Sporotrichosis in Peru: Description of an Area of Hyperendemicity

Peter G. Pappas, Ildefonso Tellez, Alexandria E. Deep, Delia Nolasco, Walter Holgado, and Beatriz Bustamante

Sporotrichosis is a sporadic and rare mycotic infection in most of the developed world. In many parts of the developing world, sporotrichosis is much more commonly recognized, but epidemiological data are generally lacking from these regions. We report epidemiological, clinical, and treatment data from 238 cases of culture-proven sporotrichosis occurring in a relatively remote area of the south central highlands of Peru that were retrospectively collected during 1995–1997. Most cases (60%) occurred in children aged ≤14 years, and the most commonly affected anatomic site was the face. Disease was clinically confined to the skin and subcutaneous tissue in all patients. The incidence of sporotrichosis in this region ranged from 48 to 60 cases per 100,000 persons and was highest among children aged 7–14 years, approaching 1 case per 1000 persons. Sporotrichosis is a significant mycosis in the rural highlands of Peru, with an incidence exceeding those of other invasive mycoses in individuals without human immunodeficiency virus infection.

Sporotrichosis is a chronic cutaneous and subcutaneous infection caused by the thermally dimorphic fungus Sporothrix schenckii. The disorder was originally described in 1898 by Schenck at the Johns Hopkins Hospital in Baltimore who together with Smith recognized that the infection was probably due to a previously undescribed fungal pathogen [1]. Two years later, their observations were confirmed by Hektoen and Perkins [2] in a report of a second case and a detailed morphological description of the pathogen, together with the results of their studies involving laboratory animals. Soon after these reports, other cases from the United States and western Europe were recognized, especially in France, where large numbers of cases were reported in the early 20th century [3]. Subsequently, S. schenckii has been identified worldwide, and cases of sporotrichosis have been reported from all continents; however, in recent years, most reported cases have been from sites in North America and South America (especially Mexico, Colombia, Uruguay, and Brazil) [4–9].

Many outbreaks of sporotrichosis have been described in the literature [4, 7–15] and account for a significant proportion of reported cases. The largest reported outbreak occurred from 1941 through 1944 in South Africa; almost 3000 miners were infected, and the outbreak was attributed to contaminated mine timbers [10]. Once the timbers were treated with fungicides, the outbreak was terminated. Other smaller outbreaks have been described in forestry workers, gardeners, and florists [11–15]. In the largest United States outbreak to date, 84 cases of cutaneous sporotrichosis occurred in seedling planters from multiple states, and the outbreak was eventually traced to sphagnum moss harvested in Wisconsin [11]. A more recent outbreak in Florida tree nursery workers was also traced to sphagnum moss [15]. The results of these outbreak investigations have led to important insights into the epidemiology of sporotrichosis in the epidemic setting, but there is very limited understanding about the epidemiology of sporotrichosis in areas of the world where the disease is hyperendemic. Furthermore, there is very little information concerning the incidence of sporotrichosis since it is not a reportable condition in most countries.

Beginning in 1986, 2 of us (W. H. and B. B.) began work in an isolated area in the south central highlands of Peru where cutaneous sporotrichosis is hyperendemic. A mycology laboratory was established, and a protocol for treatment was implemented. Epidemiological and clinical investigations in this region have been limited, but data from 3 series detailing the demographic and clinical features of patients with sporotrichosis in this region, together with our own observations, suggest that sporotrichosis is hyperendemic in the area [16–18]. Indeed, Centro Medico Santa Teresa (CMST) in Abancay, Peru, has consistently diagnosed and treated 60–100 cases an-
nually, and there have been >1000 cases in this region since 1987. In this report we describe 238 cases of sporotrichosis seen at CMST over a 3-year period (1995–1997) to better understand the clinical and epidemiological features of the disease in this unique setting.

