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Immune Restoration Syndrome and Cryptococcosis Associated with Kaposi's Disease at Brazzaville University Hospital, About A Case Plus Review of the Literature

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ABSTRACT

Immune Restoration Syndrome (IRIS) is a frequent phenomenon in profoundly immunocompromised individuals who are late starters on highly active antiretroviral therapy. It is often under-notified due to a lack of available technical resources in resource-limited countries, where viral load and TCD4 lymphocyte cell assays are not always available. In tropical Africa, the active search for opportunistic infections prior to initiation of ART has not yet become part of the practice of some doctors, and some patients find their health situation exacerbated sometime after the start of treatment. Immune restoration pathologies include neuromeningeal cryptococcosis (CNM) and Kaposi's disease, which classify patients as WHO stage 4. Diagnosis of immune restoration is clinically suspected, while confirmation is immuno-virological, with a significant increase in TCD4 cell counts and a critical reduction in viral load at an early stage. The association of Cryptococcosis and Kaposi's disease testifies to advanced immunodepression in people who start antiretroviral treatment late, as was the case in the present study.

Keywords

IRIS, Cryptococcosis, Kaposi, CHU, Brazzaville, Congo.

Introduction

The advent of antiretroviral tritherapy has significantly altered the natural history of HIV/AIDS infection, with a spectacular improvement in quality of life and longer life expectancy among this population of infected people. However, some patients who start ART late will see their health situation deteriorate as a result of a paradoxical inflammatory reaction linked to an opportunistic infection that was evolving quietly and untreated until then. This picture corresponds to IRIS-demasking [1]. Worldwide, the frequency of onset of this inflammatory syndrome varies from one country to another. In Africa, the prevalence of IRIS associated with tuberculosis is % in Senegal and % in Côte d'Ivoire [2,3]. In countries with a high prevalence of Cryptococcosis, such as Senegal, the association of IRIS and Cryptococcosis is not new, having already been identified in the work of Daye Ka [4]. In the Congo, the prevalence of neuromeningeal cryptococcosis remains just as high in a population of people living with HIV [5]. At an advanced stage of HIV/AIDS disease, the association of CNM and Kaposi's disease remains frequent, and is discovered when antiretroviral treatment is started early as part of immune restoration, as was the case in this patient, whose association is described below.

Medical Observation

The patient, initials I.J., male, born January 16, 1976, aged 48, no profession, single with no children, was evacuated from Ouesso in the Sangha department on September 5, 2024 for treatment of a

febrile coma. For over a month, the patient had been suffering from a prolonged fever lasting more than 21 days, treated in Ouesso for malaria with artemisinin derivatives without success. The onset of fronto-temporal and retro-orbital headaches prompted a retroviral serology test, which proved positive. The viral load reached 5000 copies, and the patient was put on antiretroviral treatment with Tenofovir + Lamuvidine and Dolutegravir, i.e. Acriptega 1 tablet/day. After two weeks on this treatment, he went into a coma, and was taken to the Brazzaville hospital for further treatment.

He is neither diabetic nor hypertensive. He has never had a BCG vaccination. He occasionally drinks alcohol and does not smoke tobacco. He has no history of trauma or prison confinement. Never operated on, he is the 3rd of 5 children, all in good general condition. The parents are alive and there is no evidence of chronic illness in the family. Examination on arrival revealed a patient in poor general condition with good mucocutaneous staining, anicteric with good hydration status and thick skin folds of undernutrition. Calves are supple, no IMO. Temperature was 39°c, heart rate 120 beats per minute, respiratory rate 22 cycles per minute. Room air SPO_2 was 97%.

Examination of the equipment revealed a coma with a Glasgow score of 8, meningeal stiffness with Kernig's sign present. Generalized hyperchromic spots all over the body associated with angiomatous, bluish lesions located on the soft palate, nasal root and thoracoabdominal areas (Figure 1). The heart was regular, with no additional noise. The lung fields and lymph nodes are unobstructed. The rest of the examination was unremarkable. Cerebrospinal fluid analysis revealed a rock-clear fluid with 40 elements, 100% lymphocytic. Hyperproteinorachia at 5g/l and hypoglycorachia at 0.1 g/l. Mycology revealed the presence of numerous cryptococci. Histological analysis of the bluish skin lesions revealed angiomatous lesions..... Plasma viral load on October 15, 2024, one month after initiation of ART, returned to 157 copies/mL and CD4 count to 600/mm3. The diagnosis of IRIS with CNM associated with KAPOSI disease was accepted. The patient was treated with Fluconazole 1600mg/d for 15 days, then 800mg/d, Ancontyl 100 mg/kg/d, Bleomycin 15mg/kg every 15 days, Corticosteroid 20mg/d for 2 weeks, then halved. Continuation of antiretroviral therapy (TDF+3TC+DTG) at a dose of 1cp/d via nasogastric tube, then orally. Progression at D 22 was marked by regaining consciousness with a Glasgow score of 15, apyrexia for more than 72 hours, and the patient was discharged at Days 28.

