Fahr's syndrome: a rare clinico-radiologic entity

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INTRODUCTION

Fahr's syndrome is a genetically dominant, degenerative disorder characterised clinically by multiple neurological and psychiatric symptoms occurring secondary to calcification in brain parenchyma with subsequent neuronal loss. Presence of bilateral and symmetrical intracerebral calcifications in the basal ganglia, thalamus, dentate nucleus and centrum semiovale region due to unknown aetiology is referred to as Fahr's disease or idiopathic striopallidodentate calcinosis. Fahr's syndrome includes Fahr's disease as well as secondary causes of striopallidodentate calcinosis.^{1,2} Though the disease can present in childhood or adolescence the usual age of presentation is 4th–5th decade.

CASE REPORT

A 56-years-old female with a 6–12 months history of worsening forgetfulness, generalised seizures and headache came for non-contrast computed tomography (NCCT) of brain. She was allegedly having mild degree of similar complaints for last 3–4 years with medical treatment for which no records were available. Clinical examination revealed normal orientation to time, place and person with normal level of consciousness. There was mild degree of dysarthria, dysdiadochokinesia and ataxia; however, no evidence of any spasticity was noted. Rest of the neurological and physical examination was unremarkable.

Laboratory examinations including blood levels of glucose, iron, calcium, ferritin and parathormone were within normal limits. ECG and EEG examinations were within normal limits. NCCT brain revealed bilateral and symmetric, extensive, irregular, amorphous, intraparenchymal calcifications involving the white matter in the frontal, parietal, temporal and occipital lobes; basal ganglia, thalamus and dentate nucleus (Figures 1–4).

In the white matter, the calcification was noted at the cortico-medullary junction with no evidence of any adjacent atrophy. In addition, midline irregular calcification was noted in the pons (Figure 1).

Based on the clinico-radiological and biochemical findings, the provisional diagnosis of Fahr's syndrome due to idiopathic striopallidodentate calcinosis or Fahr's disease was strongly suggested. As there was no known cause, the patient was advised anti-convulsants and regular follow-up. The latter was unremarkable for nine months.

Figure 1 Non-contrast transaxial scan shows midline calcification in pons and bilateral symmetric calcification in dentate nuclei.

Figure 2 Non-contrast transaxial scan shows bilateral symmetric calcification in temporal lobes.

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Figure 3 Non-contrast transaxial scan shows bilateral symmetric calcification in basal ganglia, thalami and fronto-parieto-occipital white matter.

Figure 4 Non-contrast transaxial scan shows bilateral symmetric calcification in fronto-parietal white matter.

DISCUSSION

Although the exact prevalence of Fahr's syndrome is not known yet intracranial calcifications can be detected incidentally in up to 0.3–1.2% of NCCT examinations of brain.³ Although bilateral and symmetric basal ganglia calcification is known to be associated with multiple medical conditions, the exact etiology is still unknown.⁴ Genetic alterations have been attributed to genes in the region of chromosome 14.⁵ Many of these conditions involve the basal ganglia only or predominantly. The condition that has been closely described with diffuse, bilateral, symmetric striopallidodentate calcinosis is primary hypoparathyroidism.^{1,6,7} Other causes include lupus, tuberous sclerosis, Alzheimer's disease, myotonic muscular dystrophy and mitochondrial encephalopathies.⁸ When there is no explainable cause for striopallidodentate calcinosis, the condition is termed as Fahr's disease. None of the previously described cases of Fahr's disease has been associated with calcification in pons, as seen in our index case.

