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CASE REPORT

Visceral Leishmaniasis with an Unusual Presentation in an HIV Positive Patient

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حالة نادرة لداء الليشمانيا الحشوي لدى مريض مصاب بفيروس نقص المناعة المكتسب ، مع مراجعة أدبيات

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الملخص: داء الليشمانيا الحشوي هو مرض حيواني المنشأ ينتج عن الإصابة بطفيلي من سوطيات الدم من جنس الليشمانيا، ويتميز بانتشار جغرافي واسع. الحالات التقليدية عادة ما تصيب الأطفال في المقام الأول وتظهر على شكل حمى مصحوبة بفقر الدم مع تضخم الكبد والطحال وارتفاع معدلات الجاماجلوبيولين وقلة الخلايا الشامل. يتم تشخيص المرض عن طريق فحص مسحة نخاع العظم بالإضافة إلى فحوصات أخرى كالزرع والفحص المناعي. يمكن أن تظهر الأعراض بشكل مغاير لما هو معتاد في الغالب عند المرضى المصابين بفيروس نقص المناعة المكتسب وعند كبار السن ذوي المناعة العادية. ندرج هنا حالة نادرة لمرض الليشمانيا الحشوي لدى مريض مصاب بفيروس نقص المناعة المكتسب يبلغ من العمر سبعة وعشرين عاما حيث كان يعاني من آلام في البطن مع إسهال شديد مصحوبا بغثيان وتقيؤ لمدة أربعة أسابيع دون وجود الأعراض أو العلامات التقليدية المميزة للمرض. تم تشخيص الحالة عن طريق إيجاد الطفيلي في الفحص النسيجي لخزعات مأخوذة من ألاثنى عشري والقولون، ثم تم تأكيد التشخيص عن طريق فحص مسحة نخاع العظم.

مفتاح الكلمات: داء الليشمانيات الحشوي ؛ فيروس نقص المناعة المكتسب ؛ خزعة ألاثنى عشري.

ABSTRACT: Visceral leishmaniasis is a disease caused by a haemoflagellate protozoan of the genus *Leishmania*. It has a wide geographical spread. Classic cases are found primarily in children and present with typical features that include fever, anaemia, hepatosplenomegaly, hypergammaglobulinaemia, and pancytopenia. The diagnosis is usually achieved by bone marrow smears, culture and serology; however, it can manifest itself atypically, mostly in patients infected with HIV and geriatric immunocompetent patients. We report an unusual case of visceral leishmaniasis diagnosed in a 27 year-old HIV-infected male who presented with abdominal discomfort and diarrhoea of four weeks duration associated with nausea and vomiting, but with no typical symptoms or signs of visceral leishmaniasis. The diagnosis was established through the identification of the *Leishmania* organism in duodenal and colonic biopsies and confirmed by subsequent bone marrow smears.

Keywords: Visceral leishmaniasis; HIV; Duodenal biopsy; Case report; Iraq

Leishmaniases are a group of zoonotic diseases caused by a haemoflagellate protozoan of the genus *Leishmania*. The parasites are present in the macrophages of a wide variety of vertebrates. They are transmitted to man from the animal reservoir through the bite of female sand flies of the Phlebotomus species.[1] There are several species of *Leishmania* that can infect human and result in a spectrum of diseases known as leishmaniasis.[2] Depending on the mode of presentation there are three main types: cutaneous leishmaniasis, which is often self-limiting, mucosal leishmaniasis and visceral leishmaniasis.[3] Visceral leishmaniasis affects mainly the mononuclear phagocytic system of the bone marrow, liver and spleen[1] and is caused mainly by *Leishmania* donovani and *Leishmania* infantum species.[2] It shows a wide geographical spread in more than 88 countries all over the world.[4]

Clinically, typical cases of visceral leishmaniasis are found primarily in children.[4] It's features include fever, anaemia, hepatosplenomegaly, adenomegaly, hypergammaglobulinaemia, and pancytopenia, but it can also manifest itself atypically, mostly in patients infected with HIV and geriatric immunocompetent patients.[5] The definitive diagnosis of visceral leishmaniasis is achieved by identification of the organism in a bone marrow biopsy. The characteristic Leishmania amastigotes are round to ovoid in shape and can be identified after routine haematoxylin-

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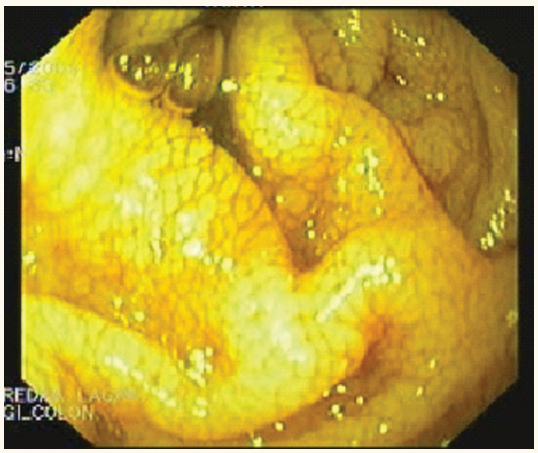

Figure 1: Upper GIT endoscopy revealing whitish nodular appearance of the duodenal mucosa.