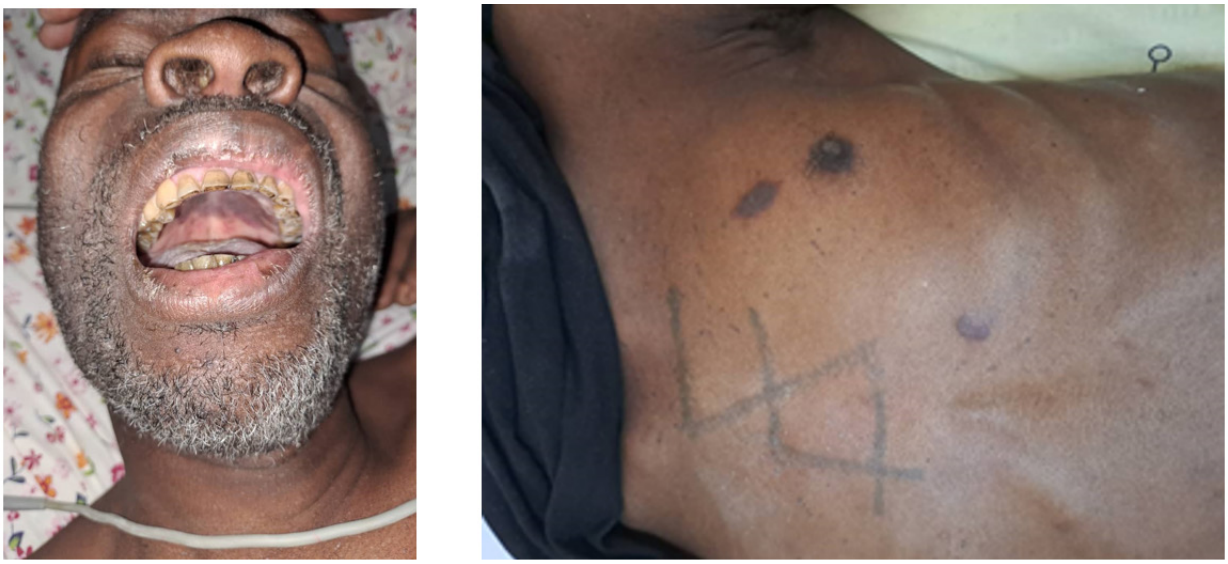

Figure 1: Skin and palatal vault lesions with purplish macules.

Discussion

IRIS was defined in 2008 by the International Network for the Study of HIV-associated IRIS (INSHI) as the occurrence, at the time of introduction or modification of ARVs, contemporary with an increase in CD4 and/or a decrease in viral load (-0.5 log10) and/or an improvement in general condition of inflammatory symptoms be related to an underlying condition, without any other diagnosis and with improvement within 12 to 20 weeks [6].

The frequency of immune restoration in a population of patients immunosuppressed by HIV/AIDS is relatively high, but sometimes underestimated due to the weaknesses of technical facilities in southern countries [1]. The predominant sex appears to be male, but this varies from study to study. The first documented case of IRIS-Tuberculosis in the Infectious Diseases Department of the Brazzaville University Hospital was that of a 38-year-old man immunosuppressed by HIV type 1, in whom the first inflammatory symptoms appeared two months after initiation of ART [7]. The incidence of immune restoration remains variable, ranging from 10 to 25% of cases, depending on the country and the degree of immunosuppression of patients considered as notified by French [8]. The 4-week delay following the onset of inflammatory-

