CASE REPORT

Fahr's disease: a differential diagnosis of frontal lobe syndrome

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Fahr's disease refers to a rare syndrome characterised by symmetrical and bilateral intracranial calcification. The basal ganglia are the most common site of involvement and most cases present with extra-pyramidal symptoms. We describe two men with Fahr's diseases who presented with prominent frontal lobe symptoms. The first man presented with frequent uncontrollable bursts of laughter and crying spells. He later developed mild dysarthric speech and choreoathetoid movement. The second man presented with progressive changes in personality and behaviour. In both cases, there were no parkinsonian features. Computed tomographic scans of both patients demonstrated extensive symmetrical calcification over the basal ganglia and dentate nuclei. A repeated imaging scan in the second patient revealed progressive cerebral atrophy but reduction in the calcification. No underlying cause for the bilateral calcification was found. As frontal lobe symptoms are usually inconspicuous in the early stage, the presence of these symptoms might be overlooked in clinical practice when compared with those suffering from prominent movement disorders.

Introduction

Bilateral striopallidodentate calcinosis (BSPDC), commonly known as Fahr's disease, is a rare syndrome characterised by symmetrical calcification over the basal ganglion and dentate nucleus. The basal ganglia are the most common site of involvement. Most cases present with extra-pyramidal symptoms initially. We report two cases that had different clinical presentations and minimal extra-pyramidal symptoms.

Case reports

Case 1

In July 2004, a 38-year-old unemployed man presented with bursts of inappropriate and uncontrollable laughter for over 5 years. He had been medically and psychiatrically assessed for 4 years and had been diagnosed as having the early prodrome of schizophrenia and social anxiety. He was treated with psychotherapy and did not take any regular psychiatric medication. He had several episodes of urinary incontinence, slurred speech, and uncontrollable crying spells with no evidence of depressed mood. He lost his job and his marriage failed. However, he did not have significant memory impairment and was able to maintain normal independent daily living. There was no family history of mental illness, dementia, or major physical illness. During examination, he was seen to have frequent uncontrollable bursts of laughter. He had dysarthric speech and mild choreoathetoid movement of his upper limbs. He did not have depressive or psychotic symptoms. He scored 28/30 in his mini-mental state examination. He had deficits on frontal lobe tasks including verbal fluency and task shifting. No parietal lobe signs, parkinsonian signs, nor any clinical features suggestive of hypoparathyroidism were found. A medical work-up revealed normal serum calcium and phosphate levels and an unremarkable electroencephalogram. A plain computed tomographic (CT) scan showed extensive and symmetrical hyperdense lesions over the caudate, dentate nuclei, and frontal lobe. He was prescribed sodium valproate and sulpiride for symptomatic relief of his emotional incontinence.

Case 2

In September 2001, a 59-year-old retired married man presented to the psychiatric clinic with a history of self-neglect and 'irresponsible' behaviour. Family members reported that his personality had changed progressively over the past 5 years, and he had become reckless and sexually disinhibited. He toileted in public areas, had poor personal hygiene, and harboured morbid jealousy towards his wife. There was no known family history of psychiatric illness or

Key words
Basal ganglia diseases; Calcification, physiologic; Frontal lobe

Hong Kong Med J 2007;13:75-7

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華氏綜合症：額葉綜合症的鑑別診斷

華氏綜合症（Fahr's disease）是一種非常罕見的病症，病者通常有左右對稱的腦鈣化跡象。而這些腦鈣化通常分佈在基底核，患者一般會有錐體外徑的徵狀。本文記述兩名患有此病的男性，他們早期均有明顯的額葉徵狀。第一位患者開始時會不受控制地大笑大喊，後來演變成發音含糊及有舞蹈手足徐動症。第二位患者則呈現性格與行為上的改變。兩人並沒有帕金森病徵狀；但他們的腦部電腦素描均顯示在基底核及齒狀核有大範圍及左右對稱的鈣化，原因不明。重複的電腦素描顯示第二位患者的大腦逐漸萎縮但鈣化減少。由於額葉病徵往往在早期病發時不明顯，與一些患上運動障礙的病人比較，華氏綜合症的診斷容易被忽略。

