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CASE REPORT

A case report of cutaneous leishmaniasis: a misleading clinical presentation

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Abstract

Background The diagnosis of cutaneous leishmaniasis (CL) is often difficult because of the diversity of clinical presentations, its often-misleading appearance and the very long incubation period (time between the endemic stay and the onset of skin lesions).

Case We report the case of an otherwise healthy 67-year-old man who presented with inflammatory skin lesions on the scalp and face for the past 7 years. The lesions were first mistaken as cutaneous sarcoidosis, mycobacterial infection, and cutaneous lymphoma. Finally, the diagnosis was made by RT-PCR analysis on a punch-biopsy specimen, which was positive for *Leishmania infantum*.

Discussion and conclusion To date, the choice of treatment for complex cutaneous leishmaniases is based on the *Leishmania* species. Our patient successfully responded to liposomal amphotericin B.

Keywords Leishmaniasis · Skin · *Leishmania infantum*

Introduction

Cutaneous leishmaniasis (CL) is a parasitic disease transmitted by sand fly bite and the incidence of which has been increasing in recent years [1]. In Europe, CL is frequently unrecognized and late diagnosed because of unfamiliarity by physicians due to its wide variety of clinical manifestations and its non-specific histology [2]. With histology the diagnosis is often overlooked and even with a specific histology picture, the Giemsa stain in it, misses in many cases the parasite, unless PCR is done. The incubation period of old world CL can be long (1 week to 1 year or more [3]), which also contributes to a frequent delay in diagnosis [2]. Moreover, this parasite is responsible for chronic skin lesions that can heal spontaneously.

Case description

An otherwise healthy 67-year-old man presented to the dermatology outpatient clinic at the Cliniques universitaires Saint-Luc, Brussels, Belgium, with a 7-year history of inflammatory lesions of the scalp and face. The patient lived in Belgium, but was of Italian origin and regularly travelled to the province of Molise in southern Italy. The skin lesions had appeared in 2012, initially in the form of an erythematous macule on the scalp which had grown slowly. At the time of the consultation, the lesions covered almost the entire scalp, forehead, ears and left part of the face. They appeared as large erythematous scaly patches, highly infiltrated and ulcerated in places (Fig. 1). The patient reported the recent onset of bilateral palpebral oedema and pain on the scalp. Besides the presence of small bilateral cervical lymph nodes, clinical examination was otherwise

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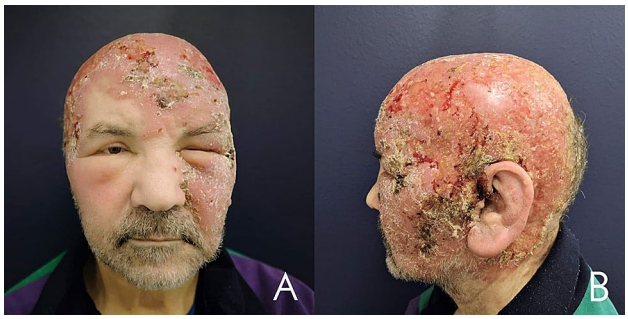

Fig. 1 Initial clinical aspect of the face and scalp. Infiltrative, erythematous and ulcerated plaques covering the scalp, forehead, ears and left part of the face (**a**, **b**)

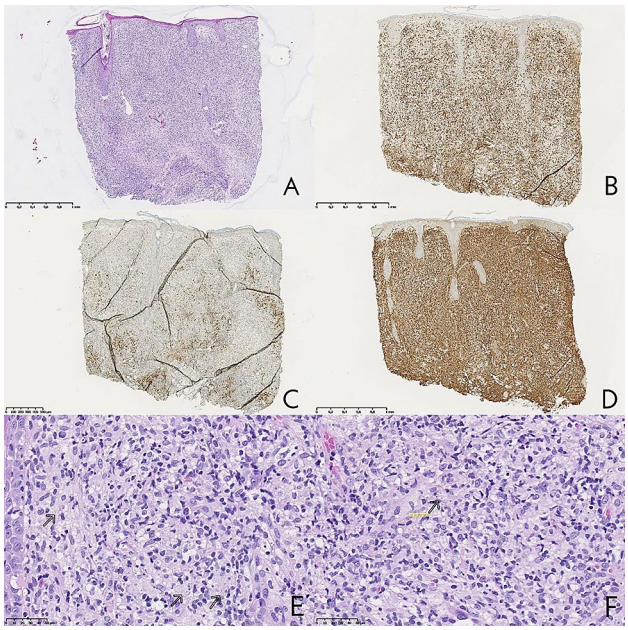

Fig. 2 Histological examination. Histological image showing a large dermal inflammatory infiltrate associating small lymphoid cells and numerous histiocytes (**a**). Immunostaining. Immunomarkers show that the inflammatory infiltrate is mainly composed of cytotoxic CD8 + T lymphocytes as well as a large histiocyte population (CD163). CD8 + immunostaining showing numerous CD8 + T lymphocytes in the dermis (**b**). CD20 + immunostaining showing a low population of B lymphocytes (**c**). CD163 immunostaining which confirms the presence of a large histiocyte population associated with lymhoid infiltrate (**d**). At higher magnification, leishman bodies (↗) in the amastigotes form are observed in the cytoplasm of macrophages or extracellularly. These are small in size. An experienced pathologist is needed so as not to miss the diagnosis (**e**, **f**)