type symptoms after initiation of triple antiretroviral therapy is classic and has already been reported in the literature by several authors [1,8,9]. Several factors influence the time to onset of symptoms, in relation to immune restoration. Patient age, degree of immunosuppression and duration of HIV infection have been shown to influence IRIS, irrespective of the pathology of immune restoration [8,10]. Profoundly immunocompromised patients, in the absence of early detection and effective management, may have several undetected opportunistic infections, manifesting themselves on the introduction of highly active triple antiretroviral therapy. In South Africa, the incidence of immune restoration syndrome (IRIS) was 10.4% in 2008, and cryptococcosis was the second most common immune restoration pathology after tuberculosis [11]. The diagnosis of IRIS is suspected when clinical signs of an inflammatory nature appear in a patient initiating highly active antiretroviral therapy at an early stage. It was confirmed by immunology, with increased CD4 cells and a critical reduction in viral load, all within a short time. Our patient began ART with a viral load of 20,000 copies/ml according to the Xpert HIV-1 Viral Load Kit, and CD4 cells at 50. Five weeks later, he presented with a persistent fever of 39.5°C, tachycardia at 120 beats per minute, and coma-like disorders of consciousness with a Glasgow score of 8. Viral load using the same technique came back at 157 copies/ml or 2.20 log and cD4 at 400 C/ul. The diagnosis of IRIS was therefore confirmed. Cerebrospinal fluid analysis revealed a rock-clear fluid with 1200 elements, 100% lymphocytic. Hyperproteinorachia at 5 g/l and hypoglycorrhea at 0.2 g/l. Direct examination with India ink staining revealed numerous cryptococci. Histological analysis of cutaneous and mucosal biopsies revealed fibro-connective tissue infiltrated by vascular proliferation consisting of small-calibre vessels with narrow lumens. The presence of a diffuse, moderate, lymphocytic inflammatory infiltrate is consistent with Kaposi's disease in the plaque stage. The association of Cryptococcosis and Kaposi's disease in the context of IRIS was accepted.

The patient was treated with Fluconazole 1600 mg for 15 days, then 800 mg for 8 weeks, ancotyl 100mg/kg for 15 days. Bleomycin 15mg/kg every 15 days. ART was continued and we added corticosteroid therapy, notably dexamethasone at a dose of 20 mg/d for 2 weeks, then 10 mg for 2 weeks. With this treatment, the patient regained consciousness, with a Glasgow score of 15 and stable apyrexia for over a week. He was discharged on day 28 of his hospitalization. IRIS usually has a favorable prognosis spontaneously in the more or less short term, and not all cases require treatment. Since IRIS is unmasking, the underlying pathology needs to be managed with appropriate treatment, as was the case for cryptococcosis and Kaposi's disease in this patient. Optimal treatment reduces the length of hospital stay, and mortality from IRIS is low overall [1,6].

Conclusion

Immune restoration syndrome is a frequent event in the profoundly immunocompromised, but is often underestimated due to a lack of technical resources. Its morbidity is mainly related to prolonged hospitalization, additional investigations and prolonged anti-infectious treatments. Its prognosis is less unfortunate, as was the case in this patient.

References

1. Müller M, Wandel S, Colebunders R. Immune reconstitution inflammatory syndrome in patients starting antiretroviral therapy for HIV infection. A systematic review and meta-analysis. Lancet Infect Dis. 2010; 10: 251-261.
2. Poda GEA, Seydi M, Manga NM, et al. Sundrome de reconstitution immunitaire au cours du traitement antirétroviral au sénégal. Méd et maladies infect. 2009; 39: 350-351.
3. Aoussi EF, Ehui E, Dembélé JP. Cryptococcose neuro-méningée et VIH à lère des antirétroviraux en Côte d'Ivoire. Méd et maladies infect. 2012; 33: 1-6.
4. Ossibi Ibara BR, Manga NM, Daye Ka, et al. Prevalence and associated factors to cryptococcosis in the Infectious Diseases Departement of the national University Hospital Center of Fann in Dakar (Senegal). Microbiol Infect Dis. 2018; 2: 1-4.
5. Ossibi Ibara BR, Mabiala babela JR, Attinssounon Cossi A, et al. Cryptococcosis neuro-brain in 42 patients at the University hospital of Brazzaville. Am J Infect Dis. 2017; 15: 45-49.
6. Meintjes G, lawn SD, Scano F. Tuberculosis-associated immune reconstitution inflammatory syndrome: Case definition for use in resource-limited settings. Lancet Infect Dis. 2008; 8: 516-523.
7. Ossibi Ibara BR, Bemba ELP, Okemba Okombi FA, et al. Premier cas documenté d'IRIS-Tuberculose dans le service des maladies infectieuses du Centre Hospitalier Universitaire de Brazzaville. J Fran Viet Pneu. 2015; 19: 1-89.
8. French MA, Price P, Store SF. Immune restoration disease after antiretroviral therapy. AIDS. 2004; 18: 1615-1627.
9. Barber DL, Andrade BB, Sereti I. Immune reconstitution inflammatory syndrome : The trouble with immunity when you had none. Nat rev Microbiol. 2012; 10: 150-156.
10. Meya DB, Manabe YC, Boulware DR. The immunopathogenesis of cryptococcal immune reconstitution inflammatory syndrome: Understanding a conundrum. Curr Opin Infect Dis. 2016; 29: 10-22.
11. Murdoch. AIDS. 2008.