Patients and Methods

Description of the site. Patients were identified for this study through a retrospective review of results of the mycology laboratory at CMST for a 3-year period (1995–1997). CMST is a 10-bed inpatient and outpatient facility serving the city of Abancay and the province of Apurimac in the south central Peruvian highlands. Abancay (elevation, 2377 m) is a medium-sized city located in a semiarid region of the Peruvian highlands and is the departmental capital of Apurimac. In 1997 the city had a population of 106,362 (population figures are based on 1995 data from the Peruvian National Institute of Statistics and Informatics and were adjusted annually through 1997 according to a growth rate of 0.9%). The region is very mountainous, and access to the city is limited by the difficult terrain. Most of the population is native to Peru.

The region is poor economically, and the economy is largely based on agriculture and regional services. There is no significant manufacturing industry in the region. There are 3 other hospitals in Abancay, but because of CMST’s regional reputation as a sporotrichosis center, together with the excellent support of the mycology laboratory, most patients with suspected cases of sporotrichosis are referred to CMST for culture confirmation and therapy.

Case definition. A case of sporotrichosis was defined as an S. schenckii-positive culture of a specimen from any site obtained during the 3-year period from 1 January 1995 through 31 December 1997 at CMST. Culture specimens for isolation of S. schenckii were obtained by skin scraping or needle aspiration from a suspicious site. Time (days) to culture positivity was noted. The identification of S. schenckii was based on the isolation of a morphologically typical fungus with conversion to the yeast phase at 35°C.

Data collection. Upon identification of a case, the corresponding medical record was reviewed, and data were recorded on a standardized case report form. Each patient was assigned a unique study number. The data collected included detailed information concerning residence, demographics, duration of symptoms, date of diagnosis, underlying medical illnesses, occupational and other exposure risk, history of trauma, clinical findings, response to therapy, and any other pertinent data.

Treatment and clinical outcome. Therapy and response to therapy were recorded in each patient’s medical record. Length of therapy (weeks) and reason(s) for terminating therapy were noted. Outcome (success or failure) was determined by the clinician and based on clinical criteria. When available, data on follow-up of successfully treated patients were noted.

Data entry and analysis. Data from each case report form were further analyzed by use of Epi-Info Version 6 (Division of Surveillance and Epidemiology, Centers for Disease Control and Prevention, Atlanta, GA). Statistical methods employed for this analysis included frequency, mean, median, variance, standard deviation, and cumulative percentage calculations.

Results

Demographics. We identified 238 patients with culture-proven sporotrichosis who were seen at CMST in the 3-year period from 1 January 1995 through 3 December 1997. The demographic features of these patients are detailed in table 1. There were 133 males (56%) and 105 females (44%); 143 (60%) of the patients were aged <15 years. During this same period, 45% of the patients seen at CMST were aged <15 years. Significant underlying diseases were evident in 47 patients (20%); these diseases were most commonly malnutrition, alcoholism, chronic hepatitis B, and diabetes mellitus. Most patients were students (52%) or toddlers (18%); only 7% of the patients were farmers. A history of local trauma preceding the development of sporotrichosis was reported by 24 patients (10%).

Mycology. For all 238 patients, the diagnosis of sporotrichosis was based on typical clinical presentation and culture of a specimen from the involved site that was positive for S. schenckii. Thirty of these isolates were transported to the United States to a mycology research laboratory (University of Alabama at Birmingham School of Medicine) for species confirmation, and all 30 isolates were reconfirmed as S. schenckii. Cultures became positive within 8 days in 211 cases (89%); all the remaining 27 cultures (11%) were positive within 29 days.

Clinical features. Duration of symptoms before seeking medical attention was quite varied. Seventy-eight patients (33%) were seen within 4 weeks after initial symptoms; 55 (23%), 5–8 weeks; 36 (15%), 9–12 weeks; 31 (13%), 13–26 weeks; and 16 (7%), 27–52 weeks. Twenty-two patients (9%) had symptoms that lasted >1 year before seeking medical attention.

