Case Report: Sporotrichosis from the Northern Territory of Australia

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Abstract. We report three cases of lymphocutaneous infection caused by the thermally dimorphic fungus, *Sporothrix schenckii* from Australia's tropical Northern Territory. Two cases were acquired locally, making them the first to be reported from this region. All three cases presented with ulceration in the limb; however, the classical sporotrichoid spread was present only in the first two cases. Their occurrence within several weeks of each other was suggestive of a common source of environmental contamination such as hay used as garden mulch. Diagnoses were delayed in each case, with each patient having substantial exposure to ineffective antibiotics before the correct diagnosis was made. These cases bring the total number of reported sporotrichosis cases in Australia since 1951 to 199. Lessons from these cases are to consider the diagnosis of sporotrichosis in lesions of typical appearance, even in geographical settings from where this pathogen has not previously been reported.

INTRODUCTION

Sporotrichosis is a cutaneous infection caused by *Sporothrix schenckii*, a widely distributed dimorphic ascomycete fungus found in decaying vegetation, soil, and contaminated organic matter.¹ The classical clinical appearance of lesions spreading along lymphatic channels gives rise to the term “sporotrichoid” spread, which can also be caused by *Nocardia* species, *Mycobacterium marinum* and *Leishmania brasiliensis*.² Infection usually occurs by traumatic inoculation of soil, plant, or organic materials contaminated with the fungus. The lesions are usually restricted to skin and subcutaneous tissues, although depending on inoculum load and host immune responses, systemic dissemination can occur.³

Sporothrix schenckii is recognized to have a near-global distribution, except for latitudes further from the equator than 50° north or south.¹ In Australia, cases tend to cluster in temperate or sub-tropical settings.⁴ Numbers are sparse, with 196 cases having been reported since 1951, mostly from the states of Queensland and New South Wales (Table 1 and Figure 1). Australian cases occur either as outbreaks, attributed to a contaminated source such as moldy hay,^{19,20} or may be endemic to certain areas,⁴ although at far lower rates than hyperendemic foci such as that in Peru.²¹ Zoonotic transmission of this fungus can occur from scratches or bites of animals such as armadillos, squirrels, dogs, and cats,^{18,21} and a spider bite has also been implicated as a potential inoculating culprit.¹⁸ There has been a suggestion of clustering of cases during higher rainfall periods.⁴ The Northern Territory of Australia is a tropical setting at 12°S with an annual monsoon season and no previous reported cases of sporotrichosis.

Important differential diagnoses exist locally that can also cause chronic ulceration with or without sporotrichoid spread. These include nocardiosis, cutaneous melioidosis (*Burkholderia pseudomallei*), chromoblastomycosis, and group A streptococcal pyoderma.²² Another plant-associated fungal pathogen of particular importance in the Northern Territory, also implicated in occasional skin lesions, is *Cryptococcus gattii*.²³

Here, we report three cases of sporotrichoid lymphocutaneous infection diagnosed in Australia's Northern Terri-

tory. Additionally, *Quambalaria cyaneus* was isolated from one biopsy sample, although that was not likely to be contributing to the clinical presentation.

CASE REPORTS

Case 1. A 47-year-old caucasian male used as a Groundsman was referred to the Infectious Diseases Outpatient Clinic at the Royal Darwin Hospital with an 8-week history of ulceration of the dorsum of the knuckle of his right index finger (Figure 2A). There was sporotrichoid spread ascending the forearm (Figure 2B) and a tight cord-like appearance of the upper arm lymphatic channel (Figure 2C). He described multiple potential inoculating events before the onset of the lesion, which had been in May (the end of the monsoon season). These included lifting wet hay bales using twine encompassing the bales, using his hand to remove leaves from a blocked gutter, and fixing an irrigation pipe that involved submerging his hands in muddy water. He had been treated with several courses of cephalexin and amoxicillin-clavulanic acid by his general practitioner without improvement in the lesions.

His past medical history included squamous cell carcinoma (SCC) of the tongue diagnosed in 2007, treated with chemoradiotherapy with no evidence of recurrence seen on a positron emission tomography scan in 2009. He did not take any regular medications and has no known drug allergies. He had a history of moderate alcohol intake of six standard drinks daily.

