Case Report

Expansive brain lesion in a patient with AIDS

Lesão expansiva cerebral em paciente com aids

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ABSTRACT

A cerebral tuberculoma is a potential complication of disseminated tuberculosis in people living with HIV/AIDS, especially in developing countries. We report the case of a 52-year-old woman with advanced HIV disease and confirmed pulmonary tuberculosis, who presented with mental confusion, syncope, and a multilobulated intracranial tumor. She exhibited clinical and radiological worsening after 3 months of treatment (already in the maintenance phase), which resulted in therapeutic doubts: cerebral toxoplasmosis was the main differential diagnosis and empirical treatment was initiated. We also decided to reinitiate the complete tuberculosis regimen and add corticosteroids to it. Examination of a second sample of cerebrospinal fluid showed acid-fast bacilli; however, a stereotactic biopsy did not show any etiologic agent. After a prolonged hospital stay of 2 months, the patient was discharged to an outpatient clinic where she followed up for almost 2 years presenting evident clinical improvement, but with only partial improvement in terms of neuroimaging.

Headings: AIDS-Related Opportunistic Infections; Tuberculoma, Intracranial; Toxoplasmosis, cerebral; Case report.

RESUMO

Os tuberculomas cerebrais constituem potenciais complicações da tuberculose disseminada em pessoas vivendo com o HIV/aids, principalmente nos países em desenvolvimento. Relatamos o caso de uma mulher de 52 anos com doença avançada pelo HIV e tuberculose pulmonar confirmada, a qual apresentou confusão mental, síncope e uma lesão tumoral intracraniana de aspecto multilobulado. Houve piora clínica e radiológica depois de três meses (já na fase de manutenção) do tratamento específico, fato que implicou em dúvidas terapêuticas, tendo a toxoplasmose cerebral como o principal diagnóstico diferencial, a ponto de também merecer tratamento empírico. Optou-se por reiniciar o esquema completo para tuberculose e associar corticosteróides. Uma segunda amostra de líquor exibiu bacilos ácido-álcool resistentes, mas a biópsia estereotáxica não identificou nenhum agente etiológico. Após uma internação prolongada de dois meses, a paciente recebeu alta hospitalar para seguimento ambulatorial, onde vem sendo acompanhada já por quase dois anos com melhora inequívoca do ponto de vista clínico, porém ainda parcial em relação às neuroimagens.

Descritores: Infecções oportunistas relacionadas com a aids; Tuberculoma intracraniano; Toxoplasmose cerebral; Relato de Caso.

INTRODUCTION

Neurological manifestations occur in approximately 1% of tuberculosis cases, the most common form being meningitis[1]. However, expansive lesions in the central nervous system (CNS) can also occur in neurotuberculosis, a condition that is particularly challenging to diagnose in people living with HIV/AIDS (PLWHA) due to the presence of key

differential diagnoses such as cerebral toxoplasmosis, primary CNS lymphoma, chagoma, syphilitic gumma, and pyogenic abscess[1-3].

In this report we present the case of a patient with AIDS presenting a sizeable brain lesion suggestive of tuberculoma and discuss the difficulties in diagnosing and treating this lesion.

CASE REPORT

A 52-year-old woman with HIV, whose condition had not been medically followed up for more than 10 years, visited an infectious disease outpatient clinic complaining of weight loss, respiratory symptoms, and shingles infection. At the time, the physician prescribed acyclovir and restarted antiretroviral therapy (ART) with dolutegravir, tenofovir, and lamivudine, but did not investigate further. Moreover, the patient had an HIV viral load of 320,000 copies/mL and a $CD4^+$ count of 88 cells/mm³.

Approximately 15 days after initiating ART, her respiratory symptoms worsened and she presented mental confusion and syncope; she was then admitted to another department. There, she was diagnosed with pulmonary tuberculosis after testing positive using sputum smear microscopy. Treatment with rifampicin (R), isoniazid (H), pyrazinamide (Z), and ethambutol (E) was initiated, and the same ART regimen was continued; however, with a double dose of dolutegravir because of the use of rifampicin. There are no reports of the use of corticosteroids at this time.

