Medical Mycology Case Reports 7 (2015) 23–25

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

Fixed cutaneous sporotrichosis treated with topical amphotericin B in an immune suppressed patient

Vikram K. Mahajan*, Karaninder S. Mehta, Pushpinder S. Chauhan, Mrinal Gupta, Rajni Sharma, Ritu Rawat

Department of Dermatology, Venereology & Leprosy, Dr. R.P. Govt. Medical College, Kangra (Tanda) 176001, Himachal Pradesh, India

ARTICLE INFO

Article history:
Received 4 November 2014
Received in revised form
7 January 2015
Accepted 23 January 2015
Available online 24 January 2015

Keywords:
Amphotericin B gel
Cutaneous sporotrichosis
Fixed cutaneous sporotrichosis
Lymphocutaneous sporotrichosis
Sporothrix schenckii
Thermotherapy

ABSTRACT

Both fixed cutaneous and lymphocutaneous sporotrichosis are associated with significant morbidity due to chronicity. Although treatment with itraconazole, saturated solution of potassium iodide or terbinafine is recommended in most cases, the described patient with fixed cutaneous sporotrichosis could not tolerate any of these. Her lesion healed after 8weeks of topical amphotericin-B (0.1% w/w). Topical amphotericin-B appears useful treatment modality for uncomplicated cutaneous sporotrichosis when systemic treatment needs deferment, remains contraindicated, or in pediatric patients.

1. Introduction

Sporotrichosis is an implantation mycotic infection due to thermo-dimorphic fungus *Sporothrix species*, a common saprophyte of soil and plant detritus. Current data of molecular biology shows high genetic diversity and distinct epidemiology for *Sporothrix species* encompassing a complex of several cryptic species; *S. maxicana*, *S. globosa*, *S. brasiliensis*, *S. luriei*, *S. schenckii sensu stricto* (*Sporothrix schenckii sensu lato*) and *S. globosa* (in UK, Spain, Italy, China, Japan, USA, and India) [1]. The usual mode of infection is from traumatic inoculation of the pathogen in the skin. Personnel handling plants or plant material (agriculturists, foresters, gardeners, florists and nursery workers) are at risk of being infected occupationally in most endemic regions. Lymphocutaneous sporotrichosis (70–80% cases) and fixed cutaneous sporotrichosis are the two common clinical presentations of cutaneous sporotrichosis [2,3]. Fixed cutaneous sporotrichosis is comparatively less common and occurs as localized, asymptomatic, erythematous, papulo-plaque, papulo-pustule, nodule or verrucous plaque, a non-healing ulcer or a small abscess at the inoculation site. Disseminated or systemic disease (ocular, meningeal, pulmonary or osteoarticular sporotrichosis) is rare and usually seen with immunocompromised state. An early treatment is imperative as the spontaneous resolution is an exception and chronicity of the diseases results in significant morbidity. Treatment with itraconazole, saturated solution of potassium iodide (SSKI) or terbinafine has been recommended (in order of preference) in most cases of cutaneous sporotrichosis [4]. However, topical amphotericin B has been not used previously for treating cutaneous sporotrichosis. We share our experience of treating this patient with some degree of immunosuppression who had complete healing of fixed cutaneous sporotrichosis after 8 weeks with topical liposomal amphotericin B (0.1% w/w). This has implications for the treatment of uncomplicated cases where conventional drugs remain contraindicated/intolerable.

2. Case

This 53-year-old Indian female from agricultural background developed small asymptomatic papule over right cheek that had enlarged and ulcerated over a period of 3 months. She could not recollect any history of prior trauma. Treatment with systemic and topical antibiotics from a peripheral center had not benefited her. Medical history revealed that she had been on treatment with methotrexate (7.5 mg/week) for rheumatoid arthritis, ramipril (5 mg/day) for hypertension, and metformin (500 mg/day) and glimepiride (2 mg/day) for diabetes mellitus for almost past 10 years. Cutaneous examination (Fig. 1a) showed a well-defined

* Corresponding author.
E-mail address: vkm1@rediffmail.com (V.K. Mahajan).

