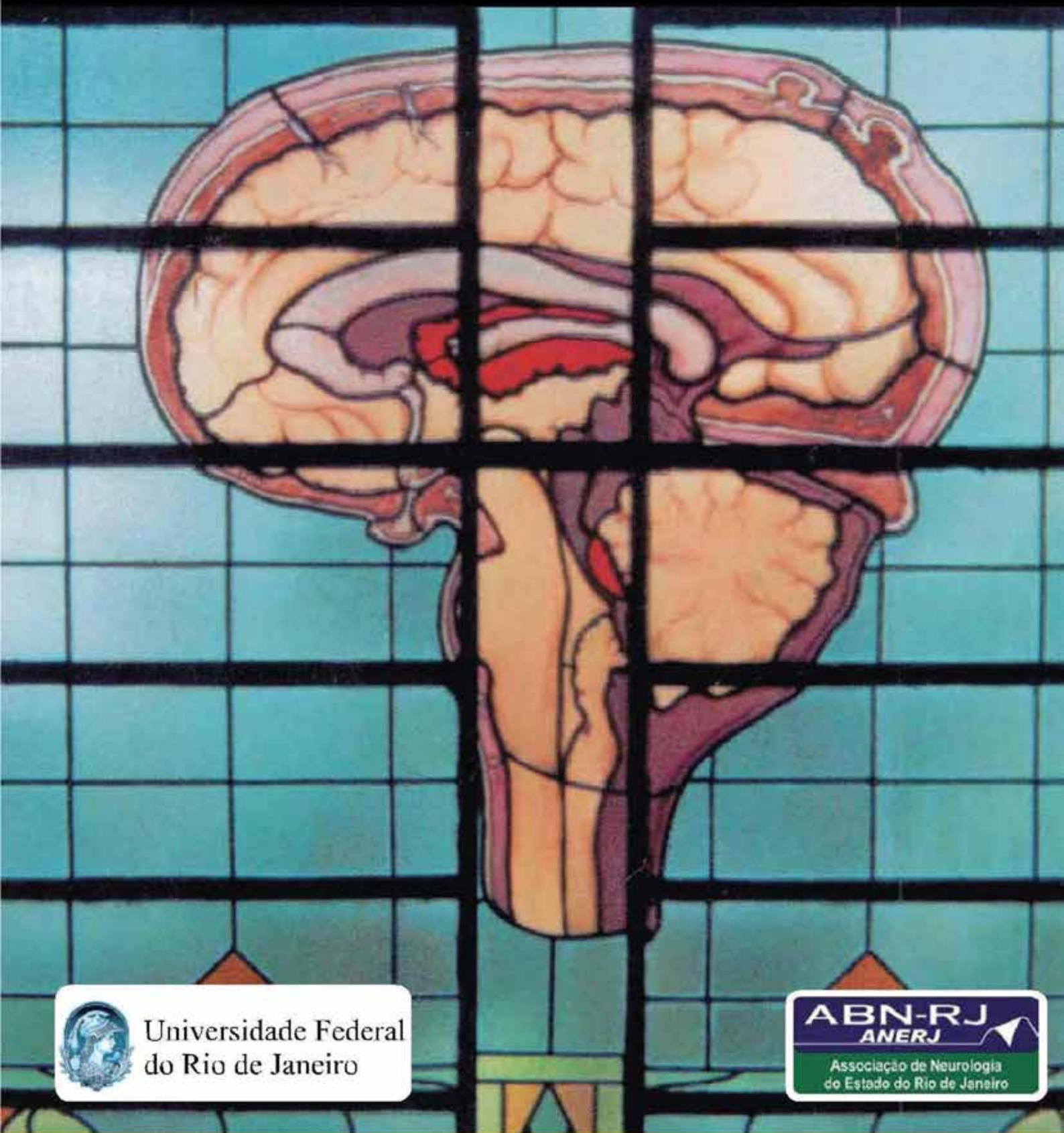
Revista Brasileira de
NEUROLOGIA
Órgão Oficial do Instituto de Neurologia Deolindo Couto
Vol. 57 • Nº 2 • ABR/MAI/JUN - 2021



Universidade Federal do Rio de Janeiro
ABN-RJ ANERJ Associação de Neurologia do Estado do Rio de Janeiro

ISSN 0101-8469 CODEN RBNEES ISSN eletrônico: 2447-2573 Acesso pelo LILACS-Express

Revista Brasileira de
NEUROLOGIA
Órgão Oficial do Instituto de Neurologia Deolindo Couto

Sumário

REVISTA BRASILEIRA DE
NEUROLOGIA

Órgão Oficial do Instituto de Neurologia Deolindo Couto

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CIP-Brasil - Catalogação na Fonte
Sindicato Nacional dos Editores de Livro - RJ

R349
Revista Brasileira de Neurologia/Instituto de Neurologia Deolindo Couto, Universidade Federal do Rio de Janeiro [vol 1 - nº 1 (1949)]

Continuação do:
Jornal Brasileiro de Neurologia [vol 19 - nº 6 (1983)]
Trimestral a partir do vol 37 - nº 1 (2001) [descrição baseada no vol 34 - nº 6 (1998)]

1. Neurologia - Periódicos brasileiros.
I. Universidade Federal do Rio de Janeiro. Instituto de Neurologia Deolindo Couto. II. Título: Jornal Brasileiro de Neurologia.

98-1980 CDD 616.8 CDU 616.8

ISSN 0101-8469
CODEN RBNEE

Different etiologies of superficial siderosis

Diferentes etiologias de siderose superficial

Lady Jane da Silva Macedo[1], Andreza Oliveira Alves[1], Antonione Santos Bezerra Pinto[1], Giuliano da Paz Oliveira[1,2,3]

ABSTRACT

Superficial Siderosis (SS) is an uncommon condition caused by hemosiderin deposition into the subarachnoid space. SS is characterized by cerebellar ataxia, progressive sensorineural hearing loss and pyramidal signs, but is often an unrecognized disorder. Magnetic Resonance Imaging (MRI) is the diagnostic procedure of choice due its high sensitivity to hemosiderin deposits in addition to being a non-invasive exam. This paper aims to describe a case of SS and to perform a literature review about SS etiologies, neuroimaging features and clinical characteristics. A 65-year-old man came to a neurology outpatient clinic with seizures and cerebellar ataxia with a history of car accident and severe traumatic brain injury 45 years ago. MRI SWAN showed a hyposignal in the cisterns of the base and on the cerebellar surface and T1-weighted images left hippocampal sclerosis.

Keywords: siderosis, magnetic resonance imaging, epilepsy.

RESUMO

A Siderose Superficial (SS) é uma condição rara causada por depósitos de hemossiderina no espaço subaracnóideo. SS é caracterizada por ataxia cerebelar, perda neurosensorial auditiva progressiva e sinais piramidais, mas é frequentemente uma desordem de difícil diagnóstico. A Ressonância Magnética (RM) é o exame de escolha para o diagnóstico devido a sua alta sensibilidade aos depósitos de hemossiderina, além de ser um exame não invasivo. Este artigo tem como objetivo descrever um caso de SS e realizar uma revisão da literatura sobre as etiologias da SS, suas características na neuroimagem e suas características clínicas. Um homem de 65 anos de idade procurou o ambulatório de neurologia com convulsões e ataxia cerebelar. Ele informou histórico de acidente automobilístico e lesão cerebral traumática grave há 45 anos. A RNM SWAN mostrou hipossinal nas cisternas da base e na superfície cerebelar e as imagens em T1 evidenciaram a presença de esclerose hipocampal esquerda.

Palavras-chave: siderose, imagem por ressonância magnética, epilepsia.

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Conflict of interest: The author declares that there is no conflict of interest.

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Funding statement: There is no financial support.

Ethical aspects: The research was approved by the Ethics Committee on Research of Universidade Federal do Piauí (CAAE 03106518.3.0000.5214). The patient signed an informed consent authorizing the publication of the case.

INTRODUCTION

Superficial Siderosis (SS) is a rare condition caused by the deposition of hemosiderin along the pial and subpial structures of the central nervous system due to low-grade bleeding into the cerebrospinal fluid (CSF). SS is mainly caused by subarachnoid hemorrhage due to idiopathic bleeding, which represents around 35% of the cases[1-4]. Hemosiderin deposition mainly affect the upper vermis, the cerebellar leaves, the frontal and temporal lobes, the ventricular epithelium, choroid plexus epithelium, brain stem, spinal cord, nerve roots and cranial nerves I and VIII[5].

