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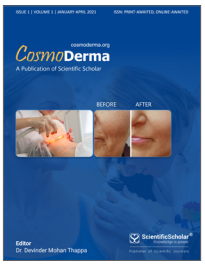

Tropical Dermatology

Sporotrichosis: A brief review

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ABSTRACT

Sporotrichosis is a chronic mycotic infection caused by dimorphic fungus *Sporothrix schenckii*, a common saprophyte of soil and plant detritus. According to recent phylogenetic studies, it is a complex of at least six cryptic species with distinct biochemical properties, geographical distribution, virulence, disease patterns, and therapeutic response. *S. globosa* is the commonest isolated strain in India and evidently responsible for most cases of treatment failure. The disease is endemic in tropical/subtropical regions with occasional large breakouts. In India most cases have been reported along the sub-Himalayan regions.

The characteristic cutaneous and subcutaneous infection follows traumatic inoculation of the pathogen. Zoonotic transmission attributed to insect/bird bites, fish handling, and bites of animals is perhaps because of wound contamination from infected dressings or indigenous/herbal poultices and so is human-to-human spread.

Progressively enlarging papulo-nodule(s) at the inoculation site develop(s) after a variable incubation period which will evolve into fixed cutaneous sporotrichosis or lymphocutaneous sporotrichosis. Primary pulmonary sporotrichosis following inhalation of conidia and osteoarticular sporotrichosis due to direct inoculation are rare forms. Persons with immunosuppression (HIV, immunosuppressive and anticancer therapy) may develop disseminated cutaneous sporotrichosis or systemic sporotrichosis particularly involving central nervous system. Clinical suspicion is the key for early diagnosis and histologic features remain variable. The demonstration of causative fungus in laboratory culture is confirmatory.

Oral itraconazole is the currently recommended treatment for all forms of sporotrichosis but saturated solution of potassium iodide is still used as first-line treatment for uncomplicated cutaneous sporotrichosis in resource poor settings. Terbinafine has been found effective in the treatment of cutaneous sporotrichosis in few studies. Amphotericin B is used initially for the treatment of severe or systemic disease, during pregnancy and in immunosuppressed patients until recovery, and follow-on therapy is with itraconazole until complete (mycological) cure. Posaconazole and ravuconazole remain understudied while echinocandins and voriconazole are not effective.

Keywords: Disseminated sporotrichosis, Fixed cutaneous sporotrichosis, Itraconazole, Lymphocutaneous sporotrichosis, Sabouraud glucose agar, *Sporothrix schenckii*, SSKI

SPOROTRICHOSIS: A BRIEF REVIEW

Sporotrichosis, the most reported subcutaneous mycosis, is caused by a dimorphic fungus *Sporothrix schenckii*. It is sporadic worldwide particularly in temperate, subtropical, and tropical regions but large outbreaks are not uncommon. Frequent occurrences are reported in Japan, China, India, Australia, and Central and South America. In India most cases have been reported along the sub-Himalayan regions [Table 1].[1–7]

Table 1: Salient features of patients with cutaneous sporotrichosis as reported in few important Indian studies.

