fahr's disease	
	Others	Aging process	
	Hereditary familial condition with metabolism abnormalities from calcium, phosphor and PTH	Familial hypoparathyroidism, pseudohypoparathyroidism type 1a	
	Hereditary familial condition without metabolism abnormalities from calcium, phosphor and PTH	Aicardi-Goutiere syndrome, dihydropteridine reductase deficiencies,Cockayne type 1 syndrome, Fahr's disease	
	Hereditary familial condition with unknown chromosomal location	Raine sindroma, Encephalopathy syndrome with intracranial calcification, White matter lesion, pseudo-TORCH syndrome	

Table 3. Clinical Manifestation in Fahr's Syndrome

Author(Year)	Clinical Presentation		Study type
	Organ	Specific Presentation	
Saleem et al (2013)[2]	Neurologic	Loss of consciousness Tetany Seizure Epilepsy Gait abnormality Spastic Speech disorder Dementia Myoclonus Coma Paroxysmal choreoatetosis Dystonia choreoatetosis Papiledema pleositosis CSF	Literature Review
	Movement disorder	Easily fatigued Unstable gait Involuntary movement Muscle cramping	
	Neuropsychiatric disorder	Psychosis Depression Apoplexia Intellegency disorder Inability to make decisions	
Marlena et al (2009)[21]	Neurologic	Recurrent syncope	Case Report
	Cardiologic	Hypocalcemic cardiomyopathy	

CONCLUSION

Fahr's syndrome is a constellation of syndrome that is increasingly common to be found although the knowledge about this disease is still largely unknown. Clinicans are encouraged to include this syndrome in the differential diagnosis when a patient presents with neurologic complaints that are suggestive of Fahr's syndrome. Finding out the underlying disease(s) or comorbid(s) is also imperative as it will affect the treatment for the patient.

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