The clinical syndrome is characterized by sensorineural hearing loss, cerebellar ataxia, signs of pyramidal tract dysfunction and dementia[6]. For a long time the diagnosis of superficial siderosis could only be made by post-mortem,[1,7] but with the modernization of radiological imaging methods, including blood-sensitive sequences, it is possible to diagnose SS using Magnetic Resonance Imaging (MRI)[7,8].

The aim of this study is to describe a case of superficial siderosis with mesial temporal sclerosis and to evaluate SS etiologies, imaging characteristics and features of diagnosis.

CASE REPORT

A 65-year-old man came to the neurology outpatient clinic reporting episodes of seizures characterized by behavioral arrest and oral automatism (chewing and sucking) accompanied by aphasia, lasting 3 to 5 minutes. He maintained consciousness during the episodes and had no post-ictal clinical manifestation. Episodes occurred on average once a day for 3 months. He had a history of car accident with severe traumatic brain injury 45 years ago without a neurosurgical approach at the time. He reported being a 40 pack-year smoker but denied any comorbidities. On physical examination he presented a broad-based gait, dysmetria and bilateral dysdiadokinesia, more prominent on the right.

Sleep electroencephalogram did not show epileptiform paroxysms. Cranial MRI revealed hypersignal in T2/FLAIR in periventricular and cerebellar white matter which suggest areas of gliosis, associated with marked cerebellar atrophy (fig. 1). In the images weighted in magnetic susceptibility, a hyposignal was highlighted in the basal cisterns and in the cerebellar surface (fig. 1: F, G, H). The left hippocampus had distorted morphology and a slight hypersignal in T2 / FLAIR images. Based on these findings the patient was diagnosed with superficial siderosis associated with mesial temporal lobe epilepsy due to left hippocampal sclerosis. Cervical, thoracic and lumbar spine MRI did not characterize spinal cord injuries or superficial siderosis in this topography. The patient was treated with lamotrigine 75mg 12/12h with a 70% reduction in the frequency of epileptic seizures.

The research was approved by the Ethics Committee on Research of Universidade Federal do Piauí (CAAE 03106518.3.0000.5214). The patient signed an informed consent authorizing the publication of the case.

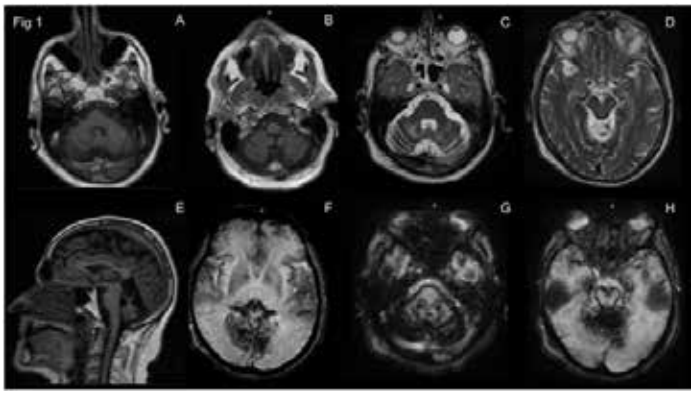

Figure 1. Prominent cerebellar sulci consist with diffuse cerebellar atrophy (A, B, E: T1WI). Hypointensity at the pial surface of midbrain, surface of cerebellum and cerebellar atrophy (C, D: T2WI; F-H: SWAN).

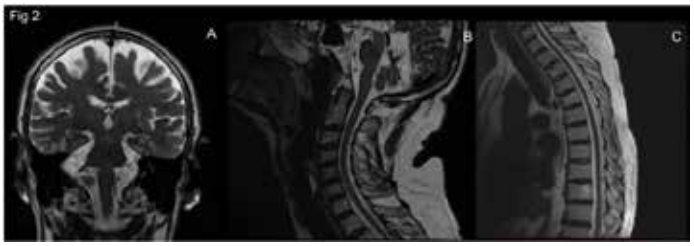

Figure 2. Discrete hypersignal and morphological distortion in the left hippocampus consist with mesial temporal sclerosis (A: T2WI). Absence of injuries or superficial siderosis (B, C: T2WI).

DISCUSSION

SS is an uncommon and often unrecognized disorder[9]. The only established causes of SS are chronic or intermittent extravasations of blood into the subarachnoid space [2,6,10]. Various etiologies can cause SS and they can be classified into brain and spinal disorders (Table 1). The main brain disorders that cause SS are CNS tumors, such as craniopharyngioma, paraganglioma and ependymoma, amyloid angiopathy, head trauma and history of brain surgery. Spinal cord disorders can also cause SS and the main causes are arteriovenous fistula, neural tube defect, spinal meningeal diverticulum and dural ectasia. Despite that, idiopathic bleeding is still the main cause of subarachnoid bleeding [4,10,11].

Idiopathic bleeding is the main cause , but it also can be caused by a central nervous system (CNS) tumor, arteriovenous malformations, meningocele, history of trauma or CNS surgery and is also common in patients with advanced cerebral amyloid angiopathy [4,10,11]. Spontaneous intracranial hypotension has also been associated with superficial siderosis[11].

Studies report that SS pathogenesis occurs from the breakdown of erythrocytes followed by the release and deposit of hemosiderin throughout the arachnoid and pia mater. Accumulation of blood products causes the symptoms through an inflammatory process, including reactive gliosis, neuronal loss and demyelination,[10] especially in the posterior region of the cerebellum and cranial nerves [2,10]. The most affected nerve is the vestibulocochlear, probably due its long glial segment that predisposes it to iron deposition[9].

Table 1. Causes of Superficial Siderosis.

Etiologies of superficial siderosis
Brain
CNS tumor (craniopharyngioma, paraganglioma e ependymoma)
Amyloid angiopathy
Hemorrhagic transformation of cortical infarction
Reversible cerebral vasoconstriction syndrome
Cerebral venous thrombosis
Head trauma
History of brain surgery
Spinal/medullary
Arteriovenous fistula
Neural tube defect
Spinal meningeal diverticulum
Dural ectasia
Intradural herniated disc
Brachial plexus / root avulsion injuries
Spinal meningeal diverticulum
Spinal cavernous malformation in the vertebral body
Back trauma
Others
Drugs (anticoagulants and antiplatelet agents)
Idiopathic

Although clinical condition can vary depending on hemosiderin distribution, almost all reported cases of SS were diagnosed in patients with clinical symptoms that are now considered typical presentation for the disease: cerebellar ataxia, progressive sensorineural hearing loss, cognitive impairment and pyramidal signs. Usually, the symptoms develop slowly and progressively [12,13].

MRI is largely more sensitive to hemosiderin deposits than computerized tomography (CT), therefore MRI is the diagnostic procedure for the diagnosis of SS [9]. Brain or spine intra-arterial digital subtraction angiography and surgical exploration can be performed as well[7]. SS appearance on MRI is characterized by signal loss on T2 gradient recalled echo (GRE) and susceptibility-weighted imaging (SWI) sequences following the gyral cortical surface in a curvilinear pattern[1]. Typically T2 hypointensity can be consistently seen outlining the cerebellum, brainstem, and pial surface of the cord. These imaging findings can also be seen in the sylvian, interhemispheric fissures and hemispheric convexities [9]. Although T2 GRE has a high sensitivity, SWI sequence is superior to identify microbleeds [1].

Even with MRI the diagnosis of SS can still be missed because the findings in images can be overlooked, once the abnormalities follow the contour of the brain. Frequently an experienced neuroradiologist is required. In some cases cerebrospinal fluid (CSF) evaluation can be useful and may reveal xanthochromia or red blood cells. Because it is an invasive procedure, CSF puncture is only performed when SS is suspected but imaging diagnosis is not conclusive [9].

Iron chelators, such as deferiprone can be used in some cases[14]. However, patients with SS are usually treated with symptomatic therapies, since there is not an evidence based treatment for this condition. When the source of bleeding is identified it is possible to perform surgical removal. Cochlear implants can be indicated for patients with progressive sensorineural hearing loss. Antiepileptic drugs may also be used in patients with SS and comorbid epilepsy [14].

CONCLUSION

SS is an uncommon and often unrecognized disorder, characterized by cerebellar ataxia, progressive sensorineural hearing loss and pyramidal signs. MRI is the diagnostic procedure of choice because of its high sensitivity to hemosiderin depositions. SS is a challenging condition for clinical practitioners due to its defying diagnosis and nonspecific symptomatology.

