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Fahr's Syndrome; True Clinical Orphan: Experience of A Young Togolese and Review of The Literature

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ABSTRACT

Background: *There is no clinical sign to suspect Fahr's syndrome when examining the patient.*

Objective: *To report the experience of a Togolese 32-year-old reseller and do a review of the literature.*

Case Presentation: *A 32-year-old Togolese woman, reseller, has long wandered from consultation to consultation for headaches and psychiatric symptoms such as insomnia and nightmares. When she was received in neurological consultation, the imaging revealed symmetrical calcifications of the basal ganglia and the biology confirmed an endocrinopathy which is hypoparathyroidism.*

Conclusion: *This case study underlines that only imaging allows to suspect Fahr's syndrome. However, imaging does not allow to make a difference with Fahr's disease. The peculiarity of Fahr's syndrome is its frequent association with an underlying pathology that is most often hypoparathyroidism.*

Keywords

Fahr's syndrome, Clinical orphan, Togolese, Sub Saharan Africa.

Introduction

Fahr's disease and Fahr's syndrome are two conditions characterized by calcification in certain areas of the brain that result in neurological and/or psychiatric sequelae in patients [1]. For years, the terms Fahr's disease and Fahr's syndrome have been indistinctly used [2]. Fahr's disease was described by Karl Theodor Fahr in 1930 as a rare familial (autosomal dominant) disorder that presented with idiopathic basal ganglia calcification, as seen in the neuroimaging study [3]. One of the peculiarities of Fahr's syndrome is its frequent association with hypoparathyroidism [4]. However, to date, there is no specific clinical sign to suggest this condition during the examination of the patient which makes this disease a truly syndromic orphan. We report the experience of a Togolese 32-year-old reseller and do a review of the literature.

Case Report

A 32-year-old Togolese woman, reseller, has been admitted to a general practice for chronic headaches evolving since six weeks. These headaches were diffuse, without photo or phonophobia. They evolved in an apyretic context and without associated vomiting. There was no aura. They were badly calmed by the

usual analgesics. There is no comorbidity in her medical history. However, there was a notion of her mother's death two weeks before the onset of symptoms. Her examination was normal. She received analgesic treatment after a check-up made of complete blood cell count, uremia, serum creatinine and hepatic enzyme assay, all of which were normal. The persistence of headaches associated with a notion of insomnia and nightmares with sensation of diffuse cramps motivates the demand for a psychiatric opinion. The psychiatric consultation done, she was put on Amytriptiline 25 mg daily associated with 1 mg of Lorazepam each night. The symptoms remained stationary with paroxysms of coldness and cramp treated each time as malaria. Following a major episode of generalized tetany, a neurological consultation is then requested. On physical examination, the patient was afebrile, with normal blood pressure at 135/66 mm Hg. The oxygen saturation was 98% on room air. She had a body mass index (BMI) of 27.3 kg/m^2. Neurological examination revealed clear consciousness and no cognitive impairment. No focal motor or sensory deficit was detected. There was no cerebellar sign. The cranial nerves examination was normal. The cardiac and lung examination results were unremarkable. No goitre was palpated.

Previous laboratory examinations were completed and reveled a hypocalcemia at 1.59 mmol/l (normal: 2.14 to 2.57 mmol/l), and normal phosphoremia level of 1.80 mmol/l (normal: 0.80 to 3.38 mmol/l). Magnesium was also normal. The serum electrolytes levels were normal. The Thyroid panel including a thyroid-stimulating hormone (TSH), free thyroxines (FT3, FT4); was normal. A serum parathyroid hormone (PTH) level was not evaluated because of the unavailability of this test in our laboratories. The HIV test and the search of hepatitis B and C were negative in the serum. The electrocardiogram (ECG) showed sinus rhythm.

CT scan of brain was done and demonstrated symmetrical spontaneous hyperdensity of the lentiform nuclei and the head of the caudate nuclei (Figure). An electroencephalogram (EEG) was also performed and was normal.

