Visceral Leishmaniasis Revealed By Portal Hypertension: About a Case

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ABSTRACT
Visceral leishmaniasis is a vector-borne disease due essentially, at the level of the Mediterranean, to infection by leishmania infantum. Usually rare in adults, its prevalence has recently increased, including in immunocompetent person, with an annual number of new cases between 1.5 and 2 millions. The visceral form can be a diagnostic challenge because of the great variability of its clinical presentations. We describe the very atypical case of a rare form of visceral leishmaniasis (VL).

Introduction
Visceral leishmaniasis is a vector-borne disease due essentially, at the level of the Mediterranean, to infection by leishmania infantum. Usually rare in adults, its prevalence has recently increased, including in immunocompetent person, with an annual number of new cases between 1.5 and 2 millions. The visceral form can be a diagnostic challenge because of the great variability of its clinical presentations. We describe the very atypical case of a rare form of visceral leishmaniasis (VL).

Case report
58 years old patient, with no known comorbidities , lived all year round in north-west Morocco (Sidi-Kacem region), in rural areas. For the past year, the patient has had pain in the left hypochondrium with moderate intensity, without radiation, associated with a single episode of spontaneously resolving jaundice, all evolving in a context of apyrexia and preservation of the general state. Clinically, there was splenomegaly and hepatomegaly with a sharp lower edge. In addition, the rest of the clinical examination, particularly the cutaneous and mucous examination, is normal. The first manifestations were pancytopenia, with neutropenia, anemia and thrombocytopenia in progressive worsening .The myelogram did not allow establishing a haematological diagnosis or directing the diagnosis. An abdominal ultrasound performed showing an enlarged liver (hepatic arrow = 20cm) with a homogeneous splenomegaly (210 x 82 mm) and a dilated and permeable portal vein. Our diagnostic approach was leaning towards portal hypertension, an assessment was carried out in this direction, the hepatic echo-doppler, hepatic angio-CT as well as the MRCP which show a liver of chronic hepatopathy with signs of portal hypertension and a dilated tortuous splenic vein, the inferior vena cave (IVC) , hepatic veins and bile ducts are permeable. The esogastric fibroscopy is normal. A fibroscan carried objectified a severe fibrosis (F3). Viral serologies (HBV, HCV, HIV, EBV, CMV) returned negative, a normal iron testes as well as the autoimmune tests . Protein electrophoresis is normal, and the patient has no biological inflammatory syndrome. The cardiac origin is eliminated with a normal echocardiography. The etiological investigation brought back to make an hepatic biopsy whose histological study showed a liver with preserved architecture , with ballooned hepatocytes and the presence of many bodies of leishmaniasis at the level of the intra sinusoidal macrophages associated with a peri-sinusoidal fibrosis. The anti-leishmaniasis serology performed secondarily by the ELISA technique , was positive (antibodies level at 1258). Antimoniate therapy with meglumine (Glucantime) was introduced for a period of 28 days, with a significant result , clinical improvement and the regression of biological abnormalities.

Discussion
Leishmaniasis is a vector-borne disease linked to infection by a flagellated protozoan belonging to the genus Leishmania [4] which is transmitted by the bite of a blood-sucking vector dipterous insect: the female sandfly [5]. Depending on the parasitic species involved and the defense mechanisms put in place by the host, the disease can take the form of a seed coat or systemic disorder [4]. There are three clinical entities: cutaneous-mucous, cutaneous and visceral leishmaniasis [1]. Visceral leishmaniasis is present in 69 countries spread over all continents except Oceania [4, 6]. It is usually caused by L. infantum around the Mediterranean, in Central Asia, in China and in South America. The global incidence of visceral leishmaniasis is estimated at 500,000 cases / year, leading to 50,000 annual deaths [4, 6]. In Morocco, the morbidity of visceral leishmaniasis due to L. infantum fluctuates on average around 152 cases per year. Rare in adults, its prevalence is clearly increasing. This change in the epidemiological profile of Mediterranean visceral leishmaniasis can be explained by the combination of several factors dominated by the multiplication of the causes of immunosuppression, whether viral such as HIV infection,
or iatrogens induced by certain drugs, such as corticoids, immunosuppressants and antimitotics [2, 7].