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Clinical and radiological features of main dementias

Aspectos clínicos e radiológicos das principais demências

Jean Lima Fontenele[1], Cássy Geovanna Ferreira Moura[1], Giuliano da Paz Oliveira[1,2]

ABSTRACT

Dementia is a syndrome characterized by a decline of two or more cognitive functions, affecting social or professional life. Alzheimer's Disease is a neurodegenerative disorder that represents 53% of dementia cases; memory loss, inability to recognize faces, impaired judgement, disorientation and confusion are possible common symptoms. Vascular Dementia is responsible for 42% of dementia cases, due to cerebrovascular pathologies, and the clinical aspects are related to the extension and location of the brain injury. Lewy Bodies Dementia is a neurodegenerative disorder that represents 15% of dementia cases, and its symptoms include visual hallucinations, parkinsonism and fluctuating cognitive decline. Frontotemporal dementia is a group of clinical syndromes, divided in Behavioral-variant, characterized by disinhibition, compulsions, apathy, aberrant sexual behavior and executive dysfunction; and Primary Progressive Aphasia, which is subdivided in Nonfluent-variant and Semantic-variant. Vitamin B_{12} deficiency is a reversible cause of dementia, with a wide clinical feature, that includes psychiatric symptoms such as depression and irritability, hematological symptoms related to anemia (e.g. dyspnea and fatigue), and neurological symptoms including dementia and neuropathy. Normal pressure hydrocephalus is also reversible, presenting forgetfulness, changes in mood, decline of executive functions, reduced attention, and a lack of interest in daily activities as symptoms. The radiological findings vary depending on the etiology of dementia. For that reason, understanding neuroimaging and clinical aspects is important to diagnose effectively.

Keywords: dementia, neurology, neuroimaging.

RESUMO

A demência é uma síndrome que consiste em um declínio de um ou mais domínios cognitivos, que afeta o desempenho social ou profissional do indivíduo. A Doença de Alzheimer é um transtorno neurocognitivo que representa 53% dos casos de demência; seus sintomas podem incluir perda de memória, incapacidade de reconhecer rostos familiares, julgamento comprometido desorientação e confusão mental. A Demência Vascular é responsável por 42% dos casos de demência e é causada por doenças cerebrovasculares, seus achados clínicos são relacionados com o local e com a extensão do dano cerebral. Já a Demência por Corpos de Lewy é uma doença neurocognitiva que representa 15% dos casos de demência, cujos sintomas incluem alucinações visuais, parkinsonismo e flutuação cognitiva. A Demência Frontotemporal, por sua vez, é um grupo de síndromes, que se dividem em variante comportamental — caracterizada por desinibição, compulsão, apatia, hipersexualidade e disfunções executivas — e Afasia Progressiva Primária, subdividida em variante não-fluente e variante semântica, que cursam com disfunções da linguagem. Há, ainda, a Deficiência de Vitamina B_{12}, uma causa reversível de demência. Ela possui um quadro clínico variado, que inclui sintomas psiquiátricos, como depressão e irritabilidade, sintomas hematológicos relacionados a anemia, como dispneia e fadiga) e sintomas neurológicos, que incluem demência e neuropatias. Uma outra causa reversível é a Hidrocefalia de Pressão Normal, que se apresenta com esquecimentos, alterações de humor, perda de função executiva e redução da atenção e do interesse nas atividades cotidianas. Os achados de neuroimagem variam dependendo da etiologia da demência. Assim, compreender os aspectos clínicos e radiológicos é importante para um diagnóstico efetivo.

Palavras-chave: demência, neurologia, neuroimagem

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Conflict of interest: all authors have not conflict of interest.

Financial support: all authors have no financial support to declare.

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INTRODUCTION

According to NIH criteria, published in 2011, dementia is characterized by cognitive or behavioral symptoms affecting work or usual activities, representing a decline from previous levels of functioning and performing, when these findings are not explained by delirium or major psychiatric disorder. The diagnosis of dementia is made based on history-taking from the patient and an informant, besides mental status examination or neuropsychological testing[1].

Patients with dementia may present two or more cognitive domains impaired, which can be: ability to remember new information; judgement, handling of complex tasks and reasoning; visuospatial abilities; language; personality, behavior or comportment[1].

This syndrome usually affects elderly with neurodegenerative disorders; however young onset dementia is not considered rare[2]. There are secondary causes for dementia, therefore a series of blood and imaging exams are necessary to identify reversible diseases, such as Vitamin B_{12} deficiency, thyroidopathy or resectable tumors[3].

The overall prevalence of dementia ranges from 5 to 7%[4]. A neuropathological study in Brazil revealed Alzheimer's Disease (AD) alone or combined with other disease represents 53% of the dementia cases, followed by Vascular Dementia (VaD) unaccompanied or combined with other etiology with 42%, and Lewy Bodies Dementia (LBD) itself or in combination with other diagnoses representing 15%, while 14% of autopsied patients who had clinical criteria for dementia did not have enough neuropathological findings at autopsy[5]. It is also worth mentioning the existence of Normal Pressure Hydrocephalus (NPH), which can be one of the causes of dementia. Patients can also be diagnosed with mixed dementia, a condition in which a person has symptoms attributed to more than one type of dementia[6,7].

The clinical presentation of dementia is wide, varying according to the cause, and involves a cognitive impairment such as amnesia, loss of functional independence, behavioral disinhibition, and language changes[8]. A cognitive neurological exam and a detailed medical history obtained from both the patient and a close family member or friend are necessary to diagnose dementia[1].

Cognitive tests can be used as screening to help the examiner to make a diagnosis. Montreal Cognitive Assessment (MoCA), for example, is composed of questions and challenges evaluating 12 items. Another option is the Mini-Mental State Examination (MMSE), with 30 questions to analyze 7 different cognitive domains. Both tests range the score from 0 to 30 points[3].

Modalities of neuroimaging exams such as magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT) can be relevant to classify, evaluate and help the diagnosis of dementias[3].

ALZHEIMER'S DISEASE

AD is a neurodegenerative disorder responsible for 53% of the dementia cases (5). The pathophysiology of AD involves a build-up of amyloid-ß and tau proteins. This aggregation leads to formation of neuritic plaques and neurofibrillary tangles, which causes neurodegeneration, then, consequently, synaptic and neuronal loss[9].

The typical clinical presentation of AD is an insidious loss memory with other cognitive declines, such as inability to recognize faces, impaired judgement, disorientation, confusion, and neuropsychiatric symptoms, like delusions and hallucinations, affecting the functions at work or in daily activities. Family members or friends usually report repetitive questioning, forgetfulness of recent memories and where they kept objects, besides difficulty to cook and control finances[10, 11].

MRI of AD is classically represented by hippocampal atrophy and global brain volume reduction, most evident in mesial temporal lobe (MTL)[12]. Other imaging modalities can be useful to diagnose AD as the cause of dementia. For example, single-photon emission computed tomography (SPECT) and F-fluorodeoxyglucose positron emission tomography (FDG-PET) show, respectively, a hypoperfusion and hypometabolism patterns, which are important to make a precocious diagnose and to identify AD degeneration changes in other brain areas such as inferior parietal and lateral temporal cortex, precuneus and posterior cingulate[9, 13].

VASCULAR DEMENTIA

VaD is a group of disorders that represents 42% of dementia cases, which accompanies or precedes cognitive impairment due to cerebrovascular pathologies. VaD is also frequently present in combination with AD. VaD can be originated by strokes, hemorrhages, white matter rarefaction or infarction. Its main risk factors are hypertension, dyslipidemia, diabetes, atherosclerosis, and cerebrovascular diseases[5, 14, 15].

This type of dementia has a wide clinical feature, which varies with the severity of brain injuries and its location. The clinical manifestation comprises cognitive symptoms such as forgetfulness and confusion, and neuropsychological symptoms, including depression, apathy, and changes in behavior or mood[14, 15].

VaD has many possible etiologies, such as cerebrovascular pathologies, small vessel disease, leukoaraiosis, reduced cerebral perfusion, cerebral amyloid angiopathy, mixed lesions and lacunar infarcts[15].

There are several possible findings of neuroimaging exams in VaD, which help determine the subtypes of VaD and detail the aspects of lesions. For instance, brain Computed Tomography (CT) or MRI are both able to detect atrophy and large vessel diseases, although MRI is more sensitive than CT. Brain MRI can also show white matter lesions, microinfarcts, territory of vascular injury, cerebral microbleeds (usually seen in cerebral amyloid angiopathy), contributing to determine the etiology of VaD[16, 17].

LEWY BODIES DEMENTIA

LBD is a progressive cognitive decline that represents 15% of all cases of dementia, as the second most common neurodegenerative dementia, and it is characterized by the presence of Lewy bodies (LB) and its main constituent is the protein α-synuclein[5, 18].

LBD manifests with motor, cognitive, neuropsychiatric and autonomic symptoms. The core clinical features of LBD are: recurrent visual hallucinations, one or more of the cardinal signs of parkinsonism, fluctuating cognitive decline, and REM sleep behavior disorder. Other symptoms include autonomic dysfunctions (mainly orthostatic hypotension and constipation), hypersensitivity to antipsychotics, hypersomnia, hyposmia, depression, apathy, anxiety and delusions [9, 18-22].

