Multiple Tuberculous Brain Abscesses in an HIV-infected Patient Successfully Treated with Highly Active Antiretroviral Treatment (HAART) and Antituberculous Treatment

Running head: Tuberculous Brain Abscesses and HIV Infection

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Summary

Tuberculous brain abscesses (TBA) are an unusual clinical presentation of central nervous system tuberculosis occurring extremely infrequent in developed countries, and almost always in immunocompromised patients. Before the introduction of Highly Active Antiretroviral Therapy (HAART), TBA were associated with a high mortality rate in AIDS patients. We describe an HIV-infected patient presenting with multiple TBA who recovered completely with a combination of HAART and antituberculous treatment.

Keywords: Mycobacterium tuberculosis

Brain abscess
HIV infection
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Introduction
The AIDS epidemic has led to a resurgence in all forms of tuberculosis (TB), including central nervous system (CNS) tuberculosis [1,2,3]. Several clinical presentations are possible and sometimes associated, including tuberculous meningitis, tuberculous brain abscesses (TBA) and brain tuberculomas. TBA remains a very rare condition almost always reported in AIDS patients [4,5] or in patients with miliary tuberculosis [6]. Because of limited clinical experience, there are no definitive recommendations concerning the optimal management of TBA. Many questions remain to be answered. How long should the anti-TB treatment be given? Should corticosteroids be associated? What are the indications for surgical resection or stereotactic aspiration? In patients co-infected with HIV, when and how should Highly Active Antiretroviral Treatment (HAART) be administrated?
We describe an HIV-infected patient, presenting with multiple TBA, who was successfully treated with anti-TB treatment together with HAART.

Case report
A 47-year-old Belgian man was admitted in February 2000 because of impaired consciousness and anorexia since a few weeks. He had used intravenous drugs for years and was substituted with methadone since 4 months. He had been diagnosed to be infected with the Human Immunodeficiency Virus (HIV) and the Hepatitis C Virus (HCV) in 1994, but had never been treated with antiretrovirals.
On physical examination, his temperature was 36°C, his blood pressure 130/90 mmHg and his body weight 70 kg. He was lethargic but well oriented in time and space. He presented with an important impairment of sensitivity and co-ordination of his left hemibody and a central ataxia. There was no motor deficit nor neck stiffness. A generalised muscular atrophy, multiple slightly enlarged cervical lymph nodes, a painful hepatomegaly (5 cm under the costal margin) and massive ascitis were noted. Laboratory findings showed an haemoglobin of 11 g/dl, a platelet count of 258000/mm3, a leukocyte
count of 11300/mm³, and a CD4+ lymphocyte count of 136/mm³. Other abnormalities included blood urea nitrogen: 170 mg/dl, creatinine: 3.1 mg/dl, natrium: 129 mmol/l, potassium: 5.1 mmol/l, albumin: 2.1 g/dl, and C-reactive protein: 11.8 mg/dl. The level of aspartate amino-transferase was 34 IU/l, of alanine amino-transferase 70 IU/l, and of alkaline phosphatase 218 IU/l. The HIV viral load was > 750000 copies/ml. Blood cultures showed no growth of bacteria including mycobacteria. A chest X-ray revealed a bilateral pleural effusion without cardiomegaly nor infiltrates. A Computed Tomographic (CT) scan of the abdomen showed multiple enlarged para-aortic lymphadenopathies and a large amount of ascitis. Analysis of the pleural and peritoneal effusions confirmed their transudative nature, and cultures remained negative for bacteria including mycobacteria. No malignant cells were detected. A CT scan of the brain revealed two lesions, one with a diameter of 2 cm located at the pontine level of the brainstem and the second with a diameter of 0.5 cm located beside the left frontal cortex (Fig.1). Both lesions were characterised by contrast ring-enhancement, surrounded by oedema. Magnetic Resonance Imaging (MRI) of the brain detected a third small lesion in the left cerebellum. Anti-toxoplasmosis treatment was initiated, including clindamycin and pyrimethamine. He received also broad-spectrum antibiotics for possible pyogenic cerebral abscesses and diuretics. His general condition improved slowly, but without neurological recuperation. Two weeks later, because there was no radiological change of the cerebral lesions, a stereotactic biopsy of the pontine lesion was performed. Histology revealed focal micro-abscesses with areas of caseous necrosis, with numerous acid-fast bacilli at Ziehl-Neelsen coloration. A pan-sensitive Mycobacterium tuberculosis strain was isolated from the brain biopsy specimen. Anti-tuberculous therapy (isoniazid, rifampicin, pyrazinamide and ethambutol) was started, in association with dexamethasone initially 4 x 4 mg daily. Later the dosage of corticosteroids was slowly decreased and finally stopped after 3 months. HAART was also initiated, including zidovudine, lamivudine and abacavir. Sedimentation rate and C-reactive protein levels decreased slowly, his renal function normalised completely, his
liver function and his neurological disturbances improved gradually. Anti-TB treatment was discontinued after one year. At that moment, the patient had gained 30 kg, and had no residual neurological complaints. A CT scan of the brain confirmed the complete disappearance of the lesions. His CD4+ lymphocyte count was 320/mm3 and his viral load was undetectable (< 50 copies/ml).

