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Case Report

Multi territory ischemic stroke in a patient with Fahr's disease: Report of a rare case ☆,☆☆

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ABSTRACT

Fahr's disease is a rare neurodegenerative condition characterized by widespread cerebral calcium accumulation and cell death, mostly in the bilateral basal ganglia and dentate nuclei of the cerebellum. Concurrent findings of Fahr disease with multi territorial ischemic stroke and falx lipoma has been rarely reported till date. We discuss the case of a 75-year-old female Pakistani by birth, with Fahr's disease who presented with an ischemic stroke.

Introduction

Fahr's disease also named as bilateral striopallidodentate calcinosis (BSPDC), was first described in 1930 and ever since as a rare genetic neurodegenerative disease characterized by presence of idiopathic abnormal calcifications in bilateral basal ganglia and also at other locations including hippocampus, thalamus, cerebral cortex, dentate nucleus, and cerebellar subcortical white matter [1]. There is usually absence of an underlying cause explaining the excess calcium deposition like biochemical imbalance, toxins, endocrine disorders, infections or trauma history. If 1 or more of these are attributable causes, it is described as Fahr's syndrome. Although the exact pathogenesis is not known, however T2 hyperintensity on MRI may suggest progressive inflammatory or metabolic process which consequently calcifies [2]. Calcium and other minerals are found deposited in walls of capillaries, arterioles, venules and perivascular spaces [3].

Commonest manifestations are movement disorders (50%) predominantly parkinsonism, cognitive impairment, speech disorder and cerebellar dysfunction [4]. These calcifications allude probability of ischemic stroke, however very few cases with stroke as presenting symptom have been described. We hereby describe a case of Fahr's disease presenting with stroke symptoms.

Case presentation

About 75 years old female presented to emerhgency department with high blood pressure followed by slurred speech. Urgent CT scan head without contrast was performed.

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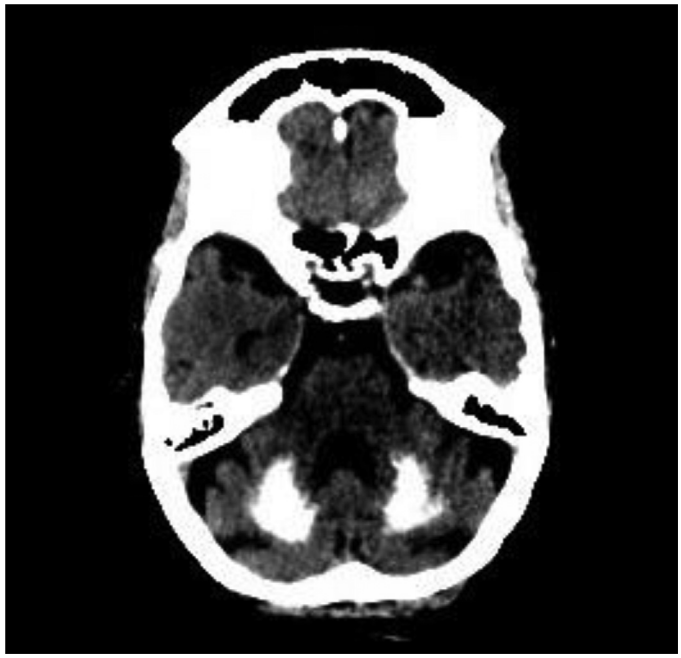

Fig. 1 – CT noncontrast axial showing bilateral cerebellar calcifications in dentate nuclei.

Extensive bilateral symmetrical calcifications were noted involving dentate nuclei of bilateral cerebellar hemispheres as well as basal ganglia. Accentuated hypodensity in right frontoparietal lobe as well as right basal ganglia with effacement of cortical sulci was also noted suggestive of acute infarct in right MCA (middle cerebral artery) and ACA (anterior cerebral artery) territory. Frontal horn of right lateral ventricle was slightly effaced likely due to mass effect of the aforementioned establish territorial infarct. There was subtle contralateral midline shift of 3.5 mm. Few internal hyperdensities were also noted with CT attenuation of 60 HU, likely representing hemorrhagic conversion of infarct. Tiny lipoma along the anterior midline falx was seen, too small to characterize. Few additional accentuated hypodensities were seen involving subcortical and periventricular white matter, likely representing chronic microvascular ischemic changes. There was no uncal or tonsillar herniation (Figs. 1–9).