Parkinsonism related to LBD has an atypical pattern. Tremor is less frequent, usually classified as a postural tremor, not a resting tremor, which is frequently seen in Parkinson Disease. Moreover, there is a low response to dopaminergic treatments in parkinsonism related to LBD[18].

In order to diagnose LBD, the physicians mainly depend on its clinical features, however neuroimaging could also help. At a first sight, brain MRI and CT can reveal no significant features and it is marked by a preservation of medial temporal lobe structures and hippocampus. Nevertheless, brain MRI may reveal focal atrophy of the midbrain, and hypothalamus which indicates neuronal death due to the accumulation of LB. It also can show generalized decrease in cerebral volume, most marked in parietotemporal regions[18, 21].

SPECT and PET may provide important information, such as FDG-PET imaging usually shows presence of occipital hypometabolism. In addition, it can also observe changes in perfusion or metabolism in the occipital and parietal regions[9, 18, 21].

FRONTOTEMPORAL DEMENTIA

Frontotemporal dementia (FTD) is defined as group of clinical syndromes characterized by progressive decline in executive functioning, behavior and/or language, that is associated with a series of neurodegeneration process (neuronal loss and astrocytic gliosis) of the frontal and/or temporal lobe, which results in a focal atrophy in these lobes[23].

This dementia is subdivided into three clinical subtypes: Behavioral-variant (bvFTD) and Primary Progressive Aphasia (PPA), which is subdivided in Nonfluent variant Primary Progressive Aphasia (nfvPPA) and Semantic-variant Primary Progressive Aphasia (svPPA), both having language disorders. bvFTD is the most common, and it is characterized by progressive emotional decline, changes in behavior and personality, presenting, for example, disinhibition, compulsions, apathy, aberrant sexual behavior and executive dysfunction. On the other hand, the svPPA variant patient may present a loss of knowledge of the meanings of words and compulsions. In addition, nfvPPA cases are characterized by progressive motor-speech impairment and difficulty in sentence construction[24, 25].

Neuroimaging findings on brain MRI or CT in bvFTD include frontal or anterior atrophy and on SPECT or PET, it is possible to observe hypoperfusion or hypometabolism in those same areas. Unlike bvFTD, neuroimaging findings on brain MRI in cases of nfvPPA include atrophy in the left posterior fronto-insular and perisylvian area, and on SPECT or PET is observed hypoperfusion or hypometabolism in these areas. In svPPA the findings on brain MRI are anterior temporal lobe atrophy and on SPECT/PET temporal hypoperfusion/hypometabolism can be observed[16, 23, 24].

DEMENTIA DUE TO VITAMIN B_{12} DEFICIENCY

Vitamin B_{12} deficiency is a common reversible cause of dementia. This syndrome has a very wide clinical spectrum, which includes psychiatric symptoms (mainly depression and irritability), hematological symptoms related to anemia (e.g. dyspnea and fatigue), and other neurological symptoms including neuropathy. A retrospective study concluded that dementia due to vitamin B_{12} is characterized by behavioral changes in most cases, followed by memory loss. There is also a spinal cord manifestation, which is called subacute combined degeneration (SCD), and consists in disturbance of position sense, spastic paraparesis or tetraparesis and symmetric dysesthesia. Neurological symptoms may precede hematologic signs of vitamin B_{12} deficiency, and they are the main reason for seeking medical care[26, 28-30].

The neuroimaging of vitamin B_{12} deficiency consists in a typical myelopathy, involving the central and peripheral nervous system. FLAIR and T2-weighted MRI in involved brains show hyperintensity in periventricular white matter. In cases of SCD, it can be found a T2-weighted hyperintensity symmetrically, especially in posterior, lateral or both columns in the cervical and thoracic portions of the spinal cord[26].

NORMAL PRESSURE HYDROCEPHALUS

Normal pressure hydrocephalus (NPH) is one of the reversible and treatable causes of dementia, defined as a syndrome characterized by an abnormal presence of cerebrospinal fluid in the ventricles, cognitive impairment, gait ataxia, and urinary urgency and/or incontinence, which can be reversible. Gait impairment is usually the main clinical feature of NPH, and it is characterized as slow and broad-based, which is associated with posture and balance abnormalities. Furthermore, NPH is considered the most common type of hydrocephalus in adults[6, 31].

When enlargement of the ventricles involves prefrontal brain structures patients may present cognitive symptoms. In these cases, the clinical features of cognitive decline are presented in the subcortical form, which is characterized by forgetfulness, changes in mood, decline of executive functions, reduced attention, and a lack of interest in daily activities. In addition, visuospatial perception and visuoconstructive skills can be affected[31-33].

The Large-volume lumbar puncture (Tap Test) is a test that assesses gait and cognitive functions before and after lumbar

punctures to drain cerebrospinal fluid (CSF) in patients with NPH. The procedure can reproduce the effect of a definitive shunt. From 60% to 80% of the patients with cognitive symptoms improve after CSF shunt surgery, explaining why dementia can be reversible in such cases[6, 31, 32].

Neuroimaging findings on brain MRI or CT in NPH are enlargement of the lateral and third ventricles. The Evans' index is a ratio used to evaluate this ventricular enlargement, which compares the widest frontal horn of the lateral ventricles to the widest transverse diameter of the skull [31, 34]. This index is useful for the diagnosis of NPH, because when it is more than 0.3 it indicates enlargement of the ventricles[38].

Other neuroimaging findings can also be present, such as callosal angle of 40° or greater, enlargement of the temporal horns without hippocampal atrophy, and disproportionately enlarged subarachnoid space hydrocephalus (DESH). It can be noted by the widening of sulci near to vertex. On SPECT/PET hypometabolism and reduction of cerebral blood flow can be observed[31, 34].

Table: Prevalence, clinical features and imaging findings of some dementias.

	Prevalence	**Clinical Features**	**Imaging findings**
Alzheimer's Disease	Represents 53% of the dementia cases.*	Memory deficits, visuospatial function and language impairment. Delusions, hallucinations and depression may occur.	Brain MRI: Hippocampal atrophy and global brain volume reduction. SPECT/PET: inferior parietal and lateral temporal hypoperfusion/ hypometabolism.
Vascular Dementia	Represents 42% of the dementia cases.*	Cognitive symptoms: forgetfulness and confusion.Neuropsychological symptoms: depression, apathy, and changes in behavior or mood.	Brain CT or MRI: atrophy and large vessel diseases. White matter lesions, microinfarcts, encephalomalacia, cerebral microbleeds.
Lewy Bodies Dementia	Represents 15% of the dementia cases.*	Visual hallucinations, parkinsonism, cognitive decline, REM sleep behavior disorder, hypersomnia, hyposmia, constipation, depression, apathy, and anxiety.	Brain MRI: Atrophy of the midbrain, and hypothalamus. SPECT/PET: Occipital hypoperfusion/ hypometabolism.
Frontotemporal Dementia	Less than 14%.	BvFTD: changes in behavior and personality, disinhibition, compulsions, apathy, aberrant sexual behavior and executive dysfunction. NfvPPA: Progressive motor-speech impairment, and difficulty in sentence construction. SvPPA: Loss of knowledge of the meanings of words, and compulsions.	BvFTD MRI: Frontal or anterior atrophy. BvFTD SPECT/PET: frontal or anterior hypoperfusion/ hypometabolism nfvPPA MRI: atrophy in the left posterior fronto-insular and perisylvian area. nfvPPA SPECT/PET: left posterior fronto-insular and perisylvian hypoperfusion/ hypometabolism. svPPA MRI: Anterior temporal lobe atrophy. svPPA SPECT/PET: temporal hypoperfusion/ hypometabolism.
Dementia due to Vitamin B_{12} Deficiency	Less than 14%.	Psychiatric symptoms: depression and irritability; Hematological symptoms: dyspnea and fatigue; Neurological symptoms: neuropathy, dementia (behavioral changes and memory loss)	Typical myelopathy in the central and peripheral nervous system. FLAIR and T2-weighted MRI hyperintensity in periventricular white matter; T2-weighted hyperintensity symmetrically in posterior, lateral or both columns in the cervical and thoracic portions of the spinal cord in cases of SCD.
Normal Pressure Hydrocephalus	Less than 14%.	Cognitive impairment (forgetfulness, changes in mood, decline of executive functions, reduced attention, and lack of interest in daily activities), gait ataxia, and urinary urgency.	Brain MRI or CT: enlargement of the lateral and third ventricles, Evans' ratio > 0.3, callosal angle of 40° or greater, enlargement of the temporal horns, and Disproportionately Enlarged Subarachnoid Space Hydrocephalus (DESH). SPECT/PET: Hypometabolism of periventricular regions and reduction of cerebral blood flow.

