Fahr's Disease Vs. Drug Induced Movement Disorder: Case report and Literature Review

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Introduction

Fahr's disease is Familial Idiopathic Basal Ganglia Calcification characterized by bilateral intracranial calcification and associated with neuropsychiatric manifestations. Fahr's disease referred to Fahr's (German neurologist) who described a case with bilateral calcifications in the basal ganglia and other parts of the brain in 1930, despite the fact that he was not the first to describe this kind of calcification nor did he contribute significantly to the understanding of this disorder. Most cases of Fahr's disease are autosomal dominant, but familial and sporadic cases had been documented and autosomal recessive cases had been reported. In dominant cases, most of afflicted family members by cerebral calcification are asymptomatic and even some of them may not show calcification changes till they get older. Although there is...
no strong evidence and some researchers doubt it, TULIP1 gene on chromosome 14q has been suggested to be the responsible gene (For what? Farah's disease?) 4-7. Fahr's disease cases are usually diagnosed by exclusion of other causes of Fahr's syndrome e.g. hypoparathyroidism, neurobrucellosis, CNS TB, toxoplasmosis, Wilson disease and Huntington's disease.

Case Report
A 26-year-old single retired soldier, schizophrenic patient, admitted to psychiatric ward on 2004 after seeing the outpatient psychiatric clinics in the Military Hospital with his family. The patient's family reported that he started to develop abnormal involuntary movement of the trunk and upper limbs which worsen progressively and interfered with his daily live activity during the last six months prior to his visit. They also admitted that he had low self care, aggressive behavior but denied any recent history of thought, perception or cognitive abnormalities. Actually, the patient was seen in the out-patient clinics before, where his condition was diagnosed as drug induced movement disorder -extrapyramidal side effect secondary to his antipsychotic medication- (Resperidone 4 m.g, Procyclidine 5 m.g and Fluanxol depot 30 mg every 4 weeks), antipsychotic discontinued and his anticholinergic drugs increased without any improvement.

The patient was diagnosed as a case of schizophrenia for 4 years after he suddenly developed paranoid delusions with aggressive behavior. During this period the patient was admitted three times in three different tertiary hospitals, diagnosed as a case of Paranoid schizophrenia, and prescribed different kinds of typical and atypical antipsychotic medications, but he didn't fulfill his medication and his condition deteriorated progressively inform of positive and negative symptoms' of schizophrenia (and he has been retired? What does this mean? The patient retired because of the negative effect his case had or because of him not complying with his medication?).

The patient is the 4th amongst his 10 siblings, 7 males and 3 females, whom were all healthy with no history of psychiatric or neurological disorders. His parents denied any heredity of similar conditions of abnormal movements in the family. The examination of the patient's neurological and mental state showed a calm, cooperative, older than his stated age, thin, unclean dressing with poor self hygiene patient.

The patient demonstrated an abnormal bizarre choreoathetoid movement of trunk and upper limbs, dysarthric speech and euthymic mood with appropriate affect and his perceptual feeling intact. Upon examinations of his thought and cognition revealed no abnormalities. Other physical examinations were unremarkable.

Upon the patient's admission at a neurologist was consulted and an MRI scan and the following investigations were done: CBC, U&E, LFT, parathyroid hormone, HIV, syphilis, Hepatitis viruses screening & urine drug screening.

All of the patient's lab tests were within normal limits and his MRI showed the following: Calcific changes, which involved basal ganglia bilaterally, both dentate nuclei and subcortical area and centrum semiovale of both hemispheres (Figure 1). After that, a radiologist asked for a CT scan, which confirmed the finding and revealed extension of calcification to caudate nuclei, inferior aspect of thalami and cerebellum (Figure 2, 3).
Figure 1: MRI Brain demonstrated calcific changes which involved basal ganglia bilaterally.

Figure 2: CT Brain revealed calcification of caudate nuclei.
Therefore, the patient's condition was diagnosed as Fahr's Disease after the exclusion of other disorders like, Wilson disease and metabolic disorder related to parathyroid hormone.

Upon admission to (Where?), the patient received a small dose of clozapine, which was discontinued, then Tetrabenazine was prescribed by neurologist, who added Sodium valproate later. The patient's condition did not show any marked changes and was discharged in order to be admitted to a long-term rehabilitation facility. However, after that, patient was seen once at an ER with the same presentation, but no more visits were made since then.

Discussion

The most common sites of calcifications are basal ganglia and dentate nuclei of cerebellum. Hence, one of the other names of the disease is Bilateral Striopallidodentate Calcification (BSPDC). However, calcification can involve centrum ovale, Thalami, cerebral cortex, subcortex and no part of the brain could be spared. The extension of calcification is directly related to the psychiatric manifestations, but not to the neurological ones, which could explain the presentation of the acute psychosis in the patient in this study. Functional brain neuroimaging showed different inconsistent findings according to the clinical presentation, showing part of the brain affected by calcification.

Postmortem histology studies of the lesions showed mainly calcium compositions, but other items like phosphorus, iron, magnesium, aluminum and zinc had been identified as well. However, no important
clinical issues were related to these components. 

Fahr's disease has a broad spectrum of clinical neurological presentation. Patients can be presented with movement disorders, executive and cognitive impairment, seizures, pain, pyramidal symptoms, cerebellar signs and other different presentation, depending on which part of the brain was affected by lesion. Manyam BV et al. 2001 analyzed presentations of sixty one symptomatic cases and found that movement disorders were the most common presentation, which accounted for 55% of clinical presentations Parkinsonism 57%, chorea 19%, tremor 8%, dystonia 8%, athetosis 5% and orofacial dyskinesia 3%. About 40% of patients with Fahr's disease present initially with psychiatric features. Cognitive, psychotic, and mood disorders are the most common presentations. Fahr's disease may present as a progressive subcortical dementia in elder patients and those who were presented earlier with other psychiatric presentations e.g. psychosis, mood disturbance, are most likely to progress to dementia. Paranoid and psychotic features occur between the ages of 20 and 40. They may take the form of delusions, persecutory ideas, auditory and visual hallucinations or fugue state. Mood disturbances are the most frequent psychiatric presentations and eventually afflict two-thirds of the patients and up to one-third may be affected by anxiety disorders. Fahr's disease has poor prognosis since there is not an effective calcium chelating agent or another modality, which could affect intracranial calcification masses. Neuropsychiatric complications of the illness had different responses to antiparkinsonic and antipsychotic medications, though markedly less improvements than those seen with genuine diagnoses. In mood disorders, antidepressant agents showed good responses.

In the case presented in this study, it is not clear if the past active psychotic episodes of the patient were a genuine schizophrenic manifestation (supported by typical age at presentation and progressive course of the illness over long period) or just an early psychiatric presentation of Fahr's disease that preceded the movement disorder. Since the presentation is sudden, no family history of schizophrenia and because of the extensive calcification that was most likely to be there at the start of psychosis, the researchers suggest the later diagnosis, starting psychotic patients on antipsychotic need close monitoring and observation for any side effect development like movement abnormalities especially if there is no response to anticholinergic medications. Cerebral imaging is strongly indicated when patients without a family history of psychosis are presented with sudden psychosis or a case of unordinary movement complication to antipsychotic medication not responding to the usual interventions. Professionals in the psychiatric field should be more educated about other differentials and causes of medications' side effects in advance.

References:

ganglia calcification (Fahr's disease) without neurological, cognitive and psychiatric symptoms is not linked to the IBGC1 locus on chromosome 14q. **Hum Genet 2002;** 110(1):8-14.


