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NEURO-INFLAMMATORY SYNDROME OF IMMUNE RESTAURATION IN REANIMATION: ABOUT A CASE

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ABSTRACT

The authors recall, through an observation, the rare nature of immune restoration neuroinflammatory syndromes (IRIS) of the immunocompromised patient, and report the case of a 31-year-old patient admitted to medical intensive care for hypoxemic-serious pneumonia. The etiology was a pulmonary cryptococcosis indicative of HIV infection at the AIDS stage and effectively treated with a combination of antifungals. The initiation of HAART has been very virologically effective with viral load collapse and improved CD4 cell counts. The evolution was marked by the occurrence of a neuro-IRIS associated with a rapidly fatal cancerous toxoplasmosis.

Keywords : *Pulmonary cryptococcosis. ART. IRIS. Toxoplasmosecérébrale*

INTRODUCTION

The introduction of antiretroviral therapy (ART) in the management of human immunodeficiency virus (HIV) infection has significantly reduced the incidence of opportunistic diseases through immune restoration. This restoration may, however, be the cause of the onset of inflammatory immune restoration syndrome. It gathers all clinical and biological manifestations related to an excessive immune response directed against the antigens of an infectious agent or not. This syndrome can be expressed in different ways including the paradoxical aggravation of an opportunistically treated infection.

The authors report, through an observation of pulmonary cryptococcosis revealing HIV infection at the AIDS stage, a case of inflammatory immune restoration syndrome associated with a rapidly fatal cerebral toxoplasmosis and insist on the importance of referring to this diagnosis each time. circumstances of occurrence are met.

MATERIALS AND METHOD

Observation

This is a 31-year-old woman, married and mother of a 6-year-old child admitted to intensive care in a chart of serious hypoxemic pneumonia. In its antecedents, one finds a notion of shingles intercostal occurred three months before, and a significant slimming quantified to ten kilograms in two months. Its history goes back to 15 days by the occurrence of a cough, painful, whooping-cough, rebellious to the symptomatic treatment and dyspnea of effort. Acute respiratory failure

completes the picture. Clinical examination at admission found a conscious patient, feverish at 40 ° C, tachypneic at 42 cycles per minute. The saturation with ambient air is 67% It goes up to 92% under oxygen therapy at 12 l / min. The ends are cyanotic. It is tachycardic at 102 beats per minute, the blood pressure is at 108/66 mm Hg. The chest X-ray shows a diffuse interstitial syndrome with a frosted glass appearance, without associated pleural effusion (Figure 1). Thoracic CT shows predominant atelectasis at the left lower lobe. CT scan with contrast medium is normal.

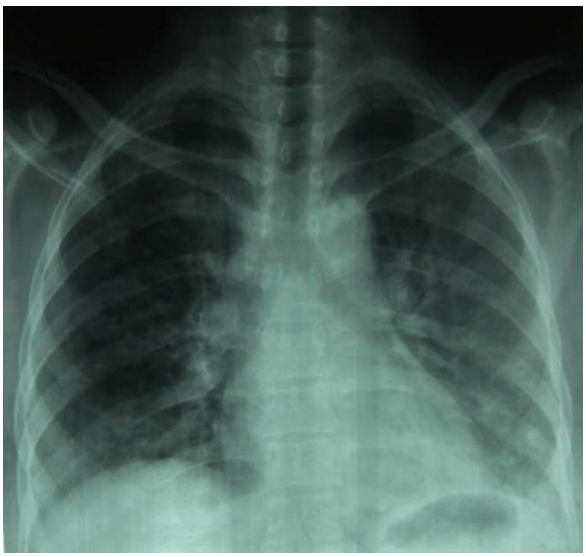

Figure 1: X-ray of the chest face to the admission of the patient

The leucocytes are at 5950 / mm3. The white formula has a pronounced lymphopenia of 8%. The C-reactive protein is 93.5 mg / let procalcitonin at 0.155 ng / ml. Arterial gasometry revealed respiratory alkalosis with a pH at 7.49, PaCO2 at 27 mmHg and hypoxemia with PaO2 at 76 mmHg.

