Idiopathic bilateral basal ganglia calcification (Fahr’s Disease) presenting with psychotic depression and criminal violence: A case report with forensic aspect

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SUMMARY

Fahr’s disease is a rare neuropsychiatric disease characterized by bilateral intracranial calcification, primarily in the basal ganglia. The more general term, Fahr’s syndrome, is used for primary and secondary basal ganglia calcification, regardless of the etiology, but the term Fahr’s disease is used to describe primary, idiopathic cases. Fahr’s disease may present with neurological symptoms, such as parkinsonism and extrapyramidal symptoms, dysarthria, paresis, convulsion, and syncope. Psychiatric disorders, including behavioral disorders, psychosis, and mood disorders, as well as cognitive disorders can occur. CT is useful for the diagnosis of Fahr’s disease. Herein we present a patient diagnosed as Fahr’s disease that presented with symptoms of depression, delusions, and auditory hallucinations. The 47-year-old male patient was hospitalized in a forensic psychiatry inpatient clinic due to aggressive behavior and was subsequently diagnosed with major depressive disorder with psychotic features. While hospitalized he was treated with antidepressant and antipsychotic drugs, as well as electroconvulsive therapy, resulting in significant improvement in his symptoms. As bilateral basal ganglia calcification was observed via CT, the patient was diagnosed as Fahr’s disease. This case report emphasizes the importance of cranial imaging and detailed laboratory examination when evaluating patients with psychosis and affective symptoms. Pathologies such as Fahr’s disease must be included in the differential diagnosis, especially in cases with neurological symptoms and cranial imaging findings.

Keywords: Fahr’s disease, depression, psychotic disorders

INTRODUCTION

Basal ganglia calcification (BGC) is referred to various terms such as Fahr’s disease (FD), Fahr’s syndrome (FS), pallidal calcification, striato-pallido-dentate calcification, and calcinosis nucleorum cerebri (Baba et al. 2005; Manyam 2005; Lauterbach 2000). FS is a more general term used for primary and secondary BGC regardless of the underlying etiology, whereas FD is used for primary idiopathic BGC (Ashtari and Fatehi 2010; Lauterbach 2000; Lauterbach et al. 1998). The etiology of FS is varied and includes developmental abnormalities, history of infections and inflammatory diseases, and exposure to toxins and radiation; however, endocrinopathies such as hypoparathyroidism and metabolic disorders—including changes in calcium metabolism—are more prevalent (Doğan et al. 2011; Casamassima et al. 2009; Koçak et al. 2009; Kökeş et al. 2009; Manyam 2005).

FD, first described by Fahr in 1930, is a rare and usually inherited condition characterized by neurological and psychiatric symptoms; however, in some cases it may be sporadic in nature (Bozkurt et al. 2011; Doğan et al. 2011; Akçali et al. 2009; Manyam 2005; Lauterbach 2000). It may present and follow a course with extrapyramidal symptoms, such as parkinsonism, chorea, tremor, and dystonia, neurologic disorders such as dysarthria, paresis, seizure, and syncope, psychiatric disorders such as behavioral disorders, psychosis, and mood disorders, and dementia and cognitive disorders (Baba et al. 2005; Benke et al. 2004). The most common symptoms are movement related, followed by cognitive symptoms (Manyam 2005).
FD is a progressive condition; abnormal calcium deposition generally starts during the third decade of life and neurological symptoms occur 2 decades later. There are also reports of pediatric FD cases (Bozkurt et al. 2011; Srivastava et al. 2010; Lauterbach 2000; Lauterbach et al. 1998) and several asymptomatic cases (Ashtari and Fatehi 2010; Akçali et al. 2009; Kökeş et al. 2009). The prevalence of FD is estimated to be <0.5% (Bozkurt et al. 2011; Lauterbach 2000) and it occurs more commonly in males (Kökeş et al. 2009; Manyam 2005).

CT is reported to be more sensitive for the diagnosis of FD and is better able to show regions of intracranial calcification (hyperdense lesions) than MRI (Doğan et al. 2011; Yilmaz et al. 2010; Akçali et al. 2009; Kotan and Aygül 2009; Lazar et al. 2009; Günsün et al. 2006; Manyam 2005; Aslantekin et al. 1999; Lauterbach et al. 1998). In addition, there are studies that used positron emission tomography (PET) (Benke et al. 2004) and single photon emission CT (SPECT) (Shouyama et al. 2005). Intracranial calcification is typically symmetrical and primarily occurs in the globus pallidus, as well as in the putamen, caudate nucleus, dentate nucleus, centrum semiovale, thalamus, and cerebellum (Yilmaz et al. 2010; Kökeş et al. 2009; Baba et al. 2005; Manyam 2005).

The basal ganglia constitute a functional unit that plays a role in motor learning, movement, attention and filtering, working memory, and implicit learning. Furthermore, they are thought to play a significant role in reward processes. Two interrelated circuits are mentioned to be associated with the pathophysiology of depression: 1. The limbic circuit, which connects the amygdala and anterior cingulate to the ventral striatum, and the medial and ventral lateral prefrontal cortex; 2. The prefrontal circuit, which connects the basal ganglia to the lateral prefrontal cortex. Pathological interactions between these 2 systems are suspected of playing a role in major depression. In clinical practice, the high frequency of depression in patients with Parkinson's disease and Huntington's disease supports the theory of basal ganglia involvement in the development of depression (Ring and Serra-Mestres 2002).

