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CASE REPORT

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Parkinsonism in a patient with AIDS and cerebral opportunistic granulomatous lesions

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Abstract The localization of opportunistic infections in the basal ganglia in patients with acquired immunodeficiency syndrome (AIDS) can cause movement disorders, such as choreoathetosis, dystonia, hemiballism and, more rarely, parkinsonism. We describe the case of an AIDS patient who developed cerebral opportunistic granulomatous lesions and, subsequently, a parkinsonian akinetic-rigid syndrome. In agreement with cases reported in the literature, the parkinsonian syndrome developed only when the lesions bilaterally involved basal ganglia. The critical localization of the opportunistic lesions in the direct and indirect strio-pallidal pathways possibly associated with the HIV-related neurotoxicity might have contributed to determine this clinical picture.

Key words AIDS • Cerebral toxoplasmosis • Parkinsonism

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Introduction

Movement disorders are unusual manifestations of cerebral toxoplasmosis in patients with acquired immunodeficiency syndrome (AIDS). A 6%-8% prevalence of these neurological signs has been reported in the literature. Hemiballism, chorea, rubral tremor and dystonia are the most frequent involuntary movements, while parkinsonian symptoms are extremely rare [1-3].

Basal ganglia involvement can be investigated by neuroimaging techniques and/pathological studies, but magnetic resonance imaging (MRI) is preferable to accurately study the anatomic areas of the encephalon involved, to verify its integrity and to determine the clinical-morphological correlations. However, previous studies have demonstrated that neuroradiological images do not always correlate with clinical expressions. In fact, in hemichorea-hemiballism the lesions are usually localized in the controlateral caudate nucleus or putamen, thalamus or subthalamic nucleus, while parkinsonism has been particularly noted when the lesions involve both lentiform nuclei [1-5].

Herein, we describe the case of a patient with cerebral opportunistic lesions and AIDS who developed an akinetic-rigid syndrome only when the lesions of the basal ganglia became bilateral.

Case report

The patient, a 31-year-old white male, was an intravenous (IV) drug user was was found to be seropositive for human immunodeficiency virus (HIV) in April 1991. In January 1993 he had an episode of oropharyngeal thrush, and in October 1993 he developed a feverish bronchitis.

In May 1995 he was admitted to our hospital for confusion and dysarthria. MRI revealed a hypointense signal (on T1- and T2-weighted images) corresponding to a granulo-

matous lesion at the dural level in the right temporo-occipital region suggesting cerebral tuberculosis. Analysis of the cerobrospinal fluid (CSF) by polymerase chain reaction (PCR) indicated positivity for *Mycobacterium tuberculosis*, and reinforced the diagnostic hypothesis. One month after initiating treatment with ethambutol (1.5 g/day) and pyrazinamide (2 g/day), the MRI findings and neurological signs improved.

In July 1995, a control MRI exam showed a further improvement of the granulomatous lesion (initial calcification), but also evidenced two new localizations involving the left lentiform nucleus and the left parietal region at the cortical-subcortical junction, consistent with cerebral toxoplasmosis. This neuroradiological situation did not correlate with any extrapyramidal disorder or new neurological sign. Diagnosis of cerebral toxoplasmosis was reinforced by the presence of *Toxoplasma gondii* DNA in the CSF (determined with PCR), while PCR for tuberculosis was negative. Therefore the patient was administered pyrimethamine (50 mg/day) and sulfadiazine (4 g/day).

After 30 days the patient was admitted to hospital for a sudden worsening of his neurological disorders. Neurological examination revealed behavioral abnormalities (abulia), right VII cranial nerve impairment and a bilateral rigid-akinetic syndrome. The main characteristics of this syndrome were: facial hypomimia; speech moderately impaired but understandable; difficulty to rise from a chair, stooped posture, short step gait and occasional freezing of the gait when turning; moderate limb cogwheel rigidity; and global bradykinesia characterized by moderate loss of finger dexterity, poverty and slowness of initiation and execution of hand movements, severe loss of leg agility associated with frequent hesitation in initiating movements or arrest in ongoing movement. MRI demonstrated an abscessed lesion in the left lenticular nucleus, while other inflammatory lesions were revealed in the right lenticular nucleus and the right frontobasal region. In addition, the previous tuberculous lesion seemed to be superinfected with toxoplasmosis (Fig. 1). The patient was submitted to the mini-mental state (MME) examination although the result (27/30) excluded AIDS dementia complex.