Patient followed by the ultrasound to assess the carotid dopplers. Mixed calcified/noncalcified plaque were seen at right carotid bifurcation extending into ICA causing upto 50 % luminal narrowing.

PSV was raised in right ICA of 180 cm/s. While PSV in right CCA was 40 cm/s. Peak systolic velocity ratio = ICA/CCA = 4.5. Mixed calcified / non calcified plaque at left carotid bifurcation was also seen extending into ICA without causing any significant stenosis (Peak systolic velocity ratio = ICA/CCA = 0.5).

Patient also underwent other important examinations including ECG which showed normal sinus rhythm with PVC's, however lab markers and Echocardiography were essentially normal.

Thus, it is a very rare case to be reported having concurrent findings of Fahr disease along with multi-territory ischemic stroke and a tiny falx lipoma.

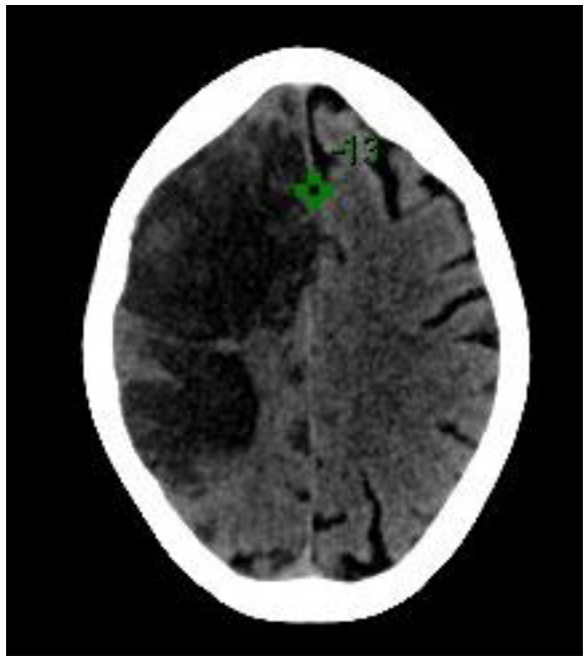

Fig. 2 – CT noncontrast axial showing falx lipoma.

Discussion

Fahr's disease, also known as idiopathic basal ganglia calcification (IBGC), is a rare neurodegenerative disorder characterized by diffuse, symmetric intracranial calcium deposition and associated cell loss, primarily in the bilateral basal ganglia

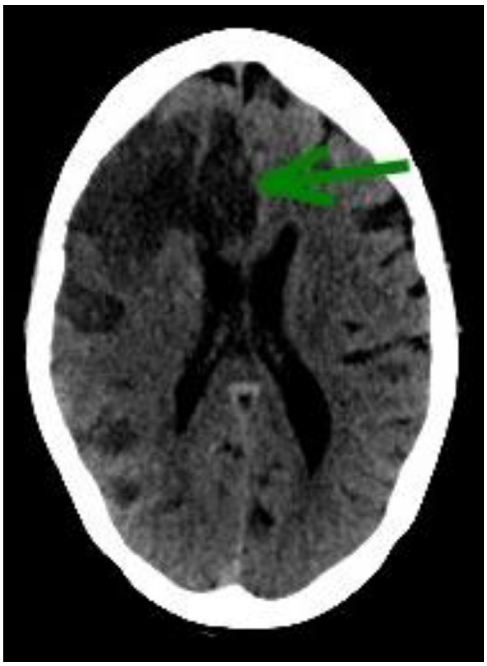

Fig. 3 – CT noncontrast axial showing right ACA and MCA infarct.