The patient underwent intravenous bi-antibiotic therapy combining clavulanate amoxicillin 1g / 6h and ciprofloxacin 500mg / 12h. the aggravation of the respiratory distress, in spite of a well-conducted antibiotherapy leads to aventilatory care with intubation and artificial ventilation. The doubt about the patient's immunocompetence resulted in an HIV serology that is made positive. The viremia is greater at 822,000 copies / ml. Immuno-depression is profound since the CD4 count was 27 / ml. The viral serologies B and C were negative. The IgGantitoxoplasmic search is positive.

The diagnosis of pulmonary cryptococcosis was related to the isolation of a cryptococcus neoformans in the culture of the bronchoalveolar lavage fluid. Analysis of the cerebrospinal fluid was not performed. The blood cultures produced were negative. Standard therapy is based on amphotericin B (1 mg / kg / day) combined with flucytosine (50 mg / kg / every 6 hours) [1,2]. The clinical improvement is notable. The patient is extubated at day 5 and leaves the intensive care unit on day 8. Follow-up is provided in the infectious diseases department and in addition to the treatment of pulmonary cryptococcosis, an ART was introduced on D + 22. It is a fixed combination of efavirenz (600 mg), emtricitabine (200 mg) and tenofovirdisoproxil fumarate (245 mg).

The patient is readmitted to the intensive care unit at day 47, in a table of confusionnelfébrile syndrome (glasgow score is at 11/15) of rapid installation. It is preceded by deficiency signs in the form of muscle weakness in the right upper limb. Cerebral CT with injection of iodinated contrast medium shows necrotic center cockade images with contrast enhancement at the periphery

associated with a peri-lesional edematous component responsible for a moderate mass effect on surrounding structures.

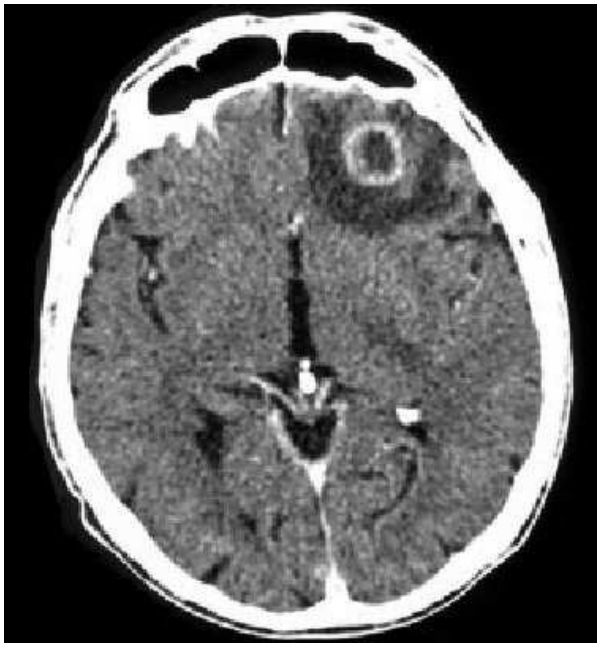

Figure 2: Cerebral CT with injection of contrast medium.

The CD4 count is 242 while the viral load has dropped to 52,000 copies / ml. Parsulfametoxazol-trimethoprim treatment was initiated in combination with oral corticosteroid therapy (prednisone: 1 mg / kg) and ART. The evolution was fatal and the patient died at 4 days of readmission, in a table of irreducible intracranial hypertension.

RESULTS AND DISCUSSION

French et al. report in 1992, the first statement of immune restoration syndrome (Immune Reconstitution InflammatorySyndrome or IRIS Anglosaxons) associated with tuberculosis. In a series of 64 HIV-positive patients with CD4 <200 and a tuberculin anergic, the introduction of azidothymidine (zidovudine) was the cause of a tuberculin shift in 47% of them [3] , demonstrating a restoration of cell-mediated immunity.