Punch biopsies were obtained for microbiological and histopathological processing. Despite the provisional diagnosis of “sporotrichosis” being written on the pathology request form, the pathologist concluded that the sample showed inflammatory SCC. Features included intense, acute dermal inflammation and necrosis. Implantation of squamous epithelial cell elements caused by penetrating trauma was listed as a differential diagnosis and a more extensive repeat biopsy was suggested, which was arranged while fungal cultures remained in progress. Bacterial cultures including for *B. pseudomallei* were negative, and *B. pseudomallei* serology was also negative. A further biopsy was arranged, given the unexpected report of inflammatory SCC, which was disturbing given the patient's history of SCC. The ulcerated lesion overlying the knuckle and the one forearm lesion were then biopsied. The follow-up histopathology again reported SCC, which was withdrawn on review, in light of the emerging fungal culture

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TABLE 1
Human cases of *Sporothrix schenckii* reported in Australia

Reference	Year	Location	Number of cases
Robinson ⁵	1951	New South Wales	1
Barrack and Powell ⁶	1952	New South Wales	1
Minty and others ⁷	1956	Queensland	1
Mead and Ridley ⁸	1957	Queensland	2
Durie and others ⁹	1961	New South Wales	1
O'Donnell ¹⁰	1962	Western Australia	1
Muir and Pritchard ¹¹	1963–1981 (published 1984)	New South Wales	12
Robertson ¹²	1967	Queensland	2
Black and McAleer ¹³	1975	Western Australia	1
Auld and Beardmore ¹⁴	1965–1977 (published 1979)	Queensland	37
Beardmore ¹⁵	1979	Queensland	1
Bullpitt and Weedon ¹⁶	1978	Queensland	39
Conias and Wilson ¹⁷	1998	Queensland	16
Moaven ¹⁸	1999	Western Australia	1
Feeny and others ¹⁹	2003–2004 (published 2007)	Busselton-Margaret River Region, Western Australia	49
Sivagnanam and others ⁴	2000–2010 (published 2012)	New South Wales mid-north coast	31
Subedi and others (current report)	2013	Northern Territory	2
		Queensland	1
Total			199

results. The first fungal culture report to be received was that of *Quambalaria cyaneus* in the forearm lesion, identified by DNA sequencing (internal transcribed spacer region) at the National Mycology Reference Center (NMRC). Subsequently, fungal cultures both from the original biopsy and the later finger and forearm biopsies all yielded *S. schenckii*. The patient was commenced on itraconazole 200 mg daily. The lesions regressed substantially, and treatment was continued for a total of 3 months at which stage the lesions were healed.

Case 2. A 54-year-old Caucasian male presented to the Royal Darwin Hospital with a 6-week history of ulcerated lesion on the dorsum of his left hand with sporotrichoid spread ascending the left forearm. He was treated in the com-

munity with several courses of amoxicillin-clavulanic acid with no improvement. There was no history of specific inoculating injury, although he was a keen gardener. Hay is often used as a garden mulch locally but it is unclear whether he was directly exposed to hay as was Case 1. He has no significant past medical history and did not take regular medications. There was no history of overseas or interstate travel. On examination, there was a 5 × 4 cm ulcerated lesion on the dorsum of his left hand with nodular lymphangitis (Figure 3).

Several punch biopsies were taken from the ulcerated area and submitted for histopathology, microscopy, and culture including for fungi and mycobacteria. He was commenced on empirical treatment of *Nocardia* with

FIGURE 1. Distribution of all *Sporothrix schenckii* human Australian isolates reported in Australia. Blue circles represent outbreaks attributed to moldy hay.^{14,19} Case numbers are attributed to State or Territory if no specific geographic location was recorded.

FIGURE 2. (A) Lesion overlying index finger knuckle. (B) Lesion ascending the forearm. (C) Cord like appearance of lymphatic channel in upper arm.

trimethoprim-suphamethoxazole two double strength tablets twice daily while awaiting further results.

