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Casi clinici

Case report

Visceral leishmaniasis and HIV co-infection: a rare case of pulmonary and oral localization

Leishmaniosi viscerale e co-infezione da HIV: un raro caso di localizzazione polmonare ed alla mucosa orale

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INTRODUCTION

Visceral leishmaniasis (VL) has increased as a complicating infection in subjects with human immunodeficiency virus (HIV) in countries bordering the Mediterranean sea [1]. Since 1985 about 45 cases of HIV/Leishmania co-infections have been reported in Sicily. Fever, spleen and liver enlargement may often not be apparent in these patients and biochemical abnormalities such as pancytopenia and hypergammaglobulinaemia could be related to HIV disease. Besides atypical clinical features such as unusual localisation of the parasite, are commonly found [2].
We report a case of VL with pulmonary and oral mucose localisation in a patient with acquired immune deficiency syndrome (AIDS).

CASE REPORT

A 46-year-old bisexual man, was admitted to the Infectious Diseases Department of "Ferrarotto" Hospital of Catania in August 1995 with irregular fever (39 °C) and asthenia for two weeks. Clinical examination revealed liver enlargement (the lower margin 2 cm below the costal margin) and spleen enlargement (lower margin 3 cm below the costal margin). Laboratory investigations showed reductions in Haemoglobin (Hb) level 12,5 gr/dl, White Blood Cell (WBC) count 2300/mm^3, and Platelet (PLT) count 9,000/mm^3, hypergammaglobulinaemia. Leishmanial serology indirect immunofluorescence (IFAT) was positive with a titre of 1:320. The bone marrow aspirate showed amastigotes of Leishmania, and the parasite, isolated in NNN medium, was *Leishmania infantum* zimodeme MON1. CD4+ cell count was 10/mm^3. HIV serology (ELISA and Western blot) was positive. The patient received 20 days treatment with two daily intramuscular injections of N-methyl-glucamine antimoniate (60 mg/kg). After treatment the fever disappeared and there was noticeable increase in platelet count (269.000/mm^3).
AIDS diagnosis was made on the basis of oesophageal candidiasis, revealed by oesophagogastro-duodenal endoscopy. Moreover, the patient started antiretroviral therapy with zidovudine 500/die and zalcitabine was followed as an out-patient. In November 1996 the patient had fever and a cough. A chest X-ray showed an excavative lesion in the right lung. Bronchoalveolar lavage (BAL) was performed and was negative for microbial agents, the presence of leishmania not being investigated. In January '97 CMV infection was diagnosed and the patient received 20 days' treatment with Gancyclovir. After six months because of persistent fever, a cough, asthenia and malaise the patient was readmitted to the Hospital. Clinical examination showed cyanosis. Liver and spleen were still enlarged, and two small Kaposi's skin lesions were present. Haemoglobin was 12.9 g/dl, leukocyte count 5100/mm^3 (984 lymphocytes), PLT count was 144,700/mm^3, CD4+

count was 40/mm^3. Both chest X-ray and CT SCAN (Figure 1) showed a further lesion localised in the left lung and an increase in the dimensions of the previous one. Bronchoscopy showed the presence of hyperaemic and oedematous areas and in the BAL amastigotes of Leishmania were found both inside and outside the epithelial cells, together with erythrocytes, granulocytes, macrophages and hyperplastyc epithelial cells; whereas the search for other pathogens (by stain and culture) was negative. Once more, the patient received 20 days treatment with two daily intramuscular injections of N-methyl-glucamine antimoniate together with steroid and oxygen therapy. Following antimonial therapy the patient improved, fever and the cough disappeared, and the chest X-ray showed a reduction of the lesions. Protease inhibitor was added to the antiretroviral treatment (highly active anti-retroviral therapy) (HAART).

In June 1997 the patient was re-admitted to hospital because of irregular fever (39 °C) and asthenia. Leishmania amastigotes were found in the peripheral blood; CD4+ count was 10/mm^3; other clinical and laboratory investigations did not show any important changes and the chest X-ray showed the lung lesions to be smaller than before. An oral mucose ulcer was found and the smear of the lesion made by mucosal scarification showed numerous Leishmania amastigotes. The search for amastigotes of Leishmania in the peripheral blood was still positive.

In the last few years, the patient has presented irregular fever, diarrhoea, weight loss and conspicuous spleen and liver enlargement. He has been treated with HAART and has received, periodically, secondary Leishmania prophylaxis with different regimens. The patient is now in hospital because of neurological symptoms. The viral load is undetectable whereas CD4+ cell count is 12/mm^3 and CD8+ cell count 99/mm^3.

DISCUSSION

Leishmaniasis is endemic in Sicily and when it occurs in immuno-compromised patients it is difficult to eradicate. In these the amastigotes of Leishmania are often found in unusual sites. In our patient the onset of the first episode of VL was typical. It was observed when the patient was in advanced HIV disease (CD4+ 10/mm^3).