Pathophysiologically, the IRIS corresponds to a restoration of the specific anti-microbial immune responses, an inflammatory and lymphoproliferative response as well as a production of pro-inflammatory cytokines (IL6) responsible for the clinical symptomatology.

Its incidence is difficult to assess and varies with the opportunistic condition considered and with time from the start of ART. It can occur in most opportunistic infections, particularly tuberculosis, cerebromenofenic cryptococcosis, viral hepatitis B. In the case of disseminated cryptococcal disease, this incidence may exceed 30% [4]. Although toxoplasmosis is the most common cause infectious diseases of the central nervous system of the immunodepressed patient, IRIS associated with cerebral toxoplasmosis remains rare [5]. Martin-Blondel et al reported in a retrospective study over 9 years the largest series described in the literature with 9 cases of neuro-IRIS associated with cerebral toxoplasmosis [6].

IRIS recognizes three main risk factors:

Initial immunosuppression (with CD4 count <50 / ml) [7,8], initial spread of infection and early onset (1 to 2 months) of ART after the start of antifungal therapy in cryptococcosis.

In addition, a conversion of IDR to tuberculin is frequently observed [9].

The diagnosis is above all presumptive. It will be supported by a compatible clinical presentation, an evocative chronology, the existence of risk factors for SRI [10], the confirmation of the efficacy of ART with a significant decrease in viral load (> 1 log fall) and the elimination of the most frequent differential diagnoses with the help of some additional examinations (Table 1).

It could be newly acquired infection, failure to treat a previously identified infection (resistance, nonobservance) or adverse effects of treatment

MAJOR CRITERIA (2 major or 1 major A + 2 minors)	
	A: Atypical presentation of an opportunistic or tumoral pathology in patients responding to ART
- - Localized disease - - Inflammatory inflammatory reaction - - Atypical inflammatory response in tissues - - Progression of organ involvement or pre-existing lesion size increase after initial improvement under specific treatment prior to initiation of antiretroviral therapy and after exclusion of drug toxicity or other diagnosis	
	B: Decrease in viral load HIV> 1 log10 copies / ml
MINOR CRITERIA	
- - Increase of CD4 lymphocytes after antiretroviral treatment - - Increase of the specific immune response (ex: IDR) - - Spontaneous resolution without specific treatment with continued antiretroviral and anti-infectious treatment	

Table 1: Diagnostic criteria for immune reconstitution syndrome [11].

Therapeutic management is based on expert recommendations, not validated by clinical studies, and consists in initiating the specific treatment of the infectious agent at the origin of IRIS. On the other hand, it seems that corticosteroid therapy associated with the resumption of ART may limit the recurrence of SRI [12].

The discontinuation of ART is not recommended: There is certainly a decrease in drug interactions and toxicities as well as the number of tablets, however, the reintroduction of ART leads to an almost systematic relapse of IRIS and mortality. is twice as high in the group or treatment was reintroduced late [13].

The prevention of infectious IRIS is mainly based on the search and systematic treatment of a latent opportunistic infection in the deeply immunocompromised patient before the introduction of ART. Short corticosteroid therapy is recommended in severe clinical forms (prednisone 0.5-2 mg / kg / day 2 weeks).

Despite the diagnostic and therapeutic difficulties and the potential complications related to the occurrence of the immune restoration syndrome, its prevention must not lose sight of the considerable contribution of ART in terms of reducing mortality.

CONCLUSION

IRIS is a common event (20% if an opportunistic infection is indicative of HIV). Difficult diagnosis often retrospective and polymorphous presentation. Although rarely serious, its management is always complex. In this case, it must lead to the introduction of corticosteroid therapy, or even the discontinuation of a previously initiated ART.

However, it should not be overestimated because the risks associated with IRIS lead to delayed ART, the benefit / mortality of which is clear when the CD4 cell count is <100 / mm3.

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