He was reviewed in the Infectious Diseases Outpatient clinic 3 weeks later when he was noted to have new lesions in the anterior forearm. Histopathology from the punch biopsy showed skin with intense acute and chronic inflammation. Focally, at the margin of the biopsy there were several multinucleated giant cells present. Culture from the tissue eventually yielded a yeast-like organism which was identified as *S. schenckii* at the NMRC ~3 weeks after the biopsy had been performed. The patient was commenced on itraconazole 100 mg daily, increased to 200 mg daily with an acidic soft drink after a trough itraconazole level of 423 µg/L was noted. His lesions regressed within weeks of commencing the itraconazole and were deemed to have been cured when treatment was ceased after 3 months of therapy.

Case 3. A 47-year-old Caucasian male was seen at the Infectious Diseases Outpatient Clinic at the Royal Darwin Hospital on the same date as Case 1, with a 9-week history of a progressive ulcer with associated nodules of his right shin. The lesion

developed after he went bushwalking in the Airlie Beach region in Queensland (latitude 20°S). He had been systemically well with no fevers. He has no significant past medical history. Cultures from a swab of the lesion had yielded *Pseudomonas aeruginosa*, hence he had been treated with ciprofloxacin 750 mg twice daily for 2 weeks with some improvement.

On examination, there was a lesion of the right shin with central ulceration. Several satellite lesions were near the area of ulceration but there was no sporotrichoid spread (Figure 4, shown after partial response to treatment). Punch biopsy was performed. While awaiting biopsy results, ciprofloxacin was continued but after 3 weeks, *S. schenckii* was reported from the biopsy sample. Hence, ciprofloxacin was ceased and fluconazole 400 mg daily commenced, changed to itraconazole 200 mg daily when the antifungal susceptibilities became available. The MIC of fluconazole was 32 µg/mL and itraconazole 0.5 µg/mL as determined by the Clinical and Laboratory Standards Institute (CLSI) M38-A2 standard,²⁴ fairly typical of *S. schenckii*.²⁵ His lesion was slow to resolve, and itraconazole was continued for 6 months. On review

FIGURE 3. Case 2. Hand lesion with sporotrichoid spread ascending the forearm.

2 months after completion of therapy, scarring was evident but there was apparent cure of active infection.

DISCUSSION

The cases of sporotrichosis we report are notable for their occurrence in a new location (Australia's tropical Northern

Territory, Cases 1 and 2), the somewhat atypical appearance without classical sporotrichoid spread and slow treatment response in Case 3, the concurrent isolation of *Q. cyaneus* with *S. schenckii* from one patient's lesion, and the unexpected histopathology report of SCC. These cases bring the total number of reported sporotrichosis cases in Australia to 199 (Table 1). This is likely to be a substantial underestimate of true national case numbers, because the infection is not notifiable. Because sporotrichosis remains relatively uncommon, the lack of recognition of this infection in general practice, leading to ineffective antibiotic treatment often for weeks to months before correct diagnosis, is likely to be an ongoing problem. Local recognition of the possibility of this disease occurring in the Northern Territory is therefore of major importance. We acknowledge it is possible that the two apparently local cases were acquired after contact with contaminated material such as hay, which might have been imported from interstate, meaning that the organism did not originate in the Northern Territory.

The identification of *Q. cyaneus* in Case 1 was of great interest because it was the only isolate from the initial biopsy, causing us to wonder whether it might be the pathogen responsible for the sporotrichoid lesions. However, the subsequent isolation of *S. schenckii* from a repeat biopsy of the same lesion, and a forearm lesion, make it far more likely that *Q. cyaneus* was not implicated in the pathogenesis of the lesions, in keeping with the existing understanding of this organism.²⁶⁻²⁸

Quambalaria cyaneus is a basidiomycetous plant pathogen,²⁹ which has undergone a number of taxonomic reassignments including, previously, *Sporothrix cyaneus* and *Fugomyces cyaneus*.^{30,31} There are no human case reports of the isolation of *Q. cyaneus* from human specimens or as a cause of human pathology. However, when previously known as *S. cyaneus*, this organism was postulated to have had a pathogenic role in one immunosuppressed patient with pulmonary nodules.²⁶ *Sporothrix cyaneus* features in just two other human reports as a potential pathogen²⁷ or an environmental contaminant appearing in bronchial washings.²⁸ *Quambalaria* species cause pathology such as canker and shoot blight in Australian native trees of the *Eucalyptus* and *Corymbia* genera (red flowering gums)³² different trees from those with which *Cryptococcus gattii* is associated.³³