The clinical presentation is less suggestive in adults, even immunocompetent than in children: the frequency of splenomegaly and fever barely exceeds 80% of cases depending on the series, in particular in case of infection by leishmaniasis infantum [2, 4]. Our case illustrates the diagnostic difficulties that infection with the protozoan L. infantum can pose. The clinical presentations, often misleading, evoke systemic diseases or portal hypertension. Visceral leishmaniasis can be limited to asymptomatic carrying as it can take rapidly evolving and fatal forms. In addition to these clinical abnormalities, there are biological disorders. Thus, cytopenia is most often found and can affect the three lines [2, 4, 8].

The electrophoresis of serum proteins as well as the measurement of the sedimentation rate also contributed to the diagnostic orientation. Indeed, an inflammatory syndrome is often found, includes: hyperproteidemia, polyclonal hypergammaglobulinemia with an albumin / globulin ratio often reversed and an accelerated rate of sedimentation [1, 2]. Conventionally, the diagnosis of certainty requires a bone marrow sample, with a smear stained with May Grünwald Giemsa, or by performing a splenic or hepatic biopsy [15]. Direct examination highlights amastigote forms typically within phagocytic cells. The small parasite (2-5µm) is characterized by the simultaneous presence of the round or oval nucleus and the punctate or elongated kinetoplast [4]. When available, molecular diagnosis is an excellent tool for diagnosis, post-therapeutic monitoring of leishmaniasis and for the study of asymptomatic subjects carrying the parasite. The PCR test detects parasitaemia <1 parasite / ml. The sensitivity is similar on blood samples, visceral leishmaniasis elicits a significant humoral response with a high level of specific antibodies which are routinely detected by direct immunofluorescence techniques (Ac> 1/80 °), and ELISA (Ac> 50) [4, 10].

The portal hypertension is attributed to an abnormal splanchnic vasculopathy secondary to the action of pro-inflammatory mediators, leading to the development of fibrosis. Pancytopenia is part of the visceral leishmaniasis presentation, sometimes accompanied by satellite signs of autoimmunity.

Antimony derivatives remain the standard treatment for visceral leishmaniasis in many countries [2]. The recommended antimony dosage by the world health organisation (WHO) is 20 mg / kg / day. The intramuscular administration is recommended because of its lower toxicity. The recommended duration of treatment is 28 days. Adverse effects are observed in approximately 15% of cases [2]. Treatment failures recently reported notably in India, France and Italy suggest the existence of a resistance of leishmanias vis-à-vis antimony [4]. Thus new therapeutic perspectives have been proposed. Treatment with amphotericin B, which is an inhibitor of the synthesis of sterols constituting the membrane of leishmanias, represents an alternative to stibiated derivatives [2]. Indeed, amphotericin B has shown excellent efficacy with success rates exceeding 95% in the immunocompetent for total dosages of 10 to 20 mg / kg [4, 11]. Nevertheless, it presents numerous undesirable effects limiting its use, in particular those linked to the infusion, cardiac toxicity, hypocalcemia and renal insufficiency [12]. The use of amphotericin B, associated with lipid complexes, has made it possible to increase the therapeutic doses, reduce the duration of treatment and side effects, and consequently obtain better efficacy [2, 13].

Recently, new effective oral methods, sitamaquine and especially miltefosine have been used successfully in the treatment of visceral leishmaniasis [2, 14]. In our patient treated with antimony derivatives, the evolution was marked by the occurrence of healing in the absence of any adverse effect or signs of intolerance.

**Conclusion**

Visceral leishmaniasis is on the rise in adults in Morocco with an increasing annual incidence rate in endemic regions such as Sidi Kacem region. The diagnosis is often delayed because of the various manifestations that the disease can take, such as the case of our patient revealed by portal hypertension. The biological data are not very specific. The diagnosis certainty based on the detection of the parasite in biological fluids or in tissues. Without delay, the initiation of specific treatment is vital. However, the best way to fight against this zoonosis remains prevention by detecting and treating patients early and eradicating vectors and the animal reservoir host (dogs).

**Images**

**Histological study of liver biopsy showing numerous leishmaniasis bodies at the level of intrasinusoidal macrophages with moderate hepatic fibrosis**

**Bibliographic references**