


CASE REPORT

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Cryotherapy for treatment of sporotrichosis—rapid cure with adjuvant cryotherapy: case report

Prajwal Pudasaini^{1*} , Sushil Paudel¹, G. C. Sagar¹ and Sadiksha Adhikari²

Abstract

Background Sporotrichosis is a subcutaneous mycosis caused by various sporothrix fungus species. This ubiquitous fungal infection is more commonly seen in field/farm workers in tropical and subtropical regions. This prevalence could largely be attributed to the climatic condition favorable for harboring fungi in these regions. Cutaneous infection often occurs via inoculation of fungus into the intact skin owing to traumatic skin injuries. Clinically apparent lesions can occur anywhere in exposed part of the body and mostly these occur over upper extremities, which are prone to trauma during field, farm, agricultural works, and pet handling. Other sites of involvement are lower extremities, face, eyes, and mucous membrane rarely. Onset of clinical feature is usually seen in 2–4 weeks after inoculation of the dimorphic fungus. Various cutaneous manifestations of sporotrichosis can occur ranging from those limited to skin with ulcero-nodular lesions along lymphatics to systemic dissemination to lungs and meninges rarely. Localized form of cutaneous sporotrichosis occur in those with high degree of immunity, whereas the systemic disseminated forms occur in immunocompromised individuals. Treatment of sporotrichosis is done with oral antifungal for months until clinical recovery and in recalcitrant cases with systemic dissemination-intravenous infusion of Amphotericin-B can be used. However, this prolonged dosing until clinical recovery can be hazardous to those with hepato-cardiac comorbidity and also in pregnant females. Given the systemic side-effects that can underlie the use of antifungals for prolonged duration, treatment should be sought towards adjuvant physical modality along with oral antifungal, which decreases the risks of systemic side effects.

Case presentation Here we report two cases- one fixed cutaneous form and other lymphangitic form of sporotrichosis, in a 32 year old and 40 year old Asian male working in rural part of Nepal. Both the patients had long standing history of ulceronodular lesions over extremities along the lymphatic channels, who were treated successfully with adjunct physical modality of treatment i.e., cryotherapy of 4–5 sessions along with oral itraconazole 200 mg for 4–5 weeks. There was complete resolution of lesion with rampant remission and no recurrence post therapy till date.

Conclusion As there is possibility of prolonged use of over-the-counter antifungal medication, lack of regular follow up and lack of laboratory monitoring, especially in the rural parts of Nepal, therapy should be tailored toward onsite physical treatment with cryotherapy in addition to oral antifungals, which can be cost effective and with decreased systemic side-effects. With proper diagnosis, overall prevalence of the disease can be estimated and clinical therapeutic trials can be performed with timely prevention of dreadful systemic complications.

Keywords Cryotherapy, Sporotrichosis, Case report

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Case reports

Background

Sporotrichosis is one of the common forms of subcutaneous mycosis, caused by species of the sporothrix fungi viz *Sporothrix schenckii* (sapronotic transmission via plants), *S. braziliensis* (zoonotic transmission via cats), *S. mexicana*, *S. globosa*, and *S. lerei* [1]. Sporotrichosis has been reported from various regions of Nepal for years [2]. Sporotrichosis is mostly confined to skin, lymphatics, and subcutaneous tissue, except in those who are severely immunocompromised, who inhale the fungus to lungs and can rarely progress to systemic involvement of meninges and joints [3]. Cutaneous manifestations of sporotrichosis are largely divided into the lymphangitic form and the fixed form. Among these, the commoner form involving the lymphatics occurs via direct inoculation of sporothrix via traumatic skin injuries, predominantly over exposed skin sites—upper extremity [4, 5]. Presence of disseminated systemic sporotrichosis is a rare finding and its occurrence in those without underlying immunocompromised status is even rarer [6]. The common lymphangitic form presents with ulcero-nodular lesion with purulent discharge along with tender regional lymphadenopathy over extremities mostly unilateral and rarely bilateral [7]. Cutaneous sporotrichosis rarely occurs via systemic dissemination of disease as a part of widespread systemic spread to viscera including the skin, especially in those who are severely immunocompromised [8]. This etiological association with the underlying infectious foci has led to the systemic seeding in lungs, brain, and joints for underlying infection in those with cutaneous manifestation [3]. As there is possibility of prolonged use of over the counter antifungal medication, lack of regular follow up and lack of laboratory monitoring, especially in rural parts of Nepal, therapy should be tailored toward onsite physical treatment with cryotherapy along with oral itraconazole at 200 mg per day, which can be cheap and with decreased systemic side-effects, useful in those with cardio-hepatic comorbidities and also in pregnant females. As there is lack of availability of culture media and fluorescent microscopes in rural parts of Nepal, diagnosis relies on a vigilant clinical eye and good histopathological section [9]. The histopathology of sporotrichosis, which is usually helpful, shows epidermal hyperkeratosis, acanthosis with dermal granuloma, and neutrophilic abscess. Occasionally, cigar shaped fungus with asteroid bodies is seen [10]. Adjuvant use of physical modality of treatment, such as cryotherapy has reportedly been beneficial in recalcitrant, infiltrated, nodulo-ulcerative lesion, thereby decreasing the therapeutic time course [11, 12]. Given the systemic organ related side effects that underlies prolonged treatment of this chronic granulomatous fungal infection, treatment