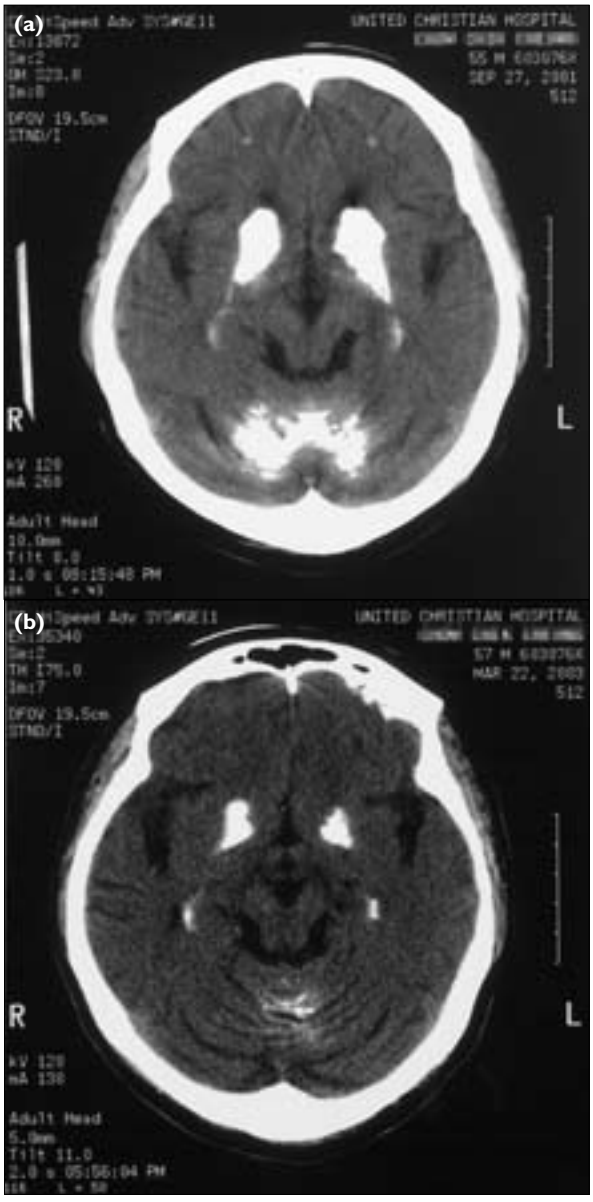

FIG. (a) Plain computed tomographic brain scan reveals cerebral atrophy and extensive calcification over basal ganglia, red nuclei, and dentate nuclei. (b) A repeated scan 2 years later reveals progressive cerebral atrophy and reduction in calcification

neurological illness. Psychiatric examination revealed a patient with a fatuous smile and disinhibited attitude. His score in the mini-mental state examination was 27/30 and he had prominent frontal lobe signs including impairment of verbal fluency, task shifting, judgement, and general knowledge. He had obvious concrete thinking and perseveration. Neurological examination revealed expressive dysphasia, dysarthria, and a wide-based gait. He did not have parkinsonian features. Blood investigations, including serum calcium and a phosphate level, were normal. A plain CT scan showed cerebral atrophy and extensive calcification over the basal ganglia, red nuclei, and dentate nuclei (Fig a). His mental condition continued to deteriorate over the next 2 years. He was treated with low-dose antipsychotics to control the disinhibition and behavioural problems. Apart from personality and behavioural changes, he had progressive memory impairment and became institutionalised. A repeated imaging scan revealed progressive cerebral atrophy but a reduction in the calcification (Fig b).

Discussion

Fahr's disease is a condition characterised by symmetrical intracranial calcification with a predilection for the basal ganglia and dentate nuclei. As the basal ganglia and dentate nuclei are always involved in a symmetrical pattern, the descriptive term BSPDC was suggested.[1] Nonetheless, Fahr's disease is still the most widely used term for this illness. It is supposed to be a very rare disease with unknown prevalence. The typical age of presentation is in middle age, which was seen in our cases, although an early-onset type mimicking schizophrenia with a more progressive deteriorating course resulting in presenile dementia has also been reported.[2] Both sporadic and familial types have been documented in the literature.[3]

The clinical features of 99 patients suffering from BSPDC have been summarised in a registry.[4] Movement disorder was the most common presentation in this group of patients. The majority of these cases presented with parkinsonian symptoms. Chorea and athetosis, as seen in our first case, were also reported. Cognitive impairment, speech disorder, and cerebellar symptoms were less common manifestations. Both of our cases presented with prominent frontal lobe symptoms and relatively subtle extra-pyramidal symptoms on their initial presentations. In addition, the frontal lobe symptoms had been present in both patients for at least 4 to 5 years before the correct diagnosis was made. As frontal lobe symptoms are usually inconspicuous during the initial stage and patient insight might be impaired, the presence of these symptoms might be overlooked in clinical practice, unlike those of patients suffering from prominent movement disorders.