All patients had cutaneous or lymphocutaneous disease; no patients were determined to have extracutaneous involvement. Cutaneous and subcutaneous lesions were categorized into 3 separate clinical classifications: lymphocutaneous disease, fixed lesions, and multifocal (disseminated) cutaneous disease. Pa-

<table>
<thead>
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<th>Characteristic</th>
<th>No. (%) of patients</th>
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<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>133 (56)</td>
</tr>
<tr>
<td>Female</td>
<td>105 (44)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>0–6</td>
<td>66 (28)</td>
</tr>
<tr>
<td>7–14</td>
<td>77 (32)</td>
</tr>
<tr>
<td>≥15</td>
<td>95 (40)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>123 (52)</td>
</tr>
<tr>
<td>Toddler</td>
<td>44 (18)</td>
</tr>
<tr>
<td>Housewife</td>
<td>27 (11)</td>
</tr>
<tr>
<td>Agricultural worker</td>
<td>16 (7)</td>
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<tr>
<td>Military service</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>17 (7)</td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>214 (90)</td>
</tr>
<tr>
<td>Yes</td>
<td>24 (10)</td>
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patients with lymphocutaneous disease had classical nodular lymphangitis, usually involving an extremity, with characteristic “marching” progression proximally from a distal lesion. Patients with fixed lesions had 1 or 2 ulcerative or plaquelike proliferative lesions without classical nodular lymphangitis. Multifocal cutaneous disease was defined as ≥3 lesions involving at least 2 anatomic sites. On the basis of these definitions, 130 patients (55%) had lymphocutaneous eruptions, 85 (36%) had fixed lesions, and 23 (9%) had multifocal cutaneous disease. Within each group, patients had nodular, ulcerative, or proliferative types of lesions. Most patients (57%) had a mixture of nodular and ulcerative lesions, whereas 39% had only ulcerative disease; the remaining patients had either plaquelike or papulosquamous disease.

Anatomic location and number of cutaneous lesions were described for each patient. The face was the most common anatomic site (figure 1); 109 patients had facial lesions. A disproportionate number of children had facial lesions: 86 (60%) of 143 children versus 23 (24%) of 95 adults. The upper extremity was the second most common anatomic site, followed by the lower extremity, neck, thorax, abdomen, and buttocks. The clinical characteristics of the patients are summarized in table 2.

**Figure 1.** Multiple facial lesions of sporotrichosis that were associated with significant scarring in a 14-year-old boy from the south central highlands of Peru.

**Table 2.** Characteristics of lesions and sites of involvement in 238 patients with sporotrichosis who were seen at Centro Medico Santa Teresa in Abancay, Peru.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>No. (%) of patients</th>
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<tbody>
<tr>
<td>Class of lesions</td>
<td></td>
</tr>
<tr>
<td>Lymphocutaneous</td>
<td>130 (55)</td>
</tr>
<tr>
<td>Fixed</td>
<td>85 (36)</td>
</tr>
<tr>
<td>Multifocal (disseminated) cutaneous</td>
<td>23 (9)</td>
</tr>
<tr>
<td>Site of involvement</td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>109 (46)</td>
</tr>
<tr>
<td>Upper extremity</td>
<td>78 (33)</td>
</tr>
<tr>
<td>Lower extremity</td>
<td>49 (21)</td>
</tr>
<tr>
<td>Neck</td>
<td>17 (7)</td>
</tr>
<tr>
<td>Thorax</td>
<td>11 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Multiple</td>
<td>18 (8)</td>
</tr>
<tr>
<td>Lesions</td>
<td></td>
</tr>
<tr>
<td>Nodular and ulcerative</td>
<td>136 (57)</td>
</tr>
<tr>
<td>Ulcerative</td>
<td>92 (39)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (4)</td>
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during 1995–1997. Incidence was calculated for each of the 3 years, and age-related incidence was calculated by use of population figures according to age for Abancay. These data are displayed in table 3.

On the basis of these calculations, we calculated that the overall incidence of sporotrichosis was 48–60 cases per 100,000 population during the study period. The incidence was 59–73 cases per 100,000 population among children aged 0–6 years and 57–93 cases per 100,000 population among children aged 7–14 years. The incidence among adults (aged ≥ 15 years) varied from 25 to 57 cases per 100,000 population; although this difference was significant (P = .005), the overall number of patients was relatively small, and there were no known changes in climatic conditions, risk factors, or access to medical care that would account for this difference. The mean incidence for the 3-year period among children aged 0–6 years, children aged 7–14 years, and adults was 67, 75, and 36 cases per 100,000 population, respectively. On the basis of the date of diagnosis, there were no significant differences in seasonal incidence.

