Visceral leishmaniasis infection in a rheumatoid arthritis patient treated with infliximab

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ABSTRACT

Anti-TNFα strategies can result in significant clinical benefits in rheumatoid arthritis (RA), but with an increased rate of opportunistic infections. Visceral leishmaniasis (VL) is a severe disease that can develop in immunocompromised hosts, principally in HIV patients. VL in RA patients treated with TNFα antagonists is an extremely rare event, and only one case has been described. Here we report a case of VL, occurring after 9 infusions of infliximab in association with azathioprine, in a patient who developed blood cytopenia, fluctuant fever, and splenomegaly.

Introduction

Anti-TNFα strategies have had a marked impact in the treatment of RA, demonstrating efficacy in reducing disease activity and in retarding radiographic progression. In general, the benefit/risk ratio is quite favourable, however higher incidence of serious adverse events has been described. Infections, particularly tuberculosis and opportunistic infections, are among the most serious adverse events, especially given delays in diagnosis due to subtle or atypical presentation (1-3). Visceral leishmaniasis (VL) is a severe disease that can develop in immunocompromised hosts, principally in HIV patients (4). VL is an extremely rare event in RA patients treated with TNFα antagonists, and only one case has been described (5, 6). Here we report a case of VL, occurring after the 9th infusion of infliximab in association with azathioprine, in a patient who developed blood cytopenia, fluctuant fever, and splenomegaly.

Case report

A 53-year-old Caucasian woman, living in the Cevennes area (south of France), with RA (diagnosed in 1999) was treated with infliximab (3mg/Kg) for one year along with azathioprine (100mg/day) and corticosteroids. The RA disease was no longer active once the anti-TNFα treatment was started, however, after the 9th infusion of infliximab she had night sweats and moderate asthenia.

Discussion

Leishmaniasis is a parasitic disease caused by the transmission, in endemic areas, of the promastigote stage of the protozoan Leishmania from wild or domestic reservoirs (usually canine in the Mediterranean basin) to other mammals by sandfly bites. Leishmania spp. are obligate intraphagocytic microorganisms of the mononuclear phagocytic system. Unless the microorgan-
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Visceral leishmaniasis (VL) is a zoonotic disease caused by the protozoan parasite Leishmania major, which infects the mononuclear phagocytes, and infection control depends on adequate activation of the infected macrophages to kill parasites and inhibit their replication (7). In vitro studies with murine macrophages revealed that soluble factors secreted by activated T cells mediate the activation of macrophages to produce nitric oxide (NO), resulting in killing or controlling L. major parasites (8). Macrophage activation by soluble factors (cytokines) depends on gamma interferon (IFN-γ) as well as tumor necrosis factor (TNF) (9, 10).

In humans, the Leishmania disease includes visceral, cutaneous, and mucocutaneous forms. Usually parasites of L. infantum complex are prone to induce a visceral form of the disease, and less frequently, cutaneous forms. Immunosuppression facilitates the diffusion of the parasite, and the clinical picture is worsened (11). Diagnosis relies on the detection of the parasite in bone marrow smears, in the culture of blood or bone marrow on NNN medium, and with the polymerase chain reaction (PCR) of blood or bone marrow on NNN medium, and with the polymerase chain reaction (PCR) of blood or bone marrow on NNN medium, and with the polymerase chain reaction (PCR). In endemic areas, we should screen the patient for VL before treating with biologic agents.

In a recent case of VL reported in a patient treated with immunosuppressive therapy, the risk of opportunistic infections and the difficulties of diagnosis in these areas medical teams should be informed of this risk.

**Conclusion**

To our knowledge, this is the second case of VL reported in a patient treated with TNFα antagonists (etanercept). This confirms the risk of opportunistic infections and the difficulties of diagnosis in these immunosuppressed patients. Although pancytopenia or thrombocytopenia could be due to a haematological form of lupus or rheumatoid arthritis, dysplasia and lymphoma, or side effects of methotrexate or other drugs, the association of fever, asthenia, hepatosplenomegaly, and pancytopenia should prompt the search for Leishmania in patients living in endemic leishmaniasis areas and treated with TNFα antagonists.

**References**