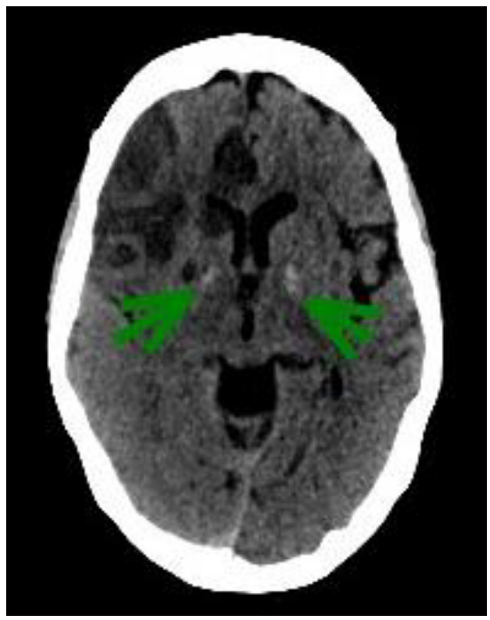

Fig. 4 – CT noncontrast axial showing bilateral basal ganglia calcifications and right sided ACA/MCA infarcts.

and dentate nuclei of the cerebellum, in the absence of other causes of secondary calcification. Karl Theodor Fahr originally characterized the condition in 1930 [1]. Patients often report with persistent, increasing cognitive decline, mental issues, and extrapyramidal symptoms. The specific process is not entirely apparent. It is proposed that calcifications in Fahr's illness may be attributable to a metastatic deposition, related to local disruption of the blood-brain barrier (BBB), or a disturbance of neuronal calcium phosphorus metabolism [5]. Fahr's disease can present in autosomal dominant, familial, or sporadic forms. Recent genetic study has revealed

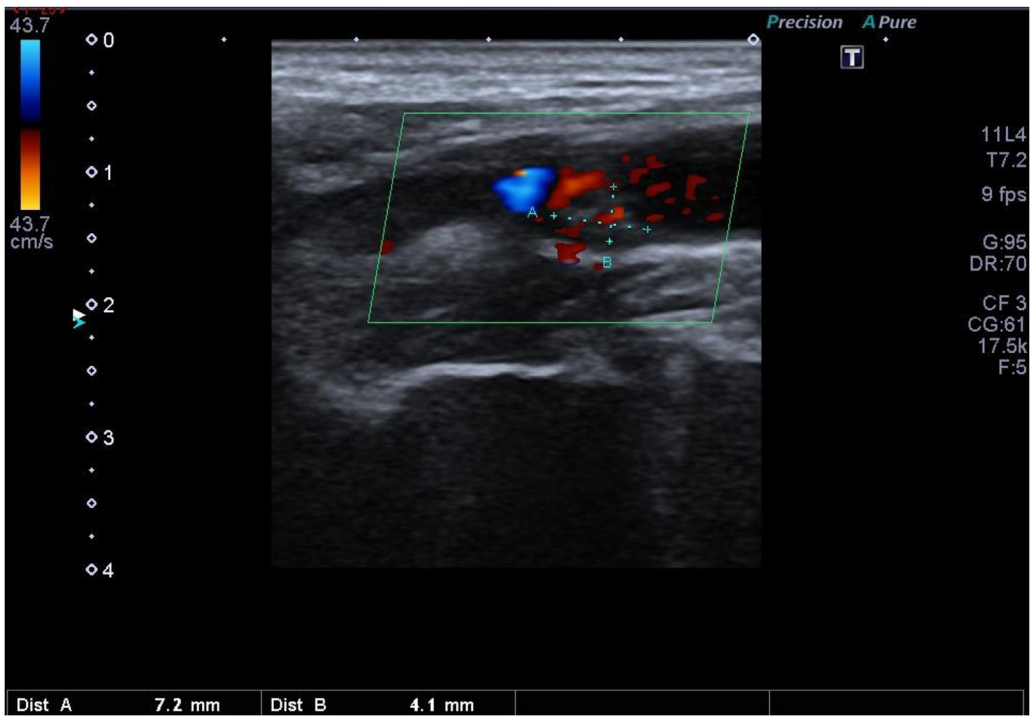

Fig. 5 – Mixed calcified/noncalcified plaque at right carotid bulb.

