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PNEUMOCYSTIS JIROVECII AND CRYPTOCOCCUS NEOFORMANS CO-INFECTION IN AN HIV-INFECTED PATIENT : A CASE REPORT

Adadi Soukaina* Parasitology and Mycology Department, Central Laboratory of Medical Analysis, Hassan II University Hospital, Sidi Mohamed Ben Abdellah, Fez, Morocco *Corresponding Author

Elamouri Jihade MD, Parasitology and Mycology Department, Central Laboratory of Medical Analysis, Hassan II University Hospital, Sidi Mohamed Ben Abdellah, Fez, Morocco

Zineb Tlamçani PROF, Parasitology and Mycology Department, Central Laboratory of Medical Analysis, Hassan II University Hospital, Sidi Mohamed Ben Abdellah, Fez, Morocco

ABSTRACT Opportunistic fungal infections have a high morality rate, occurring most often in immunocompromised subjects. We report the case of a 19-year-old girl who presented with progressively worsening dyspnea, hypoxemia requiring oxygen supplementation with bilateral pulmonary cystic lesions, treated with antibiotics for a presumptive diagnosis of pneumonia. The patient did not improve clinically. A diagnostic bronchoscopy was performed, which revealed findings consistent with pulmonary pneumocystis. The patient tested positive for HIV, and had a positive cryptococcal antigenemia. She was put on treatment adapted to each fungal infection with a favorable evolution.

KEYWORDS : pneumocystis - cryptococcosis – HIV

INTRODUCTION :

Fungal infections during AIDS are increasingly recognized. They can occur at any stage of infection, with profoundly immunocompromised individuals having increased susceptibility to a range of infections that are not common in the immunocompetent host. However, concomitant opportunistic infections (OIs) may coexist. We report the case of a newly diagnosed HIV-positive young woman with a double fungal infection due to *Pneumocystis jiroveci* and *cryptococcus neoformans*.

Case presentation:

A 19-year-old student, with no notable pathological history, the history of her illness dates back to two months before her hospitalization by the installation of a dyspnea of progressive aggravation, and atypical chest pain, all evolving in a context of fever, accompanied by asthenia, emaciation not quantified, with loss of appetite. This prompted him to consult a general practitioner, who prescribed symptomatic treatment. As the symptoms did not improve, the patient was referred to the university hospital for further treatment.

On clinical examination, she was slightly polypneic with an oxygen saturation at 96% in room air, heart rate at 116/min, cachectic and pale. The cardiovascular examination showed pericardial friction on auscultation, with the presence of well limited round erythematous papules of firm consistency measuring 0.5 cm with umbilical center located on both legs and the posterior face of the left arm and left thigh on mucocutaneous examination. In addition, the pleuropulmonary examination and the rest of the physical examination were unremarkable.

The patient underwent an initial biological workup showing a hypochromic microcytic anemia, with lymphopenia at 690/mm, and a radiological workup (thoracic CT scan) showing bilateral thin-walled pulmonary cystic lesions, with the presence of foci of bronchial dilatation, medial adenopathies, and a large pericardial effusion. The patient underwent drainage of the effusion.

A complementary serological test was requested, showing a positive HIV serology with an estimated viral load of 3960 copies/ml and a positive cryptococcal antigenemia with a titre higher than 1/1000 after detection of soluble cryptococcal circulating antigens by agglutination on latex particles (figure1).

Figure 1: positive cryptococcal antigenemia with a titer higher than 1/1000 by latex particle agglutination technique (pastorex*)

A sample of bronchioloalveolar fluid was subjected to a mycological study, and direct examination after staining with toluidine blue had isolated the presence of cystic forms in typical deflated balloon compatible with *Pneumocystis jirovecii* (Figure2). Thus their demonstration by the direct immunofluorescence technique (figure 3).

In addition, the patient underwent a biopsy of the lesion on the posterior aspect of the right leg, with an anatomopathological study in favor of molluscum contagiosum.

Our patient thus presents a pulmonary pneumocystis-cryptococcosis co-infection, with a molluscum contagiosum skin lesion in the context of a recently diagnosed acquired immunodeficiency.

Treatment with trimethoprim-sulfametoxazole, amphotericin B, with local treatment of the skin infection was started, as well as initiation of antiretroviral therapy 3 days later.

The evolution was marked by the installation of a deep febrile neutropenia resistant to the treatment leading to an inflammatory syndrome of immune reconstitution, hence the stop of the antiretroviral drugs and the addition of a corticotherapy with a good clinical and biological evolution. The patient was discharged from the hospital with an appointment for initiation of antiretroviral therapy.

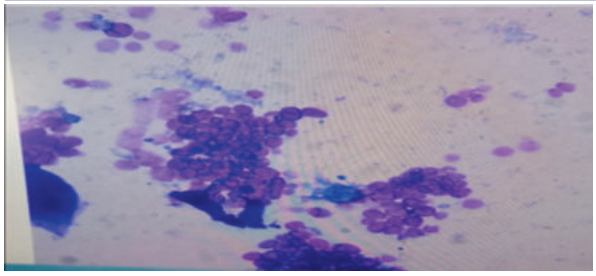

Figure 2: *Pneumocystis jirovecii* cysts stained with toluidine blue giving a deflated balloon appearance.

