Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/14106
DOI URL: http://dx.doi.org/10.21474/IJAR01/14106

RESEARCH ARTICLE

RELAPSING VISCERAL LEISHMANIASIS IN HIV INFECTED PATIENT WITH PERSISTENT LOW TCD4 COUNT: A CASE REPORT

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Manuscript Info

Manuscript History
Received: 20 November 2021
Final Accepted: 23 December 2021
Published: January 2022

Key words:-
Visceral Leishmaniasis, HIV, Relapse, Renal Injury, Pulmonary Involvement

Abstract

Visceral leishmaniasis in HIV-infected patients is marked by a high mortality rate and its frequent relapses. It is characterized by the involvement of organs that are not usually affected in non-immunocompromised patients. We report a case of relapsing visceral leishmaniasis in an HIV-infected patient. HIV infection was discovered simultaneously as the first episode of visceral leishmaniasis. Even after recovery of visceral leishmaniasis and effective antiretroviral treatment with a negative viral load during three years, the TCD4 count remained low, contributing to visceral leishmaniasis relapse. The clinical presentation of the relapse was more severe and atypical, with renal and respiratory involvement leading to his death. Through this case and a literature review, we will discuss the relation between TCD4 count and visceral leishmaniasis in this coinfection.

Introduction:-

Leishmaniasis is a vector-borne parasitic disease caused by a group of protozoa belonging to the Leishmania genus.[1] Visceral leishmaniasis (VL) is the most severe form of leishmaniasis, especially in human immunodeficiency virus (HIV) infected patients. Compared to non-immunocompromised patients, VL-HIV coinfected patients have more severe forms of VL, greater parasite loads, a higher mortality rate, and more frequent relapses. In addition, organs not typically involved in VL may be parasitized in this coinfection.[2] Moreover, HIV infection increases the risk of developing VL from 100 to 2320 times depending on the endemicity of each region. [2]

Herein, we report the case of a 39 years old man followed for an HIV infection at the acquired immunodeficiency syndrome (AIDS) stage discovered during his first episode of VL. Three years after that episode, the patient was admitted to our department for a relapse of VL with a multi-visceral impairment, including respiratory and renal injury. These conditions made the treatment more complex and the prognosis worse, leading to death. Such cases illustrate the difficulty of managing VL in HIV-infected patients. Based on this case report and a literature review, we will discuss the relation between the low TCD4 count and leishmaniasis and its relapses.

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Case Report

A 39 years old man was admitted to the infectious diseases department of the university hospital center of Marrakesh for the first episode of VL. The patient presented a prolonged fever, cachexia, pancytopenia, and splenomegaly. The visualization of amastigotes of Leishmania in the bone marrow aspirate confirmed the diagnosis of VL. HIV infection was diagnosed during this episode. The patient was at the AIDS stage (buccal and esophageal candidiasis with cachexia), his initial TCD4 cell count was at 21 cell/mm3, and the initial viral load was at 2.06 106 copies/ml.

The patient was treated with meglumine antimoniate (20 mg/kg/day) for sixteen days, switched after the onset of pancreatitis to the combination of fluconazole (400mg/day), and allopurinol (300mg/day) for fourteen days. After one month of treatment, the patient achieved remission with an improvement of his general condition, amelioration of laboratory parameters, and absence of amastigotes of Leishmania in bone marrow aspirate. The patient received antiretroviral treatment (ART), including efavirenz, emtricitabine, and tenofovir. Three years after this episode, the patient was asymptomatic, his viral load became undetectable, but the TCD4 cell count remained low during all the follow-up period (the highest was 110cell/mm3).

Three years after the first episode, the patient was readmitted to our department for VL relapse. He presented a chronic dry cough (for more than two months), fever, wasting, and asthenia. The clinical assessment found a pallor, tachypnea, bilateral crackles, abdominal pain, and splenomegaly. The laboratory tests showed pancytopenia (Hb 5.3 g/dL-WBC 1730/mm3 -lymphocytes 170/mm3-platelet count 113 000/mm3). TCD4 cell count was 66/mm3. HIV RNA was less than 50 copies/ml. Bone marrow aspirate microscopy visualized the amastigote form of Leishmanias into macrophages, confirming VL relapse diagnosis. Kidney function was impaired. Blood urea nitrogen was at 1.47 g/l and serum creatinine at 37mg/l, giving a glomerular filtration rate of 19ml/min. Furthermore, he presented hematuria, leukocyturia, and the 24-hour proteinuria was at 1.08 g/ day. The result of a urine bacterial culture was negative. Electrolytes and liver function tests were normal. Sputum tests were negative.

Ultrasound examination of the abdomen revealed splenomegaly and hyperechogenic renal cortex. A thorax CT scan found a right posterior basal consolidation with a moderate homolateral pleural effusion and bilateral micronodular pattern.

The patient received fluconazole (400mg/day) and allopurinol (300 mg/day) adapted to his renal function for 28 days with a mild improvement in his respiratory symptoms and renal function. However, the pancytopenia persisted. The control of Bone marrow examination revealed the persistence of the amastigotes of Leishmania. Therefore, we started Meglumine antimoniate (20mg/kg/day) because of our country's non-availability of liposomal amphotericin B (L-Amp B). The patient's pancytopenia, renal function, and dyspnea subsequently worsened, requiring oxygen therapy and several sessions of hemodialysis. The patient died due to respiratory and circulatory failures.