***** Prevalence data related to alone or associated with other etiologies cases found in a cross-sectional study of neuropathological findings with 1,092 patients in Brazil. This study considered patients without criteria for any neuropathological diagnose as a group that represents 14% of dementia cases, which includes Frontotemporal Dementia, Dementia due to Vitamin B12 Deficiency, and Normal Pressure Hydrocephalus5.

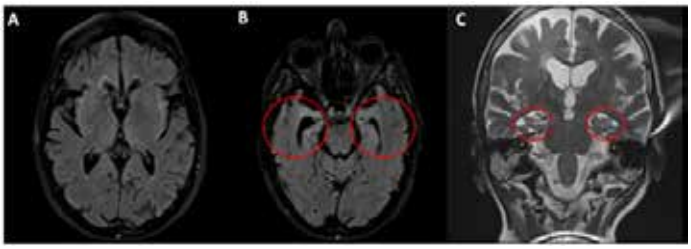

Figure 1. FLAIR axial (A and B) and T2-weighted coronal (C) brain MRI showing global brain volume reduction, predominantly in the mesial temporal lobe, characterized by increased volume of choroidal fissure and lateral ventricle temporal horn, with moderate hippocampal atrophy (circles in B and C) (Scheltens 3). There were also white-matter hyperintense signal, compatible with microangiopathy (Fazekas 2). An 80-year-old woman presenting a progressive amnesia started two years earlier. She did not remember recent events or where she placed objects. She also had poor speech with repetitive questions. At neurological examination, she had no focal neurological signs, however she obtained 22 points at the MMSE and 19 points at the MoCA, with impairment mainly in memory and visuospatial functions. Reversible dementias were ruled out after laboratory screening. These findings indicated AD as diagnosis, and donepezil was applied as treatment.

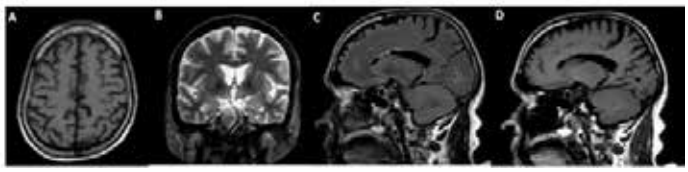

Figure 2. T1-weighted axial (A), T2-weighted coronal (B), FLAIR (C) and T1-weighted (D) sagittal brain MRI, highlighting global brain atrophy, inconspicuously more pronounced in parietotemporal regions, with enlargement of lateral ventricles. A 68-year-old man, merchant, with gradual lapses progressing for eight months. He forgets goods orders and important events, impacting work. In the last three months, he started presenting a poor speech with few words, many nightmares and visual hallucinations. These characteristics fluctuate during the day. He reached 18 points on MEEM, which reveals a decline in executive and visuospatial functions. Neurological examination showed hypomimia, bradykinesia, symmetrical cogwheel rigidity of upper limbs, reduced verbal fluency and several paraphasias. Potentially reversible dementias screening was negative. The sum of clinical and radiological characteristics allowed the diagnosis of DCL.

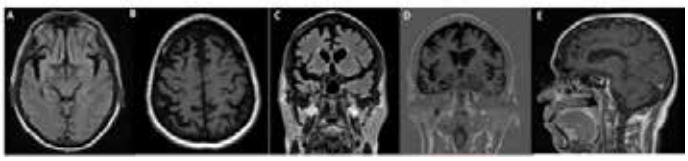

Figure 3. FLAIR (A) and T1-weighted (B) axial brain MRI, FLAIR (C) and T1-weighted IR (D) coronal brain MRI and T1-weighted sagittal brain MRI (E), showing an asymmetric global brain volume reduction, more evident in the right frontotemporal region. A 63-year-old man with a 2-year history of progressive behavioral changes, with compulsive buying disorder, which causes him many debts. In addition, increased food intake, especially consumption of sweets. In the last 9 months, the patient started to present hypersexual behavior and a small vocabulary speech. Neurological exam showed a bilateral palmomental reflex and Myerson's sign. Patient obtained 26 points on MMSE with impairment of memory and executive functions. Potentially reversible dementias screening was negative. These sets of findings allow a diagnosis of bvFTD. Then, it was proposed long term treatment with antipsychotic medication.

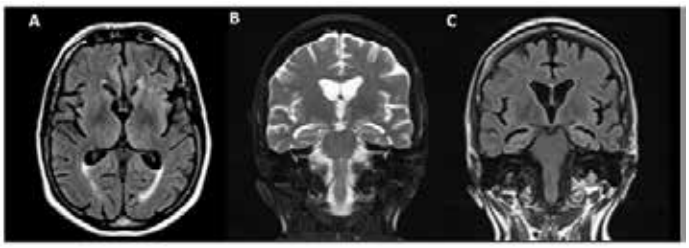

Figure 4. FLAIR axial brain MRI(A), T2-weighted (B) and FLAIR (C) coronal brain MRI, showing global brain atrophy, more evident in posterior temporal lobes and left insula and hippocampus. A 68-year-old woman, presenting language difficulties in the last two years. She started with slow and paused speeches, but comprehensible. These characteristics gradually evolved towards an unintelligible talk, ungrammatical utterance and phonological paraphasias. On neurological examination, it was found anomia and a non-fluent speech, even with efforts, however word and objects recognition were preserved. Based on these clinical features, the diagnosis of nfvPPA was made and the multidisciplinary treatment with speech therapy and music therapy was performed.

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White Matter Hyperintensities: Initial Assessments

Hiperintensidades da Substância Branca: Avaliações Iniciais

Eliasz Engelhardt[1], Felipe Kenji Sudo[2], Gilberto Sousa Alves[3], Denise Madeira Moreira[4]

ABSTRACT

The white matter hyperintensities (WMH, leucoaraiosis) represent the most common kind of ischemic vascular lesion of the white matter due to small vessel diseases, and occurs frequently in the elderly. Consequent to the neuroimaging identification arouse the need for their assessment. The group of Fazekas proposed a systematized semi-quantitative visual scale to score such lesions where two parameters were considered, extent and localization. The original scale was further modified, to a simplified version. Although other more complex scales have appeared, researchers remarked that the relatively simple Fazekas scale, in comparison to the complex ones and to volumetric measures, appeared to be sufficient when analyzing relationships between clinical parameters and WMH load in a clinical setting.

Keywords: hyperintensities, leucoaraiosis, visual scale

RESUMO

As hiperintensidades da substância branca (HSB, leucoaraiose) representam o tipo de lesão isquêmica mais comum da substância branca decorrente de doenças de pequenos vasos e ocorre frequentemente em idosos. Consequente à identificação por neuroimagem surgiu a necessidade de sua avaliação. O grupo de Fazekas propos uma escala visual semiquantitativa sistematizada para pontuar tais lesões, onde foram considerados dois parâmetros, extensão e localização. A escala original foi modificada para constituir uma versão mais simplificada. Embora outras escalas mais complexas tenham aparecido, pesquisadores comentaram que a relativamente simples escala de Fazekas, em comparação às mais complexas e a método volumétrico, mostrou-se suficiente quando é analisada a relação entre parâmetros clínicos e a carga de HSB em um cenário clínico.

Palavras-chave: hiperintensidades, leucoaraiose, escala visual

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Conflict of interests: none.

Financial support: none.

INTRODUCTION

The white matter, which makes up around one half of the human brain volume, is a very frequent target of "small vessel diseases" (SVD), which appear under varied kinds of ischemic and hemorrhagic lesions[1,2,3]. The ischemic types comprise the "white matter hyperintensities" (WMH), and the "lacunar infarcts" (lacunes), as visualized on magnetic resonance imaging (MRI)[2,3]. The WMH represent the most common kind of lesion of the white matter, and occurs frequently in adults over 65 years old with a prevalence rate of ~60 - 80% in the general population[4]. Such lesions are even more extensive in those with vascular or Alzheimer's disease type of dementia, where they may reach ~90% when compared with cognitively normal older adults, suggesting its role in dementia pathogenesis and neurocognitive dysfunction[5].

