АРХИТЕКТУРА

FAHR'S DISEASE: A TUNISIAN SERIES OF TWO CASES.

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АННОТАЦИЯ : Болезнь Фара - это редкая патология, которая определяется наличием двусторонних и симметричных кальцификаций базальных ганглиев головного мозга при отсутствии какого-либо другого атероматозного поражения. Клиническая картина очень разнообразна, ассоциируя психоневрологические и иногда эндокринные признаки. Диагноз рентгенологический и по существу компьютерная томография. Были упомянуты несколько этиологий (эндокринная, генетическая, идиопатическая...) и обсуждались несколько патогенных гипотез (метаболическая, сосудистая, иммунологическая ...). В данной работе мы предлагаем изучить клинические, параклинические и этиопатогенные особенности этой патологии с помощью новой серии.

Наше исследование сфокусировано на двух пациентах: одна женщина и один мужчина в возрасте 22 и 44 лет, госпитализированных в интенсивной терапии по поводу судорожных состояний в одном случае и синдрома Лайелла в другом случае. Оба случая, о которых мы сообщаем, иллюстрируют ассоциации различных патологий с болезнью Фара: пан-гипопитуитаризм (1-й случай), синдром Лайелла с пустулезным псориазом (2-й случай). Лечение было симптоматическим в обоих случаях, и прогрессирование было благоприятным в 1-м и неблагоприятным в другом (смерть 2-го пациента). Прогноз болезни Фара является переменным, и его лечение является чисто симптоматическим. Только лечение ассоциированного гипопаратиреоза позволяет в некоторых случаях стабилизировать эволюцию, следовательно, возникает интерес к постановке диагноза заболевания и поиску такой связи.

ABSTRACT: Fahr's disease is a rare pathology that is defined by the presence of bilateral and symmetrical calcifications of the basal ganglia of the base of the brain in the absence of any other atheromatous lesion. His clinical picture is very varied associating neuropsychiatric and sometimes endocrine signs. The diagnosis is radiological and essentially computed tomography. M ultiple etiologies have been mentioned (endocrine, genetic, idiopathic ...), and several pathogenic hypotheses have been discussed (metabolic, vascular, immunological ...). In this work we propose to study the clinical, paraclinical and etiopathogenic characteristics of this pathology through a new series.

Our study focuses two patients: one women and one man aged 22 and 44 years, hospitalized in intensive care for convulsive conditions in first cases, and for Lyell syndrome in other. All the cases that we report illustrate associations of different pathologies to Fahr's disease: a pan hypopituitarism (1st case), a Lyell syndrome with pustular psoriasis (2nd case). The treatment was symptomatic in all cases and the progression was favorable in the 1st case and unfavorable in the other (death of the 2nd patient). The prognosis of Fahr's disease is variable and its treatment is purely symptomatic. Only the treatment of an associated hypoparathyroidism allows in certain cases to stabilize the evolution hence the interest to carry the diagnosis of the disease and to seek such an association.

Ключевые слова: болезнь Фара - центральные серые ядра, болезни - кальциноз - гипопаратиреоз - компьютерная томография - диагностика по магнитному резонансу

Key words: Fahr's disease - Central gray nuclei, diseases - calcinosis - Hypoparathyroidism - Computed tomography - Diagnosis by magnetic resonance

INTRODUCTION:

Fahr's disease is a relatively recent nosographic entity. Although the notion of central basal ganglia calcifications is old, the appointment of "Fahr's Disease" hardly dates back to the 1930s [1].

It is a rare condition, whose great disparity of clinical presentations makes the diagnosis difficult to evoke and the circumstances of discovery very varied.

However, since the advent of the CT scan, a new approach is possible by highlighting clinical forms.

The etiopathogenic theories remain numerous and subject to many debates.

The diagnosis being radiological, the cerebral computed tomography is the key examination that makes it possible to make the diagnosis of Fahr's disease [2].

We report in this work two observations that illustrate the difficulties of clinical diagnosis, the contribution of CT as well as nosological, etiopathogenic and therapeutic problems posed by this condition.

OBSERVATIONS:

Observation N ° 1:

This is a 44-year-old patient admitted to CAMU's medical resuscitation unit for convulsive coma.

In his personal history, we note the notion of neurosurgical intervention that would be followed by cerebral radiotherapy, pleurisy of unspecified etiology and unexplored primary enuresis. His family history could not be detailed; the patient having been raised in an orphanage.