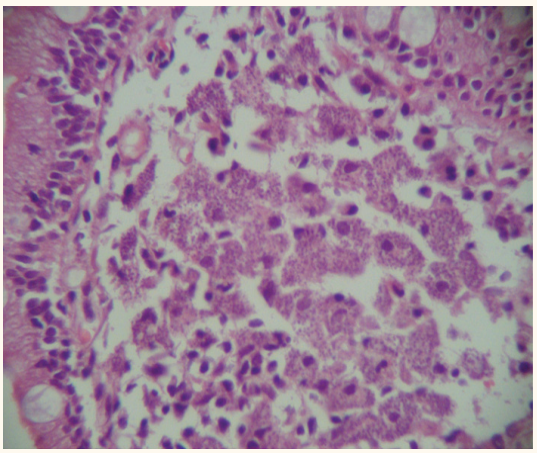

Figure 2: Duodenal biopsy showing many macrophages with abundant intracytoplasmic leishmaniae.

eosin or Giemsa staining.[4,6] Other diagnostic tools include isolation of promastigotes by Novy-McNeal-Nicolle (NNN) culture[2,4] and serological tests to detect antileishmanial antibodies, but the latter have low sensitivity.[3,4] Histopathological identification of leishmania organisms in tissue sections is quite easy and very sensitive;[4] however, the diagnosis of leishmaniasis in paraffin sections may be difficult in some conditions, such as when the parasites are present in unusual sites which is frequently observed in visceral leishmaniasis that develops in immunocompromised patients.[2,7] This is a presentation of an unusual case of visceral leishamniasis diagnosed in an HIV-infected patient, with atypical clinical features, who was unexpectedly diagnosed through the identification of the *Leishmania* organism in an unusual site.

Case report

The patient was a 27 year-old Yemeni male, diagnosed with HIV infection 8 years previously, who presented with abdominal discomfort and diarrhoea of four weeks duration associated with nausea and vomiting, but no fever or anorexia. The diarrhoea (5–6 times a day) was watery and accompanied by mucus, but with no blood. On physical examination, the patient was conscious, oriented, afebrile and not pale. His vital signs were stable. His chest was clear and abdominal examination showed mild subumbilical tenderness, but no abdominal mass or organ enlargement was detected. No lymphadenopathy was present. The patient was not receiving any antiretroviral therapy.

Laboratory investigations showed leukocytes $10.88x10^3/\mu l$, 83% neutrophils, 8.4% lymphocytes and 8.4% monocytes. The haemoglobin level was 136 g/l, erythrocytes sedimentation rate 16 mm/hour. Urine examination showed mild proteinuria and his serum creatinine was mildly elevated at 2.1 mg/dl. Stool samples were negative for *Cryptosporidium* and *Clostridium difficile* toxin and repeated stool culture revealed no pathogens. His CD4 cell count was 210 cells/mm3. An abdominal ultrasound showed no abnormalities. An upper GIT endoscopy showed normal oesophageal and gastric mucosa; however, the mucosa of the second part of the duodenum showed congestion with a peculiar whitish nodular appearance [Figure 1]. A colonoscopy showed normal colonic mucosa. Multiple biopsies were taken from the oesophagus, stomach, duodenum and colon for histopathological examination to exclude microscopic lesions and opportunistic infections.

The histopathological examination demonstrated widening of the duodenal villi with infiltration of duodenal and rectal mucosa by a large number of macrophages filled with intracytoplasmic *Leishmania* amastigote parasites (Donovan bodies) [Figure 2]. Gastric and oesophageal biopsies showed no significant pathologic changes. The case was diagnosed as visceral leishmaniasis. Subsequent bone marrow aspirate (showing Leishman–Donovan bodies) confirmed the diagnosis [Figure 3]. The patient was treated with sodium stibogluconate (20 mg/kg/day), but he was lost to follow-up after 1 week of therapy.

