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LEISHMANIASIS DISSEMINATED INFECTION IN MULTIPLE MYELOMA: CUMULATIVE IMMUNOSUPPRESSIO N IN A PATIENT PLURIRELAPSED AND TREATED WITH HIGH DOSE THERAPY

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INTRODUCTION

Immune dysfunction is a preeminent biological and clinical feature of Multiple Myeloma (MM) patients. It can lead to severe infections that are both a major cause of morbidity and mortality. Moreover it can promote tumour growth and resistance to chemotherapy. Numerous defects of the immune system have been described including hypogammaglobulinemia, impaired lymphocyte function, steroid-related immunosuppression; moreover also neutropenia secondary to chemotherapy or bone marrow infiltration.

AIMS

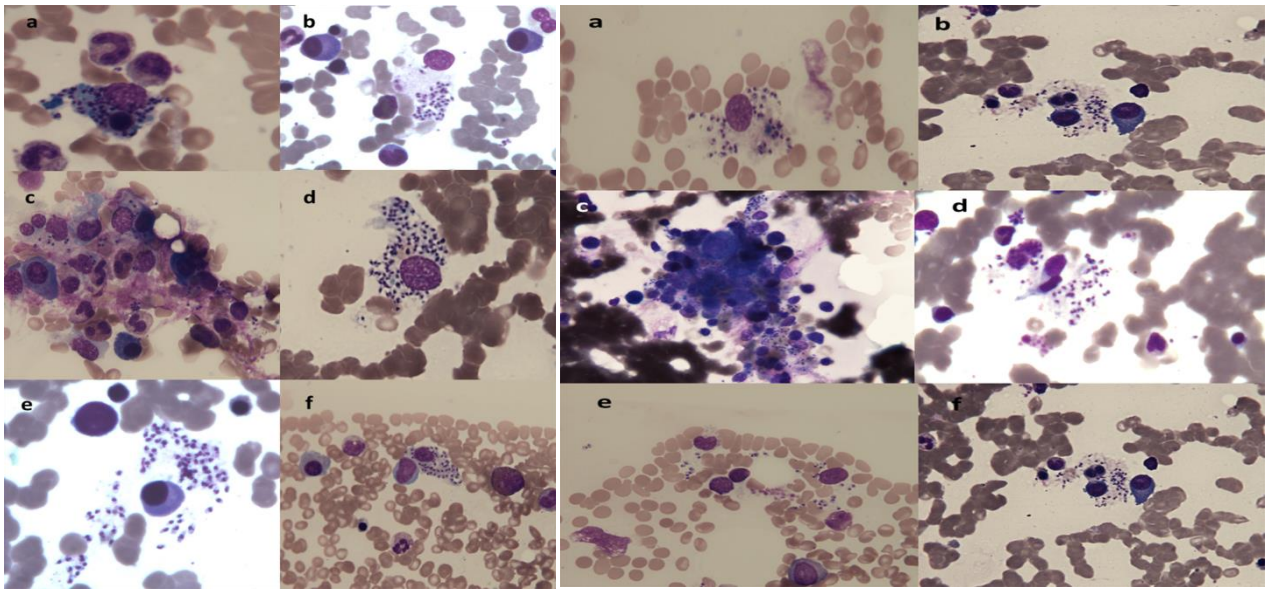
We describe the occurrence of visceral leishmaniasis in an overtreated MM patient developing pancytopenia and recurrence disease, without fever.

MATERIAL AND METHODS

A 68-year old Italian man was diagnosed with IgG-k MM in stage IA. He was initially treated with lenalidomide and dexamethasone according to EMN 441 Italian protocol (four cycles), followed by Cyclophosphamide and peripheral blood progenitor cell mobilization and collection.
For recurrent disease a second-line therapy according to PAD regimen (pegylated liposomal doxorubicin, bortezomib and dexamethasone) was administered, obtaining a very good partial response (VGPR), after 4 cycles of treatment.
Tandem autologous haematopoietic stem cell transplantation (HSCT) was carried out upon conditioning chemotherapy with melphalan 200 mg/m^2 obtaining a VGPR; maintenance therapy with low dose thalidomide (100 mg) was prematurely discontinued owing to severe bradycardia. Some months later a new treatment with Len-Dex regimen (lenalidomide 25 mg for 21 days every 28 days and dexamethasone 40 mg weekly) was delivered because of progressive disease. After 1 year the dexamethasone was reduced and finally stopped, while the patient showing persistent VGPR/CR. However after 25 cycles of treatment the patient developed asthenia, pancytopenia, mild hepatosplenomegaly, with increasing monoclonal paraprotein, showing a relapse of MM

RESULTS

The bone marrow aspirate and biopsy was performed showing monoclonal CD 138 positive k plasma cells (about 50% of cellularity) and several amastigotes in the cytoplasm of macrophages and granulocytes consistent with visceral Leishmaniasis (VL, Figures). Serological workup obtained a positive antibody titer for Leishmania species. Polymerase chain reaction (PCR) performed on the bone marrow aspirate confirmed the presence of Leishmania species, with sequence analysis positive for Leishmania Donovani. After treatment with liposomial amphotericin B the bone marrow smear became negative, without amastigotes. Now we are planning the next line therapy, probably with Bendamustine.



Figures 1-2:several amastigotes in the cytoplasm of macrophages and large clusters of Leishmania consistent with visceral leishmaniasis.

CONCLUSION

VL is a tropical vector-borne infection and is an extremely rare example of opportunistic infection found in MM patients treated with immunomodulatory drugs (IMID) and proteasome inhibitors. Only a few cases have been described. In our patient prolonged steroid therapy, high dose chemotherapy, tandem HSCT and the disease itself could lead to a cumulative immunosuppression. The role of novel agents (bortezomib and lenalidomide) could be relevant in modulating the cell-mediated immune response; therefore VL might represent a rare complication of biologic therapies. Some studies suggest that bortezomib suppresses the activity of human plasmacytoid dendritic cells, significantly decreases the number of CD4+ and CD8+ T cells and reduces the production of interferon-gamma. Hence a careful investigation of opportunistic infections in MM patients should always carried out. Someone suggests it would be desiderable monitoring CD4 lymphocytes in peripheral blood as in HIV-positive patients, especially in patients after several lines of chemo-immuno therapy.