Such WMH, as coined by Zimmerman and collaborators, were initially observed on T2 sequence of MRI (1.5 T), introduced in the beginning of 1980s as an increase of the signal of this change of the white matter[6,7]. A better visualization of WMH was achieved on FLAIR (fluid-attenuated inversion recovery) sequences that appeared (1985)[6,8], becoming soon one of the preferred sequences for this purpose[9]. Such white matter changes can also be detected on CT generated images, introduced in the late 1970s, as decreased densities of the white matter ("white matter hypodensities"), although with a lesser sensitivity in comparison to MRI[6,10]. Concurrently, the term "leucoaraiosis" (rarefaction of the white matter [*leuko*=white and *araios*=rarefaction]), "meaning a diminution of the density of representation of the white matter", was coined by Hachinski and collaborators (1986), to designate these white matter changes, which appear as hypointense (hypodense) on CT and hyperintense on MR[11,12].

SCORING THE WMH

Consequent to the MRI findings arouse the need to assess the magnitude and the localization of such WMH, and the researchers also recognized the association of the load of such lesions with cognition in normal aging, and pathological states. Zimmerman and collaborators (1986)[7] have proposed an initial scoring method, aiming mainly the periventricular region. Next, Fazekas and collaborators proposed a systematized scoring scale of such lesions, which became to be known as the "Fazekas scale", where he considered two parameters, extent and localization (1987)[10]. The original Fazekas scale (oF) comprises a semi-quantitative visual assessment of these lesions in two locations: [a] "periventricular hyperintensities" (PVH), following the contour of the lateral ventricles with variable breadth and degrees of irregularity, and [b] "deep white matter hyperintensities" (DWMH), extending from the paraventricular region through the centrum semiovale, and also the deep white matter, with a 4-point grading of each region (total range 0 to 6) (1987)[10] (Box) (Figure).

Much later, the LADIS study group introduced a modified Fazekas scale (mF), "taking into account only deep and subcortical white matter lesions" (DSWM), with a 4-point severity scale (total range 0 to 3) (Box) (Figure). Their initial interest was to correlate the leucoaraiosis load with disability development (cognitive, functional, motor, autonomic) over a time period, and was used successfully by this kind of research (2001-2015)[9,13,14].

Nevertheless, it was felt by numerous researchers that, despite the practicality of the simplification, the original Fazekas' rating presented some advantages, offering more detailed information considering the localization of the lesions, considering that there are overt differences between the PVH and the DWMH, regarding the affected underlying white matter structures[12,15,16,17,18]. However, it should be pondered, that in the subjects with advanced WMH the PVH and DWMH often adjoin each other. Thus, a stringent distinction of these two regions appears to be disputable in advanced stages[12].

The two visual scales that appeared later were more complex, and also distinguished the differential localization of the lesions, the "Scheltens scale" (range 0 to 84), which discriminates the PV and the DWM regions, and additionally the basal ganglia and infratentorial structures (1993)[19], and the "Wahlund (ARWMC) scale" (range 0 to 30), which differentiate also right and left hemisphere lesions, besides those of the basal ganglia (2001)[20].

Worth full to observe, that the LADIS group, which besides the modified Fazekas scale used also complex ones (Scheltens, ARWMC) and volumetric measurement, remarked that the relatively simple modified Fazekas scale appeared to be sufficient when analyzing relationships between clinical parameters and WMH load in a clinical setting [21,22,23].

Box. Characterisitcs of the Fazekas scales[9,10].

ORIGINAL FAZEKAS		MODIFIED FAZEKAS
PVH	**DWMH**	**DSWM**
0=absent	0=absent	- - -
1=caps or pencil-thin lining	1=punctate foci	1=[mild] punctate lesions with a maximum diameter of a single lesion below 10 mm and areas of 'grouped' lesions smaller than 20 mm in any diameter
2=smooth halo	2=beginning confluence of foci	2=[moderate] single lesions between 10-20 mm in any diameter, areas of 'grouped' lesions more than 20 mm in any diameter, no more than 'connecting bridges' between individual lesions
3=irregular hyperintensities extending into the deep white matter	3=large confluent areas	3=[severe] single lesions or confluent areas of hyperintensities of 20 mm or more in any diameter
total score= [(0 – 3) + (0 – 3)] = 0 - 6		**total score = 0 - 3**

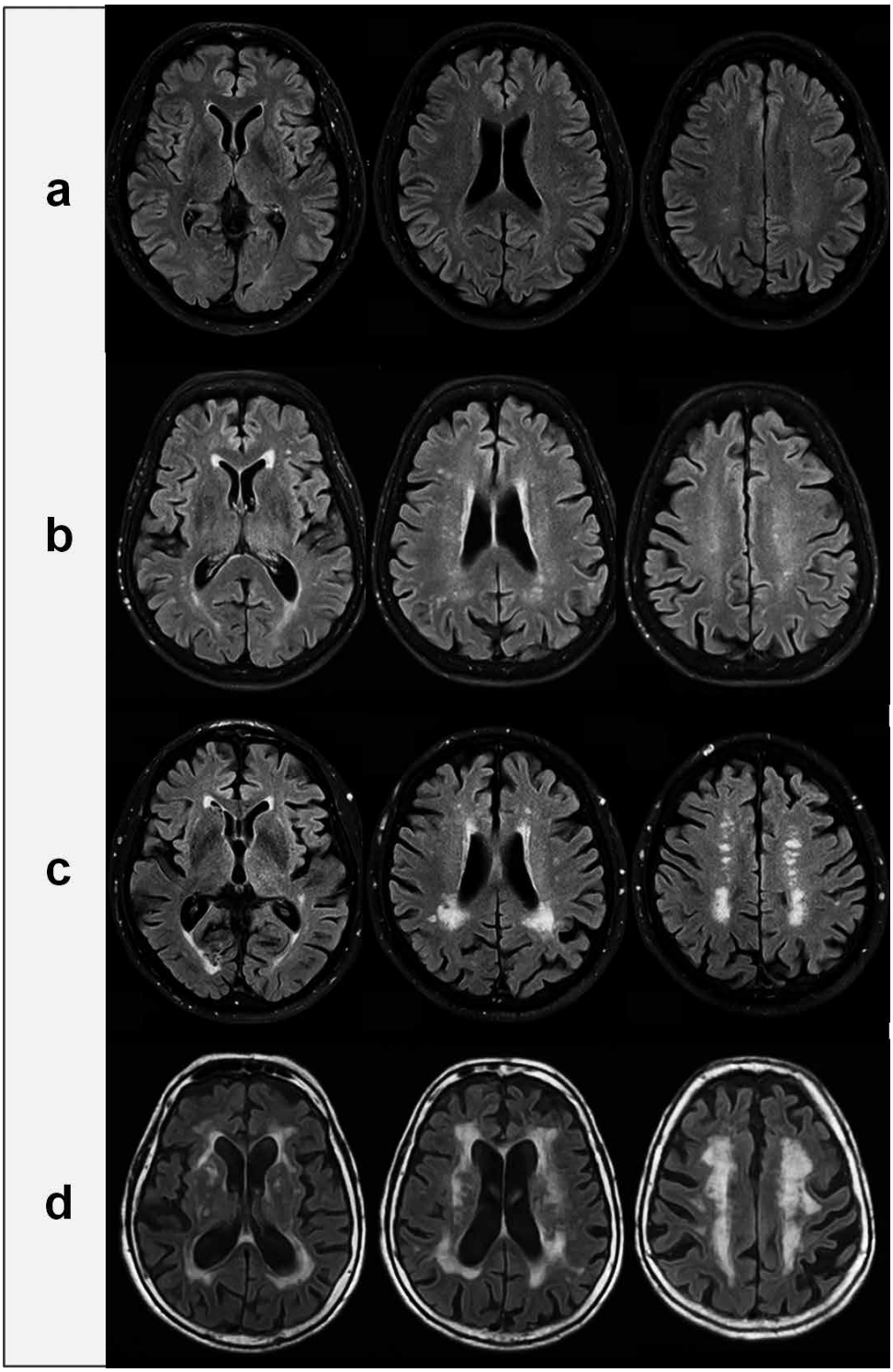

Figure. Fazekas scoring scales. [oF=original Fazekas, mF=modified Fazekas].
MRI – FLAIR sequence: axial sections at basal ganglia, lateral ventricles and supraventricular levels for visualization of WMH [PVH and DWMH].
Grades of severity:
a=absent [oF=0+0, mF=0], b=mild [oF=1+1, mF=1], c=moderate [oF=2+2, mF=2], d=severe [oF=3+3, mF=3]

COMMENTARIES

The advent of the contemporaneous neuroimaging machines, which appeared in the late 1970s (CT), and early 1980s (MRI) permitted for the first time to analyze the brain structure, in normal and pathological states (tumors, vascular diseases, among others), in a direct manner[6]. In this way, the WMH (leucoaraiosis), a result of SVD were identified, followed by the relatively simple visual scoring scale, proposed by Fazekas and collaborators, adopted by a large number of researchers of the clinical neuroimaging field, in its original form or in a modified version[9,10]. It was followed by more complex visual scoring scales, and also by volumetric measures[9,24]. However, it was remarked that the Fazekas scale, even in its modified form, appeared to be sufficient to analyze, in a clinical setting, the relationships between the WMH load and the varied disabilities that developed over a period of time[21,22,23].