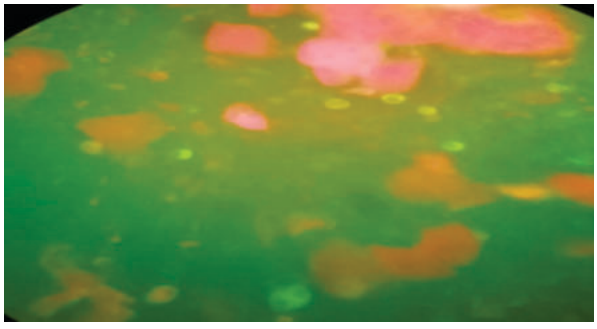

Figure 3: *Pneumocystis jirovecii* cysts in direct immu nofluorescence

DISCUSSION:

Morbid co-infections are relatively common in HIV-positive patients in the AIDS stage [1]. With the development of combination antiretroviral therapy, morbidity and mortality secondary to human immunodeficiency virus (HIV)-related opportunistic infections have decreased. However, many patients still pay a high price for these infections because they are diagnosed late [2]. CD4 T-cell counts have been shown to be a good marker of immune status during infection, and their levels have been used to estimate the risk of OI for each patient [1]. Cryptococcosis and pneumocystis, 2 severe and deep opportunistic mycoses that occur in the advanced stages of HIV immunosuppression with very low CD4 counts.

Cryptococcosis is one of the most common infections in people with advanced acquired immunodeficiency syndrome (AIDS) with a defective cellular immune component and is a major contributor to AIDS-related mortality worldwide [3]. Despite the increasing availability of antiretroviral therapy (ART), cryptococcosis remains a major cause of death among HIV-positive patients in developing countries [4,5,6].

Screening for subclinical cryptococcal infection by cryptococcal antigen immunoassay is highly effective in identifying patients at risk for developing cryptococcosis, allowing these patients to be targeted with preventive antifungal therapy to prevent the development of severe and morbid disease [7,8].

Pneumocystis is known as the classic infection of AIDS [9]. It is a frequent cause of respiratory disease in patients with a pathology generating cellular immunosuppression, mainly in those who do not receive prophylaxis [10].

The existing immunosuppression responsible for pneumocystic disease may favor infection with other opportunistic pathogens. Concomitant infection with *Cryptococcus neoformans* is not common, and to date has apparently been reported only rarely in the literature. In Morocco, only sporadic cases have been reported: 2 cases at the Mohammed VI University Hospital in Marrakech over a period of 14 years from January 2007 to March 2021 [11], and only 1 case diagnosed at the University Hospital in Casablanca over a period of 5 years from January 1, 2010 to June 30, 2015 [12]. With some other sporadic cases reported in the world, notably in North America [10,13,14] and Africa [15,16]

Some studies associate the risk of developing fungal infections with CD4 cell thresholds, which makes it possible to evaluate the risk incurred by each patient with respect to opportunistic infections [1]. Therefore, Pneumocystis and Cryptococcosis generally occur in HIV-positive patients with a CD4 T cell count below 200 cells/mm3 [1]. However, in our case, in the absence of CD4 count, and since the patient had an AIDS stage disease, with a high viral load, we can deduce that she had a low CD4 count (less than 200).

The initiation of antiretroviral therapy in HIV-infected patients restores protective immune responses against a wide variety of pathogens and significantly decreases mortality. But in some patients immune reconstitution is associated with a pathological inflammatory response resulting in substantial short-term morbidity and even mortality. In cryptococcosis, the incidence of immune reconstitution inflammatory syndrome (IRIS) is variable, ranging from 4 to 15%/year [17]. The risk factors reported are: antiretroviral treatment started within sixty days of the diagnosis of cryptococcosis, a very high level of cryptococcal antigen in the cerebrospinal fluid, fungemia, low CD4+ T lymphocytes, antiretroviral treatment concomitant with the diagnosis of cryptococcosis, and a high viral load [17]. Therefore, in our patient the IRIS was most likely secondary to the initiation of antiretroviral therapy 3 days after the start of antifungal therapy, and to the high viral load. Therefore, the initiation of antiretroviral therapy should be delayed for up to 10 weeks after the start of antifungal therapy, especially for patients with certain features predictive of IRIS, as mentioned previously [18].

For the prevention of multiple and concurrent opportunistic fungal infections, specific safety measures should be adopted, such as early and regular medical examination, prompt diagnosis and appropriate antifungal prophylaxis. These are necessary to decrease the morbidity and mortality associated with these infections in HIV-positive patients, which in turn may increase their longevity[19].

CONCLUSION:

The diagnosis of fungal coinfections demonstrates the vulnerability of patients with HIV in advanced stages of the disease. Thus, detection of AIDS cases in the early stages of infection is necessary for prompt and adequate introduction of antiretroviral therapy and use of prophylaxis to control opportunistic infections.

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