Endemic of Zoonotic Sporotrichosis

Profile of Cases in Children

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Background: Sporotrichosis in childhood is rare in most countries. Isolated cases and small outbreaks related to recreational activities or without identification of the transmission mechanism have been reported.

Methods: Series of case reports. The isolation of *Sporothrix schenckii* from exudates or fragments of lesions obtained from the patients was used as the criterion of inclusion in the study.

Results: A total of 81 cases of sporotrichosis in children younger than 15 years of age were diagnosed at the Evandro Chagas Research Institute, Fiocruz, Brazil, between 1998 and 2004. These cases are part of the endemic disease occurring in Rio de Janeiro related to contact with domestic cats. There was a predominance of girls in the 10–14 year age group. The most frequent clinical form was the cutaneouslymphatic form located on the upper limbs. Itraconazole was used as the first-choice treatment. Sixty-six patients were cured, 9 were lost to follow-up, and 6 had spontaneous regression of the lesions.

Conclusions: This is the largest series of childhood sporotrichosis with zoonotic transmission. The clinical presentation of sporotrichosis in children followed the same pattern of the disease in adults in this ongoing endemic.

Key Words: sporotrichosis, child, zoonosis, endemic, Brazil

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Sporotrichosis is a subacute or chronic mycosis caused, in most cases, by traumatic inoculation of the dimorphic fungus *Sporothrix schenckii*. The lesions are usually restricted to the skin, subcutaneous cellular tissue, and adjacent lymphatic vessels. In children, the most common clinical form is the localized cutaneous type, especially on the face.[1]

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The first case of sporotrichosis was reported by Schenck in 1898[2] and the second by Hoektoen and Perkins in 1900[3] in a 5-year-old boy who developed an ulcer and nodular lymphangitis after hurting his index finger with a hammer. Since then, isolated cases and small outbreaks among children, related to recreational activities or without identification of the transmission mechanism, have been reported. The largest series of childhood sporotrichosis was reported by Pappas et al[4] in Peru, in which 60% of the 238 cases described involved children less than 15 years of age, with no transmission mechanism being identified. In Brazil, the largest series was reported in Rio Grande do Sul where 122 cases were diagnosed between 1958 and 1997 in patients less than 20 years of age, including 42 younger than 10 years.[5,6]

Sporotrichosis is distributed worldwide, especially in tropical and subtropical zones. Classically, infection is associated with the handling of soil, plants, and organic matter contaminated with the fungus.[7,8] Zoonotic transmission has been sporadically described until the report of an epidemic in Rio de Janeiro, Brazil, related to contact with domestic cats with sporotrichosis.[9,10] Cats develop sporotrichosis characterized by lesions rich in parasites and often accompanied by severe manifestations and death.[10–12] Other animals have been reported as possible transmitters of the disease but without any significant zoonotic potential.

Between 1998 and 2004, 755 cases of human sporotrichosis were diagnosed at the Evandro Chagas Clinical Research Institute (IPEC), Fiocruz, Brazil. Of these, 81 were children younger than 15 years, a number representing the largest series of zoonotic sporotrichosis in children described in the literature.

PATIENTS AND METHODS

The study was approved by the Research Ethics Committee of Fiocruz. All patients attended the Infectious Diseases Outpatient Clinic of IPEC. After we obtained parental informed consent, the patients were subjected to clinical evaluation and collection of material from the lesions. All samples were submitted for routine mycological examination as follows: (1) direct microscopy of wet mount preparations with 4% sodium hydroxide; (2) seeding onto Sabouraud-dextrose agar and mycobiotic agar (difco), incubation at 25°C and observation during 4 weeks for fungal growth. Suspected isolates were subcultivated on potato-dextrose-agar medium (difco) at 25°C for macroscopic and microscopic morphologic

studies and dimorphism was demonstrated by conversion to the yeast-like form on BHI agar medium (Difco) at 37°C.

The isolation of *Sporothrix schenckii* from exudates or fragments of lesions obtained from the patients was used as the criterion of inclusion in the study.

Itraconazole 5 mg/kg/d was used as the first-choice treatment for children up to 20 kg body weight, and doses of 100 mg given once daily was used for children above this weight. Children unable to swallow capsules received potassium iodide, starting with 1 drop 3 times per day, which was increased from 1 drop per day to 10 drops 3 times per day. The medications were provided free of charge to all patients. After conclusion of treatment, the patients were followed up for 6 months to 1 year.

RESULTS

Patients and Demographic Data

Table 1 shows the main characteristics of the patients. Between 1998 and 2004, 81 cases of sporotrichosis were diagnosed in children younger than 15 years. The youngest child was 2 years old and the oldest was 14 years old. There was a predominance of girls (49 of 81, 60.5%), especially in the 10–14 year age group. The total male-to-female ratio was 1:1.5. All children older than 4 years of age were in school.

