ALZHEIMER'S DISEASE WITH SEVERE FRONTAL LOBE ATROPHY, SIMULATING FOIX-CHAVANY-MARIE SYNDROME, AND NOT OF THE ANTERIOR OPERCULAR LESION. A CLINICAL ANATOMY STUDY

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ABSTRACT
Foix-Chavany-Marie is a syndrome characterized by the dissociation between the loss of voluntary innervation of the facio-labio-pharyngo-glosso-masticatory paralysis muscles with the preservation of the involuntary musculature innervation. The topography affects the bilateral frontal operculum or its corticofugal projections. Neuropsychological testing failed to show any associated language defect. The clinic-neuroradiological and autopsy correlations of this clinical picture were discussed. We described a case of Alzheimer's disease that evolved with severe frontal lobe atrophy, simulating Foix-Chavany-Marie syndrome, but no anatomical lesion in the anterior opercular gyri.

Keywords: Foix-Chavany-Marie syndrome; Left anterior operculum atrophy; Automatic-voluntary dissociation; Alzheimer's disease.

DOENÇA DE ALZHEIMER COM SEVERA ATROFIA DO LOBO FRONTAL, MIMETIZANDO A SÍNDROME DE FOIX-CHAVANY-MARIE, SEM LESÃO OPERCULAR ANTERIOR. UM ESTUDO ANÁTOMOCLÍNICO

RESUMO
A síndrome de Foix-Chavany-Mary é uma síndrome que se caracteriza por dissociação entre a perda da inervação voluntária da musculatura facio-lábio-faringo-glosso-mastigatória mantendo preservada a inervação involuntária desses músculos. A topografia afeta o opérculo frontal, ou suas projeções córtico-fugais. Avaliação neuropsicológica, estudos de neuroimagem e de autópsia foram discutidos. Descrevemos um caso de doença de Alzheimer que evoluiu com severa atrofia do lobo frontal como uma síndrome de Foix-Chavany-Marie, mas sem lesão anatômica em ambos os giros *opercular* anteriores.

Palavras-chave: Síndrome de Foix-Chavany-Marie; Atrofia opercular anterior esquerda; Dissociação automática-voluntária; Doença de Alzheimer.

INTRODUCTION

Foix-Chavany-Marie syndrome (FCMS) is a type of pseudobulbar palsy characterized by automatic-voluntary dissociation of the voluntary movements of the masticatory muscles. FCMS can occur at any age, in acute, subacute, or chronic forms, with an incidence lower than 1/1.000.000[1]. FCMS is caused by congenital[2] or acquired unilateral or bilateral lesions of the anterior opercular gyri[1,3,4]. There are at least six distinct etiologies of FCMS due to cerebrovascular disease[5,6], central nervous system infections[1,7,8], neurodevelopmental disease[9], neurodegenerative disorders[10,11], benign Rolandic epilepsy due to perinatal asphyxia[12] and traumatic injury[13]. In 1926, the syndrome was described by Charles Foix (1882-1927), Jean Alfred Émile Chavany (1892-1959), and by Julien Marie (1899-1987)[14],

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although, the first case was reported in Germany by Magnus in 1837[15]. The authors described a case of Alzheimer's disease that evolved with severe frontal lobe atrophy simulating Foix-Chavany-Marie syndrome.

METHOD

Clinical diagnosis of FCMS was done on a male patient according to Bruyn[1]. Neuropsychological assessment was carried out[16]. He was also submitted to other examinations such as magnetic resonance imaging (MRI), and electro-encephalography (EEG). The neuropathological examination was performed according to CERAD[17] and Braak-Braak classification[18], and the stain used was hematoxylin and eosin. The brain was maintained in 10% formalin for 4 weeks and cut into coronal sections. Pieces of the inferior and middle frontal, upper temporal, inferior parietal, occipital lobes, hippocampus cortex, basal ganglia, midbrain, including the substantia nigra, and cerebellum were routinely processed. On microscopic study, paraffin was embedded in sections to be cut at 6 to 8 micrometers thick and stained with hematoxylin-eosin.

CASE REPORT

We describe a 70-year-old, right-handed male mechanic, with 4 years of schooling was taken to the Neurology Service at *Hospital Universitário Oswaldo Cruz da Universidade de Pernambuco* – Brazil, on September 14, 2001 with a complaint of forgetfulness for the last 4 years. The patient spoke only when asked and he would answer in a few words. Medical history of benign prostate hypertrophy, hypertriglyceridemia, and seizures were present. He had habits of smoking and alcohol intake during the weekends. The patient was taking diphenylhydantoin, phenobarbital, and alfuzosin hydrochloride. There is no case of dementia in his family. General clinical examination was normal, but on the neurological evaluation, he was conscious, his speech was slow and his comprehension was impaired.

