Case Report: Late Emergence of Cutaneous Leishmaniasis in an Immunocompromised Patient in a Non-Endemic Setting

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Abstract. We report a case of reactivation of cutaneous leishmaniasis caused by *Leishmania major* in a 40-year-old man from Afghanistan, in the context of immune suppression. His last potential exposure was 7 years before the clinical presentation. To our knowledge, this is the most temporally distant reactivation of cutaneous leishmaniasis reported in a non-endemic country.

CASE REPORT

A 40-year-old male of Afghan origin, living in Melbourne, Australia, was referred to our infectious disease service with a diagnosis of cutaneous leishmaniasis. The patient first presented to his general practitioner with a skin lesion on his proximal left fourth finger. This emerged over 2 months (Figure 1). The doctor performed a punch biopsy which demonstrated *Leishmania* amastigotes on histopathology (Figure 2). DNA from the paraffin-embedded biopsy was extracted and the internal transcribed spacer 1 region amplified. Restriction enzyme digestion and subsequent analysis allowed identification to the species level (*Leishmania major*). The sample was not sent for culture.

The patient has a history of seronegative arthropathy, ankylosing spondylitis, chronic hepatitis B, and ulcerative colitis. He was commenced on immunosuppressive therapy in 2007 with azathioprine (150 mg daily) and prednisolone enemas. Two flares of ulcerative colitis were controlled by high doses of oral prednisolone in 2008, but since 2009, he has had a stable bowel and joint disease. His current immunosuppressive medications were azathioprine (100 mg daily) and sulfasalazine (2 g twice daily). He has never received any biologics or tumor necrosis factor- α inhibitors. His immunosuppressive regimen was not altered since 2016 when the azathioprine dose was reduced to 100 mg daily. The patient commenced on entecavir (0.5 mg) at the time of initial immunosuppression, to treat chronic hepatitis B. The hepatitis B viral load has remained undetectable.

The patient was born in Afghanistan and moved to Iraq before immigrating to Australia 16 years previously. His most recent travel outside of Victoria, Australia, was to visit friends and relatives in Afghanistan and Iraq, 7 years before the clinical presentation of leishmaniasis. He had no history of previous leishmaniasis or similar skin lesions.

Clinical examination revealed one large raised lesion (15 mm) and one smaller proximal lesion (5 mm) (Figure 1). He had mild epitrochlear lymphadenopathy in the affected limb. No other abnormalities were found on clinical examination.

Full blood count and hepatic and renal biochemistry tests were all within normal limits. HIV serology was negative.

He was treated with oral miltefosine (50 mg orally, three times a day for 28 days). Systemic rather than topical therapy

was chosen, given the unusual clinical situation and his immunosuppression. Miltefosine was chosen as a balance of efficacy, safety, and cost. Three months later, the lesions had decreased in size and appeared clinically inactive.

DISCUSSION

Leishmania is caused by protozoa in the genus *Leishmania* and is transmitted by sand fly vectors. Visceral and cutaneous leishmaniasis differ in their epidemiology, with India, Bangladesh, Sudan, South Sudan, Ethiopia, and Brazil bearing 90% of visceral leishmaniasis cases, whereas cutaneous leishmaniasis is most common in the Americas, Mediterranean, and Middle East.¹ Leishmaniasis is not described in Southeast Asian countries except for Thailand, where two cases of visceral leishmaniasis were described between 2006 and 2010. There is no human leishmaniasis in Australia or the Pacific, although there are cases of cutaneous leishmaniasis in red

FIGURE 1. Photo of the left hand with two cutaneous lesions at the base of the fourth finger. The ulceration of the larger lesion was due to biopsy. This figure appears in color at www.ajtmh.org.

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FIGURE 2. Sixty-three times magnification of skin biopsy. Hematoxylin and eosin stain. Demonstrates amastigotes (intracellular forms). Kinetoplasts and nuclei would be visible at higher magnification. This figure appears in color at www.ajtmh.org.

kangaroos caused by a species of *Leishmania* most closely related to *Leishmania enriettii*.² This species is thought not to cause human infection.³

Immunosuppression is a well-described risk factor for both primary infection and reactivation of leishmaniasis.⁴ However, in contrast to our case, most reports of reactivation relate to visceral rather than cutaneous leishmaniasis and to higher level immunosuppression (high-dose steroid use, transplantation, and human immunodeficiency virus). All are in countries where leishmaniasis is endemic. In a report from Iran, several weeks after immunosuppression (cyclosporine and prednisolone) for a renal transplant, two previously untreated lesions became large and cauliflower-like.⁵ A report from Brazil described reactivation 1 year after transplant while on tacrolimus, mycophenolate, and prednisolone.⁶ Another report from Brazil describes reactivation of cutaneous leishmaniasis after 2 years in the context of corticosteroid treatment for rheumatoid arthritis.⁷ A patient originally from Bolivia but who received a kidney transplant in America had reactivation of cutaneous leishmaniasis 9 months after last exposure while on tacrolimus and methylprednisolone.⁸

Late reactivation related to immune suppression is consistent with the biology of cutaneous leishmaniasis. After clinical resolution of lesions (spontaneous or related to therapy), a small number of protozoa remain viable in the host.⁹ The parasites can continuously replicate within host cells and are able to modulate the host immune system in ways that are still not well understood. One mechanism described is an ability to resist host attack by nitric oxide.¹⁰ This ongoing replication and antigenic stimulation is thought to provide the basis for long-term immunity which is seen in patients in endemic countries.¹⁰

The patient was born and resided in an endemic region for many years, during which time he presumably had a subclinical infection. There was no clear precipitant for his reactivation. Given the biology of the parasite, he may be at a continual low risk of recurrence.

For similar patients, we suggest having a high index of suspicion for leishmaniasis in those from *Leishmania*-endemic countries, even if their last exposure was many years in the past. Patients who are about to be immunosuppressed should be informed about the potential risk of recurrence.

In summary, we report the reactivation of cutaneous *L. major* 7 years after the last potential exposure. Given the pathogen's ability to persist, it is surprising that late reactivation of cutaneous leishmaniasis in the setting of immune suppression is not more frequently reported.

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