Reference (Type of study)	State	Number of patients (M:F)	Occupations	History of trauma	Clinical profile				Culture for *S. schenckii* positivity rate	Treatment	Remarks
					Age range (in years)	Diagnosis	Sites involved	Duration			
Ghosh et al.,[1] 1999 (Survey report)	Himachal Pradesh	25 (12:13)	Farmer = 4 Service = 5 Business = 3 Forester = 1 OTA = 1 Housewife & farmers = 11	Trauma in 13(52%) cases Insect bites in 2 cases	23–70	LC = 17(8%) FC = 8(2)	UL = 20(80%) Legs = 3(12%) Face = 2(8%)	NM	100%	NM	Study was for Identifying endemic area by intradermal Sporotrichin skin sensitivity
Mahajan et al.,[2] 2005 (Retrospective study)	Himachal Pradesh	103 (38:65)	Housewife & farmers = 55 Farmer = 12 Service = 9 Business = 3 Forester = 2 Carpenter = 1 Students = 19	Present in 60(58.3%) cases	1½–82	LC = 50(48.5%) FC = 44(42.7%) Multifocal = 1 Herpetiform = 1 Acenform = 1	UL = 60(58.%) LL = 12(11.7%) Face = 27(26.2%) Breast/chest, neck, abdomen = 1 case each	1mo–15 yr	32%	SSKI in 97 cases Itraconazole in 6 cases	12 patients did not tolerate SSKI Healing time 4–32 weeks.
Mehta et al.,[3] 2007 (Prospective study)	Himachal Pradesh	21 (15:6)	Farmers = 15 Housewife & farmers = 6	Present in 9(42.9%) cases	12–72	LC = 14(66.7%) FC = 7(33.3%)	UL = 14(6.7%) LL = 2(9.5) Face = 5(23.8%)	1½ mo–4 yr	47.6%	NM	Study was to identify environmental sources. Cornstalk duff was the major source of infection.
Agarwal et al.,[4] 2008 (Case series)	Uttarakhand	9 (4:5)	Farmer = 1 Laborer = 1 Business = 1 Student = 1 Housewife = 5	NM	18–60	LC = 5(55.6%) FC = 4(44.4%)	Face - 1 UL - 1 LL = 7	1–15 mo	100%	SSKI in 8 Thermo therapy = 1 (antenatal case)*	No recurrence in SSKI treated cases after 12–16 weeks of SSKI treatment

(*Continued*)

Table 1: (*Contd.*)

Reference (Type of study)	State	Number of patients (M:F)	Occupations	History of trauma	Clinical profile				Culture for *S. schenckii* positivity rate	Treatment	Remarks
					Age range (in years)	Diagnosis	Sites involved	Duration			
Bhutia et al.,[5] 2011 (Case series and a review)	Sikkim	3 (1:2)	Housewife = 2 Glass factory worker = 1	Present in all 3 cases	28–51	LC = 3(100%)	UL = 3(100)	3wk–10 mo	100%	SSKI in 2 cases Itraconazole pulse** in 1 case (switched to SSKI after 2 mo)	No recurrence after 7 weeks of SSKI treatment
	West Bengal	100 (56:44)	NM	Present in 33(33%) cases	NM	LC = 67% FC = 33%	UL = 67% LL = 33%	NM	NM	SSKI in 89% cases. Itraconazole in 11% cases.	Study mentions other cases from Nagaland, Meghalaya, and Tripura without further details
	Assam	45 (28:17)	NM	Present in 40(88.9%) cases	NM	LC = 97% FC = 3%	UL = 49% LL = 51%	NM	NM	SSKI in 100% cases	
	Manipur	73 (24:49)	NM	Present in 29(39.7%) cases	NM	LC = 63% FC = 37%	UL = 49% LL = 51% Face = 16% Other = 7%	NM	NM	SSKI in 100% cases	
Verma et al.,[6] 2012 (Retrospective study)	Himachal Pradesh	100 (44:56)	Farmers = 90	Present in 47% cases	1½–88	LC = 71% FC = 28% DCS = 1%	UL = 55% LL = 22% Face 21% Abdomen = 1 Breast = 1	NM	100%	SSKI Itraconazole was used in patients intolerant to SSKI	The study is mainly from microbiology perspective and includes culture positive cases only

(*Continued*)

Table 1: (*Contd.*)

Reference (Type of study)	State	Number of patients (M:F)	Occupations	History of trauma	Clinical profile				Culture for *S. schenckii* positivity rate	Treatment	Remarks
					Age range (in years)	Diagnosis	Sites involved	Duration			
Sharma et al., [7] 2021 (Retrospective study)	Himachal Pradesh	152 (52:100)	Farmers = 25 Housewife & farmers = 85 Office workers = 15 Shop keeper = 6 Laborer + carpenter = 5 Students = 16	Present in 48%	21–60	LC = 71% FC = 28% DCS = 3	UL = 53.9% LL = 21% Face = 15% Trunk = 6.6%	1 mo–15 yr	40.2%	SSKI in 76.8% Itraconazole in 7 cases	Healing seen in 2–9 mo with SSKI. Combination of SSKI with Itraconazole showed better response than either drug alone in 2 cases

Abbreviations: DCS, disseminated cutaneous sporotrichosis; FC, fixed cutaneous sporotrichosis; F, females; LC, lymphocutaneous sporotrichosis; LL, lower limbs; M, males; mo, months; NM, not mentioned OTA, other than above; SSKI, saturated solution of potassium iodide; *S. schenckii*, *Sporothrix schenckii*; UL, upper limbs; yr, years;

*No follow up treatment or outcome mentioned.