The patient scored three points on the Mini-Mental State examination[19] (he repeated the three words), besides scored 20 out of 30 on Pfeffer scale[20]. He had the tendency to deviate the head to the left. Menace reflex was reduced to the right. Groping reflex and axial reflexes were also present. But deep tendon reflexes were abolished. He needed some support to start walking. The patient used appropriate neuropsychological evaluation protocol for dementia on the several cognitive components below[16], but his performance was very impaired due to his moderate to severe degree of dependence[20]. The patient was disoriented of

time and space, he did not know which day of the week and where he was. In the visual reproduction memory test[21], he did not respond to stimulus. Evocation memory test of words was applied, he had no capacity to answer the test. Oral expression – Spontaneous speech was not fluent. In an object-naming task, only 6 out of 30 pictures were correctly named. The verbal fluency test did not obtain a positive result of 90 seconds for each fluency, verbal and semantic. Oral understanding – When asked to describe some objects in the room, by applying the Pierre Marie test, and doing the dynamic discourse ability chart test, he could not perform either of them. In the test of the sandwich procedure, he was laughing with tears in his eyes and his finger in his mouth (embarrassed?). Repetition was very impaired for the patient, but with encouragement, he could repeat. He could not read letters or words, but he could write his name and age. There were ideational, ideomotor and constructive apraxia on the tests for pantomimes and gestures, but all the results had no meaning. The patient could not draw a circle, square, cube, or a house, but under a copy, he could draw an ellipse on the perseveration for 24 seconds with Alzheimerization sign[22]. The drawing of the clock test proved to be unintelligible (Figure 1). Complementary tests: audiometry was performed in February,1999 and showed a mild bilateral sensorineural hearing loss. Electroencephalography was carried out in April, 99 and revealed a low frequency constituted by intermittent and infrequent outbreaks of slow polymorphic and discontinuous waves in the delta frequency of a not synchronic projection, diffused and lateralized on the right frontotemporal areas. The MRI examination of the skull was performed in August, 1999. It showed moderate diffused brain atrophy with severe compensatory dilation of the anterior ventricular system, besides Fazekas's scale=III and Scheltens' scale = IV (Figure 2). The patient had progressed to the point of being totally dependent of others. During this evolution process, he progressively did not open his mouth voluntarily, although, he was able to open the mouth, swallow his food or drink fluids after the visual and tactile stimulus. On October 10, 2008, it was mentioned that 2 years before, the patient started, progressively, needing someone to help him in doing his oral hygiene several times a day – his wife would wash his face with ice water, to open his mouth or remove the saliva manually (Figure 3). On March 17, 2013, the patient was placed in a wheelchair. On January 19, 2018, the patient died at age 88, after a total clinical course of 18 years diagnosis due to a respiratory infection. Autopsy was performed on January 19, 2018. The weight of the brain was 900g. On the macroscopy showed circumferences and configurations altered by diffuse brain atrophy with a widening of the grooves. Moderate to severe diffuse cortical atrophy, especially on the frontal lobe was

founded (Figure 4). The brain had no detectable macroscopic infarcts, and there was no loss of nigra substances. On the microscopic examination, there were on the middle and inferior frontal gyri, upper temporal gyrus, inferior parietal and occipital lobes frequent senile plaques per X 100 microscopic in the studied field[17], besides moderate amyloid angiopathy, and neurons depopulation with focal spongiosis on each lobe. On the right hippocampus and entorhinal cortex, there were moderate of the neuron depopulations with spongiosis, and neurofibrillary tangles on the transentorhinal stage[18], and there was no granule-vacuolar degeneration, but on the left hippocampus and entorhinal cortex, there were sparse granule-vacuolar degeneration, and frequent senile plaques (Figure 5)[17]. Presence of microscopic cortical hemorrhagic infarcts in the phagocytic absorption phase on the right parietal lobe anterior basal ganglia with hyaline arteriosclerosis, *crivosus status* in the diencephalon and intravascular leukocytosis were found. Posterior basal ganglia with intravascular leukocytosis were found as well. There was sparse cerebellum amyloid (non-NPs) in white matter. There are in the midbrain of the neuron depopulations and the presence of Lewy bodies, some pigmentary neurons (slight changes). Neuropathological diagnosis was confirmed as Alzheimer's disease, *crivosus status* on the diencephalon, and cortical microscopic hemorrhagic infarcts.