The most common neurological manifestations include headache, seizures and movement disorders. Other specific

manifestations include gait disturbances, dystonia, paresis, speech alterations, dementia, Parkinsonism, tremors, chorea, etc.^{1,4,9} Psychiatric manifestations most commonly include cognitive and psychotic disorders that were not observed in our case.^{4,10} Psychiatric symptoms usually precede neurological manifestations.¹⁰

Combination of neuropsychiatric manifestations and striopallidodentate calcinosis is referred to as Fahr's syndrome. The term idiopathic Fahr's syndrome is used to refer clinical manifestations coupled with Fahr's disease.^{1,2}

Laboratory examinations should include tests for blood calcium and parathormone which in addition to the other routine blood tests will help in differentiating idiopathic Fahr's syndrome (unremarkable laboratory test results) from secondary cases especially due to hypoparathyroidism. NCCT brain will demonstrate the presence and extent of parenchymal calcification. None of the previously reported cases of idiopathic Fahr's syndrome has described pontine calcification as was seen in our case.^{1,3,4,7,10,11} The pontine calcification was in the midline and may have possible clinical and treatment implications in these patients and may even help to predict the prognosis in some patients. T2 GRE magnetic resonance images (MRI) sensitively demonstrate areas of calcification as areas of low signal. Demyelinated areas appear hyperintense on T1 and T2 FLAIR images. However, no significant role of MR imaging or MR spectroscopy over CT has been demonstrated. The usefulness of ^{99m}Tc-HMPAO brain perfusion SPECT in deciding clinical approach to Fahr's syndrome has been suggested.¹²

The treatment of Fahr's syndrome is directed to the identifiable cause especially hypoparathyroidism. In other cases, symptomatic or conservative therapy with clinical follow-up is the rule.¹ Prognosis is variable, cannot be predicted and is unrelated to the extent of calcification. Death usually occurs secondary to neurological deterioration.

To summarise, though Fahr's syndrome and Fahr's disease are rare entities they should be suspected in patients with neuropsychiatric disturbances and seizure disorder. Routine biochemical investigations should always be performed to rule out metabolic causes. Conversely, all patients with incidentally detected striopallidodentate calcinosis should be subjected to thorough neuropsychiatric examination and if required, biochemical tests. Knowledge of the associated conditions will not only help to rectify the treatable cause but will also prevent unnecessary treatment in others.

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CONFLICTS OF INTEREST

None.

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Journal Scan

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It is essential to underline current and future needs in polio eradication strategy. We need to perform certain studies especially on mOPV/bOPV in the settings of high WPV endemicity, especially in western UP and central Bihar. Article mentions recommendations of the third National Consultative Meetings on Polio Eradication (NCMPE) and an update on previously stated 'IAP Position'. Polio eradication committee (PEC) believes that 2010 is a crucial year for polio eradication in India—by achieving good control over transmission of type 1. According to the 'four-year' cycle, a type 1 polio outbreak is due in 2010, but it should not be allowed to happen. With the availability of bivalent OPV (bOPV) against types 1 and 3, type 3 WPV can also be drastically controlled, simultaneously. If current strategy fails PEC advocates the need of having a "plan B" ready where IPV will be used in endemic areas, as recommended earlier by PEC. PEC believes that OPV had failed to provide adequate herd effect. Mucosal immunity induced by OPV is not only ineffective against WPV infection, but it also wanes over time. Furthermore, mucosal immunity is better when vaccine efficacy is high, and ultimately it correlates more closely with the titre

of homologous humoral antibody than its mere presence. OPV's efficacy is low and the force of transmission of WPV is very high in Northern India. The role of IPV (one or preferably two doses) in rapidly boosting mucosal immunity can be worth considering here instead of broadening the age of OPV administration, as has been proposed. Success of the GPEI in India depends on how efficiently and intelligently all the available vaccines against polio are utilised. ICMR/GPEI, based on the evaluation of all the study findings suggests an alternate approach as achieve high coverage with tOPV at birth (avoiding days zero to two), six weeks, 10 weeks, 14 weeks, and 15–18 months. PEC advocates bOPV for all Supplementary Immunisation Activity (SIAs) with the number of National Immunisation Days (NIDs). PEC has recommended to the Ministry of Health (MoH)/Government of India (GOI) to start discussions to plan appropriate strategies and measures to prevent and pre-empt the outbreaks of cVDPV, especially during post-eradication era. PEC believes that rebuilding Universal Immunisation Programme (UIP) in several States has to be undertaken as an immediate priority.

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