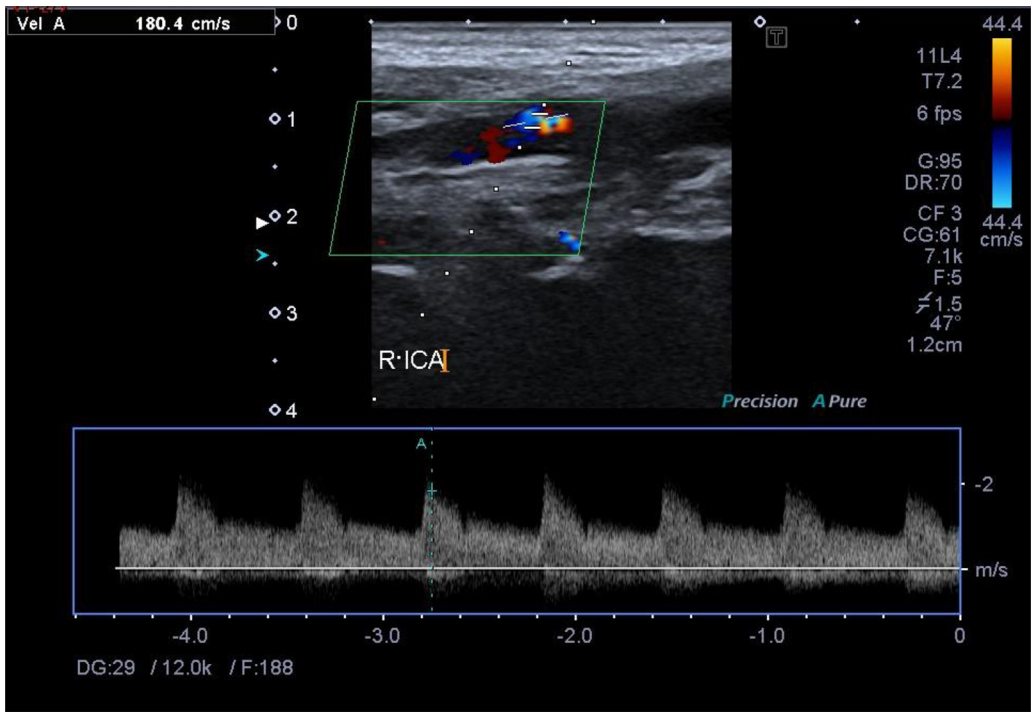

Fig. 6 – PSV in right ICA of 180 cm/s.