The study was approved by the Ethics Committee on Research involving Human Beings at the *Hospital Universitário Oswaldo Cruz* (University Hospital) under the following number: CAAE=35560620.0.0000.5192.

DISCUSSION

We describe a case of severe frontal lobe atrophy in a patient with dementia and pathological diagnosis of Alzheimer's disease, not an anterior opercular anatomical lesion, who evolved a dissociation of phases of voluntary and involuntary swallowing, simulating Foix-Chavany-Marie syndrome. Although this syndrome is a well-known feature of the asymmetric anterior opercular lesion, severe on the left[1], in this case, there were no pathological alterations in the opercular region and did not find other classic signs of neurological deficits in this patient. But, only in the last 12 years before his death, our patient was unable to swallow or spit out his saliva voluntarily, and the hygiene was done by reflexed action or manually with the help of others. The patient stopped talking, and presented voluntary manifestation of difficulties in opening his mouth, tongue protrusion, and chewing, but accepted to open his mouth to eat, only when stimulated by the touch of the spoon and

visual stimulus; similar cases were marked by progressive dysarthria and mutism, apathy, and other frontal signs. The etiology of these cases was corticobasal degeneration[23], amyotrophic lateral sclerosis[24], and Pick's disease [25], respectively. So, prefrontal and inferior frontal lobe atrophy in our patient caused functional voluntary disturbances simulating FCMS, but not the anterior opercular injury[22]. Other two cases of neurodegenerative disease had similar clinical features but not anatomic study, were also described[10,11]. Most reported cases on FCMS by several etiological types [1,2,3,4,5,6,7,8,9,10,11, 12,13], can be attributed to the unilateral or bilateral frontal opercular lesions, with variable involvement of the subcortical white matter. The etiology in most of the reported cases of automatic-voluntary dissociation is vascular involving branches of the middle cerebral artery supplying the opercular area[1]. In our anatomical study on Alzheimer's disease, we did not find any pathology that could justify a lesion in the frontal, temporal, inferior parietal, and occipital lobes besides hippocampi, except for cortical frequent senile plaques and neurofibrillary tangles on the transentorhinal stage-II[18]. It is clinically important to differentiate the diagnose, have medical treatment, speech rehabilitation, and family counseling. However, a patient admitted with advanced dementia, it is difficult to distinguish the difference among FCMS, pure anarthria, aphemia or other similar disorders [10,11,26,27]. According to the histopathological study, the tests with immunohistochemistry were not performed. But a large number of senile plaques presented on the Hematoxylin and Eosin tests in the cortical areas studied, without any other clinical or pathological factor that precluded the diagnosis, was sufficient to confirm the diagnosis of Alzheimer's disease in a patient with dementia[17]. To conclude, we described a case in the patient with dementia and histopathological diagnosis of Alzheimer's disease with severe frontal lobe atrophy, but not the anterior opercular anatomical lesion simulating FCMS. We believe that various types of cases with both frontal atrophy and automatic-voluntary dissociation of the voluntary movements of the masticatory muscles, simulating Foix-Chavany-Marie syndrome, will be identified and that further continuous clinical-pathological studies are needed.

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Confidentiality Data: The authors declare that they have followed the protocols of their work center on publication of data from patient.

Family Consent: Consent for publication was obtained.