Herein we report a patient that was hospitalized in a forensic psychiatric clinic due to delusions, auditory hallucinations, and violent behavior, and subsequently diagnosed with idiopathic bilateral BGC.

**CASE**

A 47-year-old male was admitted to assess his criminal responsibility for wounding his son with intent. The patient had a 1-month history of headache, forgetfulness, sleep disturbance, sadness, malaise, difficulty concentrating, and distress. Cranial MRI findings were normal and he was non-compliant with the recommended medical treatment. He had stabbed his son with a knife the day before admission. The patient reported that he was confused that day, and felt as though he was possessed. He reported than an inner male voice was constantly urging him to complete his last mission (to kill his son), leading him to his son's room. He did not clearly remember the moment he stabbed his son, but remembered standing still in a dazed state of mind after the attack, being very surprised, and feeling regretful. He reported that he no longer heard the inner voice after having attacked his son.

During psychiatric examination the patient was conscious, cooperative, and oriented to time and place. He spoke slowly with a low volume. He exhibited a depressive mood, and felt distressed and anxious. His associations were slow and he had difficulty concentrating on a target. He did not have delusions or hallucinations. He appeared confused, answering questions by repeatedly saying, “I don't remember” or “I don’t know”. As such, we were unable to completely discern his mindset and thought process.

The patient reported that he had presented to a psychiatrist 13 years earlier due to sleeplessness, distress, and headache, that he completely recovered after 1-year of outpatient therapy, and that he had occasional recurrence of the same symptoms since then, but hadn't sought treatment. The patient is described by his family as an introspective, quiet, careful, and respectful man without a history violent behaviour towards his son or anybody else. He had a negative history of smoking, and alcohol or psychoactive substance use. Family history of neurological and psychiatric disease was negative.

The physical and neurological examinations were unremarkable. The patient’s biochemical profile, CBC, sedimentation rate, thyroid function tests, vitamin B12 and folic acid levels, urinalysis, PA lung X-ray, and ECG were normal. The patient was negative for hepatitis, HIV markers, VDRL-RPR, and titration. Urinalysis was negative for psychoactive substances. EEG was normal, cranial CT scan showed bilateral BGC (Figures 1a and 1b) and a millimetric focus of calcification in...
the right frontal periventricular white matter (Figure 2). The patient had normal parathyroid (PTH) and 1,25 dihydroxy vitamin D3 levels.

Psychometric examination was performed using WAIS and the verbal IQ score was 108. The Rorschach protocol showed intense anxiety and dominating paranoid thoughts, with significant symptoms of depression, sense of weakness, and depressive affect.

After admission, the patient was given venlafaxine 75 mg d−1 and lorazepam 5 mg d−1. The lorazepam dose was reduced gradually and stopped upon a decrease in anxiety and the venlafaxine dose was gradually increased to 225 mg d−1 in one month. The patient’s symptoms of depression showed some improvement and the patient, having no suicidal thoughts or psychotic signs, reported that he was feeling better. In the following days, he patient expressed a sense of guilt because his son did not come to visit him and did not want to talk with him. 3 weeks later, his symptoms of depression exacerbated and he began to experience persecution and somatic delusions, reporting that his penis was cut into pieces with 4 knives in order to punish him. As the patient had suicidal ideation and psychotic symptoms, electroconvulsive therapy (ECT) was started.

During pharmacotherapy and ECT, the patient exhibited reticence and low psychomotor activity, reduced oral food and fluid intake, and avoidance of eye contact. Instead of revealing his thoughts, he muttered such expressions as, “I served my sentence”. He reported that he was tortured and that his penis was minced, and that he held the government and the Ministry of Health responsible for these actions, adding that he was forced to watch circumcisions in order to intimidate him and set an example. 10 days later, because of the persistence of his delusions of reference and persecution, the therapy was modified to haloperidol 20 mg d−1 IM, biperiden 10 mL d−1 IM with ECT, as the venlafaxine dose was reduced. Thereafter, the patient was given haloperidol 10 mg d−1 p.o., biperiden 4 mg d−1, venlafaxine 75 mg d−1, and quetiapine 100 mg d−1, along with 18 sessions of ECT. Following the discontinuation of ECT, the venlafaxine dose was increased to 150 mg d−1, haloperidol was discontinued, and risperidone 2 mg d−1 was started. One month later, the patient’s depressive and psychotic symptoms improved. The patient was followed-up with venlafaxine 150 mg d−1, risperidone 2 mg d−1 and quetiapine 100 mg d−1 and continued to improve; after 4.5 months of treatment his psychiatric examination findings were normal; therefore, it was determined that he had no legal responsibility for attacking his son and he was discharged.

