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Still Disease and Visceral Leishmaniasis in Immunocompetent Adult: A Case Report and Review of the Literature

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Case Report

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Abstract: Visceral leishmaniasis is classically associated with HIV infection On the other Hand. Adult Onset Still Disease (AOSD) is a rare entity in which the diagnosis is based on a series of both clinical and biological features. The association of visceral leishmaniasis with Still's disease is a rarity with a lot of misleading clinical features. We report a case with a review of the literature.
Keywords: Still disease, adult onset, visceral leishmaniasis, immunocompetent adult

INTODUCTION

Visceral leishmaniasis also known as kala azar is a protozoan disease caused by different species of Leishmania donovani complex which is mediated by the bite of sand flies. In adults, it is classically associated with HIV infection. However, the association of this parasitosis to autoimmune disorders such as Still's disease is exceptional. We report a case with a review of the literature.

CASE PRESENTATION

We report the case of a 38 years old adult without any particular pathological history who was admitted for febrile chronic polyarthritis at 39 ° C that has been evolving for 7 months prior to the admission with severe deterioration of the general state and weight loss of more than 20 kg. The associated signs included: Dysphagia and a generalized erythematous rash synchronous to the febrile peaks.

Physical examination revealed a diffuse maculopapular rash at the time of febrile peaks, synovitis of the intermetacarpal-phalangeal joints, proximal inter-phalangeal joints, wrists and left knee. The patient also presented multiple lymphadenopathies, the biggest enlargement of lymph nodes being axillary at 6 cm, in addition to hepatomegaly and splenomegaly. The laboratory tests carried out in order to eliminate septic, paraneoplasic and autoimmune diseases revealed: a major biological inflammatory syndrome with an increased level of C-reactive protein (CRP) at 250mg/ l and an accelerated erythrocyte sedimentation rate (ESR) at 170 mm. The initial hemogram showed a leukocytosis with 20,000 white cells/mm3 mainly neutrophilic without eosinophilia or lymphopenia, an anemia of chronic disease at 8 g/dl with a significant increase of ferritin at 15,000 ug/l. The glycosylated fraction of ferritin was collapsed at 4%. Three germs were identified in the left knee joint fluid. These included Echerichia choli, Staphylococcus Aureus, and non-hemolytic Streptococcus D. All blood cultures were sterile, echocardiography did not reveal vegetations suggestive of infectious endocarditis. The serology of HIV, viral hepatitis B and C was negative as well as the work up for pulmonary tuberculosis, including Intradermo-Tuberculin Reaction, Sputum Bacillus Koch and a chest X-Ray. The auto-immune markers were all negative (including anti-nuclear antibodies AAN, ANCA cytoplasmic anti-neutrophil antibody, rheumatoid factor and anti-peptide-citrullin antibody). X-rays of the hands and feet did not reveal structural damage. The thoraco-abdomino-pelvic computed tomography showed a visceromegaly with multiple lymphadenopathies both above and under the diaphragm, with no obvious signs of primary neoplasia. Spinal magnetic resonance imaging did not show any sign of vertebral metastasis. Bone marrow medullogram was of normal richness and the different components were correctly represented.

Furthermore, the search for Leishmania bodies by direct examination of the May-Grunwald-Giemsa

(MGG) colored marrow smear was initially negative. Myeloculture on Novy-Nicolle-Mac Neal (NNN) and parasite research on peripheral blood and marrow by gene amplification (PCR) was not available. The study of lymph node biopsy of axillary adenopathies showed follicular hyperplasia with predominance of eosinophilic polynuclear cells without sign of malignancy which led to reiterate the search for leishmania bodies at the medullary and lymph node sites without conclusive results. The laryngoscopy didn't show abnomalities. Oeso-gasto-duodenal fibroscopy with multiple gastric biopsies reaveled an erythematous pan-gastritis without any signs of malignancy. On the other hand, the non-improvement of the biological inflammatory syndrome despite a bi-parenteral antibiotherapy adapted to the antiprogram had led to retrospectively rule out the eventuality of bacterial infection. The diagnosis of adult onset Still's disease (AOSD) according to the Yamaguchi and Fautrel criteria was then established and a transitory improvement in joint and skin symptoms has been noted under aspirin medication [1, 2]. However, a pancytopenia with hypertriglyceridemia occurred announcing a Reactive hemophagocytic syndrome (RHS). The osteo-medullary biopsy showed massive medullary infiltration by Leishmania bodies confirming the diagnosis of visceral Leishmaniasis. Nevertheless, a fatal outcome was the follow up to a multi-visceral failure chart despite treatment with N-methylglucamine (Glucantime®) administered in intensive care departement.