Despite a 60-day antitoxoplasmosis therapy, only a slight regression of the lesions was observed with MRI and the symptoms persisted. In December 1995, a worsening of symptoms was noted with the onset of hallucinations, hypersomnia, difficulty in walking, and fever. In a few days the symptoms progressed to a comatous state. The relatives voluntarily released the patient from the hospital. He died at his home few days later.

Discussion

This case of rigid-akinetic syndrome demonstrated that, in addition to the more frequent choreoathetosis, other extrapyramidal disorders can also occur during the course of cerebral opportunistic lesions, even if infrequently [1-3]. Lesional parkinsonism is quite rare. In an extensive review of patients with basal ganglia lesions, Kailash et al. [5] reported a 9% rate of parkinsonism, mainly in subjects with bilateral, diffuse lesions to the lentiform nuclei. Five cases of parkinsonism in AIDS patients with different opportunistic

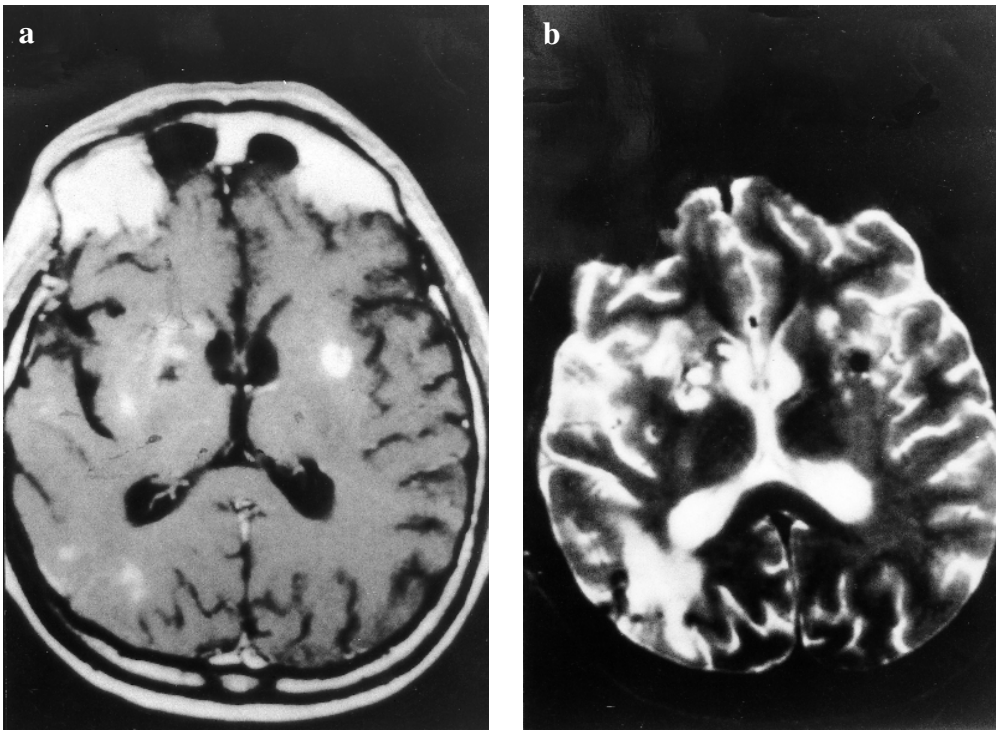

Fig. 1a, b *Axial MRI images in the acute phase of toxoplasmosis.* Abscess involving the left lenticular nucleus. Inflammatory lesions in right basal ganglia. **a** T1-weighted image. **b** T2-weighted image

lesions of the central nervous system (CNS) were reported in additional studies: two in patients with cerebral toxoplasmosis [4, 6], two in patients with progressive multifocal leukoencephalopathy [7, 8] and one in a patient with cerebral tuberculosis [9]. Four of these presented bilateral lesions of the basal ganglia; one had hemiparkinsonism related to a unilateral lesion of the lentiform nucleus.