To investigate the neurological condition, a CT scan of the skull was performed, which showed a multilobulated tumor lesion located in the left frontal parasagittal region that measured 3.6 × 1.9 cm in its longest dimensions comprising juxtaposed, hypodense oval images with ring-shaped contrast enhancement. Cerebrospinal fluid (CSF) analysis showed 1 cell/mm³, and protein levels of 100 mg/dL, negative results for sputum smear microscopy. The patient was discharged after 2 months with continuation of rifampicin and isoniazid (RH), with no documented record of the diagnostic hypotheses for her neurological condition.

Fifteen days after starting the maintenance phase of tuberculosis therapy and after about 90 days of using ART, the patient visited our hospital with mental confusion, diplopia, and loss of overall strength. At this time, the HIV viral load was 758 copies/mL and $CD4^+$ counts were 124 cells/mm³. Another CT scan of the skull was performed, which showed an increase in the size of the previously described lesion, now measuring 5.2 × 2.7 cm, and contrast enhancement was maintained. Another CSF sample was collected that tested positive for acid-alcohol resistant bacilli (BAAR), despite the negative result of the GeneXpert Ultra® test for *Mycobacterium tuberculosis*. We then decided to continue RH and initiate empirical treatment for cerebral toxoplasmosis.

Magnetic resonance imaging (MRI) facilitated better characterization of the multilobulated contour by revealing a thick capsule and central hypointensity on the T2 sequence (Figure 1A). This finding helped us to once again prioritize the hypothesis of cerebral tuberculoma; we therefore decided to reinitiate the complete RHZE regimen without suspending the toxoplasmosis treatment, which was continued for 42 days given the possibility of concomitant neurological infections. To clarify this, we requested a stereotactic brain biopsy and the histological study showed chronic inflammatory changes in the glial environment with no evidence of malignancy or granulomas. In addition, bacilloscopy, GeneXpert® for *M.*

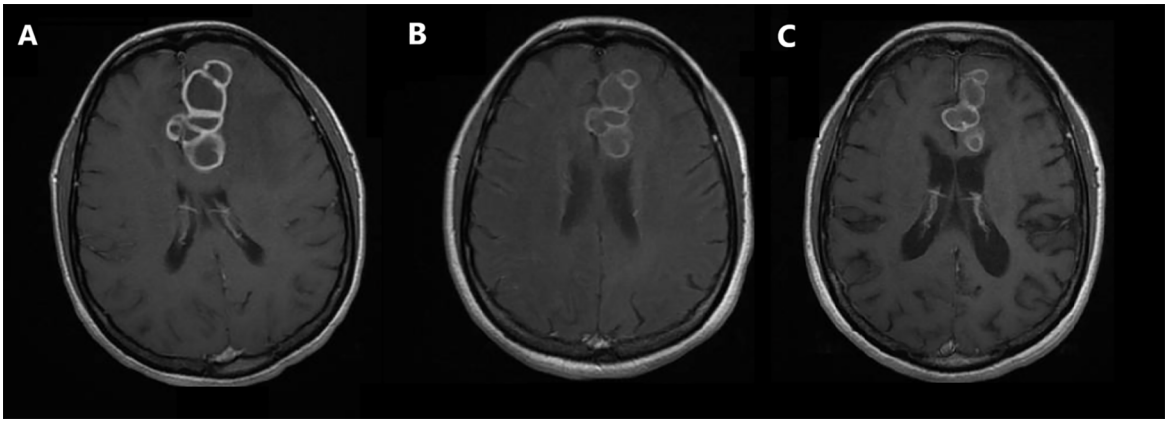

Figure 1. T1-weighted magnetic resonance imaging (MRI) in post-gadolinium axial slices). 1A- MRI performed at the time of hospitalization (after 90 days of ART and 60 days of RHZE); 1B- another exam performed after 120 days of RHZE; 1C – the last MRI performed on an outpatient basis, after almost 2 years.

Tuberculosis, fungal testing, and immunohistochemistry results were all negative, including the latest results of the respective cultures.

