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Case Report

Fahr's disease: A rare neurological disease

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ABSTRACT

A 40-year-old unmarried female presented with abnormal involuntary choreo-athetoid movements involving both upper limbs for 5 years along with features, such as bouts of disorientation, anxiety, personality changes, reckless behaviour, inappropriate laughter and progressive decline in the neurological status. On neurological examination, her speech was dysarthric with mild choreiform movements involving both upper limbs. She had MMSE score of 20/30. MRI scans of the brain plain T1- and T2-weighted axial and flair coronal images were obtained. It showed calcifications as hyper-intense lesions on T1W and hypo-intense T2W lesions in bilateral basal ganglion and bilateral dentate nuclei of cerebellum, that is consistent with Fahr's syndrome.

1. Case report

A 40-year-old unmarried female presented to our tertiary care hospital with abnormal involuntary movements involving both upper limbs for last 5 years, but no such movements were noticed in the lower limbs. These movements were suggestive of choreo-athetoid movements. The family also noticed that for the same period, the patient had features, such as bouts of disorientation, anxiety, personality changes, reckless behaviour and inappropriate laughter. For these symptoms, she was under the care of a psychiatrist, and was put under some medication. Despite this, she was having a progressive decline in the neurological status.

There was no significant family history of mental illness, dementia or any other physical illness. She did not have any features of depression. On neurological examination, the patient was alert, oriented to time, place and person. She had bursts of laughter. Cranial nerves were normal, as well as power and sensations were found to be normal. Her speech was dysarthric and mild choreic involving both upper limbs. She had a score of 20/30 on the mini mental state examination. No parietal lobe signs, Parkinson's features or any other features suggestive of long tract signs.

In order to exclude other differentials that may lead to secondary intracranial calcification, the patient went through a series of blood tests that included completed blood picture, erythrocyte sedimentary rate, serum iron studies, serum calcium and phosphate level, serum parathyroid hormone level, thyroid hormone level, serum creatinine, serum cerulo-plasmin and urinary copper, serum lactate and pyruvic acid, serological tests for syphilis, HIV and CSF study to rule out

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other metabolic, infectious causes. All these tests were essentially normal in our patient. Her electroencephalogram was also done, which was normal. MRI of the brain plain T1 & T2 weighted axial and flair coronal images were obtained. It showed calcifications as hyper-intense lesions on T1W and hypo-intense T2W lesions in bilateral basal ganglion and bilateral dentate nuclei of cerebellum that is consistent with Fahr's syndrome (Fig. 1).

2. Discussion

Basal ganglia calcification is also known as Fahr's disease or Fahr's syndrome. It is a rare inherited or sporadic neurological disorder with a worldwide prevalence of <1/1,000,000.[1–3] It was first described by German neurologist Karl Theodor Fahr in 1930.[4] It is characterized by abnormal deposition of calcium in areas of the brain that control movements including basal ganglia, thalamus, dentate nucleus, cerebral cortex, cerebellum, subcortical white matter and hippocampus.[5] Most cases present with extra pyramidal symptoms initially. Additionally, they may present with cerebellar dysfunction, speech difficulty, dementia and neuropsychiatric symptoms.[6] Fahr's syndrome typically manifests in third or fourth decade of life.

Fahr's disease is most commonly transmitted as an autosomal dominant trait, but it may also be passed on as an autosomal recessive trait, or it may occur sporadically.[1,7] A locus at 14q (IBGC1) has been suggested to be involved commonly. At the molecular level, calcification generally develops within the vessel wall and in the perivascular space, ultimately extending to the neuron. Due to defective iron transport and free radical production, tissue damage occurs which leads to the initiation of calcification. It occurs secondarily around a Nidus composed of mucopolysaccharide and related substances. Progressive basal ganglia mineralization tends to compress the vessel lumen, thus initiating a cycle of impaired blood flow, neural tissue injury and mineral deposition.[8] Endocrine disorders, particularly parathyroid disturbances are most commonly associated with Fahr's syndrome. Many neurodegenerative, inherited and infectious conditions have also been linked to etiological manifestations of Fahr's syndrome (Table 1).[8]

Presentation of disease could vary with the age and course of illness (Table 2). The clinical features usually include psychosis, cognition impairment, and symptoms of mood disorders, epileptic seizures and dementia.[9,10] Excessive extensive intracranial calcification is also associated with psychiatric manifestation.[10]

Cummings et al. (1983) have described two psychiatric symptoms in basal ganglion mineralization, as cases with psychiatric symptoms appearing in the early period (mean 31 years) and in late period (mean 49 years). Motor and cognitive symptoms in cases with basal ganglion mineralization, which appears in the late period, are more significant.[11]

Pallidal lesions may cause disorders related to motivation, judgement and insight in humans. Idiopathic basal ganglia calcification may lead to various neuropsychiatric symptoms. Patients with basal ganglia calcification present initially with psychiatric symptoms. When psychosis occurs in Fahr's disease, it usually presents in persons 20–40 years of age as a part of the so-called early adult-onset Fahr's disease. Classic schizophrenia-like symptoms have been described, including auditory hallucinations, paranoid delusions, delusions of reference and catatonia. Psychotic symptoms that are not typically associated with schizophrenia have also been described, including musical auditory hallucinations and complex visual hallucinations.[12]

The pathophysiology of psychosis in Fahr's disease remains unknown, though previous studies have found a

Table 1 – Etiological manifestations of Fahr's syndrome.

S. no.	Etiologies	
1	Endocrine disorders	Idiopathic hypoparathyroidism Secondary hypoparathyroidism Pseudohypoparathyroidism Pseudo-pseudohypoparathyroidism Hyperparathyroidism
2	Adult onset neurodegenerative conditions	Neurodegeneration with brain iron accumulation disease Neuroferritinopathy Polycystic lipomembranous Osteodysplasia with sclerosing Leukoencephalopathy
3	Infectious disease	Intrauterine and perinatal infection Cockayne syndrome Type 1 Cockayne syndrome Type 2
4	Inherited or early onset syndrome	Aicardi-Goutieres syndrome Tuberous sclerosis complex Brucellosis Coat's disease

Table 2 – Clinical features of Fahr's syndrome.

S. no.	Clinical features	
1	Neurological	Loss of consciousness Tetany Seizures Epileptic disorder Gait disorder Spasticity Speech impairment Dementia Myoclonus Coma Paroxysmal choreoathetosis Dystonic choreoathetosis Papilledema of intracranial hypertension Pleocytosis of CSF
2	Movement disorder	Clumsiness Fatigability Unsteady gait Involuntary movements and muscle cramping
3	Neuropsychiatric features	Psychosis Depression Apoplexia Deterioration of intelligence Inability to make decisions