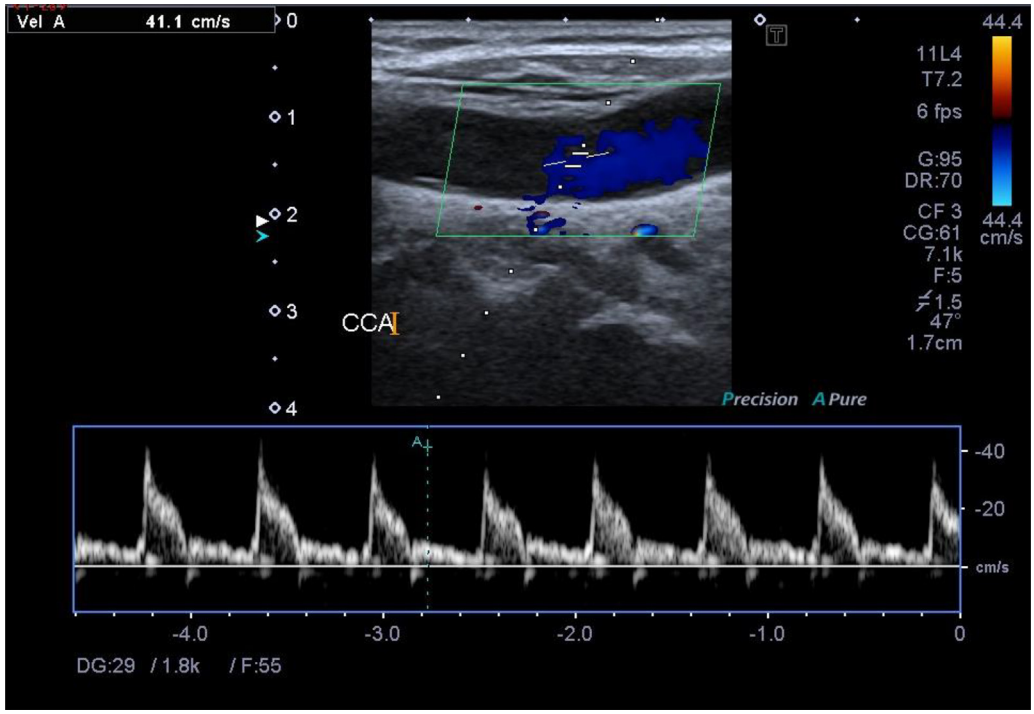

Fig. 7 – PSV in right CCA of 180 cm/s.

mutations in SLC20A2, a gene in the IBGC3 region that encodes type III sodium-dependent phosphate transporter 2 (PiT2), as a primary cause of dominantly inherited Fahr's disease [6]. Fahr's disease must be separated from Fahr's syndrome, in which basal ganglia calcification is a secondary cause. Pathologic basal ganglia calcification can be caused by idiopathic hypoparathyroidism, secondary hypoparathyroidism, hyperparathyroidism, post-thyroidectomy, birth anoxia, cysticercosis, toxoplasmosis, calcified infarction, HIV infection, and other factors [7]. In general, endocrine, toxic, metabolic,

Echo Measurement	Result	Normal(mm)	Doppler Measurement	Result	Normal(m/s)
L.V. End Diastolic	32	35 - 55	Aortic Peak Flow Velocity	01.51	0.9 - 1.7
L.V. End Systolic	21	25 - 41	Peak TR gradient		mmHg
Septal Thickness End Syst	15	14	Aortic Gradient (Peak)		mmHg
Septal Thickness End Diast	12	11	Mitral Area		3 - 5 cm2
Inf/Post Wall End Syst	14	14	Aortic Area		2 - 3 cm2
Inf/Post Wall End Diast	11	11	E/A Ratio	00.48	1.6 ± 0.5
Right Ventricle		9 - 26	IVRT	78	73 ± 13ms
Right Atrium (4-C)		27 - 37	Deceleration Time	275	199 ± 32ms
Left Atrium	38	19 - 40	Valvular Regurgitation	None / Mild / Mod / Sev	
Aortic Root	27	20 - 37	Mitral Regurgitation	Mild	
Aortic Valve Opening	15	15 - 26	Tricuspid Regurgitation		
Ejection Fraction	55 %	54-75%	Aortic Regurgitation		
			Pulmonic Regurgitation		

** *INTERPRETATION* **
- Left ventricle is normal in size.
- Left ventricle systolic function is normal.

Fig. 8 – Echocardiography.