**Iraconazole pulse therapy comprises oral itraconazole 200 mg/daily given for 1 week followed by 3 weeks of no itraconazole in a month.

Etiopathogenesis

S. schenckii, a common saprophyte of soil, decaying wood, hay, and sphagnum moss, is a complex of at least six cryptic species viz. *S. globosa* (in India, the UK, Spain, Italy, China, Japan, and the USA), S. *mexicana* (environmental, in Mexico), *S. albicans*, *S. brasiliensis* (in Brazil), *S. luriei*, and *S. schenckii* sensu stricto.[8,9] These show distinct biochemical properties (dextrose, sucrose, and raffinose assimilation), geographical distribution, virulence, disease patterns, and therapeutic response. *S. globosa* is the commonest isolated strain in India and evidently responsible for most cases of treatment failure.[10,11]

Cutaneous infection occurs following traumatic implantation of *S. schenckii* into the skin from contaminated thorns/needles, hay stalks, soil, splinters, and contaminated bizarre injuries. However, only 10%–62% of patients could recall history of trauma in most reports with few exceptions as it is mostly forgotten being innocuous and happened few weeks/months earlier.[1-7] Zoonotic transmission attributed to insect/bird/animal(s) bites, fish handling, etc. are because of wound contamination from infected dressings or indigenous/herbal poultices and so is human-to-human spread.[2] Although animals are not significant source of human infection, cats have been important vehicle in dissemination of *S. schenckii* in a long-lasting epidemic in Brazil.[12]

Since disease occurrence depends upon the fungus in the environment and its portal of entry, professionals handling plants or plant material (farmers, gardeners, florists, foresters, nursery workers) are at risk of getting infection without any predilection for age, gender, or race. The reported preponderance of males or females and individuals aged between 30 and 50 years is perhaps from their high occupational exposure risk.[7]

Clinical spectrum

The incubation period varies from a few weeks to few months (average 3 weeks). The portal of entry, the size, and the depth of the inoculums, virulence, and thermal tolerance of the fungus, and the host immune status have been suggested to influence the subsequent manifestations.[13] Sporotrichosis primarily involves the skin and surrounding lymphatics without systemic symptoms. A small, indurated, progressively enlarging papulo-nodule (primary lesion) evolves at inoculation site, which may ulcerate (sporotrichotic chancre), develop few similar satellite lesions with or without transient adenopathy.[13] It may remain as such or progress into one of the clinical forms listed in Table 2 [Figure 1]. Lymphocutaneous sporotrichosis, involvement of upper limb, dominant hand in particular, and face especially in children remain the commonest clinical presentation.

Figure 1:
(a) **Fixed cutaneous sporotrichosis:** A small crusted plaque develops at inoculation site seen here over cheek of a child. This form is common in children and responds better to treatment. Small lesion at the periphery of primary lesion indicates destabilization of the lesion because of trauma from self manipulation, surgery, or biopsy.
(b) An ulcerated lesion of fixed cutaneous sporotrichosis mimicking pyoderma ganrenosum.
(c) **Lymphocutaneous sporotrichosis**: An ulcerative lesion (sporotrichotic chancre) has developed at inoculation site over dorsal hand with a string of ulcerative plaques along the proximal lymphatics characterizes this form and the diagnosis is fairly easy.
(d) Healing of lymphocutaneous sporotrichosis lesions 8 weeks after treatment with saturated solution of potassium iodide.

Table 2: Clinical spectrum of Sporotrichosis.