Discussion

Most published reports of sporotrichosis have described moderate to large outbreaks of disease or have focused on unusual manifestations of sporotrichosis. Although these observations provide insight into the transmission and risk factors associated with disease in the epidemic setting, they are of limited value in areas of the world where sporotrichosis appears to be much more endemic, such as Central America, South America, and Africa. One obstacle preventing comprehensive epidemiological investigation of sporotrichosis in developing countries is that the disease is probably greatly underdiagnosed. In addition, the disease is not reportable in most countries. Thus, reliable data on incidence are not available from any region of endemicity. In this report, we describe 238 cases of culture-proven sporotrichosis from an area in the south central highlands of Peru in which there have been >1000 cases since 1987. The existence of a sporotrichosis program at CMST has provided an excellent opportunity to make several important clinical and epidemiological observations relative to the disease in this region.

Our data indicate that the incidence of sporotrichosis among Abancay residents is among the highest incidence of any invasive mycosis described for non–HIV-infected patients in a population-based study. The overall incidence of between 48 and 60 cases per 100,000 population is striking, and the experience of the CMST team suggests that this figure has been consistent for more than a decade. The incidence among older children is even more remarkable, approaching 1 case per 1000 population. Undoubtedly, these figures represent low estimates of incidence, since most, but not all, patients with sporotrichosis were seen at CMST, and only patients with culture-proven disease were included in this analysis. Nonetheless, these figures greatly exceed those of previously reported studies of other invasive mycoses, including cryptococcosis [19], coccidioidomycosis [20], and histoplasmosis [21], in non–HIV-infected patients in a nonepidemic setting. From a public health perspective, other invasive mycoses clearly have a substantially greater impact on mortality than does sporotrichosis, since death due to sporotrichosis is limited to a few patients with extracutaneous disease.

There were a significant number of children with sporotrichosis in this cohort and a large number of patients with facial lesions, especially children. Indeed, 60% of the patients in this study were aged <15 years, and most of these children had facial involvement. Few investigators have described substantial numbers of children in any series of sporotrichosis. Kusuhara et al. [22] and Itoh et al. [23] reported 2 large series from Japan that included 23 children (15% of 150 patients) and 35 children (18% of 200 patients), respectively, but very few details were provided beyond age, skin lesion morphology, and anatomic location; 21 (92%) of 23 and 34 (97%) of 35 children, respectively, had only facial lesions. In an unusual outbreak of sporotrichosis, 8 cases were reported from 1 residence, including 5 children (all of whom had facial lesions) [24]. In 3 smaller series of sporotrichosis in children, little note was made of facial lesions [25–27]. Observations from our cohort suggest that sporotrichosis in children is more common than is often recognized, particularly in developing regions, and most often manifests as facial lesions. The cosmetic implications of this observation are particularly important, as scarring and disfigurement are the most common consequences of untreated sporotrichosis.

A history of trauma was absent in 90% of our patients, which is consistent with the observation that most cases (>70%) occurred in toddlers or students (and not in persons involved in manual labor). Indeed, only 7% of our adult patients were

<table>
<thead>
<tr>
<th>Variable, age group</th>
<th>1995</th>
<th>1996</th>
<th>1997</th>
<th>P</th>
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<tbody>
<tr>
<td>Population in Abancay*</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0–6</td>
<td>24,648</td>
<td>24,870</td>
<td>25,094</td>
<td></td>
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<tr>
<td>7–14</td>
<td>24,206</td>
<td>24,424</td>
<td>24,644</td>
<td></td>
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<tr>
<td>≥ 15</td>
<td>55,611</td>
<td>56,111</td>
<td>56,615</td>
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</tr>
<tr>
<td>Total</td>
<td>104,465</td>
<td>105,405</td>
<td>106,353</td>
<td></td>
</tr>
<tr>
<td>No. of persons with proven sporotrichosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0–6</td>
<td>18</td>
<td>17</td>
<td>15</td>
<td></td>
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<tr>
<td>7–14</td>
<td>18</td>
<td>14</td>
<td>23</td>
<td></td>
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<tr>
<td>≥ 15</td>
<td>14</td>
<td>32</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>63</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Incidence (no. of cases per 100,000 population)</td>
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<td></td>
<td></td>
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<tr>
<td>0–6</td>
<td>73</td>
<td>68</td>
<td>59</td>
<td>.85</td>
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<tr>
<td>7–14</td>
<td>74</td>
<td>57</td>
<td>93</td>
<td>.35</td>
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<tr>
<td>≥ 15</td>
<td>25</td>
<td>57</td>
<td>25</td>
<td>.005</td>
</tr>
<tr>
<td>Overall</td>
<td>48</td>
<td>60</td>
<td>49</td>
<td>.42</td>
</tr>
</tbody>
</table>

