Case Report

A case of cutaneous leishmaniasis successfully treated with oral terbinafine in Kenya

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ABSTRACT

Leishmaniasis is a tropical disease of the skin and the reticuloendothelial system caused by a parasite of the genus Leishmania. The disease poses significant psychosocial and public health burdens in endemic areas. Its treatment poses significant challenges considering that new treatment modalities are currently unavailable. The out-dated and toxic antimonial compounds remain the standard treatment. Nevertheless, these agents are mostly unavailable and reports of resistance to these compounds are increasing. Various drugs have therefore been used off label to treat cutaneous leishmaniasis. Terbinafine, an allylamine designed for treatment of fungal infections has been used off label in the treatment cutaneous leishmaniasis in Middle East and India. However, its potential has not been fully exploited in Kenya. This case is reported of a thirteen year old boy, a resident of a leishmaniasis endemic region in Kenya who presented with a symptomless, well demarcated plaque embedded with crusts and papules on his right cheek. Fine needle aspiration cytology revealed leishmania donovani bodies confirming a diagnosis of cutaneous leishmaniasis. He was treated with oral terbinafine 250mg daily for two consecutive months together with topical application of a combination of 10% Chrotamiton + 2% Sulphur cream applied for three consecutive months. A significant improvement evidenced by substantial flattening of the lesion, conspicuous digital image changes and general clinical improvement was noted after 3 months of follow up. This observation endorses oral terbinafine, as an efficacious management of uncomplicated cutaneous leishmaniasis. To limit scarring, an appropriate topical application can be added to oral terbinafine.

Keywords: Cutaneous leishmaniasis, Oral terbinafine, Case report, Kenya

INTRODUCTION

Leishmaniasis is an indolent illness caused by a parasite belonging to the genus Leishmania. Female phlebotomine sand fly is the intermediate host and known vector of the disease. Leishmaniasis is common in the tropics and has no gender predilection. Approximately 700,000 to 1.2 million new cases of cutaneous leishmaniasis occur annually.1 Systemic disease causes up to 20 000 to 30 000 deaths annually. The disease chiefly targets the skin, mucous membranes and the reticuloendothelial organs. It can manifest as a mild self-limiting skin disease, a disfiguring mucocutaneous infection as well as an inexorably fatal systemic disease.

Cutaneous leishmaniasis (CL) is readily recognizable by its clinical manifestations. It can be confirmed through histological and serological investigations. Fine needle aspiration cytology (FNAC) is a useful method for rapidly confirming presence of leishmania parasites in resource poor countries.2
Although cutaneous leishmaniasis can heal without intervention, treatment is required because spontaneous healing takes abnormally long, results in increased morbidity, and causes a decrease in quality of life due to ugly scarring. Besides, untreated patients serve as a reservoir of leishmania parasites and therefore a potential source of disease spread. Moreover, local cutaneous disease can spread to the mucous membranes and the reticuloendothelial organs eventuating in a lethal systemic illness.

Treatment of CL is challenging. For decades, the highly toxic antimonial compounds have remained the only standard treatment for CL. Nevertheless, these drugs are not readily available in Kenya and drug resistance has been reported in many countries. Hence, clinical and pharmacological innovativeness are increasingly being used to treat this disease. Drug repositioning is one of the innovative ways commonly utilized to manage leishmaniasis. Here, drugs made for specific indications are used off-label for treatment of other diseases. Amongst many drugs used off-label and reported as effective in cutaneous leishmaniasis is terbinafine. Terbinafine works by inhibiting ergosterol biosynthesis.

Sterol is a principal component of cell wall of fungi and some species of leishmania. Inhibition of sterol synthesis results in a weakened and permeable cell wall leading to death of the microorganisms.

CASE REPORT

A 13 year old boy complained of a six month old disfiguring lesion on his right cheek. He was reviewed in a midtown private dermatology clinic in Nakuru town, Kenya. His residence is Gilgil, a leishmaniasis endemic area in the central rift region. On examination, his general health was good and his systematic review was uneventful. Lesional exam revealed a well demarcated irregularly roundish plaque approximately 10 centimeters in diameter on his right cheek. It extended to involve the right half of upper lip and the chin. On the surface of the plaque were ulcerations, hypo/hyperpigmented patches, eroded papules, scars and few hemorrhagic crusts. Small islands of uninvolved skin were seen; infiltration on the chin was noted. The upper right lip was significantly disfigured and swollen (Figure 1a). The rest of his entire skin was normal. The patient had not used any treatment for this condition in the recent past.