In our study, parkinsonism appeared when lesions involved both lentiform nuclei. In fact, a previous lesion of the left striatum was not sufficient to cause parkinsonism. To explain this clinical event, two possible mechanisms can be hypothesized. The first hypothesis involves the appropriate neuro-anatomical location. Cortically generated movement is controlled by the basal ganglia through two major striatonigral-pallidal pathways: one direct and the other indirect. When the dopaminergic drive to the striatum is normal, both pathways lead to inhibition of the medial globus pallidus and, consequently, reinforce the thalamocortical drive to the premotorial cortical areas. On the other hand, degeneration of the substantia nigra leads to hyperactivity of the subthalamus and medial globus pallidus, resulting in inhibition of the ventroanterior/ventrolateral thalamus. Thus, a lesion of the medial globus pallidus would not produce parkinsonism, while a lesion of the lateral globus pallidus (which normally would lead to inhibition of the subthalamus through the indirect pathway) might cause parkinsonism. Therefore, the appropriate location of the neuro-anatomical lesion appears to be necessary to cause parkinsonism. Lesions of the globus pallidus rarely respect the boundaries of the medial and lateral globus pallidus and, moreover, do not provoke the same changes in the direct and indirect striatopallidal pathways which can be found in nigro-striatal dopaminergic degeneration. Thus, lesional parkinsonism is quite rare and is more frequent when lesions of the basal ganglia are bilateral [5].

In our patient, diagnosis of cerebral lesions due to tuberculosis and toxoplasmosis was based on imaging studies and the results of PCR. Actually, the use of PCR has yet to be validated as a diagnostic technique for these opportunistic infections and, consequently, the etiology could remain uncertain without a postmortem confirmatory examination. Nevertheless, in this case, the etiology of the lesions played a secondary role with respect to their anatomic localization.

The second hypothesis regards HIV-related toxicity. Cerebral toxoplasmosis in patients without HIV-1 infection does not cause movement disorders, while extrapyramidal signs can occur in HIV-1 infected patients without any opportunistic infection. This is evidence to indicate that the basal ganglia are involved early in the course of HIV-1 infection. Hristo et al. [10] reported that administration of neuroleptic drugs induced extrapyramidal symptoms (mainly parkinsonism) more frequently in AIDS patients with respect to psychotic patients without AIDS. Neurotoxic substances have also been considered a pathogenetic factor of HIV-related encephalopathy, some of which can cause an increase in glutamate release or decreased glutamate re-uptake. This mechanism might also be involved in other neurodegenerative diseases including Parkinson's disease and Huntington's chorea. Therefore, glutamate neurotoxicity might represent a final common pathway for neuronal susceptibility [11]. These observations suggest that, in addition to the critical localization of opportunistic infections in the basal ganglia, the progressive HIV-neurotoxicity involving pathways may also contribute to the presence of movement disorders.

Certainly, the advent of effective antiretroviral combination therapies resulted in a sharp decline of opportunistic pathologies in HIV-positive patients. Nevertheless, cases of severe neurological infections, such as tuberculosis or toxoplasmosis, are still frequent in patients intolerant or non-compliant to these therapies or in subjects not aware of being HIV-positive. Consequently, AIDS will probably remain an important cause of movement disorders in future years.

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Sommario *La presenza di lesioni opportunistiche a livello dei gangli della base in pazienti con AIDS può causare disordini del movimento, quali coreoatetosi, distonia, emiballismo e, più raramente, parkinsonismo. Noi descriviamo il caso di un paziente con AIDS, che ha sviluppato lesioni granulomatose opportunistiche a livello cerebrale e, successivamente, un parkinsonismo rigido-acinetico. In accordo con la letteratura, nel nostro studio la sindrome parkinsoniana si sviluppava soltanto quando le lesioni coinvolgevano i gangli della base bilateralmente. La specifica localizzazione delle lesioni opportunistiche a livello delle vie strio-pallidali dirette e indirette specie se associata ad una neurotossicità HIV-correlata potrebbe determinare questo quadro clinico.*

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