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Original article

Lobar frontotemporal degeneration: a senegalese series

Dégénerescence fronto-temporale lobaire : une série sénégalaise

F Kane*[1], J Kahwagi[2], A Guène[1], I El Ghoureichy[1], M Sèye[1], S Sow[1], K Toure[1], M Ndiaye[1,3], AG Diop[1]

Résumé

Introduction : La dégénérescence lobaire fronto-temporale (DLFT) représente la 3ème cause de démence dans le monde et la plus fréquente des démences précoces. Son diagnostic aisé dans le monde, est cependant plus difficile en Afrique, particulièrement au Sénégal. Notre étude a pour but de caractériser les différents aspects épidémiologiques, cliniques, paracliniques, évolutifs et thérapeutiques de cette pathologie au CHNU Fann de Dakar.

Méthodologie : Il s'agit d'une étude prospective et descriptive de Janvier 2020 à 2021 réalisée au service de neurologie du CHNU de Fann au Sénégal. Tous les patients respectant les critères diagnostiques de Rascovsky 2011 ont été inclus. Ont été exclus ceux présentant une amnésie précoce, des pathologies vasculaires ou des lésions multifocales à l'imagerie cérébrale.

Résultats : En 1 an, 6 patients ont été répertoriés dont la majorité est de sexe féminin (66.6 %), avec un taux d'instruction faible (17%). L'âge moyen d'apparition des symptômes est de 59.1 ans avec un délai moyen entre les premiers signes et le diagnostic de 6.4 ans. La variante comportementale est la forme la plus retrouvée (83%). L'échelle de dysfonctionnement frontal est supérieure à 3 chez 83% des cas, avec une moyenne de 29/39 obtenue au Test du Sénégal. Chez tous les patients, le scanner cérébral montrait une atrophie fronto-temporale. Le traitement repose essentiellement sur la psychothérapie, les antidépresseurs et les antipsychotiques. La moitié des patients sont décédés environ 9.7 ans après les premiers symptômes.

Conclusion : La DLFT est une entité connue dans le monde mais peu d'études ont été faites en Afrique. La faible prévalence dans notre étude par rapport à celle retrouvée dans le monde, le délai important entre l'apparition des premiers signes et le diagnostic et la mortalité élevée reflètent l'insuffisance de moyens diagnostiques de cette pathologie qui est également assez peu connue dans notre contexte. Il est important de mener plus d'études sur la DLFT en Afrique afin de permettre un diagnostic et une prise en charge précoce.

Mots-clés : démence, maladie neurodégénérative, Test du Sénégal, CHNU de Fann, Sénégal, Afrique.

Abstract

Introduction: Frontotemporal lobar degeneration (FTLD) is the 3rd leading cause of dementia worldwide

and the most common early-onset dementia. Its easy diagnosis in the world, however, is more difficult in Africa, particularly in Senegal. The aim of our study is to characterize the different epidemiological, clinical, paraclinical, evolutionary and therapeutic aspects of this pathology at the CHNU Fann in Dakar.

Methodology: This is a prospective and descriptive study from January 2020 to 2021 carried out at the neurology department of the CHNU of Fann in Senegal. All patients meeting the diagnostic criteria of Rascovsky 2011 were included. Those with early amnesia, vascular pathologies or multifocal lesions on brain imaging were excluded.

Results: In 1 year, 6 patients were identified, the majority of whom were female (66.6%), with a low education rate (17%). The mean age of symptom onset is 59.1 years with an average time from first signs to diagnosis of 6.4 years. The behavioral variant is the most common form (83%). The frontal dysfunction scale is greater than 3 in 83% of cases, with an average of 29/39 obtained on the Senegal test. In all patients, brain CT showed frontotemporal atrophy. Treatment is mainly based on psychotherapy, antidepressants and antipsychotics. Half of the patients died about 9.7 years after the first symptoms.

Conclusion: The FTLD is a well-known entity in the world, but few studies have been done in Africa. The low prevalence in our study compared to that found in the world, the long delay between the appearance of the first signs and diagnosis and the high mortality reflect the inadequacy of diagnostic means of this pathology which is also relatively unknown in our context. It is important to conduct more studies on FTLD in Africa to enable early diagnosis and management.

Keywords: dementia, neurodegenerative disease, Senegal test, Fann University Hospital, Senegal, Africa.

Introduction

Frontotemporal lobar degeneration (PFLD) is a group of neurodegenerative diseases that have in common the progressive involvement of the frontal and temporal lobes. They manifest as progressive changes in behaviour, executive dysfunction and language disorders. Most manifest clinically as one of three syndromic variants: the behavioral variant (cFTD), the most common, or one of two language variants (non-fluent or semantic progressive primary aphasia). This heterogeneity, which is characterized at the clinical, genetic and neuropathological levels, makes the understanding of this pathology very complex. We report a Senegalese series of 6 patients with DFTL.