Based on the psychiatric examination, history, assessments, and signs and symptoms observed during the hospitalization period, the patient was diagnosed as major depressive disorder with psychotic features, according to DSM-IV-TR criteria. In light of the cranial CT findings, normal PTH levels, consultations with the departments of neurology and internal diseases, and clinical examination results, the patient was diagnosed as FD. No additional suggestions associated with FD were made to the patient by these departments.

**DISCUSSION**

FD is diagnosed based on the evaluation of 3 main components: idiopathic non-atherosclerotic bilateral BGC, psychiatric symptoms, and extrapyramidal movement disorders (Doğan et al. 2011; Shouyama et al. 2005). The differential diagnosis of FD should include developmental defects, infectious and toxic etiologies, calcium metabolism disorders, and endocrinopathies such as hypothyroidism that could lead to FS (Manyam 2005). In the presented case PTH and calcium levels were normal, and biochemical test results and physical examination findings indicated that there were no endocrinological, metabolic, or other internal disease. The patient had a negative history of infection, head trauma, and exposure to toxic substances. The patient was diagnosed with FD based on BGC observed via CT, in addition to psychiatric signs and symptoms.
BGC has a higher prevalence than FD, and it has been reported to be 0.93% in radiological studies (Lauterbach et al. 1998). In a study that evaluated 6248 brain CTs, 62 patients (0.98%) were observed to have BGC, whereas only 31 (0.49%) had FS (Lauterbach 2000). Akçali et al. (2009) studied patients that presented to their neurology clinic between 2002 and 2008, and observed bilateral BGC in 17 patients, of which 9 were diagnosed as FD as there was no apparent etiology. Lazar et al. (2009) conducted a study that included 1942 patients with neurological and psychiatric symptoms; all were evaluated via CT, and BGC was noted in 149 cases, of which 6 were diagnosed with FD.

Approximately 40% of cases with BGC are reported to first present with psychiatric symptoms (Srivastava et al. 2010; Lauterbach et al. 1998). Akçali et al. (2009) observed psychiatric symptoms in 4 of 9 patients with FD, of which 1 patient was diagnosed with psychotic syndrome.

Mood disorders are the most common psychiatric disorder in FD (Casamassima et al. 2009; Lauterbach et al. 1998). Lauterbach et al. (1998) reported depressive disorders in 37% of their patients with BGC. In FD, paranoid and psychotic symptoms are generally observed in patients aged 20-40 years (Srivastava et al. 2010; Gülsün et al. 2006; Lauterbach et al. 1998). Such symptoms include auditory and visual hallucinations, and paranoid delusions. Furthermore, delusions of reference and catatonia can also be seen (Gülsün et al. 2006; Lauterbach et al. 1998). FD may present as progressive subcortical dementia during the 6th decade of life, along with delirium, apathy, and amnesia (Lauterbach et al. 1998).


Some FD patients present with psychiatric symptoms, but no extrapyramidal signs or neurological pathology (Srivastava et al. 2010; Kotan and Aygül 2009). In the presented case neurological examination findings were normal.

CT has been reported to be a more sensitive diagnostic tool for FD due to its ability to show intracranial calcification, as compared to MRI (Doğan et al. 2011; Yilmaz et al. 2010; Akçali et al. 2009; Kotan and Aygül. 2009; Lazar et al. 2009; Gülsün et al. 2006; Manyam 2005; Aslantekin et al. 1999; Lauterbach et al. 1998). It is of note that cranial CT in the presented patient showed intracranial calcification, whereas EEG and cranial MRI findings were normal.

There is no specific therapy for BGC; however, some improvement can be achieved by targeting underlying hypothyroidism or other calcium metabolism disorders (Akçali et al. 2009; Lauterbach et al. 1998). There are reports of cases treated with antipsychotic and antidepressant therapy due to psychiatric symptoms (Doğan et al. 2011; Srivastava et al. 2010; Yilmaz et al. 2010; Shouyama et al. 2005; Lauterbach et al. 1998). In cases accompanied by seizures anticonvulsants can be prescribed (Koç and Tunç 2010; Akçali et al. 2009; Lee 2006). Some researchers report that psychotic symptoms may not always respond to treatment and patients can be very sensitive to extrapyramidal side effects (Srivastava et al. 2010). Some studies have reported that ECT is efficacious (Srivastava et al. 2010; Casamassima et al. 2009). Casamassima et al. (2009) administered ECT (10 sessions) to a patient diagnosed with FD and bipolar I disorder, and reported that it was reliable and effective in the treatment of psychiatric symptoms related to FD. The presented case was treated with antipsychotic and antidepressant therapy; however, ECT was later administered due to the failure of pharmaceutical treatment to achieve improvement in the symptoms and due to suicidal ideation. The presented case responded to ECT, as the symptoms started to resolve; thereafter, the treatment was continued with antipsychotics and antidepressants.

**CONCLUSION**

The presented case report highlights the importance of brain imaging and comprehensive laboratory analysis in the assessment of patients that present with symptoms of psychosis and mood disorder. In particular, in cases with neurological symptoms and cranial imaging findings, pathologies such as FD should be included in the differential diagnosis.

**REFERENCES**