Discussion

A TBA is a very unusual presentation of CNS tuberculosis. Since the last century, TBA have been reported in less than 30 patients on microbiological and pathological criteria [7]. At least ten of these patients were co-infected with HIV [3-5]. Even in developing countries, TBA seems rare, accounting for 4 to 7.5 % of patients with CNS tuberculosis without HIV infection [4]. In a recent Indian series of 50 patients with brain abscesses, *Mycobacterium tuberculosis* was found to be the causative organism in only one patient [8].

TBA should be distinguished from brain tuberculomas, even if these 2 conditions represent the two ends of the same pathological spectrum. The histological features depend on complex host-organism interactions involving the cellular immune response, the individual hypersensitivity and the mycobacterial load. A tuberculoma is a focal mass of dense granulomatous inflammatory tissue, in patients capable to mount a granulomatous inflammatory response. A TBA results from the caseation of a tuberculous focus, in immunocompromised patients, or in patients with a high mycobacterial burden. Histological findings show a focal collection of pus containing abundant acid-fast bacilli and surrounded by vascular granulation tissue, as observed in our patient. The distinction between TBA and brain tuberculomas is difficult on CT, although abscesses are usually associated with more oedema. Differentiation between these 2 patterns is easier with MRI, because a TBA generally is multiloculated and has a hyperintense centre on T2-weighted images.
Focal tuberculous lesions of the brain occur much less frequently than tuberculous meningitis [2,3]. Brain tuberculomas are more often reported than TBA. Brain tuberculomas still constitute 10-30% of intracranial space-occupying lesions in developing countries, while they are diagnosed in less than 2% of them in developed countries [10]. There is little information about the prevalence of brain tuberculomas and TBA among HIV-infected patients. Brain tuberculomas were diagnosed in 4 (10%) of 38 HIV-positive patients with intracranial mass lesions, who underwent a brain biopsy in South-Africa [11], and in 3 (7.5%) of 40 Mexican HIV-positive patients with neurological complications [12]. In contrast, among 130 U.S. HIV-infected patients with neurological complications [12], and among 250 U.S. AIDS patients who underwent a stereotactic biopsy for cerebral lesions [13], nobody was diagnosed with CNS tuberculosis. Our patient had never stayed in a region where tuberculosis is endemic, but he had used intravenous drugs for years, which is a known risk factor for TB [3,14]. It is likely that he first developed asymptomatic tuberculomas, evolving to abscesses because of his declining immunity. In general TBA have a worse prognosis than brain tuberculomas [4,6]. Of the 10 AIDS patients with TBA reported so far, at least 2 died because of tuberculosis. None of them received HAART [3,5]. To our knowledge our patient is the first published case of TBA who received concomitant antituberculous treatment and HAART.

There are no “evidence-based” recommendations for the treatment of brain tuberculomas and TBA. Most of the authors recommend an initial diagnostic needle aspiration if neurosurgical facilities are available, followed by prolonged anti-tuberculous chemotherapy, at least 9 months for tuberculomas [15], and at least 1 year for TBA [1]. Initially, 4 anti-TB drugs should be given, including isoniazid, pyrazinamide and rifampicin because these three drugs penetrate the blood brain barrier and reach adequate concentrations in the cerebrospinal fluid. Surgery or stereotactic aspiration are indicated if life or vision are threatened by raised intracranial pressure, or if the lesions fail to respond to antimicrobial therapy alone [16,17].
In conclusion, tuberculosis or tuberculous abscess should be suspected in HIV-infected patients presenting with intracranial space-occupying lesions, even if they never stayed in a country where TB is endemic. In order to diagnose this condition, a stereotactic brain biopsy should be performed. The treatment option with HAART makes a correct diagnosis and an adequate management of opportunistic infections ever more important.
References


Legend

**Figure 1**: Magnetic resonance imaging of the brain shows a large lesion (2 x 2 cm) in the brainstem, characterised by a $T_1$ and $T_2$ hypointense signal, ring enhancement after injection of gadolinium and perilesional oedema, and a smaller lesion in the left cerebellum.