The discrepancy between the clinical presentation and imaging findings has been reported.[5] There have

been clinically asymptomatic patients with positive brain imaging findings.[6] Even in those with clinical symptoms, the imaging correlation is still poor.[7] Benke et al[8] studied brain metabolism using brain positron emission tomography with ^{18}fluorodeoxyglucose in a person with Fahr's disease who presented with predominant frontal lobe syndrome and dementia. There was a massive reduction in glucose metabolism in both the basal ganglia and the frontal lobes, including the orbitofrontal and anterior cingulate areas, which correlated with the clinical picture of disinhibition and personality change. The involvement of frontal-subcortical circuits provides a hypothetical framework for the interpretation of cognitive and psychiatric problems in Fahr's disease. Thus, the atypical presentation of our two cases might be related to early involvement of the frontal-subcortical pathway. Although there was a persistent finding of basal ganglia calcification, the calcification was only part of the subsequent pathological reaction of the illness. Striatal F-dopa positron emission tomography revealed no evidence of nigrostriatal dopaminergic dysfunction.[6] There are other unidentified neurogenerative processes that might account for the diversity of clinical symptoms and their discrepancy with the imaging.

Making a clinical diagnosis of Fahr's disease relies on the combination of clinical features, brain imaging, and exclusion of other causes of intracranial calcification. The imaging findings of symmetric and extensive calcification are usually typical and conspicuous. The common sites of involvement are the basal ganglia, dentate nuclei, and centrum semiovale. In suspected cases, other differential causes of intracranial calcification must be ruled out, such as parathyroid disorders, vascular lesions, infectious diseases like toxoplasmosis, syphilis and inflammatory illnesses such as systemic lupus erythematosus. The prognosis is variable and difficult to predict, but a serial CT scan performed in one patient revealed a progressive increase in cerebral atropy,[4] and a similar finding was seen in our second case. The paradoxical diminution in the extent of calcification might be secondary to the neuronal loss. To clarify whether it is a sporadic or familial case, imaging scanning of the parents and other kindred is more reliable than clinical screening.

Genetic studies revealed an autosomal dominant inheritance in the familial cases.[9] Genetic heterogeneity and an anticipatory effect have been observed. One multigenerational family with linkage to the IBGC1 of chromosome 14 has been identified but the causal gene is still unknown. Genetic studies on other families did not replicate this result.[10] There is no prenatal or genetic test available for genetic counselling. Computed tomographic scanning remains the most effective screening tool for adult relatives. However, false negative results may still occur. The minimum age at which a negative CT scan can exclude the disease is not established yet.[4]

Treatment targets symptomatic support. The response to levodopa in those with parkinsonian features is reportedly poor.[11,12] The use of antipsychotics may be indicated in those presenting with psychotic symptoms or behavioural problems. The choice of atypical antipsychotics or those with less extra-pyramidal side-effects is warranted because of the co-existence of extrapyramidal symptoms in this group of patients.

References

1. Manyam BV. Bilateral strio-pallido-dentate calcinosis: a proposed classification of genetic and secondary causes. Mov Disord 1990;5(Suppl 1):94S.
2. Cummings JL, Gosenfeld LF, Houlihan JP, McCaffrey T. Neuropsychiatric disturbances associated with idiopathic calcification of the basal ganglia. Biol Psychiatry 1983; 18:591-601.
3. Manyam BV. What is and what is not 'Fahr's disease'. Parkinsonism Relat Disord 2005;11:73-80.
4. Manyam BV, Walters AS, Narla KR. Bilateral striopallidodentate calcinosis: clinical characteristics of patients seen in a registry. Mov Disord 2001;16:258-64.
5. Koller WC, Cochran JW, Klawans HL. Calcification of the basal ganglia: computerized tomography and clinical correlation. Neurology 1979;29:328-33.
6. Manyam BV, Bhatt MH, Moore WD, Devleschoward AB, Anderson DR, Calne DB. Bilateral striopallidodentate calcinosis: cerebrospinal fluid, imaging, and electrophysiological studies. Ann Neurol 1992;31:379-84.
7. Avrahami E, Cohn DF, Feibel M, Tadmor R. MRI demonstration and CT correlation of the brain in patients with idiopathic intracerebral calcification. J Neurol 1994;241:381-4.
8. Benke T, Karner E, Seppi K, Delazer M, Marksteiner J, Donnemiller E. Subacute dementia and imaging correlates in a case of Fahr's disease. J Neurol Neurosurg Psychiatry 2004;75:1163-5.
9. Moskowitz MA, Winickoff RN, Heinz ER. Familial calcification of the basal ganglions: a metabolic and genetic study. N Engl J Med 1971;285:72-7.
10. Oliveira JR, Spiteri E, Sobrido MJ, et al. Genetic heterogeneity in familial idiopathic basal ganglia calcification (Fahr disease). Neurology 2004;63:2165-7.
11. Berendes K, Dorstelmann D. Unsuccessful treatment with levodopa of a parkinsonian patient with calcification of the basal ganglia. J Neurol 1978;218:51-4.
12. Klawans HL, Lupton M, Simon L. Calcification of the basal ganglia as a cause of levodopa-resistant parkinsonism. Neurology 1976;26:221-5.