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Review Article

Difficulties in Therapeutic Management of a Gabonese Patient with Cerebral Toxoplasmosis Associated to Extra Pulmonary Tuberculosis in Case HIV-HBV Co-Infection

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Abstract

Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) is a major public health concern in sub-Saharan Africa. Opportunistic diseases cause substantial morbidity and mortality to human immunodeficiency virus (HIV)-infected patients. HIV-HBV co-infection is common we report the case of an association of cerebral toxoplasmosis with mediastinal lymph node tuberculosis in a patient with HIV-HBV co-infection. The diagnosis of this extra-pulmonary tuberculosis and cerebral toxoplasmosis was presumptive and was made probable by the test therapies that were effective. Concomitant treatment of these two opportunistic infections with antiretroviral therapy resulted in severe drug hepatitis that was probably favored by hepatitis B that HIV infection would have worsened. The choice of effective and less toxic antiretroviral triple therapy was difficult in the absence of recommendations for such combinations.

Keywords: Cerebral toxoplasmosis, mediastinal tuberculosis, HIV, HBV.

INTRODUCTION

Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) is a major public health concern in sub-Saharan Africa [1, 2], where 70% of the 33 million people estimated to be infected by HIV in 2009 reside. Between 2002 and 2020, ~68 million people will die of AIDS in the 45 countries most affected. Opportunistic diseases cause substantial morbidity and mortality to human immunodeficiency virus (HIV)-infected patients. HIV-HBV co-infection is common [3, 4].

The management of HIV-infected patients has been the subject of several recommendations that have been regularly updated with the aim of combining antiretroviral efficacy with less toxic effects of drugs [5]. Management modalities have also been developed for various opportunistic infections during AIDS, as well as HIV-HBV coinfection [6-8].

However, there is a lack of recommendations for two or more opportunistic infections, especially when they occur in comorbid conditions such as hepatitis B. We report, for discussion, the case of a combination of cerebral toxoplasmosis and Mediastinal lymph node tuberculosis in a patient; HIV-HBV is healing, it is very difficult to manage. It is an infectious disease.

OBSERVATION

M.D, male patient, aged 33, with no notable pathological history was hospitalized for general impairment with cough. A thoracic Computed Tomography (CT) scan showed mediastinal lymphadenopathy suggestive of ganglionic tuberculosis (Fig-1). HIV serology was positive and the CD4 count was 6 / mm3. The diagnosis of AIDS (stage C according to WHO) was then retained. The laboratory tests also revealed a HBs positive antigen and a negative HCV serology. The hepatic assessment was normal: total bilirubin at 4.4 µmol / l, AST = 43 IU / l and ALT= 43 IU / l.

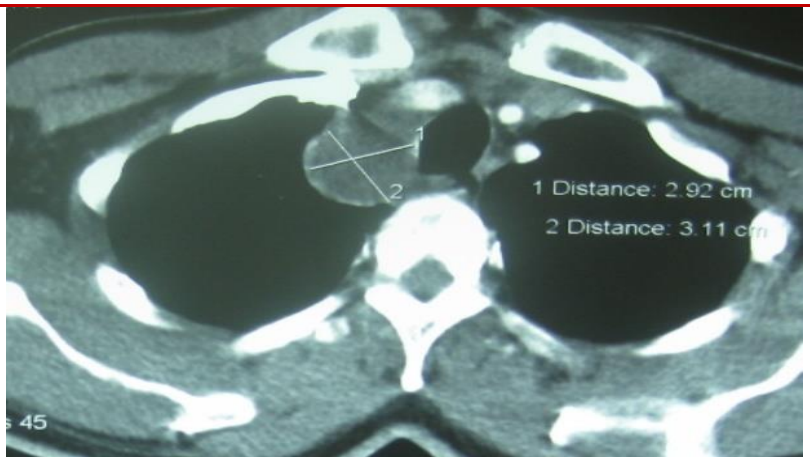

Fig-1: Thoracic CT scan showed mediastinal lymphadenopathy suggestive of ganglionic tuberculosis

The patient was then put on TB treatment based on isoniazid, rifampicin, pyrazinamide and ethambutol for a period of two months. One month later, the patient had diffused progressive headache and vomiting. A cerebral CT scan revealed lesions in the right occipital lobe, right inner capsule, left and right parietal lobe. The appearance of these lesions was more suggestive of cerebral toxoplasmosis. The titer of anti-Toxoplasma gondii IgG was 300 IU / ml. Treatment with pyrimethamine and sulfadiazine has been initiated. Fifteen days were sufficient for a significant regression of the signs of intracranial hypertension. The patient found himself under three types of treatment: triple antiretroviral combination therapy with stavudine, lamivudine and efavirenz, anti-tuberculosis and anti-toxoplasmic treatment. After three weeks of this treatment, the patient presented severe hepatitis with total bilirubin at 208 µmol / l, AST at 3670 IU / ml and ALT at 3132 IU / ml. Rifampicin and efavirenz were discontinued. After 21 days, the liver assessment was normal to conclude to a drug hepatitis. Rifampicin has been reintroduced. A cerebral and thoracic CT scan was performed; the toxoplasmic lesions and the mediastinal lymphadenopathies disappeared.