normal. The patient had previously seen several dermatologists and had received many different treatments. A first skin biopsy performed in 2015 suggested sarcoidosis with negatives PAS and BK-Ziehl colorations. The patient was treated with hydroxychloroquine with no clinical improvement. In 2017, a second skin biopsy showed necrotizing granulomatous inflammation suggesting tuberculosis. RT-PCR and culture for *Mycobacterium tuberculosis* were negative. The patient was treated with rifadine 300 mg 2x/day and nicotibine 300 mg 1x/day for 3 months. However, these treatments were ineffective. When the patient presented to our department, new skin biopsies for histological and microbiological examinations (mycobacteria culture and Leishmania PCR) were performed. Histopathological examination showed a significant lymphoid infiltrate mixed with plasma cells and a large population of histiocytes (Fig. 2a). Immunohistochemistry showed that the majority of T lymphocytes were CD8 + (Fig. 2b–d). Molecular biology analysis identified a monoclonal rearrangement of the T cells, suggesting a diagnosis of CD8 + T lymphoma. However, PCR sequencing of the heat-shock protein 70 gene (hsp70) revealed the presence of the *Leishmania donovani* complex in the skin confirming the diagnosis of CL. *L. donovani* and *L. infantum* belong to the same *Leishmania donovani* complex and they are genetically very similar. Given the patient's travel history to Italy, it was established that it was most likely a *Leishmania infantum*. Subsequently, the histological slides were reviewed and scanty Leishman-Donovan bodies were found on a single sample (Fig. 2e–f). Blood test results were as follows: C-reactive protein (CRP) at 35.7 mg/L (normal value [NV] < 5 mg/L); white blood cell (WBC) count at 6.53 10^3/µL (NV 4–10 10^3/µL) with 52, 1% neutrophils (NV 40–70%); ferritin at 675 µg/L (NV 30–400 µg/L); hemoglobin at 10.8 g/dL (NV 13.3–16.7 g/dL) with reticulocytes at 1.05% (NV 0.5–2%); platelet count at 360 10^3/µL (NV 150–450 10^3/µL), lactatedeshydrogenase (LDH) up to 300 U/L (NV 250 IU/L). Electrolytes, renal function, liver function, thyroid function and hemostasis were normal. Infectious serologies for HIV, hepatitis B and C, and syphilis were negative. Autoimmune serologies (ENA, ANCA) were also negative. An ELISA test was also positive for leishmania at 1.35 (NV ratio < 1). on A 18F-FDG PET/CT scan revealed hypermetabolic skin thickening of the scalp, face and left cervical region with multiple hypermetabolic bilateral cervical lymph nodes (Fig. 3). No other pathologic hypermetabolic foci which may suggest associated visceral or mucosal damage were found. Treatment with liposomal amphotericin B (AmBisome®, Gilead Sciences, Carringtonhill, Ireland) was initiated at 3 mg/kg/per day intravenously for 5 days with a booster of the same dose on days 10 and 30. This treatment was taken without any side effects and resulted in a rapid improvement of the lesions. No recurrence was observed after 6 months of follow-up (Fig. 4).

Discussion

This clinical case is noteworthy because of the severity and the extent of the skin lesions and because of the extremely long delay to reach the final diagnosis of leishmaniasis. The *Leishmania* species implicated was