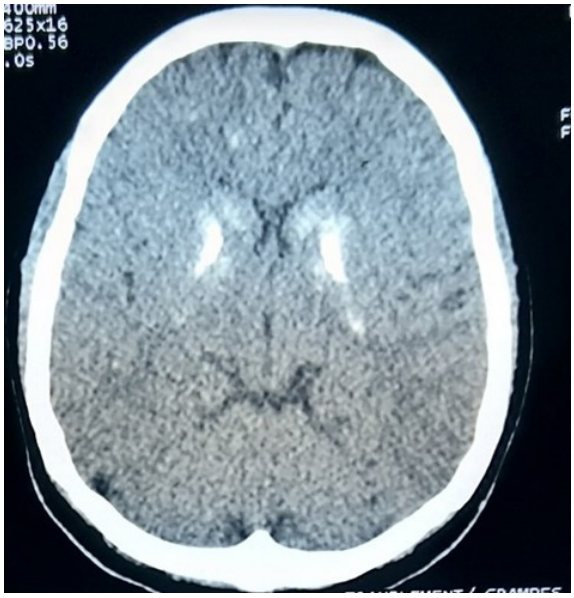

Figure: Brain CT scan showed bilateral and symetrical calcifications of lentiform nuclei and head of caudate nuclei.

Therapeutically, she received per os, 1000 mg calcium carbonate ($CaCO_3$) 2 times a day and Cholecalcifrol 100,000 IU twice a week for two weeks and then once a week. After one month, the control of serum calcium was normal and all symptoms regressed. We then retained the Fahr's syndrome secondary to hypoparathyroidism.

Discussion

Fahr's syndrome is rare and his prevalence is uncertain; however, intracranial calcifications suggestive of Fahr's syndrome are detected incidentally in approximately 0.3% to 1.2% of CT imaging of the brain [5]. It is an anatomo-clinical entity, characterized by bilateral and symmetric intracerebral calcifications, localized in basal ganglia and associated with phosphocalcic metabolic disorders [6]. There is no specific clinical sign for this condition whose diagnosis is based primarily on brain imaging including CT. Based on the literature review, the most reported clinical signs are of a psychiatric type such as anorexia nervosa, mania, dementia, psychosis, and depression [7,8]. Other atypical signs have been reported. Thus, in 2019, Ooi et al. reported a peripheral vestibular syndrome revealing Fahr's syndrome in a Chinese [9]; intracerebral hemorrhage was the mode of revelation in two patients reported by Abhijit et al. in 2011 [10]. The lack of specificity of clinical signs makes Fahr's syndrome a real syndromic orphan. This was at the origin of the wandering of our patient with a delay of the positive diagnosis. Although the diagnosis of Fahr's syndrome is based on imaging, it is often confused with Fahr's disease, which remains the main differential diagnosis. Malathi in 2016, focused on the differentiating elements between these two main disorders [1]. According to the latter, a diagnosis of either Fahr's disease or Fahr's syndrome should be considered if some or all of the following symptoms are present: a) Basal ganglia movement disorder, b) Pyramidal signs, c) Cognitive impairment, e) Gait disorder, f) Cerebellar abnormalities, g) Speech dysfunction, h) Psychiatric presentations, i) Sensory changes. But, to remember Fahr's syndrome, the following conditions must be met [1]:

- age of onset 30-40 years; evidence of symmetrical, bilateral intracranial calcification and
- presence of any of the followings endocrinopathies (idiopathic hypoparathyroidism, secondary hypoparathyroidism, pseudohypoparathyroidism, hyperparathyroidism)
- or presence of any the following (brucellosis infection, intrauterine or perinatal, neuroferritinopathy, polycystic lipomembranous osteodysplasia with sclerosing leucoencephaloathy, Cockayne syndrome, Aicardi-Gouteres syndrome, tuberous sclerosis, mitochondrial myopathy, lipoid proteinosis).

It is important to emphasize that Fahr's syndrome is different from Fahr's disease. The latter has as main characteristics, an age of onset between 40 and 60 years with a genetic trait and no associated condition [1]. The pathophysiology of intracerebral calcification in Fahr's syndrome is the subject of many hypotheses. However, the one that is unanimously is the parathyroid dysfunction or other causes of calcium metabolism overall [11]. In the pathologic

examination of Fahr's syndrome, calcium deposits were present in extracellular or extravascular space, especially around the capillaries. However, it is not clear whether abnormal calcium deposition in the brain is caused by the local destruction of the blood brain barrier or by calcium metabolic disorder of neurons [12]. Most often secondary to an underlying pathology, the management of Fahr's syndrome is tailored to these underlying associated conditions. Symptomatic treatment is most helpful. Symptomatic treatment can be pharmacological in nature [9]. When it is diagnosed and correctly managed, the prognosis is most often favorable.

Conclusion

Fahr's syndrome is a rare condition with no specific clinical signs. It is important to have it in mind in front of any intracerebral calcification especially symmetrical. Although being an orphan at the syndromic level, it is an affection that has a well-codified management which is the underlying pathology and symptoms management.

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