The admission examination found a comatose patient with GCS at 8/15, with Bravais-Jacksonian seizures located on the right upper limb with ipsilateral

single-sided disease, right facial paralysis, dysarthria, and hypothermia at 35 ° C. .

In addition, the patient has cutaneo-mucous pallor, thin and dry skin, rare, dry hair, amyotrophy of the temporal muscles, adipomastia, external genital organs of the infantile male type with absence of pubic and axillary hair, and in particular beard.

The biological assessment revealed a hypoglycemia at 3.8 mmol / l, a deep hyponatremia at 113 mmol / l with a high natriuresis at 216 mmol / 24h. The phosphocalcic balance is strictly normal as well as the renal and hepatic balance. (Table N ° 1)

Table 1. Phosphocalcic balance of the patient N°1

Phosphocalcic balance	**Values (patient)**
Serum calcium	2,35 mmol/l
Phosphoremia	1,05 mmol/l
Calciurie	1,60 mmol/24h
Phosphaturia	9,5 mmol/24h
Alkaline phosphatase	9,6 UI/l
Acid phosphatase	1,56 UI/l
PTH	47,7 pg/ml (µg/l)

The hormonal assessment concluded hypopituitarism with adrenal insufficiency, hypothyroidism and hypogonadism. (Table N ° 2)

Table 2. Hormonal assessment of the patient N ° 1

Hormone	**Values (patient)**
cortisol	170 nmol/l
ACTH	25,8 ng/l
Aldosterone	<70 pmol/l
Cortisol under hypoglycemia corticotropic insufficiency	
FT4	7,7 pmol/l
TSH	0,7 mUI/l
Test for TRH is a normal response	
FSH	0,56 UI/l
LH	0,1 UI/l
Testosterone	0,07 µg/l
PRL	80mUI/l
HRF negative response test (FSH <1 and LH <1UI / l)	
GH under insulin hypoglycemia somatotropic deficiency	

The cerebral CT revealed scattered calcifications involving both the basal ganglia and the white matter of the posterior, frontolar and oval and semi oval temporal regions. These calcifications fall within the framework of Fahr's disease. (Figure N ° 1)

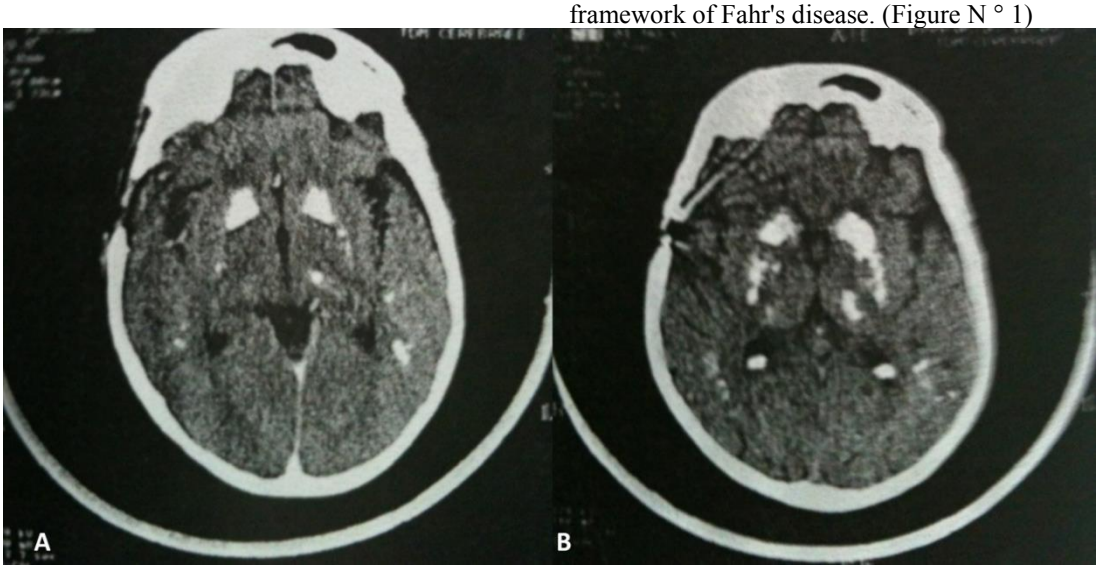

Figure N ° 1: Computed tomographic images of the observation n ° 1/ A, B: To note the bilateral and symmetrical character of the calcifications.

We also note the existence of small punctiform calcification which projects into the pituitary box lateralised on the right and which probably corresponds to a pituitary lithiasis.