Although we were unable to establish a definitive microbiological and histological diagnosis of tuberculoma, the patient's neurological symptoms gradually improved. Two months after the reinitiation of RHZE, plus 1 month of RH and the use of corticosteroids throughout these 3 months, an additional MRI showed a reduction in the volume of the lesion and smoothing of its edges (Figure 1B). At this time, the patient still had occasional focal motor seizures (regulated using sodium valproate), which contributed to a prolonged hospital stay of 70 days.

She was re-evaluated as an outpatient after almost 2 years of anti-tuberculosis treatment and ART with a double dose of dolutegravir; although there was evident neurological improvement, radiological improvement was only partial (Figure 1C). At that time, her HIV viral load was 158 copies/mL and her $CD4^+$ counts were 560 cells/mm^3. Figure 2 shows a timeline of the main events described in this report, for educational purposes.

DISCUSSION

Neurotuberculosis manifests clinically as fever, headache, mental confusion, convulsions, cranial nerve paralysis, or other focal neurological signs. Imaging exams may show signs of meningitis, vasculitis, hydrocephalus, and/or expansive lesions[2-4]. However, the existence of more than one clinical syndrome caused by *M. tuberculosis*[5,6] is not uncommon, as in the case of this patient who had diffuse meningoencephalitis in addition to an expansive lesion.

Biopsy has emerged as the gold standard diagnostic method for CNS tuberculomas[7]. However, this procedure is invasive, has variable sensitivity, and samples may not be easily accessible. The biopsy was inconclusive in the present case, either because of unrepresentative biopsy sampling or because it was performed after a long period of treatment (112 days). Because the biopsy was uninformative, we decided to complete the full treatment for neurotoxoplasmosis simultaneously with other procedures, considering the risk–benefit of this measure and the epidemiology of the disease in PLWHA.

In the context of uncertainty about a diagnosis of tuberculoma, a study published in 2020 proposed a score that combines radiological and clinical-epidemiological aspects to facilitate diagnostic reasoning and allow early treatment[8]. This scoring system (SVIMS criteria) uses major and minor criteria and the analysis of the total score has good sensitivity and specificity[8]. Our patient