http://dx.doi.org/10.1016/j.mmcr.2015.01.002

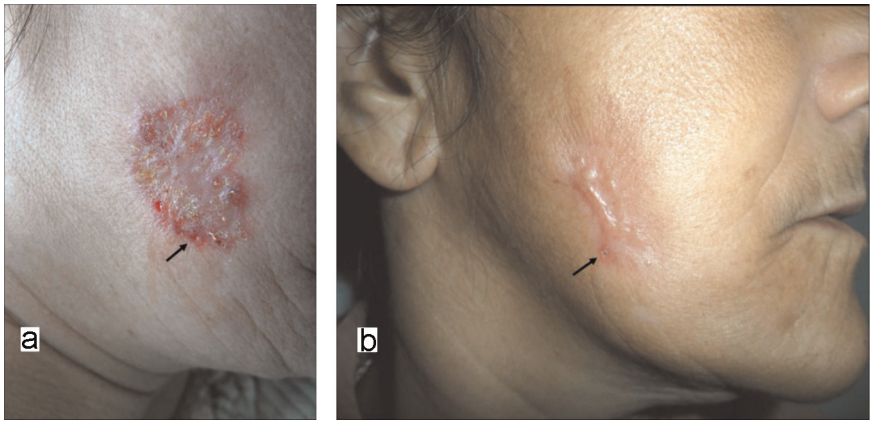

Fig. 1. (a) Large ulcerative plaque having erythematous, irregular, infiltrated borders, and crusting at places. (b) Same lesion has healed with scarring 8 weeks after treatment with topical liposomal amphotericin B gel (0.1% w/w) and thermotherapy. Arrows indicate biopsy wound.

ulcer over right cheek with infiltrated, irregular margins, having raw areas and yellowish crusting. She had no significant (regional) lymphadenopathy. Systemic examination and routine laboratory investigations including complete blood counts, serum biochemistry, urinalysis, and chest X-ray films were normal. A skin biopsy from ulcer margin revealed epidermal hyperplasia and acanthosis, and chronic granulomatous inflammatory infiltrate comprising lymphocytes, plasma cells, epitheloid cells and Langhans' giant cells in the dermis, and fibrosis at places (Fig. 2). Periodic acid Schiff (PAS) and Ziehl–Neelsen (Z–N) stained histologic sections revealed no organism. Culture of biopsy specimen showed no growth on Lowenstein–Jensen (L–J) media. Biopsy specimen incubated at 25 °C on Sabouraud's dextrose agar (SDA) without antibiotics grew cream-colored moist colonies of *Sporothrix species* within a week that turned brownish-black after further incubation (Fig. 3). The isolates were subcultured on brain heart infusion agar at 37 °C for conversion to yeast form for identity confirmation (Figs. 4 and 5). Molecular studies for its identification were not performed due to expense/non-availability. After all the results of investigations became available on day 0, the diagnosis of fixed cutaneous sporotrichosis was made. She was prescribed SSKI orally starting with 5 drops 3 times daily but developed intolerable flu-like symptoms after first dose itself. She also discontinued treatment with itraconazole, prescribed 100 mg twice daily, as she experienced vomiting, general malaise, fever immediately after its

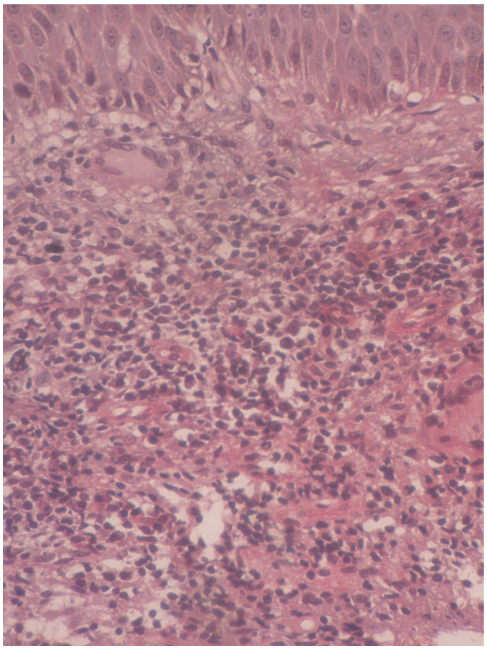

Fig. 2. Diffuse dermal chronic granulomatous inflammatory cell infiltrate comprising lymphohistiocytes, plasma cells, epithelioid cells and Langhans' giant cells (Hematoxylin & Eosin, ×40).