Discussion:-

The coinfection of Leishmania and HIV has been reported in more than 35 countries. [1] Its prevalence has decreased with the advent of highly active antiretroviral therapy, but it continues to be a public health problem in several regions like Ethiopia and Brazil.[2,3] In European Region, the annual incidence of VL-HIV coinfection is estimated at around 1100–1900 cases/year.[1]

In Morocco, there is no statistical data for this coinfection. However, according to the epidemiological situation of both diseases, several regions are considered at high risk of HIV and Leishmania infantum VL coinfection.[4] In addition, specific anti-Leishmania infantum antibodies were detected in 5% of HIV-infected patients in Marrakesh - Safi region.[4]

In the HIV epidemic, VL was recognized as an opportunistic infection. It often occurs when TCD4 cell counts are less than 200 cells/mm3.[5] The low TCD4 cell counts during VL-HIV coinfection is due to both agents' synergistic action on reducing TCD4 count by chronically activating the immune system, attacking macrophages and dendritic cells, and modifying the Th1/Th2 balance in favor of Th2.[3,6] This mechanism may explain the low TCD4 count during our patient's first episode, but it cannot explain the continued low TCD4 count until the second episode when the HIV infection was controlled, and the viral load was undetectable.

It is known that HIV-infected patients fail to entirely eliminate the leishmanial agents after remission.[7] The persistence of leishmanial agents is explained by the initially low TCD4 cell level, especially since TCD4 cells have a pivotal role in the clearance and the control of these parasites.[7,8] At the same time, the persistence of parasites after remission induces a chronic immune activation which leads to chronic depletion of TCD4 cells and maintains them at a low level.[6,8,9] This hypothesis is supported by a study done in Brazil comparing nine VL-HIV coinfected patients (6 months after remission of VL and starting ART) with a group of HIV-infected patients without prior leishmaniasis (6 months after starting ART). The VL group had low TCD4 counts not exceeding 200 cell/mm3 even with an undetectable viral load and a high CD38 count indicating immune activation. In contrast, the group without leishmaniasis had a higher average TCD4 cell count and a lower average CD38 count.[9]

The typical presentation of VL is continuous or intermittent fever, hepatosplenomegaly, and pancytopenia.[3] In addition to the typical presentation, our patient in the relapse had respiratory signs and renal impairment. Atypical presentations, including diarrhea, lungs involvement, or renal injury, are described in the literature during VL-HIV coinfection.[5,6,10]

Treatment of VL in patients with HIV infection is more complicated than the treatment of VL in immunocompetent patients. Until now, there has been no satisfying treatment therapy.[1] Several molecules can be used with variable availability depending on the country. Amphotericin B (Amp B) and pentavalent antimonials are the most used worldwide. L-Amp B is recommended as the first-line treatment of VL in immunocompromised persons in North America and Europe based on its safety profile. It can be used at a dose of 3–5 mg/kg daily or intermittently for ten doses (days 1–5, 10, 17, 24, 31, and 38).[1,11] The other Amp B formulations are the first option.[1] Pentavalent antimonials are still used in poor countries because of the high cost and access constraints. It can be used in areas where Amp B lipid formulations are unavailable.[1]

It has been suggested that combined drug regimens are the best option for VL- HIV coinfected patients. However, no published clinical trials assess the effectiveness of the combination therapy in VL–HIV coinfected patients. Information is based only on case series or case reports.[1]

In the absence of the recommended treatment and our patient's kidney failure, we were forced to use the combination of fluconazole and allopurinol. This treatment was unsuccessful, leading us to use pentavalent antimonials despite kidney failure and the risk of worsening it. All this demonstrates the difficulty of managing this disease in low-income countries with limited therapeutic options.

The risk of VL relapse is very high after VL-HIV coinfection, and secondary prophylaxis significantly reduces the rate of VL relapses. Therefore, several authors recommend it for all patients with TCD4 cells count less than 200/mm3. [1,3,11] The first line recommended regimen for secondary prophylaxis is L-Amp B at a dose of 5 mg/kg every 2 to 3 weeks until TCD4 cells count on ART reach at least 200 cells/mm3 for a minimal period of 6 months.[1]

Providing effective ART can improve immunity and reduce the relapse rate.[1] But the optimal timing after antileishmanial therapy to avoid immune reconstitution inflammatory syndrome is unclear.[5] However, an effective ART and secondary prophylaxis protect partially against relapses that may occur even under secondary prophylaxis, immune reconstitution, and undetectable viral loads.[1,11] The identified risk factors of VL relapses in coinfected patients include a TCD4 cell count below 100 cells/mm3 when VL was initially diagnosed, a poor increase in TCD4 cell count in response to ART, a lack of secondary prophylaxis, and a history of previous relapses.[1]

Conclusions:-

The clinical presentation of VL in patients with HIV infection can be atypical with renal injury and pulmonary involvement, making diagnosis more difficult. The treatment of the VL-HIV coinfection remains a major challenge because of the frequent failures and relapses, the increased drug toxicity, and the limited availability of treatment options in low-income countries. The persistence of leishmaniasis after treatment appears to be responsible for keeping TCD4 cell count low and leading to VL relapse. Further studies are needed to strengthen this hypothesis and its implication in the treatment of this coinfection.

Declaration of competing Interest

None.

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