should be focused toward adjuvant physical modality—cryotherapy with greatest therapeutic benefit, complete cure and devoid of systemic side effects especially in rural Nepal where drug overuse is often an issue [13]. Here, we report rare cases of cutaneous sporotrichosis treated with 4–5 weekly cycle of cryotherapy with freeze duration ranging from 15 to 20 seconds along with oral itraconazole for 4–5 weeks with complete cure seen post treatment and no recurrence to date. The doses and duration of cryotherapy procedure were followed in accordance to published literature and the grade of recommendations that heralded the evidence [11, 12, 14].

Case presentation

Case 1: (Lymphangitic form)

A 32-year-old Asian male from rural village of Nepal, presented with discrete plaques over left forearm and index finger in a linear distribution for 5 months. Lesion started as an asymptomatic pea sized nodule over lateral part of left index finger. Patient has repeated field work with frequent outdoor activities, but denies any sort of trauma to lesion site. Over period of 2 months, existing lesion evolved into plaque with occasional oozing and pus discharge, and new nodules evolved over forearm and index finger. He used to take over the counter topical and oral antibiotics from pharmacist nearby. Various over-the-counter medications that were used by patient included topical mupirocin ointment thrice a day for 2 weeks, topical fusidic acid and betamethasone combination cream twice a day for 4 weeks, and 500 mg of oral flucloxacillin four times a day for 2 weeks. There was apparent short-lived improvement as marked by decreased swelling and pus discharge post therapy with the later use of oral medication. However, the lesions persisted and evolved with discharge and ulcer despite the treatment. On examination, multiple plaques and nodules were present over left lateral forearm and index finger in a linear distribution. Largest erythematous plaque with central crust was present over proximal aspect of left lateral index finger. Additionally, spontaneously healed lesion with central atrophy and hyperpigmentation was seen over nearby lesion of disto-lateral forearm (Fig. 1, 2). There was no visible pus discharge or ulcer. Biopsy was done, which showed epidermal hyperkeratosis, acanthosis with dermal granuloma, and neutrophilic abscess. Few oval spores and multinucleated giant cells were also seen in the dermal granuloma suggestive of Sporotrichosis (Fig. 3). Patient was insistently reluctant to any sort of oral medication owing to previous drug reaction 1 year prior from oral medication and oral potassium iodide was deferred. Patient was started on liquid nitrogen cryotherapy with two cycles of 20 second freeze and



Fig. 1 Sporotrichoid linear pattern of nodulo-plaque lesion of left lateral forearm



Fig. 2 (Zoomed in) plaque of same patient after four sessions of cryotherapy and oral antifungal medication

10 seconds thaw every week for 4 weeks along with oral itraconazole at 200 mg, and the extension of lesion was halted with only residual pigmentation without active disease post treatment. The size and number of active/oozing nodules decreased, along with the decrement in erythema and edema associated with the plaque only leaving residual postinflammatory hypopigmentation and a halo of hyperpigmentation during 6th week post therapy. There was complete cure of the disease post treatment with no recurrence to date. New lesions have not evolved for 1 year now and the lesion has healed with no symptoms and minimal pigmentation.