Clinical form	Description	Remarks
Fixed cutaneous sporotrichosis	Less common form. Characteristic localized lesion(s) develop at the inoculation site. The lesions are asymptomatic erythematous papules, papulo-pustules, nodules or verrucous plaques, and occasionally non-healing ulcers or small abscesses. It is associated with high host resistance and better therapeutic outcome. Minimal lesions may even spontaneously subside or persist exceptionally if not treated.	The involvement of exposed body areas, the extremities in particular is most frequent. Upper limbs are involved twice as commonly as the lower limbs. Facial involvement is less frequent than that of upper limbs and seen more often with fixed cutaneous variety. Facial involvement and fixed cutaneous sporotrichosis occur more frequently in children.
Lymphocutaneous sporotrichosis	This commonest form accounts for 70%–80% of cases. Erythematous papules, nodules or plaques with smooth or verrucous surface appear along the draining lymphatic channels proximal to the inoculation lesion(s). Some nodules may soften, ulcerate and have seropurulent discharge. Indolent clinical course. Spontaneous resolution is an exception.	
Multifocal or disseminated cutaneous sporotrichosis	Less than or equal to 3 lesions involving two different non-contiguous anatomical sites. Hematogenous spread or multiple traumatic implantations of the fungus are thought to underlie this form.	May even be seen in individuals who apparently have no predisposing factors for immunosuppression.
Extracutaneous Sporotrichosis	Results from hematogenous spread from the primary inoculation site, lymph node, or lungs in patients with an immunosuppressive condition (e.g., alcoholism, diabetes, AIDS, underlying malignancy, corticosteroids, or other immunosuppressive drugs therapy). Manifests as sinusitis, osteoarticular disease, meningitis, or endophthalmitis. Pulmonary disease is rare and occurs following inhalation of conidia. Cough, low-grade fever, weight loss, mediastinal lymphadenopathy, apical lesions (85% cases), and cavitation mimicking tuberculosis, and fibrosis are usual features in pulmonary disease. Massive hemoptysis can occur.	This form is considered an emerging mycosis in HIV seropositive individuals.

Diagnosis

Clinical suspicion is paramount for early diagnosis. Cutaneous leishmaniasis, cutaneous tuberculosis, atypical mycobacteriosis, nocardiosis, and other mycobacteriosis, mycobacteriosis, nocardiosis, and other subcutaneous mycoses remain major differentials. Ulcerated lesions can mimic pyoderma gangrenosum.[14]

Histopathology

The histologic features remain variable. In lymphocutaneous sporotrichosis these vary from acute on chronic inflammation with characteristic zonation, chronic epithelioid cell granuloma with foreign body or Langhans' giant cells to non-specific chronic granulomatous inflammatory cell infiltrate in dermis.[2] The major histopathologic features of fixed cutaneous sporotrichosis include central ulceration of epidermis with hyperkeratosis at the edge, acanthosis and pseudoepitheliomatous hyperplasia. Dense mixed granulomatous cellular infiltrate in upper and mid dermis comprises lymphocytes, plasma cells, and variable number of epithelioid histiocytes, giant cells, and eosinophils with or without fibrocapillary proliferation. Cigar-shaped or asteroid bodies, oval-to-round or single budding forms of the yeast within the cytoplasm of giant cells or in the centre of asteroid bodies, or Splendore-Hoeple phenomenon is visualized occasionally.

Causative fungus

Identification of *S. schenckii* in direct examination of pus or biopsy specimen is not always possible and laboratory culture of *S. schenckii* from clinical samples is confirmatory. Its growth on Sabouraud's glucose agar at 25°C becomes visible within days. The initial cream-colored colonies turn brown/black after few weeks due to melanin production.