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Rev. Bras. Neurol. 57(2): 18-19, 2021.

Mini-relato de caso

Neuroimaging in Kearns-Sayre syndrome

Neuroimagem na síndrome de Kearns-Sayre

Nickolas Souza Silva[1]; Lady Jane da Silva Macedo[2]; Jader Cronemberger Oliveira[3]; Larissa Teles de Souza[4].

Kearns-Sayre Syndrome (KSS) is a multisystemic slowly progressive, and rare mitochondriopathy caused by mtDNA deletions. KSS manifests by a clinical triad: ophthalmoplegia, pigmentary retinopathy, and onset before the age of 20 years[1,2]. Neuroimaging shows cerebral and cerebellar atrophy; hyperintensities in basal ganglia, brainstem and cerebral and cerebellar white matter (WM); bilateral T2 hyperintensities in subcortical WM, thalami, brainstem and cerebellum[2]. KSS diagnosis is based on the clinical triad, but neuroimaging and striated muscle biopsy (SMB) might help[1,3].

The present case is about a 12-year-old female with ophthalmoplegia, bilateral eyelid ptosis and globally abolished tendon reflexes. On fundus examination, pigmentary retinopathy was reported. Axial T2-weighted image showed hypersignal in the pale globes and internal capsules (Figure A), coronal T2 presented impairment of subcortical WM (Figure B), midbrain's hyperintensities (Figure C), and T2-weighted signal hyperintensities in cerebellar hemispheres (Figure D).

With clinical diagnosis already made, patient underwent a histopathological study whose results were fibres of varying size, subsarcolemmal and intermyofibrillar accumulations of anomalous mitochondria and glycogen, myofibrillar degeneration, and presence of ragged red fibers, which is characteristic of KSS[2,3]. Subsequently, the genetic study of SMB showed smaller fragment of mtDNA, suggestive of deletion of mitochondrial genetic material, which is suggestive of KSS[2,3].

Keywords: mitochondrial encephalomyopathies, mitochondrial myopathies, Kearns-Sayre syndrome

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Conflict of interest: The author declares that there is no conflict of interest.

Funding statement: There is no financial support.

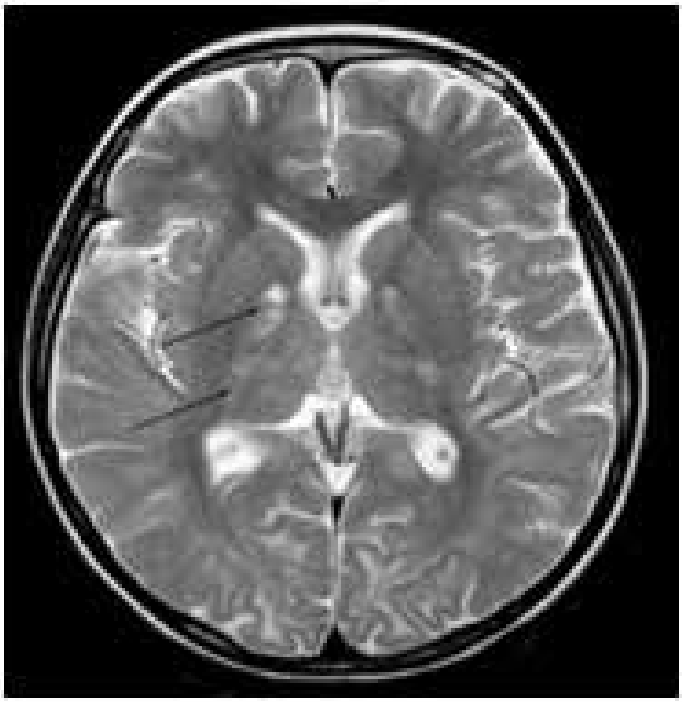

Figure A. Axial T2-weighted image demonstrating hyperintensities in the pale globes and internal capsules.

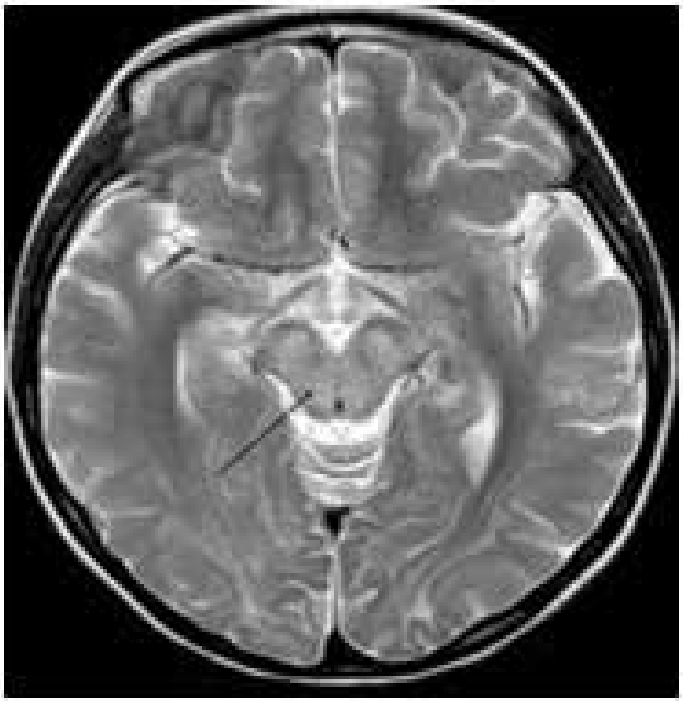

Figure C. Axial T2-weighted image showing impairment of the midbrain.

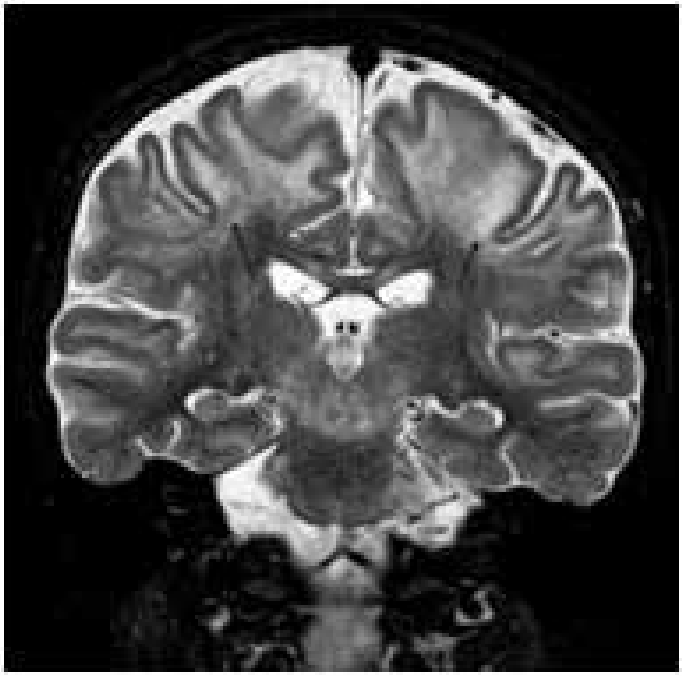

Figure B. Coronal T2-weighted image demonstrating impairment of the subcortical white matter.

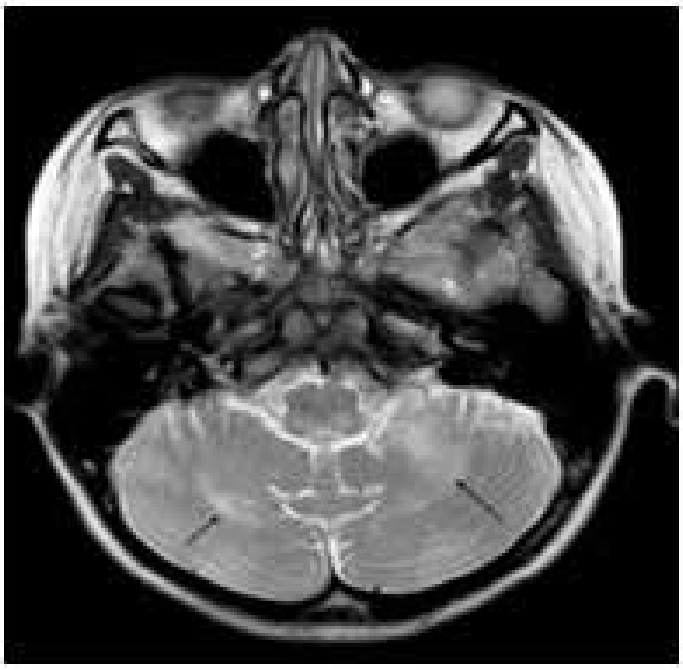

Figure D. Axial T2-weighted image with hyperintensities in the cerebellar hemispheres.