We hypothesise that *Q. cyaneus* was inoculated at the same time as *S. schenckii*, given its similar ecological niche, and colonized the wound. The national reference laboratory in South Australia had also identified *Q. cyaneus* several months prior, in another Royal Darwin Hospital (Northern Territory) patient who had a staphylococcal abscess of the shin. A sample from the shin yielded both *Staphylococcus aureus* and *Q. cyaneus*, with the latter being considered non-pathogenic. The patient responded to conventional antibiotics. *Quambalaria cyaneus* has the potential to be misidentified as *Sporothrix* species in the laboratory, hence the importance of accurate laboratory workup. In Case 1 and in the additional case seen at the NMRC, identification was by macroscopic and microscopic appearance of colonies grown on a variety of media and DNA sequencing.

Sporothrix schenckii is a thermally dimorphic fungus that assumes a filamentous form when cultured at 25°C. Colonies may be slow growing, glabrous, with a leathery to velvety texture, and pigmentation varies from white to dark grey-brown

FIGURE 4. Case 3. Shin lesion shown after regression on treatment.

FIGURE 5. (A) Sabaroud's agar at 25°C, colonies are slow growing, with a wrinkled and folded surface, forming shapes suggestive of inverted cones or volcanoes. (B) Conidiophores and conidia of *S. schenckii*. Conidia are ovoid, one-celled, and smooth-walled. Conidiophores (black arrow) arise at right angles from the thin septate hyphae and are usually solitary. Conidia are formed in clusters on small denticles by proliferation of the conidiophore, their arrangement often suggestive of a flower.

with age; microscopically, septate hyphae bear perpendicular conidiophores with sympodial clusters of denticulate conidia at the apex, and with age, ovoidal conidia may be borne directly on the sides of the conidiophore and hyphae (Figure 5). In human and animal tissues and on brain heart infusion agar at 37°C, *S. schenckii* has a yeast-like morphology with smooth cream to beige colonies; microscopically budding ovoidal to cigar-shaped budding yeast cells. Dimorphism must be shown to morphologically identify the isolate as *S. schenckii*. Molecular diagnostics are particularly helpful in situations of slow growth.³ *Quambalaria cyanescens* is distinguishable from *S. schenckii* by its velvety to powdery colony texture, production of an intense purple diffusible pigment on potato dextrose agar after several weeks incubation, and a lack of a yeast phase.

Histopathology of *S. schenckii*-infected tissue specimens often shows mixed suppurative and granulomatous inflammatory reactions in dermis and subcutaneous tissues.³⁴ The unexpected histopathological findings in Case 1 were reviewed and corrected to conclude that SCC was not present.

Regarding clinical features of sporotrichosis, the localized cutaneous form caused by traumatic inoculation is the commonest presentation. The fungus converts into yeast form and may remain in subcutaneous tissues or extend along adjacent lymphatic vessels, constituting the lymphocutaneous form.³ Osteoarticular is the second most common presentation, followed by pulmonary and systemic disease. Disseminated infection occurs rarely, most commonly in immunocompromised individuals, particularly those with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome

(AIDS).³⁵ Treatment of lymphocutaneous infection is usually achieved with itraconazole 200 mg daily.^{36,37} The recommended treatment duration is usually 3–6 months and is recommended to continue treatment of 2–4 weeks after lesions have resolved, as was used in the cases described here. Cure rates with itraconazole are over 95%.²⁸ Fluconazole (initially commenced in Case 3) is ineffective. Alternative agents include terbinafine and amphotericin B, which also have excellent activity against the organism. Treatment duration of at least 12 months is recommended for osteoarticular infections.²⁹

In conclusion, sporotrichosis needs to be considered as a differential diagnosis in patients from Australia's Northern Territory, alongside better known local endemic pathogens, which can cause sporotrichoid lesions (*Nocardia* spp.) or fixed cutaneous lesions non-responsive to conventional antibiotics (melioidosis, chromoblastomycosis, and cryptococcosis). As improved molecular diagnostics now facilitate easier distinction between similar appearing fungi such as *Q. cyanescens* and *S. schenckii*, the occurrence of *Q. cyanescens* from human specimens should continue to be monitored, to determine any possible indication of pathogenicity, and to distinguish it from *S. schenckii*, which has clearly established human pathogenicity requiring treatment.

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