Transmission and Probable Source of Infection

The cases studied were from the metropolitan region of Rio de Janeiro, and 90% of the children had a cat with the same mycosis at home or in the neighborhood and played with these animals. Thirty-three (41%) of the 81 patients reported some type of injury, including the scratch or bite of a cat with sporotrichosis in 29 (36%) and diverse injuries in 4 (5%). Among the latter, 2 patients reported contact with a sick cat. Of the 48 (59%) children without a history of trauma, 42 (52%) had domiciliary contact with a cat with sporotrichosis, 5 (6%) used to play with soil or plants, and 1 (1%) presented no risk factor for acquisition of the disease. A cat was the probable source of infection in 73 (90%) of the 81 patients.

TABLE 1. Characteristics of 81 Children With Sporotrichosis

Variable	Patients
Gender	
Female	49 (61)*
Male	32 (40)
Age group	
0–4 yr	7 (9)
5–9 yr	28 (35)
10–14 yr	46 (57)
Municipality of residence	
Rio de Janeiro	38 (47)
Duque de Caxias	21 (26)
Nilópolis	6 (7)
Others	16 (20)
Clinical form	
Cutaneous-lymphatic	55 (68)
Fixed	20 (25)
Fixed + mucosal lesion	3 (4)
Widespread	2 (3)
Primary mucosal	1 (1)
Probable transmission	
Contact with a sick cat without injury	42 (52)
Scratch of a sick cat	24 (30)
Bite of a sick cat	5 (6)
Contact with soil or plants	5 (6)
Diverse injuries	4 (5)
Ignored	1 (1)
Treatment†	
Itraconazole	61 (81)
Potassium iodide	5 (7)
Lost to follow-up	9 (12)

*Number in parentheses, percent.
†n = 75. Six patients had spontaneous regression of the lesions.

Clinical Presentation

The duration of the disease until the patients sought medical care ranged from 1 to 16 weeks (median = 4) and the number of lesions ranged from 1 to 26 (median= 5). Fifty-five (68%) patients had the lymphocutaneous form (Fig. 1) and 20 (25%) had the localized form. Three (4%) patients with cutaneous lesions on the face also had mucosal involvement, including the nasal fossa in 1 and the conjunctiva in 2. Two (3%) patients had cutaneous lesions at multiple sites and 1 (1%) patient had only lesions in the conjunctival mucosa (Fig. 2). The lesions were most frequent on the upper limbs (40 of 81, 49%), followed by the face (17 of 81, 21%) (Fig. 3), lower limbs (9 of 81, 11%), and chest (7 of 81, 9%). Lesions were also found on the back, abdomen, and neck. Lesion morphology was variable and included nodules, tubercles, papules, pustules, gummas, ulcers, ulcerative-vegetative lesions, and verrucous lesions, accompanied or not by lymphangitis. Fixed lesions manifested as isolated papules or nodules progressing to gummas and ulceration or verrucous plaques. Mucosal lesions were initially granulomatous and acquired a vegetative aspect with or without ulceration during the course of the disease.

No correlation was observed between the site of the lesion and the clinical form: half the cases with lesions on the face also had nodular lymphangitis in the neck. Likewise, fixed lesions were identified on the upper limbs, especially the arms.

The most important differential diagnoses in these patients were impetigo, bacterial abscess, and leishmaniasis. The Montenegro skin test, done in 34 patients, was positive in 11 (32%) (induration larger than 5 mm).

Associated signs and symptoms included fever at the onset of clinical symptoms in 8 (10%) patients, arthralgia without signs of arthritis in 6 (7%), and erythema nodosum in 3 (4%). Only 1 (1%) patient had secondary infection of the lesions. No significant comorbidities were identified.

Laboratory Diagnosis and Complementary Examinations

The etiologic diagnosis was made based on the isolation of the fungus from lesion secretions or biopsy fragments in all cases. A biopsy was obtained from 8 patients: 2 had a nonspecific inflammatory process and 6 had a chronic granulomatous process, with fungal elements being visualized in one. Among the 3 patients with a clinical diagnosis of erythema nodosum, this diagnosis was confirmed by histopathological analysis in one.

Before the beginning of treatment, 10 of 74 patients tested had microcytic anemia related to iron deficiency. Forty-two patients agreed to hematologic evaluation after the