Case 2: (fixed form)

A 40-year-old Asian male from rural Nepal, farmer by occupation, presented with solitary linear plaque over left lateral hand for 8 months. Lesion started as an asymptomatic pea sized nodule over lateral part of left hand. Patient had history of trauma with sickle while cutting grass 5 months prior to onset of lesion. Over

period of 4 months lesion evolved from the site of scar into plaque with occasional oozing and pus discharge. On examination, well defined erythematous infiltrated linear plaque was present over left lateral hand with scales and crust over the surface (Fig. 4). There was no visible pus discharge or ulcer. Biopsy was done which showed dermal granuloma with neutrophilic abscess. Few oval spores and multinucleated giant cells were also seen in the dermal granuloma suggestive of Sporotrichosis (Fig. 5). Patient was a chronic alcoholic with Alcoholic liver disease, under treatment and oral itraconazole and potassium iodide were deferred. Oral itraconazole and potassium iodide was initially deferred for 1 week until consultation with hepatologist was done. Later, laboratory workup for liver function test was done and patient was put on cryotherapy and oral itraconazole. Patient was started on liquid nitrogen cryotherapy at two cycles of 15 seconds freeze and 10 seconds thaw every week for 5 weeks along with oral itraconazole at 200 mg and the extension

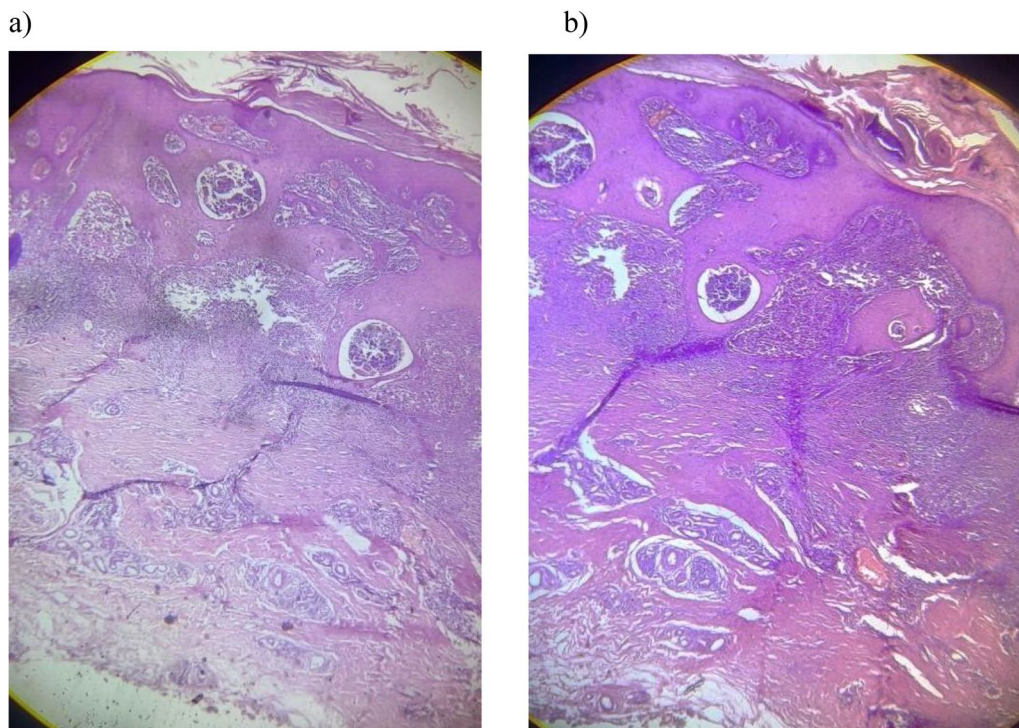


Fig. 3 **a** Involved (lesional) skin showing hyperkeratosis, irregular acanthosis with surface ulceration, and areas of pseudoepitheliomatous hyperplasia along with large intraepidermal neutrophilic abscess and mixed dermal inflammatory infiltrate with numerous accumulations of neutrophilic micro abscess (hematoxylin and eosin $\times 10$) and **b** presence of multiple scattered multinucleated giant cells, occasional eosinophilic foreign body-like structures, "Sporothrix asteroids" surrounded by ill formed granuloma in some areas (hematoxylin and eosin $\times 40$)