* Data from the Peruvian National Institute of Statistics and Informatics that were based on a growth rate of 0.9%.
farms, and the remainder were mostly housewives or military personnel or had sedentary occupations. It is of interest that a previous report from this area noted that less than one-half of the patients with sporotrichosis recalled an inoculation event [16].

Extracutaneous sporotrichosis is a well-recognized but uncommon complication of infection due to S. schenckii [28], affecting bones and soft tissue [29, 30], lungs [31], and rarely CNS [32]. This complication is particularly rare in children. On the basis of clinical parameters, there was a virtual absence of extracutaneous disease in this cohort. A similar observation was made by Lurie in 1963 [33]; of almost 3300 South African patients with sporotrichosis, only 5 developed clinically apparent extracutaneous involvement. This finding is in direct contrast with observations from several clinical trials in the United States, where up to one-half of patients enrolled had extracutaneous disease, especially osteoarticular and pulmonary involvement [34–36]. Some researchers have suggested that this disparity reflects regional differences in invasive potential among various strains of S. schenckii [4]. Indeed, Kwon-Chung [37] has suggested that thermotolerant S. schenckii strains that demonstrate an ability to grow on Sabouraud dextrose media at 37°C are more likely to cause lymphocutaneous disease and visceral organ involvement than are those strains that do not grow at 37°C. Other investigators have made similar observations [38, 39], but it has not been a consistent finding [40]. Previous strain analysis of isolates from Abancay suggests a single strain of S. schenckii [41]; however, neither thermotolerance studies nor other studies to determine optimal growth characteristics have been done.

Our observations concerning therapy confirm that when taken consistently, KI is quite effective therapy for cutaneous sporotrichosis [4, 42]. Indeed, almost all patients who completed KI therapy were cured after a median course of 12 weeks. Nonadherence, however, remains a significant problem among people in this region and affected >60% of patients in this cohort. Reasons for nonadherence to KI therapy include adverse effects, the need for frequent dosing, and the cost of therapy. We believe that the pattern of treatment described in this study probably reflects treatment patterns for sporotrichosis in most of the developing world: specifically, for treatment-adherent patients, KI is administered for 2–4 weeks after clearance of lesions; for patients with unresponsive or relapsing disease and patients intolerant to KI, ketoconazole is used as salvage therapy. In developing countries, ketoconazole is generally preferred over itraconazole because it is less expensive, even though itraconazole appears to be the oral azole of choice for treatment of cutaneous sporotrichosis, according to data from clinical trials [36, 43].

In summary, we have described 238 cases of cutaneous sporotrichosis from an area of the Peruvian highlands where S. schenckii is hyperendemic. In this retrospective study, no unusual exposure or activity could be closely associated with development of disease. The overall incidence of sporotrichosis varied between 48 and 60 cases per 100,000 persons, and among older children, the incidence approached 1 case per 1000 persons. The most common anatomic location was the face, and facial lesions were especially common in children. Extracutaneous disease was rare in this population. Clearly, sporotrichosis is an important mycosis in this region, and there is more to be learned about the regional natural history, epidemiology, and ecology of S. schenckii. The goal of disease prevention is of particular importance for this population, given the limited access to medical care and the lack of affordable therapy.

Acknowledgments

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References

17. Holgado W. Estudio de esporotricosis (Sporothrix schenckii) en el Centro...