Figure 1: (A) Before treatment; (B) One month after treatment, note apparent deterioration; (C) Two months after treatment; (D) Three months after treatment, note scarring with keloidal papule on the upper lip.

A clinical diagnosis of cutaneous leishmaniasis was made. To confirm the diagnosis, the patient was referred to a pathology laboratory for fine needle aspiration cytology (FNAC). The FNAC, done using Giemsa stain confirmed presence of Donovan bodies. Consequently, a confirmatory diagnosis of chronic cutaneous leishmaniasis was made. However, the species of the involved parasites was not delineated.
Based on previous successful reports of oral terbinafine in the management of CL, terbinafine 250 mg daily was given for one month together with a twice daily application of a combination of Crotamiton+Sulphur cream. After a month of treatment, an apparent clinical deterioration of the lesion was noted: the upper lip was more swollen, lesional infiltration had increased, new papules had occurred on areas previously spared and the lesions on the chin became more infiltrated (Figure 1b). Despite the apparent deterioration, the patient remained stable and without any systemic complaints. The same treatment was therefore continued for an additional one month. After two months of terbinafine a significant improvement had occurred. This was corroborated by both the patient and the dermatologist using clinical evaluation and progressive digital photography (Figure 1c). Following this satisfactory clinical cure, the patient was advised to continue with only topical Crotamiton+Sulphur cream for another month. At the final assessment, three months after initiation of treatment, the lesion had completely flattened, was inactive and smooth. The subsequent scar was smooth, and less disfiguring. There were few keloidal papules (Figure 1d).

The total treatment duration was two consecutive months of oral terbinafine and three consecutive months of Crotamiton+Sulphur cream application. There were no any side effects reported by the patient or observed by the dermatologist.

DISCUSSION

Leishmaniasis pose a great management challenge. Cutaneous leishmaniasis, though mostly benign, has a negative impact on life, can deteriorate and has potential to systematise. Treatment is therefore required. The mainstay of treatment for leishmaniasis has been the traditional pentavalent amoniacal compounds. Nevertheless, resistance to these agents, the associated toxicities, and their unavailability has confounded the management of leishmaniasis.

Consequently, various alternative drugs for leishmaniasis have been used with various degrees of success. Chief among them have been antifungals. The classes of antifungals commonly utilised in the treatment of cutaneous leishmaniasis include azoles and allylamines. Terbinafine, a synthetic antifungal drug belonging to the allylamine class of drugs has been used both in its topical and systemic forms for the treatment of cutaneous leishmaniasis with various successes. Reports about the success of this drug have emerged from case reports as well as from randomized clinical trials. The effectiveness of these alternative agents however depends on the type of leishmania parasite.

Terbinafine like all allylamines targets the ergosterol synthesis of fungal cell wall. Ergosterol is important for cell membrane stability. By inhibiting the synthesis of sterols, terbinafine causes cell walls of fungi to progressively weaken. Consequently, cellular contents leak out and the cell subsequently dies. Since leishmania parasites also possess sterols on their cell walls, drugs with capacity to interfere with sterol synthesis such as azoles and allylamines can arguably result in the death of leishmania parasites. Terbinafine and related allylamines can therefore be considered potential drugs for the treatment of leishmaniasis. In a study by Bahamdan et al, oral terbinafine administered daily for four consecutive weeks cleared cutaneous leishmaniasis in over 70% of treated patients, of note, is that there were no any observable or reported side effects in their study.

As was also observed in this case, oral terbinafine given at a dose of 250 mg daily for two consecutive months in conjunction with topical application of Crotamiton 10% + Sulphur 2% cream satisfactorily resolved cutaneous leishmaniasis in a boy aged 13 years. Crotamiton+Sulphur cream was selected for use as an adjunctive treatment based on the synergistic effects of the two compounds in killing parasites and minimising scarring. The apparent deterioration observed after one month of treatment in this case could represent a localized form of Jarisch-Herxheimer reaction- a reactionary phenomenon secondary to the rapid lysis of bacteria. This phenomenon has never been observed before during the treatment of leishmaniasis. Though rare, its occurrence can represent an early sign of good treatment uptake.

Despite the prolonged duration of terbinafine in this case, there were no local or systemic side effects noted during the entire period of treatment. This apparent degree of safety and success of oral terbinafine forms a basis to inspire clinicians to consider terbinafine as a first line of treatment for uncomplicated cutaneous leishmaniasis.

CONCLUSION

Oral terbinafine combined with appropriately selected topical application to improve scar aesthetics is a successful approach in the management of cutaneous leishmaniasis especially when given for a period not less than two consecutive months.

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