Methodology

This is a prospective and descriptive study from January 2020 to 2021 carried out at the neurology department of the CHNU of Fann in Senegal focusing on the sociodemographic, clinical, paraclinical, therapeutic and evolutionary characteristics of patients suffering from FTLD. The included patients met the diagnostic criteria proposed by Rascovsky in 2011 (Appendix 1). Excluded patients had early amnesia, vascular pathology, and multifocal lesions on brain imaging.

Results

The majority of patients were female (4 cases, or 66.6%) and uneducated (83%). The mean age at onset of symptoms was 59.1 years and a standard deviation of 8.32 years and the mean age at diagnosis was 65.5 years and a standard deviation of 4.62 years, resulting in a mean interval between symptom onset and diagnosis of 6.4 years. Two patients (33.3%) had a family history of dementia. The most common symptom was disinhibition. Visuospatial or agnosic disorders (inability to recognize objects or faces) were present in 5 patients (83%). Apathy and abnormality of language and speech (impaired speaking, paraphasia, perseverance) were found in approximately two-thirds of patients. More than half of the patients had hyperactivity, disturbance of social behaviours, disinhibition, perseverance or lack

of personal hygiene. Archaic reflexes and urination were present in 4 patients (66.6%). The behavioural variant was the most common form (5 cases or 83%) and the language disorder variant was present in one case (17%). The frontal dysfunction scale was greater than 3 in 5 patients (83%). The average score in the Senegal Test was 29/39 (20 and 38). Brain CT scans performed in all patients showed frontotemporal cortical atrophy (Figures 1 and 2). Blood count, HIV and syphilis serology, TSH and CSF analysis were unremarkable. Genetic testing was not performed in patients, nor was the TAU protein tested. Treatment was mainly psychotherapy, antidepressants or antipsychotics. Half of the patients died about 9.7 years after the first symptoms.

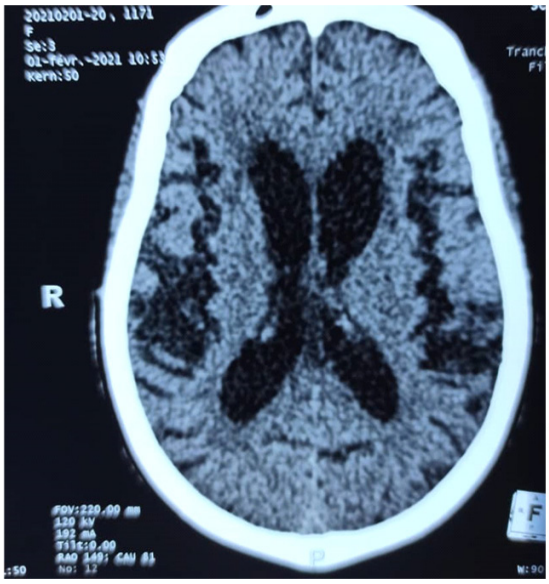

Figure 1: Subcortical cortical atrophy more marked in the right temporal

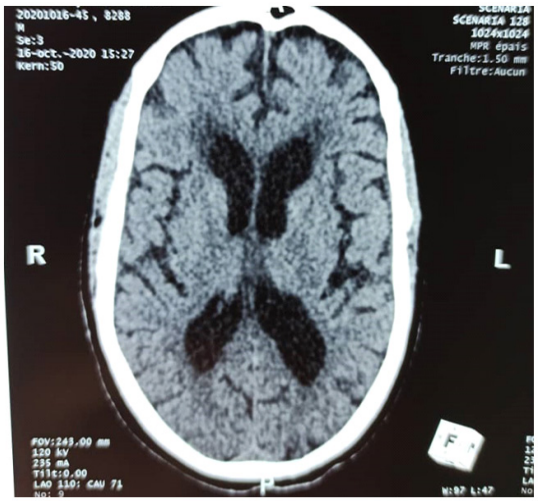

Figure 2: Subcortical cortical atrophy more marked in the bilateral frontal and temporal areas.

Discussion

Frontotemporal lobar degeneration (FTLD) is the 3rd leading cause of dementia worldwide and the most common early-onset dementia(1). In Africa, several studies have been done on neurodegenerative dementias in the elderly(2–4) , however, few studies have been done on early-onset dementia, particularly FTLD(3). In Senegal, no study has yet been done on this subject. The framework of our study, which is the Ibrahima Pierre Ndiaye Neuroscience Clinic located at the Fann Hospital, which is the last resort of the health pyramid, the socio-cultural context that makes this disease a mystical reality motivating the use of traditional medicine, and the inaccessibility of certain examinations were the limits of our study.

The low prevalence of cases in a few rare studies in Africa(3) compared to prevalence in other Western countries (5) This could be explained on the one hand by the socio-cultural context, the low rate of specialists able to make the diagnosis and on the other hand by the shorter life expectancy.