Mechanical ventilation has been reported in this patient due to the alteration of his state of consciousness associated with symptomatic (gardenal) and replacement therapy (Hydrocortisone, LT4 and Androtardyl).

The evolution has been favorable. In fact, the marked improvement in the patient's state of consciousness allowed withdrawal of respiratory assistance on the tenth day of hospitalization. But the patient kept a slowness of the ideation with depressive syndrome and ophthalmological signs: a strabismus divergent from the left eye, with a deep decrease of the visual acuity of the right eye (3/10) and a papillary pallor at the eye.

The patient was transferred to the endocrinology department to adjust the replacement therapy and to follow up.

Observation N ° 2:

A 22-year-old patient with a history of pustular psoriasis requiring multiple hospitalizations in a dermatology department with the notion of purulent otitis and tetany.

She was operated for cataract of the right eye with placement of an implant.

The patient was hospitalized in the Dermatology Department of the Charles NICOLLE Hospital in Tunis for a new outbreak of pustular psoriasis, but before the appearance of an epidermal detachment in both thighs following an injection of Aspégic in intramuscular, Lyell's syndrome was suspected and the patient was then transferred to the CAMU's medical resuscitation department.

At admission the patient is conscious, feverish at 39 ° C; she has a good hemodynamic state and a preserved diuresis. Skin examination notes finely scaly erythematous sheets, with no healthy skin reserve, scattered locally with pustules and scales on the scalp and a positive Nikolski sign. The exam also notes the presence of a positive Chvostek sign.

The phosphocalcic balance shows in addition to hypocalcemia, hyperphosphoremia, hypocalciuria and hypophosphaturia; the dosage of the PTH could not be done. (Table 3)

Table 3. Biological assessments of the patient N ° 2

Balance	***Blood***	***Urine***
calcium	1,75 mmol/l	0,9 mmol/24h
phosphorus	2 mmol/l	6,2 mmol/24h
PTH	Non faite	-
Na+	132 mmol/l	-
K+	4,5 mmol/l	14 mmol/24h
CL-	100 mmol/l	-
Cortisol	118 mmol/l	-
TP	74%	-

The remainder of the biological assessment showed hemostasis disorders with prolonged TCA and 74% PT, leukocytosis and normochromic normochromic anemia. The blood ionogram shows hyponatremia and low cortisol.

The ECG at admission finds a QT prolongation in relation to hypocalcemia. The patient was put on opioids for analgesic purposes and received calcium supplementation. But before the appearance of bilateral purulent otitis, the persistence of the fever and the precarious ground, a triple antibiotherapy based on Fortum, Oflocet and Gentamycin was started.

On the neurological level, evolution has been marked by the preservation of a good state of consciousness; but in view of the appearance of a slight pupillary asymmetry and frequent vomiting, a brain scan was performed and revealed a spontaneously hyperdense appearance of the jagged nuclei, basal ganglia and the cortical white matter frontoparietal related to Calcifications within the framework of Fahr's disease. Figure 2

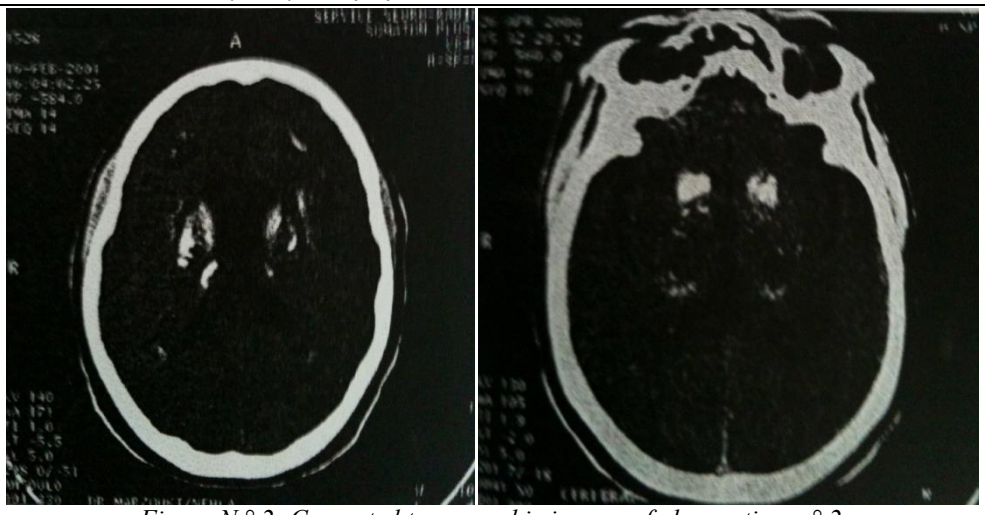

Figure N ° 2: Computed tomographic images of observation n ° 2

The hemodynamic outcome was marked by the onset of septic shock requiring vasoactive drugs, but the outcome was unfavorable and the patient died in a multi-organ failure chart.