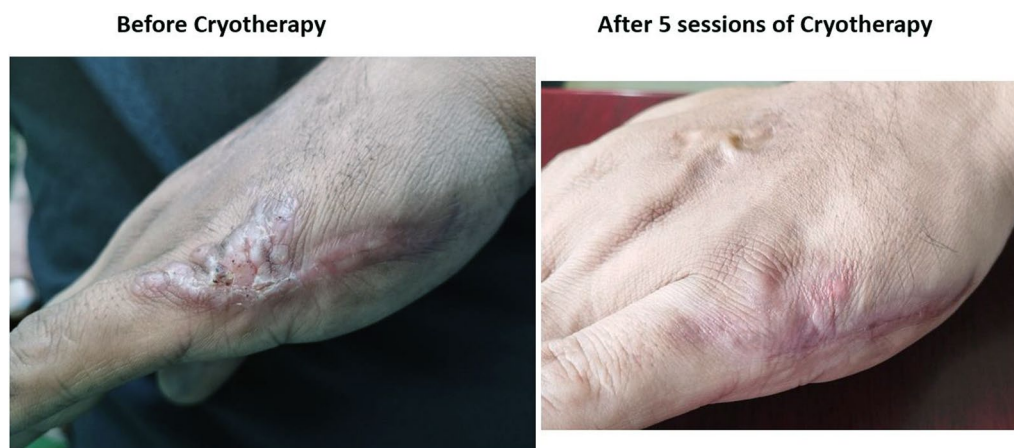


Fig. 4 Linear erythematous infiltrated plaque (left side) and complete resolution of lesion post five sessions of cryotherapy and oral antifungal (on right)

of lesion was halted with only residual pigmentation without active disease post treatment. The erythema, edema, and oozing gradually decreased during 4th week of combined therapy, only leaving residual postinflammatory hypopigmentation and a halo of hyperpigmentation on 2nd-month post therapy. Patient

was followed up with general examination for icterus and a follow up LFT 1 month post itraconazole therapy. There was complete cure of the disease post treatment with no recurrence till date. New lesions have not evolved for 1 year now and the lesion has healed with no symptoms and minimal pigmentation (Figs. 6, 7).

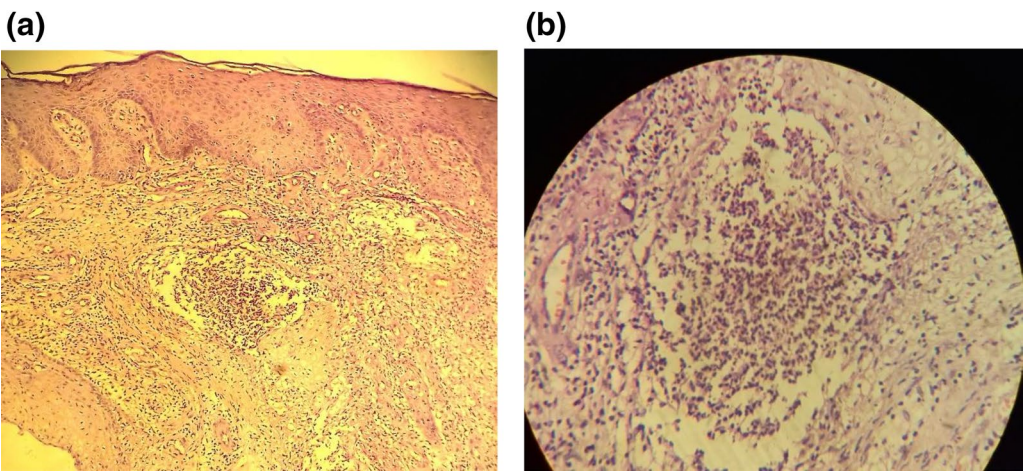


Fig. 5 **a** Involved (lesional) skin showing hyperplastic epidermis with keratinized stratified squamous epithelium showing marked hyperkeratosis, irregular acanthosis and pseudoepitheliomatous hyperplasia along with large intraepidermal neutrophilic abscess (hematoxylin and eosin × 10) and **b** presence of multiple scattered multinucleated giant cells, eosinophilic foreign body like structures, “Sporothrix asteroids” surrounded by ill formed granuloma in mid dermal region (hematoxylin and eosin × 40)