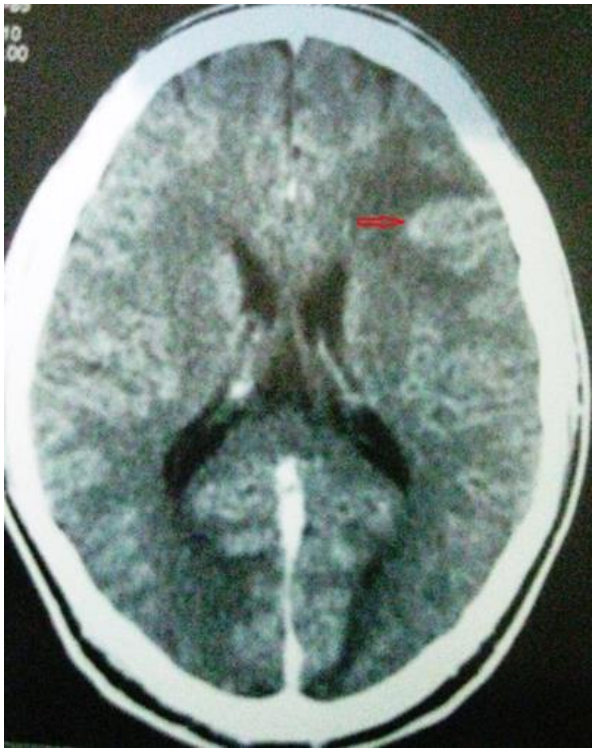

Fig-2: Brain exploratory CT revealed lesions in the right occipital lobe, right inner capsule, left and right parietal lobe

DISCUSSION

Immunosuppression, which is particularly secondary to AIDS, greatly favors tuberculosis. This is seen in disseminated and extra-pulmonary form when the immune status is seriously affected (advanced stage of AIDS for example) [9]. The contribution of HIV to the "ecosystem" of Koch's bacillus is not without reward. Indeed, tuberculosis accelerates the evolution

of this viral infection to the stage of AIDS disease [10]. Viral load can increase 160-fold when tuberculosis disease starts [11, 12]. The risk of cerebral toxoplasmosis increases with the degree of impairment of the immune system. Indeed, starting from a CD4 count of less than 100 / mm3 this risk becomes important especially in the presence of a high toxoplasmic seroprevalence as is the case for example in Libreville (Gabon) where our case originated. Indeed, it would be around 70% [18]. The conditions favoring the combination of these three conditions were all verified in our patient. The physiopathological interactions between tuberculosis and HIV (mutual Favorisation) infection would be at the origin of an accelerated evolution towards the disease AIDS stage. The profound immunosuppression that resulted would have allowed the reactivation of cerebral cysts containing Toxoplasma's bradyzoites and subsequently the establishment of cerebral toxoplasmosis [13]. The definitive diagnosis of extra-pulmonary tuberculosis is often difficult to pose, the disappearance of the clinical signs and para-clinical under therapeutic test often makes it possible to make the diagnosis [9]. However, for cerebral toxoplasmosis, the CT scan performed with and without the injection of contrast medium quite often reveals single or multiple cockade images that are quite evocative. However, in some cases, CT images are atypical or even normal [14]. These images, even typically in cockades, are not always pathognomonic of a cerebral toxoplasmosis. The main differential diagnoses in HIV-positive subjects are tuberculoma or cerebral lymphoma [15, 16].

The appearance of clinical and radiological signs after one month of antituberculous treatment and the improvement of these signs by the introduction of antitoxoplasmic treatment led to the diagnosis of cerebral toxoplasmosis. The clinical and para-clinical elements would encourage starting a specific pest control. The potential effectiveness would reinforce the presumptive diagnosis. This was the attitude observed by the medical team who cared for the patient. Diagnoses of ganglionic tuberculosis and cerebral toxoplasmosis have been reported on clinical, radiological and epidemiological elements. The clinical and para-clinical improvement of the patient under specific therapeutics made it possible to retain these diagnoses. For an HIV-infected TB patient, when the CD4 count is greater than 200 / µl, the introduction of antiretroviral therapy is recommended only after the completion of TB treatment. However, if the CD4 count is less than 200 / µl, antiretroviral therapy is recommended and should be introduced after two to eight weeks of TB tolerance [17]. After six weeks of treatment, our patient showed good tolerance to antituberculosis, the introduction of antiretroviral therapy coincided with the discovery of cerebral toxoplasmosis. The concomitant treatment of these three infections in the comorbidity field represented by viral hepatitis B is believed to be at the origin of the severe drug hepatitis observed. HIV infection promotes the multiplication of HBV making the liver more vulnerable and drug toxicity becomes common [18]. In the case of HIV-HBV co-infection, antiretroviral treatment is recommended as soon as the CD4 count is less than 500 / mm3, it must combine in triple therapy, a dual therapy with anti-HIV and anti-HBV activity: an inhibitor nucleoside (lamivudine or emtricitabine) with a nucleotide inhibitor (tenofovir) [8]. The validated triple therapy includes two nucleoside reverse transcriptase inhibitors (NRTIs) associated with either a ritonavir-boosted protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI): efavirenz. PIs and efavirenz may both be hepatotoxic. However combination with rifampicin is possible with efavirenz, contraindicated with PIs. Our patient was naive antiretroviral therapy, as reported in the literature; the association with efavirenz would be more effective, if not more than the association with PI [5]. The combination of three NRTIs, less hepatotoxic, in particular (zidovudine + lamivudine + abacavir), is without drug interaction with rifampicin, but less effective [19]. It was already reserved for situations where the load was less than 100,000 copies / ml with a contraindication on IP or NNRTI [5]. Severe hepatic impairment is a contraindication to this combination of three NRTIs as well as to these two groups of drugs: IP and NNRTI.

In conclusion the case of this patient elucidates the difficulty of therapeutic management of AIDS and multiple opportunistic infections on a terrain favorable to the hepatotoxicity of the available molecules [20]. The choice of a validated tritherapy that is both effective and less toxic was difficult, therapeutic strategies including possibly new molecules are necessary for patients associating two or more opportunistic infections and co-infected with HIV-HBV.

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