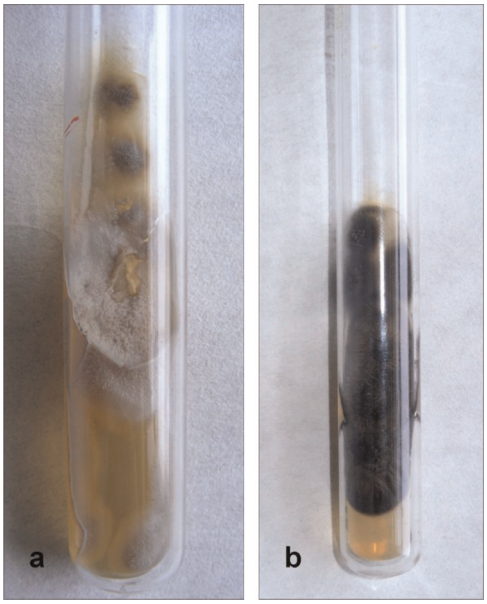

Fig. 3. *Sporothrix* spp. colony on Sabouraud's glucose agar (SDA) at 25 °C. Initial moist and cream color colony at 10 days (a) have turned brownish-black on further incubation (b).

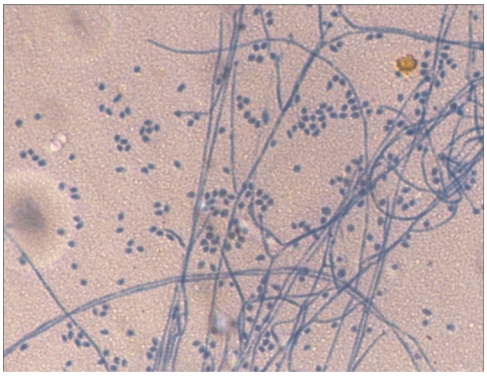

Fig. 4. Delicate branching hyphae and characteristic conidiophores of *Sporothrix* spp. seen in flower-like arrangement (Lactophenol Cotton Blue mount, ×40).

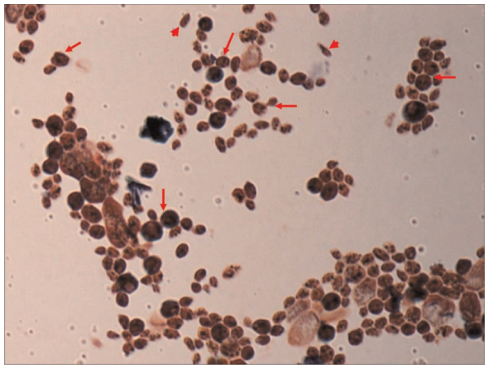

Fig. 5. Yeast phase of *Sporothrix* spp. isolate from culture on brain heart infusion agar at 37 °C seen as budding yeast cells (arrows) and cigar shaped yeast cells (arrowheads) interspersed between conidiophores (Grams' stain, × 100).

second dose. As she refused all oral therapies including terbinafine, Fungisome™ gel (liposomal amphotericin B 0.1% w/w, marketed by Lifecare Innovations Pvt. Ltd., India) was prescribed topically for twice daily application after due counseling. She was also advised to apply local heat (up to tolerable limit) to the lesion for 15–20 min twice daily with a heated stone puck wrapped in a towel. After 8 weeks ulcer showed healing with scarring (Fig. 1b) and she was advised to continue treatment for another 8 weeks. She revealed that she did not apply heat but had continued topical amphotericin B gel.