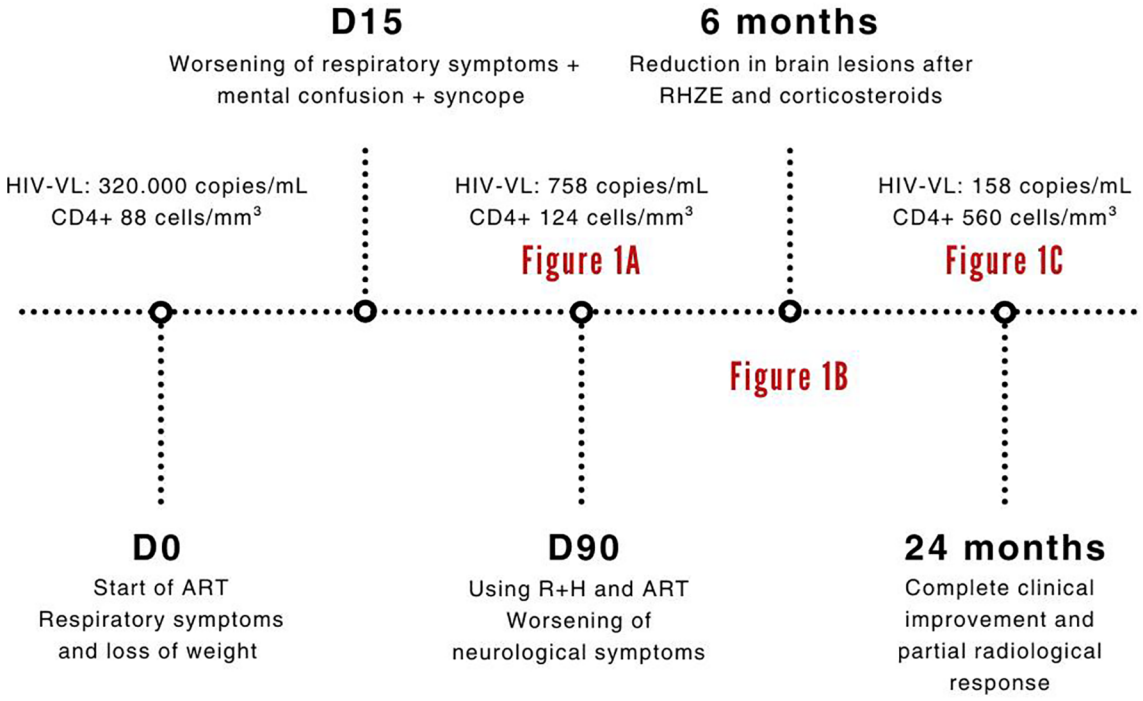

Figure 2. Timeline of the main events of the case. Legend: VL = viral load; ART = antiretroviral therapy; R + H = rifampicin + isoniazid.

presented 2 major (the radiological finding of lobulated lesions >20 mm with hypointensity in T2) and six minor criteria, including significant perilesional edema, more than one lesion in a conglomerate, and the presence of confirmed tuberculosis elsewhere[8].

The treatment of cerebral tuberculoma involves a combination of pharmacological interventions and, in selected cases, surgery[8-10]. The RHZE regimen comprises the first-line treatment; however, its duration is controversial, varying between 9 and 24 months[10]. The Brazilian guidelines recommend the usual intensive phase of 2 months with RHZE followed by a further 10 months of RH[1]. However, it is crucial to consider extending the intensive phase in cases of high bacillus load and failure of clinical/radiological response, considering the joint action of four anti-tuberculosis drugs instead of two[9,10].

Lesions larger than 2.5 cm in diameter have a poor prognosis and their treatment is prolonged (over 24 months) if they are not surgically removed[8]. In our case, we decided not to operate on the patient given her satisfactory clinical response. Surgical intervention should also be considered in cases of cranial hypertension, significant mass effect, or hydrocephalus, and ventriculoperitoneal shunting may be necessary[8].

Corticosteroids should be administered during the first 6 weeks or until a significant clinical improvement is observed, as they reduce inflammation and edema associated with the lesions[11]. Our patient only received corticosteroids at a later stage due to clinical and radiological worsening, and the benefit of their use at this stage is controversial according to reports[11].

The possibility of a patient co-infected with tuberculosis and HIV developing immune reconstitution syndrome warrants two additional comments. The first refers to the sequence of treatments. The guidelines recommend introducing ART only after a minimum of 15 days of initiating tuberculosis treatment[1]. This did not happen in our case. It would have been prudent to prioritize the investigation of the initial complaints (which resulted in a confirmed diagnosis of tuberculosis soon after) rather than reintroducing ART immediately upon the patient's first visit. The second comment refers to the possibility that the patient's clinical and radiological worsening is attributable precisely because of this sequence, i.e., due to the development of the immune reconstitution syndrome. The development of paradoxical reactions in the CNS should always be considered upon lesion regrowth after the initiation of treatment and in the presence of immune recovery markers, namely an increase in the $CD4^+$ cell counts and a significant decrease in the HIV viral load[11,12]. In our opinion, the worsening of the brain lesion revealed upon imaging examination was probably due to the progression of the infection, because BAAR was detected in the CSF, a finding that is not compatible with a paradoxical reaction[12].

CONCLUSION

Tuberculomas should be included in the differential diagnosis of brain lesions in PLWHA. This report demonstrates that establishing an etiological diagnosis of tuberculoma can be challenging, even with a brain biopsy, and that the use of a scoring system comes as an aid in this context. Prolonging the treatment and using corticosteroids concomitantly are two complementary and effective strategies that should be considered in similar cases.

"This case report deserved an official declaration of acknowledgement and ethical approval by its institution of origin and was peer-reviewed before publication, whilst the authors declare no fundings nor any conflicts of interest concerning this paper. It is noteworthy that case reports provide a valuable learning resource for the scientific community but should not be used in isolation to guide diagnostic or treatment choices in practical care or health policies.

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