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Figure 1

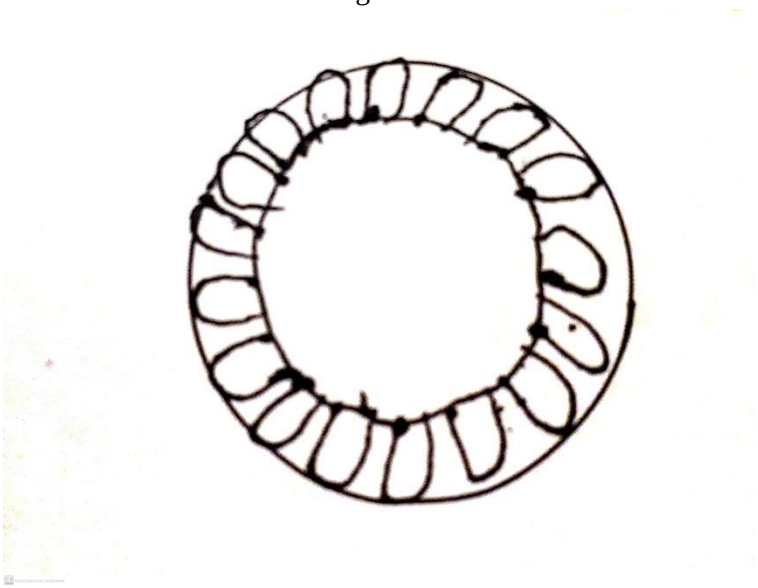

Figure 2

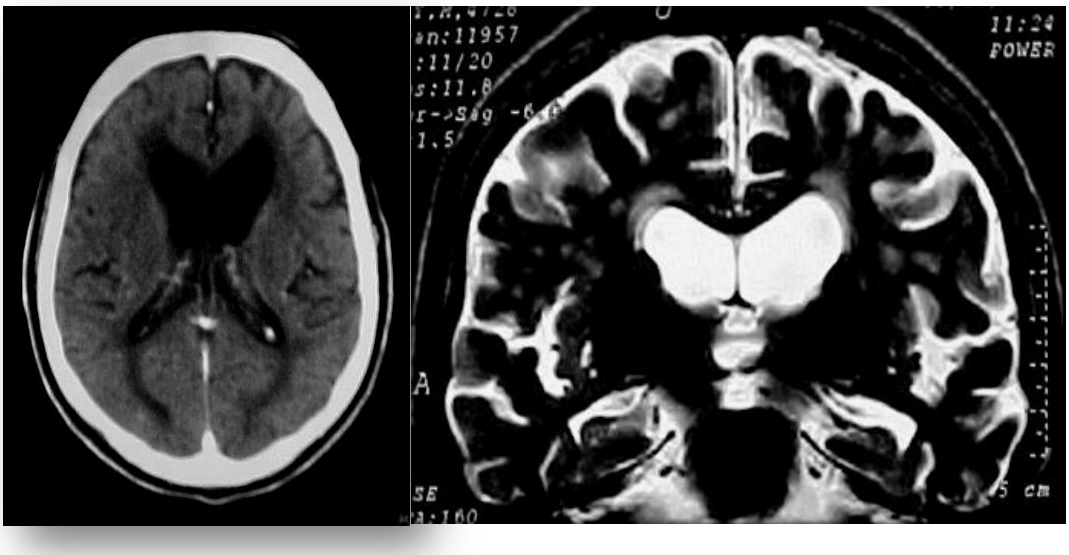

Figure 3

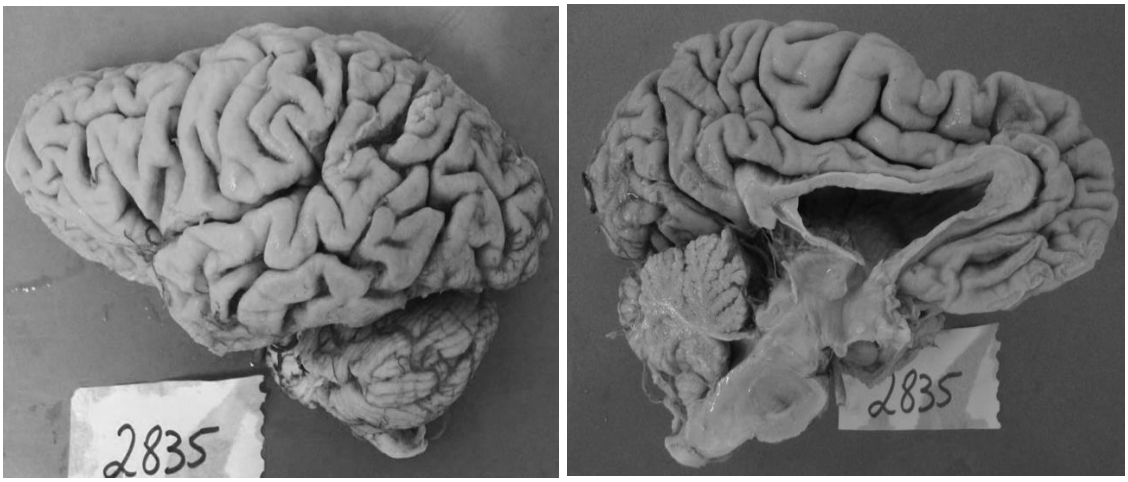

Figure 4