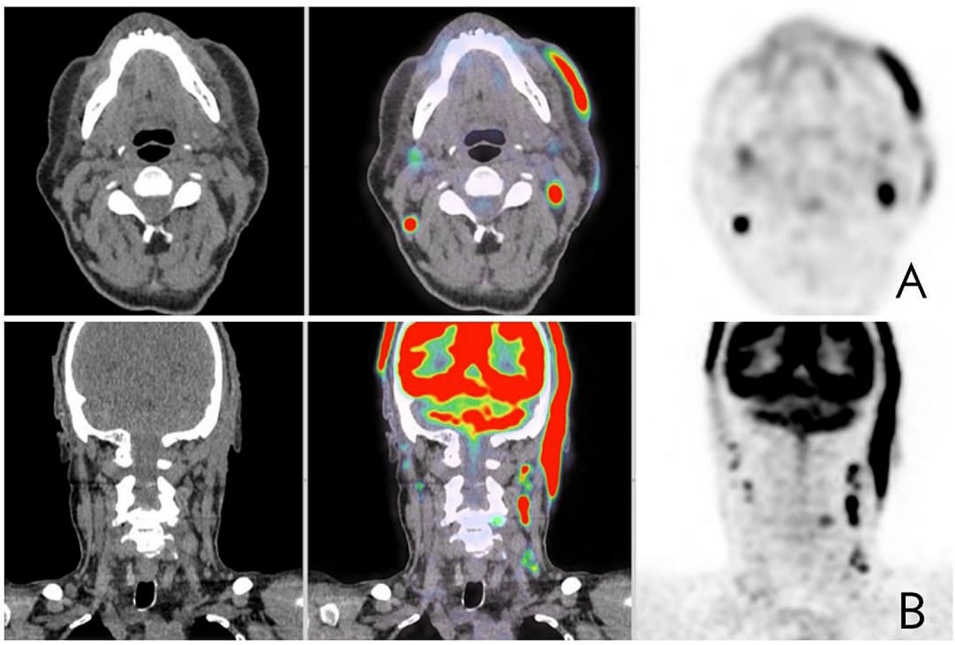

Fig. 3 FDG PET/CT (CT scan, fused PET/CT and PET image, respectively) axial view (**a**) and coronal view (**b**). Extensive thickening of the skin in the head and neck area with multiples enlarged cervical lymph nodes with high FDG metabolism (SUV max: 17.6)

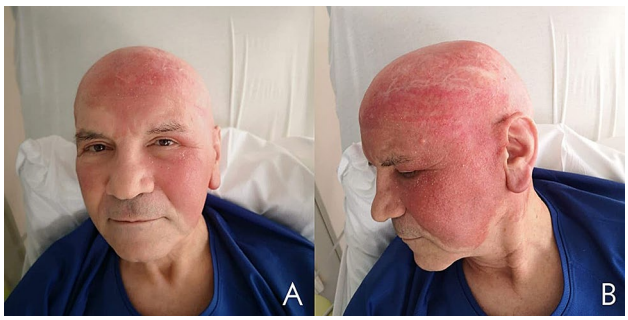

Fig. 4 Clinical aspect of the face and scalp after complete cure of 30 days of ambisoma. Disappearance of infiltration and crusts. Persistence of erythematous and atrophic scarring (**a**, **b**)

Leishmania infantum which is mainly found in Mediterranean regions and in Italy [4]. *Leishmania infantum* is most often responsible for visceral leishmaniasis but can also cause cutaneous and mucosal leishmaniasis [5]. The typical clinical form of CL with *Leishmania infantum* is a single, painless papule that usually progresses in a few weeks or months to an ulceronecrotic nodular lesion [6]. However, atypical presentations have increased in endemic areas [7]. Moreover, morphologic histological patterns can also be variable and non-specific [2]. In chronic lesions, the number of parasitized macrophages will decrease and a granulomatous inflammatory infiltrate may appear, rendering the detection of the parasite difficult [8]. It is, therefore, recommended to combine classical parasitological methods with molecular-based detection such as RT-PCR [9]. In this reported case, the presence of monoclonal T rearrangement was particularly confusing, leading to a misdiagnosis of cutaneous T-cell lymphoma.

The serious course of this leishmania infection in this immunocompetent patient may possibly be explained by the advanced age of the patient. Indeed, skin alterations due to aging can facilitate the spread of the parasite in the papillary dermis [10]. Secondly, corticosteroid treatments received at the onset of the eruption and before diagnosis of CL may also have worsened the clinical picture [11]. Thirdly, it is accepted that clinical presentation depends on the host's immune response and the virulence of the parasite [7]. A decrease in cellular immunity, notably in the TH1 response and the secretion of the cytokines inter-leukine 12 (IL 12), tumor necrosis factor alpha (TNFα) and interferon gamma (IFN γ), is associated with parasite escape and chronic lesions [12].

The Infectious Diseases Society of America (IDSA) differentiates clinical characteristics of CL that may modify management and recommend local therapy for non-self-curing simple CL and systemic therapy for complex CL [13]. In this patient who presented with complex CL, systemic treatment was required. Conventional systemic anti-leishmaniasis drugs are meglumine antimoniate (glucantime®), liposomal amphotericin B (AmBisome ®) and miltefosine [9, 10] [14]. Currently, liposomal amphotericin B appears to be the most promising choice for CL as meglumine antimoniate has significant side effects and a limited cure rate [15]. Liposomal amphotericin B is already used as a first-line and safe treatment for severe forms of leishmaniasis, such as mucosal and visceral leishmaniasis and HIV coinfected patients [10]. Oral miltefosine is an effective treatment in

new world leishmaniasis [9]. Studies are limited regarding use of miltefosine in old world CL but it could be considered as a therapeutic alternative [14].

Conclusion

CL is a major health problem in endemic countries and a growing problem in non-endemic ones due to the increasing number of travellers and migrants. It is a parasitic disease with highly variable clinical presentations which can be easily mistaken for other diseases. It is important to consider the diagnosis of CL when faced with any chronic skin lesion in a patient who has travelled to an endemic country, even months or years previously. Several biopsies must be taken, including one for a RT-PCR, which is the most sensitive diagnostic test currently available. Liposomal amphotericin B is a safe and effective treatment for complex CL.

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Compliance with ethical standards

Conflicts of interest The authors confirm that they have no conflict of interest.

Written patient consent Obtained.

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