Case 1

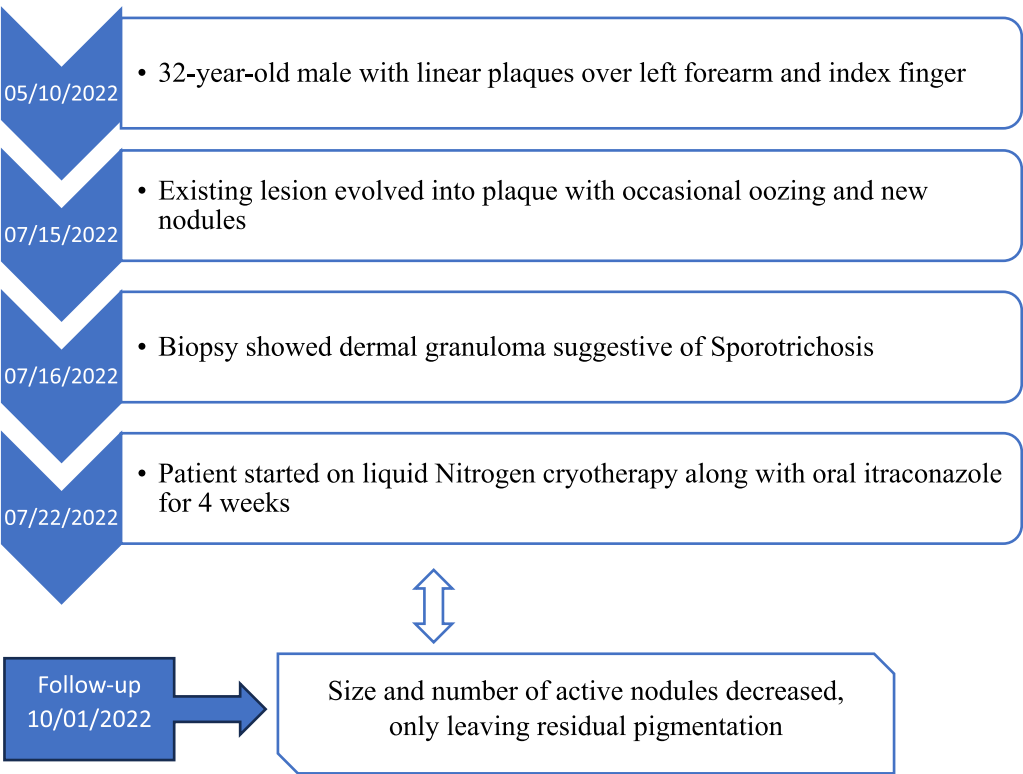


Fig. 6 Timeline depicting clinical presentation, progression, and outcome for patient 1