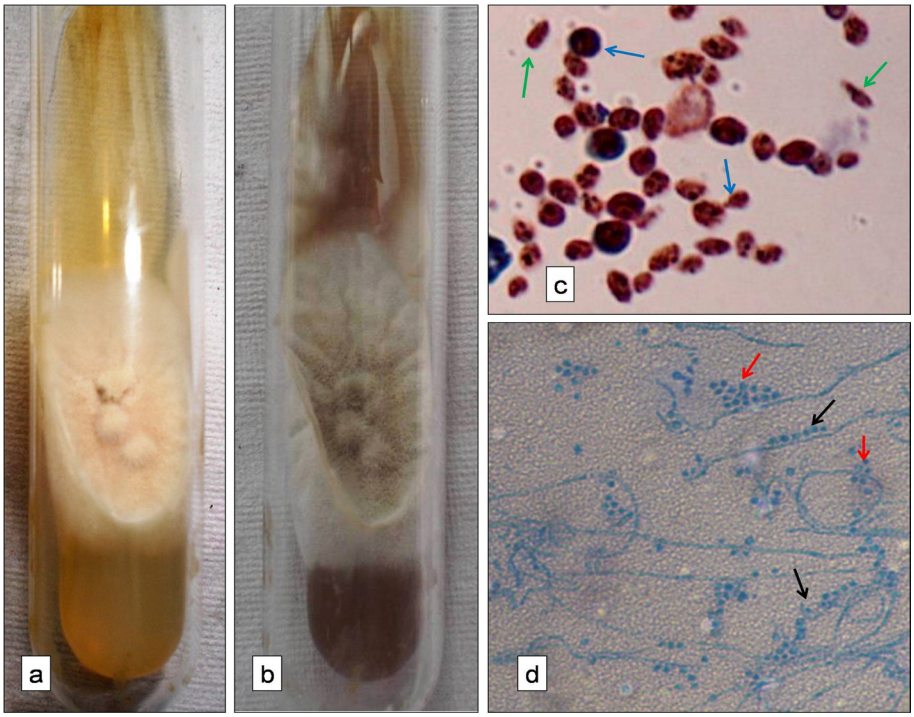

Figure 2: ***Sporothrix schenckii*** **and temperature dimorphism**.
(a) Culture on Sabouraud's glucose agar at 25°C. The initial cream colored colony;
(b) Turns brown black as it matures.
(c) *Sporothrix schenckii* isolate from subculture on brain heart infusion agar at 37°C. The budding yeast cells (blue arrows) and cigar-shaped yeast cells (green arrows) are seen interspersed between spores (Grams' stain, × 100).
(d) *Sporothrix schenckii* from culture on SDA at 25°C. The delicate branching, yeast form, and pyriform conidia in a characteristic sleeve-like pattern (black arrows) and flower-like arrangement (red arrows), (Stain, lactophenol cotton blue, × 40).

Subcultures on blood glucose-cystene agar or brain-heart infusion broth at 37°C yields yeast form. In practice demonstration of this temperature dimorphism along with colony characteristics helps in its identification [Figure 2].[6,13]

Other diagnostic tools

The diagnostic utility of intradermal tests using sporotrichin or peptide-rhamnomannan antigen in practice remains limited because of false positive (in cured or healthy persons in endemic areas) or false negative (in severe or disseminated sporotrichosis) results.[1,13] Serodiagnostic and molecular diagnostic techniques are useful for research and diagnosing rare extracutaneous forms.[13] A favorable therapeutic response to saturated solution of potassium iodide (SSKI) is also nearly diagnostic.[13,15]

Treatment

Most of the treatment recommendations are based on small case series or case reports. Any treatment found effective needs to be extended for 2–4 weeks after lesions have healed. Itraconazole (100–200 mg/d, PO) remains first-line treatment for all forms.[16] However, SSKI is still preferred for uncomplicated cases in developing countries with limited resources, and when itraconazole have failed. It is given orally in a starting dose of 5 drops thrice daily (t.i.d.) mixed with milk or fruit juice to make it palatable. The dose is increased daily by 5 drops t.i.d. up to a maximum 30 to 40 drops t.i.d. Metallic taste necessitates dosage adjustment at a lower level.[13] It is not useful in extracutaneous forms and remains contraindicated in patients who develop hypersensitivity (intolerable metallic taste, flu-like symptoms) or have pre-existing thyroid disorders because of defective autoregulation mechanism (as from surgery or radioactive iodide therapy for Graves' disease, Hashimoto's thyroiditis).[17]

An adequate control with intravenous amphotericin B (3–5 mg/kg of lipid formulation) is recommended in systemic sporotrichosis patients when the treatment cannot be deferred or before initiating long-term itraconazole therapy or when other drugs are contraindicated (as in pregnancy).[13]

Terbinafine (125 to 1000 mg/day given for 4–37 weeks) has been used effectively to treat cutaneous sporotrichosis when itraconazole had failed or remains contraindicated.[13] A combination of SSKI and itraconazole or terbinafine shows better efficacy than either drug used alone.[7]

In *in-vitro* studies posaconazole has shown good activity against five species of *S. schenckii* but activity of ravuconazole

against *S. brasiliensis* is limited; both remain understudied clinically.[13] Echinocandins and voriconazole are not effective in sporotrichosis treatment.[18,19]

The daily application of heat (42°–43°C) to the lesion for weeks using heat compresses, infrared heater, or hand-held pocket warmer is useful as an adjunct or for treating small cutaneous lesions pending specific therapy.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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