Iconography

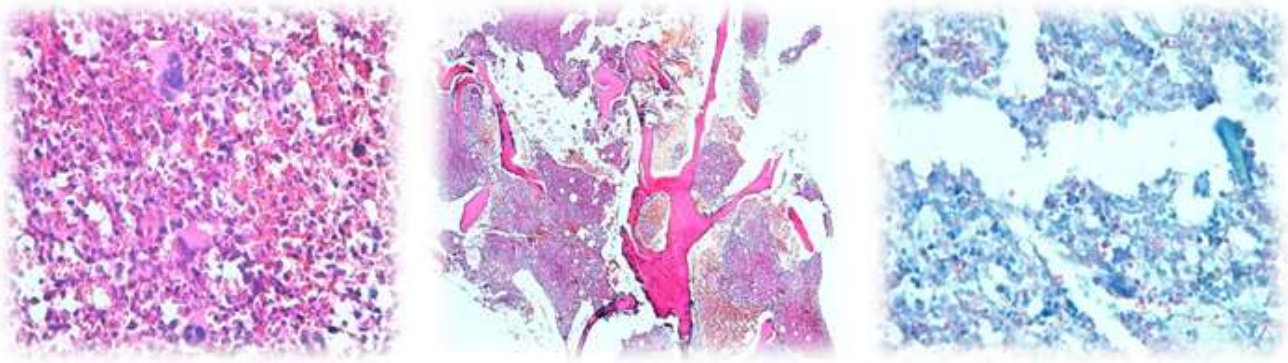

Fig-1: Demonstration of intra-cytoplasmic basophilic bodies by MGG staining 4 HE +40 HE: Hyperplasia of the three megakaryocytic, erythroblastic and granulocyte lines with the presence of pathogenic granules in intracytoplasmic histiocytes

DISCUSSION

Adult Onset Still Disease (AOSD) is a rare entity. The diagnosis is based on a series of both clinical and biological features such as : high fever, inflammatory arthralgias without rheumatoid factors or associated antinuclear antibodies, evanescent skin rash concomitant to febrile peaks, odynophagia, adenopathies, splenomegaly, hepatopathy, abdominal pain, pericarditis, pleuritis, pleural effusions, neutrophilic leukocytosis, inflammatory syndrome, hepatic cytolysis and hyperferritinemia, often with a collapse of its glycosylated fraction [1, 2]. Nevertheless, AOSD diagnosis often necessitates the arduous exclusion of potential mimickers, that is infectious, neoplasmatic, autoimmune, and other autoinflammatory diseases. Reactive hemophagocytic syndrome (RHS) is a severe and fatal hematological disorder characterized by activation of differentiated macrophages to be involved in phagocytosis of hematopoietic cells increased throughout the reticuloendothelial system. Some authors believe that AOSD may be an attenuated form of RHS, as these two entities are only the extremes of a continuum of clinical manifestations.

On the other hand, visceral leishmaniasis (VL) is a parasitic disease caused by Leishmania infantum, with vector transmission of which the animal reservoir is the dog. The annual incidence of this zoonosis is estimated between 1200 and 2000 cases per year in the Mediterranean basin [5]. Morocco appears to be the most endemic country in the Arab Maghreb with nearly 152 cases reported annually by Alvar *et al*. In adults the association of LV with HIV acquired immunodeficiency virus is conventional; it is estimated that nearly 9% of people infected with the HIV virus develop LV [7]. However, the association with Still's disease is rare. Only two similar cases have so far been reported. The first by Barešić and al. and the second in the series of Medaoud et al. who described systemic lupus (10 cases), sarcoidosis (2 cases) as the main autoimmune diseases associated to the 28 cases of LV. Liberopoulos *et al*. have demonstrated the presence of autoantibodies (antinuclear antibodies, rheumatoid factor, pANCA) in 16 cases of LV without any clinical autoimmune expression. It has therefore been suggested that LV can stimulate T lymphocytes to produce interleukins (IL) 4 and IL 10 that activate B lymphocytes to produce a broad spectrum of antibodies. The parasite could also cause tissue destruction, releasing self-antigens that stimulate self-reactivity. The possibility of cellular mimicry has also been proposed [10]. In our patient, several reasons have diverted the

diagnosis of LV: on one hand was the absence of leishmania bodies in the initial bone marrow aspiration which has been repeated twice as well as in lymph node biopsy yet of significant size. The direct identification of these bodies in the medullogram is however described in 85.9% of cases by Zait *et al* [11]. On the other hand the bacterial so infection by probable digestive translocation of multiple germs in the articular cavity made perilous the introduction of corticotherapy to compensate for RHS. And finally, the geographical origin of the patient was far from the endemic areas recognized by the authorities in Morocco. This raises fears of an extension of the epidemiological focus of the Leishmania infantum. It is sometimes difficult to impute with certainty the occurrence of macrophage activation syndrome to infection. The infectious agent could just act as a trigger on a particular immunological field. In our case Reactive hemophagocytic syndrome was probably the complication of both Stil's disease and the infection.

CONCLUSION

Visceral Lechmaniasis is on the rise in Morocco. Moreover, it is probably spreading throughout the center of the country. The association of visceral leishmaniasis with Still's disease is a rarity with a lot of misleading clinical features. The outcome might be fatal if appropriate early treatment is absent.

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