Case 2

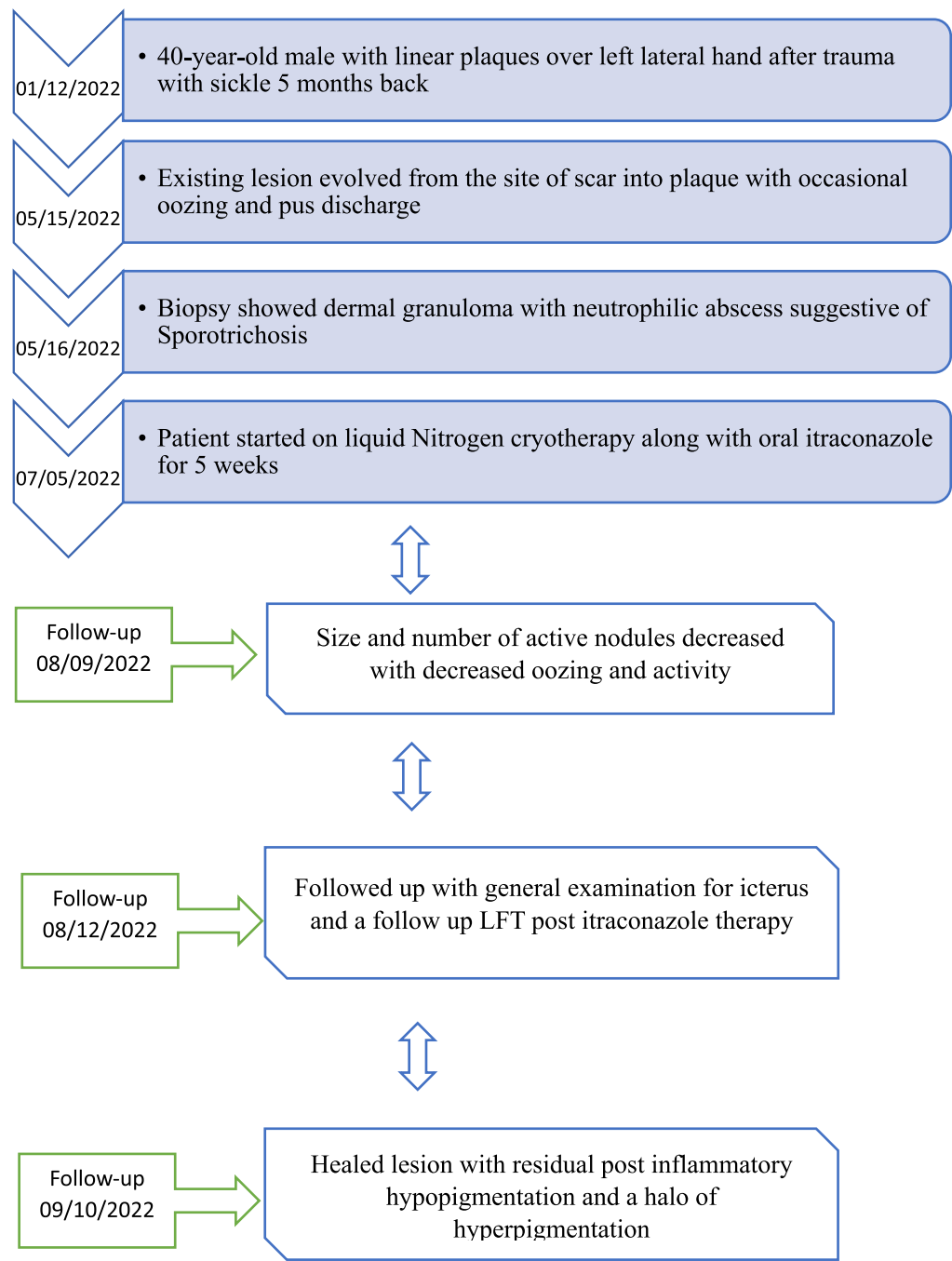


Fig. 7 Timeline depicting clinical presentation, progression, and outcome for patient 2

Discussion

Sporotrichosis is a subcutaneous fungal infection caused by various species of sporothrix fungi [4]. Clinically, the disease manifests 2–4 weeks after inoculation of fungi through trauma to the intact skin [5]. Also rarely,

disseminated sporotrichosis with secondary spread over skin can occur, along with involvement of viscera, such as lungs, meninges, and the joints [8]. Usually lesions are broadly classified into the commoner lymphangitic form and the rarer localized form. Localized lesion occurs in

those with high degree of immunity. In localized form there is containment of fungal pathogen within and there is no dissemination into the lymphatics and the viscera [15]. Disseminated Sporotrichosis involving multiple sites over trunk and extremities is a rare finding and even rarer is its occurrence in immunocompetent individuals [6]. However, disseminated sporotrichosis can occur in those with immunocompromised status, such as human immunodeficiency virus (HIV) or chronic alcoholics [16]. Patients mostly present with nodulopustular lesion along the lymphatics, predominantly over upper extremity, which is often a common site of trauma. Fixed form usually occurs localized, with infiltration, scaling, and spontaneous healing in some [4]. Some of the uncommon complications of sporotrichosis are: occurrence of therapy resistant gummatous plaque and disseminated cutaneous ulcers with scar in immunocompromised individuals with resultant social stigma and discrimination.

There are cases of sporotrichosis reported from different parts of Nepal, as it has tropical and sub-tropical climate [2].