DISCUSSION:

Fahr's disease is a rare disease that is defined by the presence of bilateral and symmetrical calcifications of the gray nuclei of the base of the brain and sometimes the serrated cerebellar nuclei in the absence of any atheromatous lesion, hypoplastic corpus callosum [1].

Sometimes asymptomatic, it can nevertheless be revealed by various disorders, in particular neuropsychic and endocrine; Fahr "syndrome" is referred to as dysparathyroidism. The diagnosis of Fahr's disease is based on radiographic examinations of the skull: simple radiographs but above all cerebral computed tomography[2].

MRI has not shown its reliability in the diagnosis of this disease. We can speak of radiological Fahr syndrome without presuming neuropsychic clinical manifestations, very diverse, which do not allow on their own, to relate the facts to their cause.

The images are characteristic. Their location, their morphology and their symmetry sign the first attack of diencephalic gray formations. In the most advanced cases, calcium deposits extend beyond the basal ganglia and radiology alone can detect these secondary locations. The frequency of discovery of a Fahr syndrome, especially at an asymptomatic stage, has increased considerably with the progress of brain imaging.

Multiple etiologies of this pathology can be discussed:

• Endocrine: a parathyroid cause should be discussed first and a study the parathyroid function should be done[5].

• Genetics: in familial forms whose hereditary transmissions have been proven and the locus of the responsible gene has been identified on the long arm of chromosome 14. A family survey is essential whenever the diagnosis of Fahr's disease is made [6].

• Idiopathic: in non-familial forms, without parathyroid involvement or for which a specific cause can not be suspected [7].

In addition, forms associated with other pathologies have recently been reported in the literature, such as those associated with hyperparathyroidism, amyloidosis, hyperostosis, juvenile hypertension, Asperger's syndrome, Dandy Walker malformation, certain dermatoses, to mitochondrial myopathy ...[8,9]

In our series, the first observation concerns a patient in his forties who presents an original association of Fahr's disease with hypopituitarism with adrenal insufficiency, hypothyroidism and hypogonadism biologically confirmed.

Our second observation illustrates an association that has never been reported in the literature. In fact, it concerns a patient with Lyell syndrome and pustular psoriasis associated with Fahr calcifications with a biological assessment in favor of hypoparathyroidism (which could not be confirmed, the patient having died before completing the balance sheet).

Despite the antiquity of its anatomical description, and more recently clinical, Fahr's disease remains rather poorly known, particularly as regards its physiopathology.

His pathogenesis is still debated. The initial mechanisms may be vascular with ischemia and secondary calcification, metabolic, endocrine or finally a simple exaggeration of a normal parenchymal cellular process (seen cases remaining asymptomatic and in which the discovery of the disease is fortuitous)[10].

Several chemical studies of parenchymal calcium deposits have attempted to elucidate the specific mechanism at the origin of their appearance. But the primum movens lesions remains unknown [10].

The entity of the disease has been questioned by some authors as much by the clinical diversity as by the physiopathological hypotheses since for them, it could be different pathologies that have as a common symptom these particular intracranial calcifications.

This same diversity makes diagnosis, long focused on anatomopathological arguments, a problem essentially scannographic.

Despite all the debates that have taken place about her subject, Fahr's disease seems to reinforce her identity, especially after the identification of the gene responsible for her family form; other sporadic cases may be related to a de novo mutation.

Our two observations are essentially of semiological interest, showing great clinical diversity, although the reason for hospitalization in the majority of cases is a comitiality going as far as a state of convulsive illness.

The indisputable contribution of computed tomography to positive diagnosis must be emphasized.

In conclusion, Fahr's disease is a rare pathology that must be considered in the presence of diffuse and symmetrical brain calcification. The therapeutic possibilities being for the moment limited, we must insist on the interest of the association hypoparathyroidism and Fahr syndrome. Indeed, the correction of hypocalcemia, due to hypoparathyroidism, by vitamin-calcium treatment has an often spectacular effect on most neuropsychic signs. This fully justifies the search for hypoparathyroidism in front of Fahr calcifications. The treatment of isolated Fahr's disease remains, moreover, only symptomatic and disappointing with an often pejorative evolution.

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