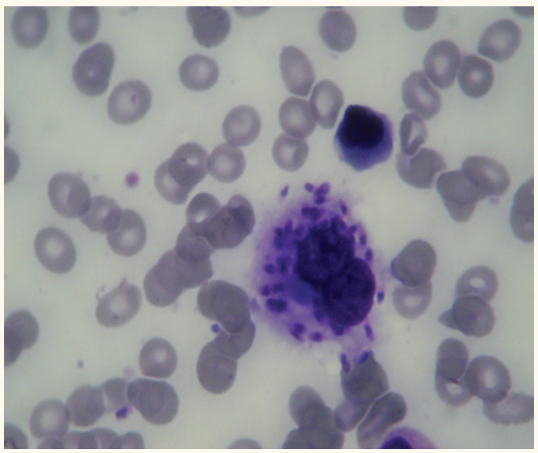

Figure 3: Bone marrow aspirate smear revealing intracytoplasmic leishmaniae.

Discussion

Although it affects mainly immunocompetent individuals, *Leishmania* is considered an opportunistic pathogen in immunosuppressed patients particularly those with AIDS.[8,9] On the other hand, HIV infection increases the risk of developing visceral leishmaniasis by 100–1,000 times in endemic areas.[10] In fact, some studies showed that visceral leishmaniasis is the fourth most common opportunistic parasitic disease in HIV-positive individuals after pneumocystosis, toxoplasmosis, and cryptosporidiosis.[4,10,11] Indeed, both HIV and leishmaniasis result in a cumulative deficiency of the cellular immune response since both agents damage similar immune resources thus promoting chronicity and, when untreated, result in death.[6,10] The first case of leishmania/HIV co-infections was diagnosed in 1985[12] and almost all cases of *Leishmania* co-infection with HIV have been described in patients with HIV-1.[13] According to data from the World Health Organization, HIV-*Leishmania* co-infection is widely distributed.[14] The most common areas are southern European countries (like Spain), and Brazil, India, Bangladesh and Nepal.[1,10] The real impact of HIV-*Leishmania* co-infection is probably underestimated owing to constraints in the surveillance and reporting of cases.

The majority of leishmaniasis cases in HIV-positive patients appear in the advanced stages of the disease. In about 80% of patients, the number of CD4 lymphocytes is less than 200/mm3 while in c. 20 % of patient.[1,4,15] In the current case, the number was low (210 cells/mm3). Leishmaniasis has different characteristics in patients with AIDS compared with immunocompetent patients.[8] Classic visceral leishmaniasis in immunocompetent individuals is found primarily in children, but in recent years an increasing number of adult cases have been observed mostly in HIV patients.[4,5,15–17] In the latter, the location is more likely to be atypical such as gastrointestinal tract, larynx, lungs, kidneys, pancreas and testes.[5,6] Organomegaly, which is one of the typical clinical features of classical visceral leishmaniasis in immunocompotent individuals, is usually absent in HIV positive adults[3] as in our case. Also cytopenia is more frequent in immunosuppressed individuals along with negative serology and higher relapse rate after therapy. [5,6,8,10] The gastrointestinal involvement and overt malabasorption in visceral leishmaniasis is reported more freqently in those with concomitant HIV infection.[3,5,8,18–20] Lesions have been seen from the oesophagus to the rectum;[6] however, the duodenum is the most common site.[5] The exact pathogenesis of the diarrhoea and malabsorption is not clear, but it has been suggested that these symptoms in enteropathic visceral lesihsmaniasis may be a combination of the mechanical occlusion of the mucosa by parasites, bacterial overgrowth, partial villous atrophy, competition between the host and the parasite for nutrients, altered motility, bile salt deconjugation and lymphatic blockade.[3]

Endoscopic examination of these patients is usually performed because of diarrhoea and epigastralgia. The findings are variable and may be unremarkable,[6,18,21] showing non-specific inflammation,[5,22] or an atrophic mucosal pattern.[8] In the current case, the mucosa of the second part of the duodenum showed congestion with a peculiar whitish nodular appearance, a rare and unusual finding also reported by others.[1] The colonoscopy showed a normal colonic mucosal pattern. Histopathological examination of intestinal (duodenal and colonic) biopsies shows intact architecture and abundant macrophages with intracytoplasmic *Leishmania* amastigotes (Donovan bodies).[5,6,19,22] Some cases may show duodenal villous atrophy.[3,22]

Conclusion

In conclusion, clinicians should be alert about the

possibility of leishmaniasis in HIV positive patients presenting with diarrhoea, particularly in patients from endemic areas. Also pathologists should pay attention to the possible finding of *Leishmania* amastigotes in biopsies from intestinal mucosa in HIV infected patients.

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