DEMENTIA AND BEHAVIORAL DISORDERS IN PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) – CASE REPORT

DEMÊNCIA E ALTERAÇÕES COMPORTAMENTAIS NA LEUCOENCEFALOPATIA MULTIFOCAL PROGRESSIVE (LEMP) – RELATO DE CASO

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ABSTRACT

Psychiatric disturbances in Progressive Multifocal Leukoencephalopathy (PML) are rarely adressed and its study can offer insights into the neurobiology of psychosis. The authors report a case of male patient, 42 years old, HIV positive, with PML and psychotic symptoms. The present case shows the need for regular neurological and neuropsychological evaluations of HIV positive patients and the importance of studying diseases that cause lesions in the white matter, such as PML, to elucidate the neurobiology of psychosis.

Key words: Progressive Multifocal Leukoencephalopathy, Dementia, Behavioral Disorders.

RESUMO

Os distúrbios psiquiátricos na Leucoencefalopatia Multifocal Progressiva (LEMP) raramente são abordados e seu estudo pode oferecer insights sobre a neurobiologia da psicose. Os autores relatam caso de paciente do sexo masculino, 42 anos, HIV positivo, com LEMP e sintomas psicóticos. O caso apresentado evidencia a necessidade de realização regular de avaliações neurológicas e neuropsicológicas de pacientes HIV positivos e a importância de se estudar doenças que causam lesões na substância branca, como a LEMP, para elucidar a neurobiologia da psicose.

Palavras-chave: Leucoencefalopatia Multifocal Progressiva, Demência, Alterações comportamentais

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INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating disease of the central nervous system caused by replication of JC virus in oligodendrocytes of immunocompromised patients. Both a decreased cellular or humoral immune response can increase the susceptibility for JC-virus induced PML[1,2].

PML was a rare disease until the advent of the HIV/AIDS pandemic, but not only HIV infected people are at risk, a wide range of otherwise immune compromised patients are a potential target for this virus[3].

The symptoms and signs more frequents in AIDS associated PML are weakness, cognitive impairment, speech abnormalities, headache, gait impairment, visual abnormalities, sensory loss and, hemiparesis, gait disturbance, dysarthria, dysphasia, hemisensory loss, visual fields defects, ocular palsies[4].

CASE

A 41 year old man, from Goiânia-GO, was admitted at the dementia ambulatory on May 2009 presenting mental confusion. The patient was diagnosed as HIV positive in 2002 when he had started antiretroviral treatment with zidovudine, lamivudine and efavirenz. His wife reported difficulties in treatment adherence since 2008 because of his cognitive deficits, mainly memory impairment (difficulties in coding, retrieval and working memory) and dysexecutive failure (insight loss, difficulties on organization, sequencing, planning and self monitoring). He did not cooperate in formal neuropsychological testing because his mental confusion and agitation.

The patient showed reduced visual acuity since March 2009 and he began to present body perception disturbance, lack of orientation in space, discrimination of objects and dynamic balance. In this occasion he began also behavior alterations featured by Othelo syndrome (pathological jealousy related to his wife), dysphoria and depressive symptoms.

On April 2009 the encephalopathy progressed reflecting the difficulty in walking, neglect of personal hygiene and progressive worsening of behavior, presenting decreased level of consciousness and severe mental confusion, oniroide state and labor delusions. In the last week before coming to the dementia ambulatory, he presented total insomnia, inappetence, confabulation, aggressiveness, soliloquy, psychosis and occasional fever.

The patient was referred to the emergency room of the Hospital das Clínicas of the Federal University of Goias. The first week after patient admission, his neurological level of consciousness was normal, he presented negativism, mutism, increased muscle tone (resulting from the administration of Haldol), generally brisk reflexes, Babinski sign on the left, with poor visual acuity, light responsive and isochoric pupils without motor deficits and meningeal signs. The cranial nerves and cerebellum have not been evaluated because of the non-cooperation of the patient. He kept at the hospital and died on August 2009 because of multiple organ failure secondary to opportunistic infection.

The magnetic resonance brain imaging (MRI) had showed large white matter lesions deeply located of both parietal, occipital and temporal lobes, spreading until the midline over of the splenium of the corpus callosum, highly suggestive of progressive multifocal leukoencephalopathy (figure 1).

DISCUSSION

Unlike the slowly evolving global changes of HIV-associated dementia, mental deterioration of PML is more rapidly progressive, together with focal neurologic deficits. Common manifestations are focal motor and sensory deficits, gait abnormalities, speech and language disturbances, cognitive disorders, headache, and visual impairment. Although the occurrence of movement disorders is rare in PML, bradykinesia, rigidity, dystonia, myoclonic jerks and myoclonic ataxia have been described[5]. On this case, the initial manifestations were correlated to visual impairment. After that, the cognitive and behavior disorders were the main alterations of encephalopathy progress.