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Imagens em neurologia

Síndrome das raízes redundantes da cauda equina

Redundant nerve roots syndrome of the cauda equine

Mayara Oliveira da Silva[1], Márcio Luís Duarte[2], André de Queiroz Pereira da Silva[3], Lucas Ribeiro dos Santos[4].

A **síndrome das raízes nervosas redundantes (RNRs)** é caracterizada por raízes espinhais serpentiformes, espessadas e tortuosas no espaço subaracnóide do canal da coluna lombar, achado relativamente comum em pacientes sintomáticos com estenose espinhal lombar (EEL)[1,2,3,4]

Existe a hipótese de que, no momento em que o diagnóstico de RNRs é feito, o distúrbio ocasionado por compressão prolongada já tenha causado danos irreversíveis à raiz atingida, promovendo resultados desfavoráveis em pacientes com EEL sintomáticos com RNRs[1].

O presente caso demonstra um homem de 58 anos com dor lombar e irradiação para o membro inferior esquerdo há quatro anos. Refere piora ao deambular, evoluindo com dormência e fraqueza. Ao exame físico o paciente apresenta teste de Lasègue positivo e flexão lombar dolorosa. A ressonância magnética apresenta abaulamento discal com componente extruso em L2-L3 comprimindo as raízes intracanais de L3 e caracterizando a síndrome das RNRs da cauda equina. O tratamento medicamentoso com anti-inflamatório resultou em discreta melhora.

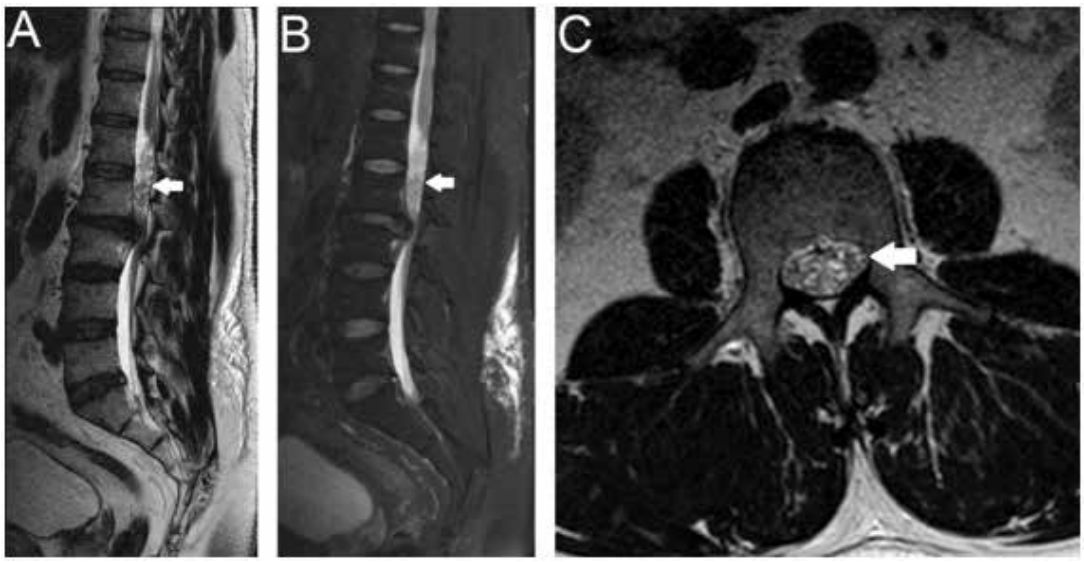

Figura. A. Ressonância magnética na sequência T2 no corte sagital; **B** na sequência T2 SPAIR; **C.** na sequência T2 no corte axial demonstrando as raízes nervosas intracanais espessadas e onduladas acima do corpo vertebral de L2, caracterizando a síndrome das raízes redundantes da cauda equina (setas brancas), com abaulamento discal difuso associado a componente extruso em L2-L3.

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Conflito de interesses: Os autores declaram não existir conflito de interesses.
Financiamento: ??

Imagens em neurologia

Diásquise cerebelar cruzada – Diagnóstico pela Ressonância Magnética

Crossed cerebellar diaschisis – Magnetic resonance Diagnosis

Márcio Luís Duarte[1,2,3], Leonardo Furtado Freitas[4], Eduardo de Oliveira Narvaez[3], André de Queiroz Pereira da Silva[1,5].

A **diásquise cerebelar cruzada (DCC)** é caracterizada pela perda da atividade funcional e do metabolismo no cerebelo contralateral à lesão supratentorial.[1,2,3,4] Este fenômeno foi usualmente observado em pacientes com infarto cerebral, tumores supratentoriais, epilepsia, encefalite, como resultado de ruptura da via cortico-ponto-cerebelar.[1,2,3,4]

A DCC é consistentemente relatada como resultado de inativação súbita do circuito, como acidente vascular cerebral (AVC), mas também pode ser encontrada em doenças crônicas, tumores cerebrais, infartos gânglio-capsulares, pequenos acidentes vasculares cerebrais, encefalite, epilepsia, enxaqueca, malformações arteriovenosas, hemorragia e doença de Alzheimer.[2,3] Nas primeiras horas após o AVC, a diásquise é potencialmente reversível em caso de reperfusão supratentorial; no entanto, DCC persistente (mais de 24 horas) está associado a danos irreversíveis e mau resultado clínico.[2]

Este caso demonstra um homem de 60 anos com sequela de isquemia aguda à direita há dois anos, com fraqueza unilateral dos membros à esquerda. O exame neurológico demonstrou a língua desviada para a direita, desvio do ângulo da boca e sinal de Babinski positivo. A ressonância magnética que detectou uma diásquise cerebelar cruzada demonstrada pelo estudo perfusional ASL (*arterial spin labeling*) que utiliza o sangue magnetizado como contraste endógeno para avaliação do fluxo sanguíneo cerebral (CBF).[5]

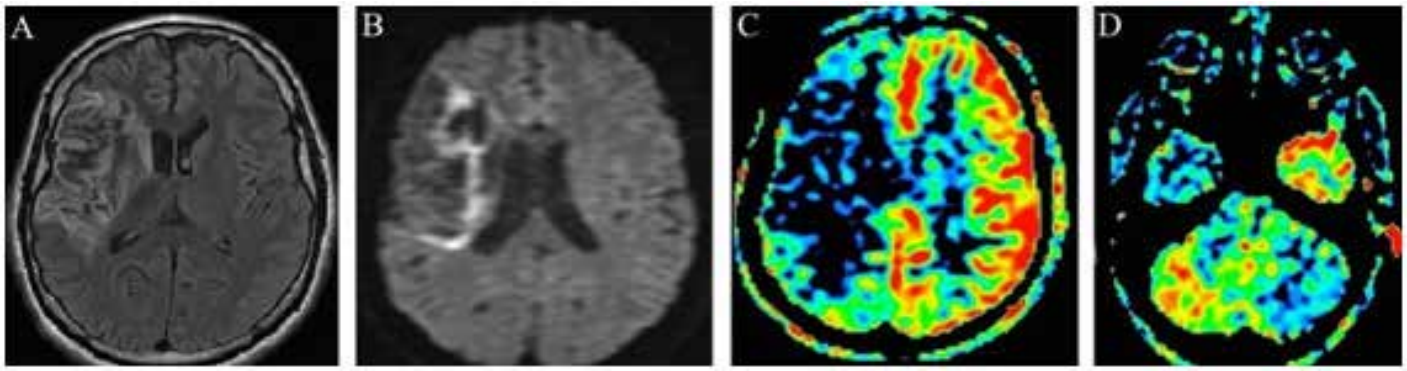

Figura. RM no corte axial na sequência em FLAIR em A, difusão em B e ASL em C e D demonstrando alterações isquêmicas com características subagudas no território da artéria cerebral média direita, que apresentam baixo fluxo sanguíneo cerebral (CBF) na sequência ASL (C). Observamos também o baixo fluxo sanguíneo cerebral no hemisfério cerebelar esquerdo, decorrente da ruptura da via córtico-ponto-cerebelar, configurando diásquise cerebelar cruzada (DCC).

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Conflito de interesses: Os autores declaram não existir conflito de interesses.

Financiamento: Não houve financiamento para este estudo.

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