The mean age of onset of the disease in our study is 59.1 years, which can be superimposed on other studies in the world where the mean age was 59.5 years in a study conducted in a hospital in Greece (6) , 54.5 years in another multicentre study conducted at the Cambridge(5). However, the diagnosis of FTLD remains difficult in some cases. A study on the natural history of FTD, conducted by a team from Lille, showed a longer time between the first symptoms and the date of diagnosis (5.9 years on average) than for an Alzheimer's-type pathology [15]. In our study, the average diagnostic interval is 6.4 years, reflecting the even greater diagnostic delay in our country. Also, the predominance was female with a sex ratio of 2 males to 4 females, however in other studies carried out around the world there was a significant difference in the sex ratio between the different groups of FTLDs; a female predominance for the semantic aphasia variant and a male predominance for the behavioral variant (cFTD) and primary progressive non-fluent aphasia(7) . These observed differences were interpreted as differences

in biological vulnerability to the 3 syndromes with vulnerability to left frontal degeneration in women, right frontal degeneration and/or bilateral temporal degeneration in men (7). This distribution of the sex ratio in the different groups could not be made in our study because of the small sample compared to other studies where they were much more representative.

More than half of our patients were illiterate (83%). On the one hand, this could be explained by the low school enrolment rate in our country. On the other hand, the low level of education would be a risk factor for dementia according to Letenneur and Lindsay(8,9).

Regarding heredity, 33% of patients had a family history of dementia compared to a multicenter study carried out in London in different neurology departments where 41.8% had a family history(10), and 29% in a U.S. study(5). A Dutch study estimated that first-degree relatives of FTLD patients are 3.5 times more likely to develop dementia, which can manifest 11 years earlier than in the general population(11).

The behavioral variant is the most common in our study (83%) compared to the variant with language disorders (17%), which is superimposed in several studies carried out around the world. It should be noted that non-fluent progressive aphasia was the 2nd most frequently diagnosed subgroup compared to semantic aphasia in a study done in California(7). After interviewing family and friends, neuropsychological tests are the second pillar of the clinical diagnosis of FTD. In some studies, the Mini Mental State Examination (MMSE) is used as a testing tool (7) while in others, the Rapid Frontal Efficiency Battery (BREF) and the DUBOIS five-word test is used instead (12). However, MMSE is not suitable for finding cognitive impairment in FTD. Indeed, it does not make it possible to highlight the frontal involvement except when it is advanced. It is therefore necessary to carry out so-called "frontal" tests to look for a dysecutive syndrome such as BREF(12). In our study, we used the Forward Dysfunction Scale and the Senegal test because it was much more adapted to our social context with the relatively low educational rate(13) . However, the paucity of studies in Africa on FTLD and the non-use of the Senegal test in other Western or American studies do not allow us to compare our results.

In case of suspicion of Alzheimer's disease and related diseases, the French National Authority for Health (HAS) recommends biological tests such as blood count, CRP, blood ionogram, calcium level, blood glucose, kidney and liver tests, TSH, vitamin B12 and B9 tests, as well as HIV and syphilis serologies (14). Brain imaging should be systematically done, MRI as a priority, and by default brain scan. In our study, we performed the blood count, TSH and HIV and syphilis serologies as well as the CSF study, the results of which were unremarkable. The brain scan performed in these patients showed frontotemporal cortical atrophy, which can be superimposed on other studies in the world where magnetic resonance imaging is most often performed but showing the same results (15). Functional imaging has also shown evidence in making it possible to differentiate between FTLD and Alzheimer's disease in several studies(16) . The genetic assessment but also the study of biomarkers could not be done in our study, nevertheless its contribution is not negligible in the diagnosis of FTLD as shown by a recent retrospective singlecenter study carried out in 2023 at the neurocognition department of Lyon(17) , where light-chain neurofilaments (Nfl) are found in the CSF and blood of patients at high levels. Also, biomarkers of Alzheimer's disease (Tau protein) were normal in CSF.

To date, no cure has been established for FTLD. However, several symptomatic treatments have been tested to improve cognitive performance. Based on the involvement of serotonergic pathways in FTD, several open-label studies have been performed with conventional selective serotonin reuptake inhibitors (SSRIs). The results suggest efficacy on disinhibition, depressive symptoms, eating disorders and behavioral disorders.(12) In our study, antipsychotics and antidepressants were used.

Half of the patients died an average of 9.7 years after

the first signs. In other studies, the average survival from first symptoms to death is about eight years (18) with extremes ranging from 2 to 20 years.

Conclusion

The FTLD is a known entity with established criteria, however in Africa few studies have been done on this topic. The low consultation rate due to the socio-cultural context, the low socio-economic level of most patients limiting explorations and the lack of specialists contribute to delayed diagnosis and burden the prognosis. With new criteria such as the Senegal test, further advances must be made in order to multiply studies on this subject and thus increase the accuracy of the diagnosis. The aim is to improve the life expectancy of patients, most of whom are relatively young, hard-working and breadwinners.

***Correspondence**

Fatou Kane .
fkane29@gmail.com

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1 : Ibrahima Pierre Ndiaye Neuroscience Clinic, Fann National University Hospital, Dakar 10700, Senegal.
2 : Centre Hospitalier National de Pikine, Pikine 16000, Senegal.
3 : Albert Royer National Children's Hospital, Dakar, Senegal.

Conflict interest : None

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