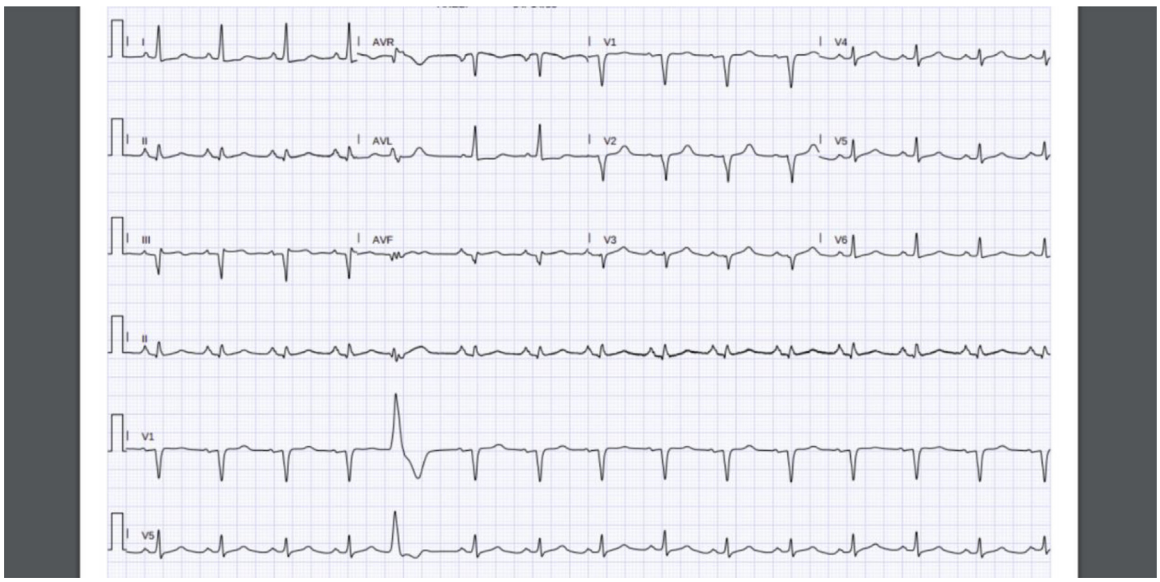

Fig. 9 – ECG.

or degenerative etiologies cause widespread and symmetrical intracranial calcification. Pathologic calcified lesions caused by infectious illness, vascular injuries, or neoplasms are often dispersed and asymmetrical in size and location [8,9].

Fahr's disease and ischemic stroke do not have a known connection. In 2 case reports, transient ischemia attack-like events were associated with Fahr's disease [10,11]. However, there have been relatively few case reports indicating acute infarction in Fahr's illness with positive MRI results and discussing its relationship with young-onset ischemic stroke. Furthermore, this is the first case report of Fahr's illness in combination with multi-territorial ischemic stroke and falx lipoma in the Asian population. Although the age at onset of neuropsychiatric symptoms in Fahr's disease is typically in the fourth to sixth decades of life, highly variable clinical manifestations have also been reported in childhood-onset cases, indicating phenotypic heterogeneity and different functional impairment in the young-aged population [12]. Furthermore, the clinical manifestations are also connected with the calcified sites, the number of calcifications, and hence alterations in functional circuits [13].

There is no particular therapy for Fahr's disease that slows the growth of brain calcification. Treatment is often symptomatic. The trial of a central nervous system-specific calcium channel blocker, such as nimodipine, failed to demonstrate effectiveness [14]. In some preclinical investigations, disodium etidronate, a biphosphonate, provided functional benefit and symptomatic relief without reducing the number of calcifications. The relationship between ischemic stroke and FD has not been fully established. Previous research has indicated that calcification occurs in the walls of capillary arteries, arterioles, and the perivascular space of FD patients, suggesting that this might be a causal mechanism [15]. For example, Nishimoto et al [16] documented a case of FD coupled with cerebral micro-infarctions and discovered reduced cerebrovascular reactivity on SPECT with an acetazolamide challenge in their patient. Based on their data, they hypothesized that a reduction in vascular diastolic capacity caused by calcification might be one of the reasons. Nonetheless, the real frequency of acute ischemic stroke in Fahr's illness is unclear because to a paucity of large-scale studies.

The crux is, the data suggest that substantial calcium deposits in afflicted arteries may lead to small-artery blockage and, ultimately, ischemic stroke. More research is needed to understand the association between FD and ischemic stroke, as well as the therapeutic strategy for these individuals.

Conclusion

Only a few case studies have revealed acute ischemic stroke or transient ischemic attack-like events in FD, thus the findings in this case will be useful in the future for predicting and managing stroke in FD patients.

Patient consent

IRB from the ethical committee taken as well as from the patient. This can be provided if asked.

Author contributions

All authors contributed equally to the drafting of study.

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