3. Discussion

Although itraconazole is recommended as first line therapy, treatment with saturated solution of potassium iodide (SSKI≡1 g/ml) is considered consistently effective, fairly safe and cost effective in resource poor settings [2,5]. Discontinuation of therapy is rarely needed except when the patient experiences flu-like symptoms/hypersensitivity that can occur even with the lowest dose [6]. Itraconazole (100–200 mg/d) given for 3–6 months is currently recommended drug of choice in all forms of sporotrichosis [4]. However, drug interactions may present potential serious toxicities and limit its use among patients with other concurrent disorders. Our patient developed flu-like symptoms and could not tolerate itraconazole perhaps due to drug (antidiabetics) interaction. She refused further oral therapy of any kind despite adequate counseling. Daily application of heat (42–43 °C) for 15–60 min several times in a day is recommended only as an adjunct to pharmacotherapy to treat small lesions in fixed cutaneous variety or pending specific therapy [4,7,8]. Its reported cure rate is 71% among 14 patients in a study by using different modes of thermotherapy [7]. The efficacy of thermotherapy could not be evaluated in her as she did not continue it. Although amphotericin B is usually reserved for systemic therapy of more severe and disseminated disease, topical treatment with Fungisome™ gel cured her lesions within 8weeks without any adverse effects. Although topical amphotericin B has been used successfully to treat persistent lesions of cutaneous leishmaniasis [9], there is no precedent for its use in cutaneous sporotrichosis treatment. Fungisome™ gel contains liposomal amphotericin B (0.1% w/w) in a specially formulated preparation containing multilamellar vesicles or nanosomes, which facilitate transport of Amphotericin B across stratum corneum because of favorable hydro-lipophylic microenvironment. Amphotericin B in these nanosomes is transferred to fungal or leishmanial cells due to its high affinity for ergosterol and its cellular precursors in cells membranes causing their lysis.

We feel that in addition to adjunct thermotherapy, topical amphotericin B is another potential therapeutic option for uncomplicated cutaneous sporotrichosis particularly where systemic treatment needs deferment (in pregnancy), remains contraindicated, or in children where availability of recommended drugs in pediatric formulations is a constraint. However, validation of its efficacy and therapeutic potential will depend upon more comprehensive studies for further evaluation.

Conflict of interest

There are none.

Acknowledgments

The expert help received from the Departments of Pathology and Microbiology, Dr. R. P. Govt. Medical College, Kangra (Tanda), H.P. (India) for histopathology and mycology studies is gratefully acknowledged.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.mmcr.2015.01.002.

References

[1] X. Yu, Z. Wan, Z. Zhang, F. Li, R. Li, X. Liu, Phenotypic and molecular identification of Sporothrix isolates of clinical origin in Northeast China, Mycopathologia 176 (2013) 67–74.
[2] V.K. Mahajan, N.L. Sharma, R.C. Sharma, M.L. Gupta, G. Garg, A.K. Kanga, Cutaneous sporotrichosis in Himachal Pradesh, India, Mycoses 48 (2005) 25–31.
[3] E.S. Rafal, J.E. Rasmussen, An unusual presentation of fixed cutaneous sporotrichosis: a case report and review of the literature, J. Am. Acad. Dermatol. 25 (1991) 928–932.
[4] C.A. Kauffman, B. Bustamante, S.W. Chapman, P.G. Pappas, Clinical practice guidelines for the management of sporotrichosis. 2007 Update by the Infectious Disease Society of America, Clin. Infect. Dis. 45 (2007) 1255–1265.
[5] C.B. Doherty, S.D. Doherty, T. Rosen, Thermotherapy in dermatologic infections, J. Am. Acad. Dermatol. 62 (2010) 909–927.
[6] N.L. Sharma, K.I.S. Mehta, V.K. Mahajan, A.K. Kanga, V.C. Vikas, G.R. Tegta, Cutaneous sporotrichosis of face: polymorphism and reactivation after intralesional triamcinolone, Indian J. Dermatol. Venereol. Leprol. 73 (2007) 188–190.
[7] M. Hiruma, A. Kawada, H. Niguchi, A. Ishibashi, I.A. Conti Diaz, Hyperthermic treatment of sporotrichosis: experimental use of infrared and far infrared rays, Mycoses 35 (1992) 293–299.
[8] C.A. Kauffman, Old and new therapies for sporotrichosis, Clin. Inf. Dis. 21 (1995) 981–985.
[9] A. Zvulunov, E. Cagnano, S. Frankenburg, Y. Barenholtz, D. Vardy, Topical treatment of persistent cutaneous leishmaniasis with ethanolic lipid amphotericin B, Pediatr. Infect. Dis. J. 22 (2003) 567–569.