Outcome of sporotrichosis and its course depends on various factors viz. type/ extent of lesion, site of occurrence, socio-economic condition, immunological status, and underlying comorbidities, such as diabetes mellitus, alcohol abuse, human immunodeficiency virus (HIV) infection, and chronic obstructive pulmonary disease (COPD) [4, 5]. Concomitant presence of these aforementioned risk factors and the host immune status will in turn affect duration of time taken in resolution of lesions, associated complications and the psychosocial consequences thereof associated with chronicity of the longstanding disease. Moreover, patient's health status will determine the type, duration and mode of therapy instituted on an individual basis [8].

Diagnosis can usually be made with good clinical acumen. Other modalities of diagnosis, such as direct microscopy (KOH stain), to detect cigar shaped budding yeasts, culture to detect whitish, closely packed yeast like colonies, nested PCR assay for diagnosis at species level, and dermoscopy to reveal diffuse erythema with orange-yellow areas, structureless white areas of fibrosis, and telangiectasias can be utilized.

The histopathology of sporotrichosis shows epidermal hyperkeratosis, acanthosis with dermal granuloma and neutrophilic abscess. Occasionally, cigar shaped fungus with asteroid bodies is seen [10]. Clinically, fixed form of sporotrichosis needs to be differentiated from other seemingly apparent granulomatous lesion, such as cutaneous leishmaniasis and/or cutaneous nocardiosis and its other variant—the lymphangitic form—should be

differentiated from the atypical mycobacterial infection (fish tank granuloma) [11].

Treatment of sporotrichosis is done with prolonged oral and systemic antifungals for months until clinical recovery [3]. However, this prolonged dosing until clinical recovery can be hazardous to those with hepato-cardiac comorbidity and also in pregnant females. Given the systemic side-effects that underlies use of antifungals for prolonged duration, treatment should be sought toward adjuvant physical modality along with oral antifungal, which leads to rapid healing of skin lesion and decreases systemic side effects owing to shortened duration of oral antifungal. Cryotherapy is one of the commonly used adjuvant physical modalities of treatment with varied evidence of efficacy in recalcitrant vegetative and nodulo-infiltrative sporotrichosis. Its utilization can be made more rampant in patients with cardiovascular comorbidities and in regions of the world where the disease is endemic with limited therapeutic armamentarium. It is based on the principle of controlled destruction of epidermal tissue using liquid nitrogen vapor, thereby increasing penetration of antifungals and stimulating the host innate immune system in response to the fungal antigens [17]. However, the major drawback has been a lack of a robust, randomized controlled trials with high level of incidence iterating its use and common side-effects, such as pain, erythema, numbness, vesiculation, ulceration, and even scarring in visibly apparent sites of body [11, 12, 14, 17].

Conclusion

As there is possibility of prolonged use of over-the-counter antifungal medication, lack of regular follow up and lack of laboratory monitoring, especially in the rural parts of Nepal, therapy should be tailored toward onsite physical treatment with cryotherapy in addition to oral antifungals, which can be cost effective and with decreased systemic side-effects. With proper diagnosis, overall prevalence of the disease can be estimated and clinical therapeutic trials can be performed with timely prevention of dreadful systemic complications.

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Author contributions

PP, SP, SA, and SG contributed to the collection of data and the management of the patient. PP and SP wrote the initial draft of manuscript. PP, SP, SA, and SG revised and prepared the final version of the manuscript. All authors have read and approved the final manuscript and agree to take full responsibility for the integrity and accuracy of the work.

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Availability of data and materials

All patient demographic data in this study are included in this published article. Further case details can be requested by emailing the corresponding author.

Declarations**Ethics approval and consent to participate**

I Dr Prajwal Pudasaini, MD hereby consciously assure that for the Cryotherapy for treatment of sporotrichosis—rapid cure with adjuvant cryotherapy: case report author has confirmed during submission that ethical approval has been obtained from the ethics committee of the institutional review board (IRB) of Civil Service Hospital, Government of Nepal (committee's reference number: CSH7201) and both the patients included in the study gave signed, written informed consent to publish this case and the accompanying images. I agree with the above statements and declare that this submission follows the policies of Journal of Medical Case Reports as outlined in the Guide for Authors and in the Ethical Statement.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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