The behavioral alterations presented by the patient seem to be associated with the white matter lesions localization. The occipital cortex has primary and secondary areas, reception and processing of visual information, and tertiary areas associated with complex functions[6]. Lesions in this brain region and its connections (cortical and subcortical) can cause dysfunctions in the perception of color, shapes (objects, faces) and the detection of movement and spatial relations and depth perception[6,7]. Meanwhile, the parietal and temporal regions and their connections are responsible for the body orientation on the space and memory (coding, retrieval and

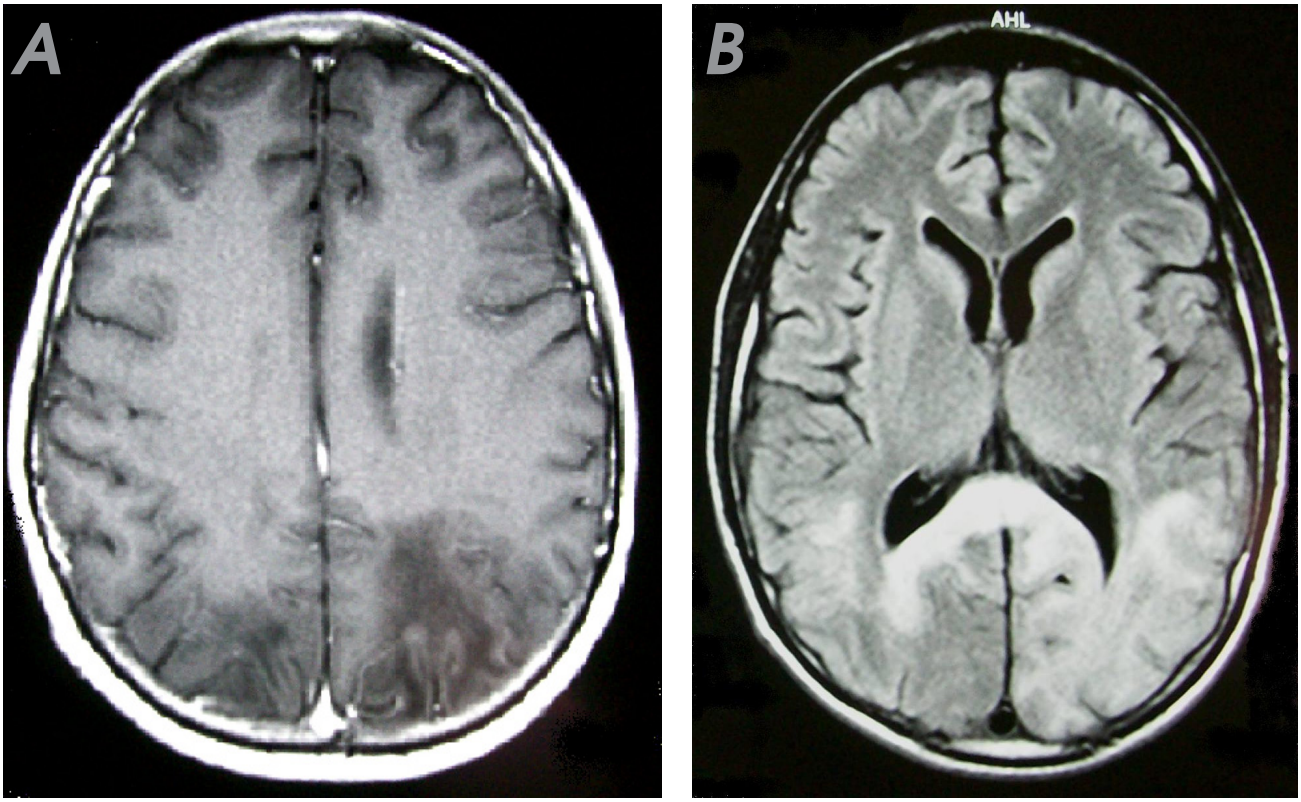

Figure 1: A- lesions with hypointensity on T1-weighted image in subcortical white matter at bilateral occipital areas. B- lesions with hyperintensity on T2-weighted image in subcortical white matter at bilateral parietal and temporal areas.

working), respectively[6,7].

The mental human process aren't restrict in specific areas on the brain and they happen with the participation of cerebral structures working as in a concert, each one contributing to the organization of these process[6]. So, the disruption of the connections among the brain structures may leads to the mental human process impairment, resulting on cognitive deficits and behavior alteration, as observed on the case reported, that presented dysexecutive failure (insight loss, difficulties on organization, sequencing, planning and self monitoring).

The psychosis in PML is not related in the literature.The presence of that can be relation to the white matter impairment, which offers an interesting model to the studies of neuroanatomic bases for psychosis origin, because this may result from the diseases that disrupt the normal formation of myelin, of corticocortical and corticosubcortical connections[8,9]. So, the illnesses that affect the white matter, as PML, seem to be related to psychosis origin and then, they could contribute to the understanding and explanation of psychosis.

Usually, the clinical outcome of patients with PML is poor with progression to death within 6 months of symptom onset[10]. The patient of the case was diagnosed with PML (when the signs and symptoms began) and he died 5 months later, reflecting the fast progression of this encephalopathy.

PML usually requires a brain biopsy or autopsy for confirmation, but radiological imaging and the detection of JCV-DNA in the CSF provide supportive evidence for the diagnosis[10]. On this case, the exam of brain magnetic resonance imaging was used for the diagnosis, making evident lesions which are preferentially in the subcortical hemispheric white matter, usually bilateral, asymmetric, and that may even be restricted to the cortical U fibers.

CONCLUSION

There are some considerations based on the case reported and on the literature reviewed: first, is the clear need of regular neurological and neuropsychological evaluation of HIV positive patients; second, is the importance to study the illnesses that affect the white matter, as PML, because it leads to ways to elucidate the neurobiology of psychosis.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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