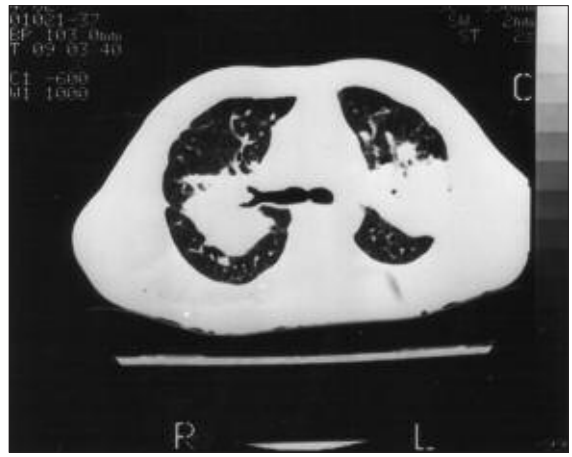

Figure 1 - Axial pulmunary CT scan with intravenous contrast showing bilateral escavative lesions, medium and superior lobus (right lung), inferior (left lung).

After ten days the patient developed oesophageal candidiasis and AIDS was diagnosed.

At the first relapse of leishmaniasis the patient presented an excavative lesion at the right lung, that at the second relapse was diagnosed as a rare form of pulmonary localisation characterised by two focal lesions one in each lung (Figure 1). The BAL performed at this stage showed the presence of Leishmania amastigotes in the fluid whereas no other pathogen was isolated. Atypical localisations of this parasite have previously been reported, and various authors have described dermonodular, mucocutaneous and gastroenteric leishmaniasis [3-6]. We have reviewed the literature and pulmonary localisation seems to be more rare than others.

After about ten months the patient developed an oral ulcerated lesion in which amastigotes of Leishmania were also found. This atypical feature has been reported in other cases [4]. These findings, together with the presence of the parasite in the peripheral blood smear confirm that in HIV positive patients the impaired immune system allows the spreading and atypical localisation of the Leishmania amastigotes more easily than in immuno-competent individuals. In individuals with HIV infection there is an immune disregulation with a lack of Th1 cells that seems to impair the cellular immune response and reduce the efficacy of therapy in these patients [7].

In the case examined here, the development of a oesophageal candidiasis and Kaposi's Sar-

coma appears to confirm that there is a two-way relationship between Leishmania and HIV in co-infected patients. Leishmania may induce an irreversible defect in T cellular immune response by triggering type 2 cytokine production, thereby favouring progression to AIDS both in asymptomatic and symptomatic HIV-positive patients. HIV may induce greater susceptibility to leishmanial infection and favour its progression to a chronic stage [8, 9].
Furthermore in HIV/Leishmania co-infected patients when the chronic stage of leishmania has been already documented anti-leishmanial treatment and HAART seem neither to eradicate nor to control leishmania.
Our patient was treated with two courses of N-methyl-glucamine antimoniate therapy and response to the treatment was incomplete with a clinical, but not parasitological recovery [2, 3]. Since 1997, the patient has been receiving HAART and periodically secondary leishmanial prophylaxis.
As the onset of VL in anti-HIV positive patients with advanced immuno-suppression could show up with atypical clinical features often due to atypical localisations of the Leishmania, in endemic areas and in HIV positive subjects, both those first diagnosed and those who do not adhere to anti-retroviral treatment, at the onset of fever and symptoms a systemic and careful parasitological follow-up is also necessary to ensure that any clinical form of leishmaniasis is not overlooked.

Key words: visceral leishmaniasis, HIV, co-infection.

SUMMARY

Visceral leishmaniasis (VL) has increased as a complicating infection in subjects with human immunodeficiency virus (HIV) in countries bordering the Mediterranean sea. The clinical course as well as organ involvement of VL are often atypical in HIV positive subjects. In this study a case of VL with pulmonary and oral mucose localisation in a patient with acquired immune deficiency syndrome (AIDS), is reported.
These findings, together with the presence of the parasite in the peripheral blood smear, confirm that in HIV positive patients the impaired immune system allows the spreading and the atypical localisation of the Leishmania amastigotes more easily than in immunocompetent individuals. In endemic areas and in HIV positive subjects a systemic and careful parasitological follow-up is necessary to ensure that any clinical form of leishmaniasis is not overlooked.

RIASSUNTO

La Leishmaniosi viscerale è una infezione endemica in Sicilia. Nei paesi del mediterraneo, l'incidenza della leishmaniosi viscerale ha subito un incremento a causa della sovrapposizione con l'infezione da HIV. In questi soggetti il decorso clinico e le localizzazioni d'organo sono spesso atipiche. In questo studio viene descritto un caso clinico di leishmaniosi viscerale con localizzazioni al polmone ed alla mucosa orale in un soggetto anti-HIV positivo. Questi riscontri e la presenza della leshmania nel sangue periferico dimostrano che in questi soggetti la compromissione del sistema immunitario favorisce la disseminazione e le localizzazioni atipiche degli amastigoti. Nelle aree endemiche e nei soggetti anti-HIV positivi, quindi, è necessaria una attenta valutazione parassitologica per evitare il mancato riconoscimento di ogni forma clinica di leishmaniosi.

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