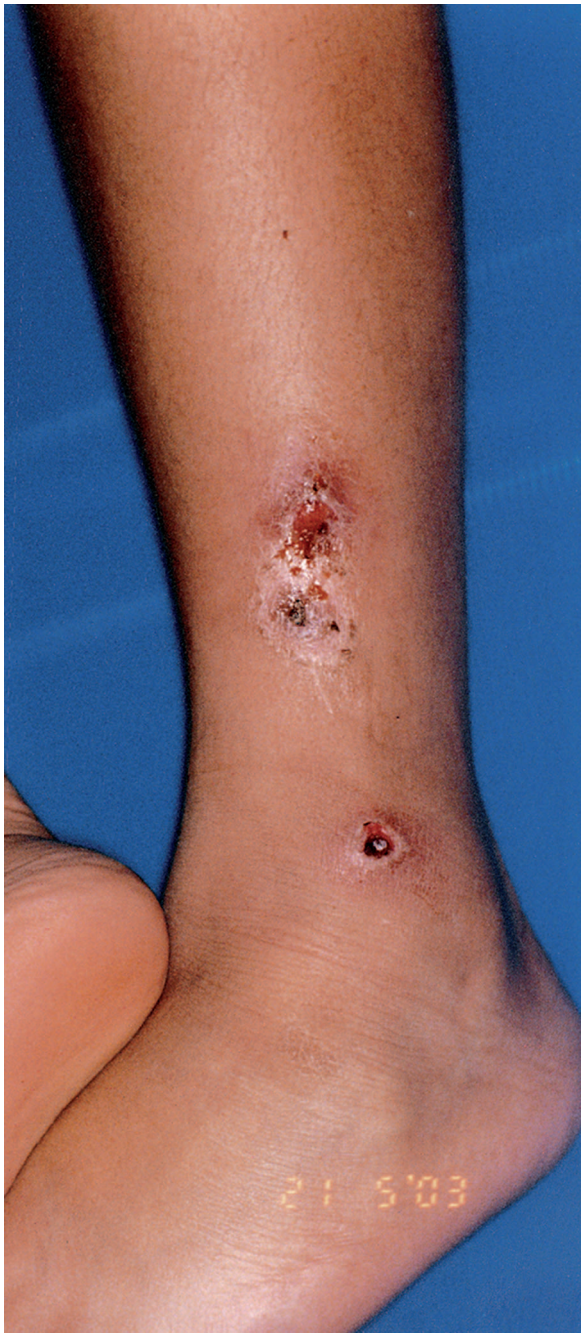

FIGURE 1. Lymphocutaneous form—1 month after treatment with itraconazole.

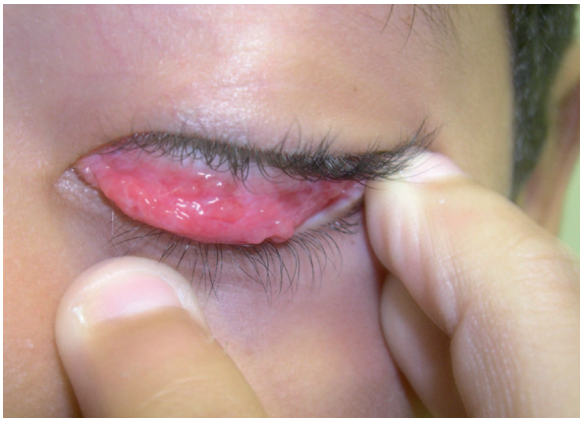

FIGURE 2. Granulomatous lesion on the conjunctiva before starting treatment.

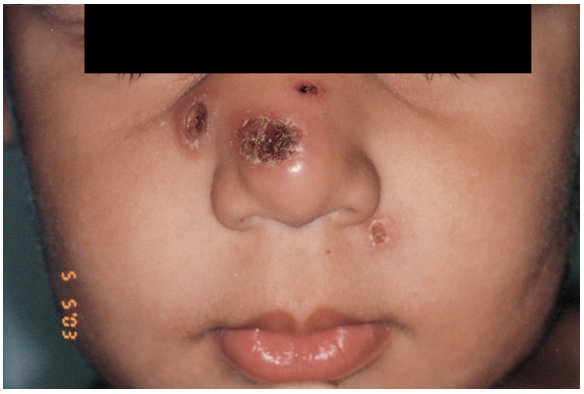

FIGURE 3. Multiple lesions on the face.

end of treatment, with anemia persisting in 7. No other abnormalities were identified.

Treatment and Course of the Disease

Spontaneous regression of the lesions occurred in 6 (7%) patients and treatment was initiated in 75 (93%): 55 received 100 mg itraconazole/d, 4 received 50 mg itraconazole/d, 2 initially received 100 mg itraconazole/d, which was then increased to 200 mg/d, and 5 were treated with potassium iodide. The dosage increase in the 2 patients was because of recurrence of the initial lesion in 1 and to the observation of active lesions after 12 weeks of treatment with 100 mg/d in the other. Six weeks after the dosage increase, the lesions were healed. Of the 75 patients undergoing treatment, 66 (88%) were cured within a period of 4–18 weeks (median = 12) and 9 (12.0%) were lost to follow-up. Among the latter, potassium iodide had been prescribed to 1 and itraconazole to the others. Spontaneous regression occurred in the 6 cases within 6–24 weeks after the onset of the disease.

Itraconazole and potassium iodide were well tolerated and none of the children had to interrupt the medication because of adverse effects.

During follow-up, other than the patient who had to be retreated because of lesion reactivation 10 months after initial cure, no recurrence was observed among the remaining patients, even those who reported to still have contact with sick cats.

With respect to the use of other medications, 12 (15%) patients had been previously seen at another health service and had received antibiotics, mainly cephalexin alone (n = 8) or in combination with another antibiotic (n = 3). In the case of the child with the conjunctival mucosal form, ciprofloxacin eyedrops had been prescribed for the diagnosis of dacryocystitis (Fig. 4).

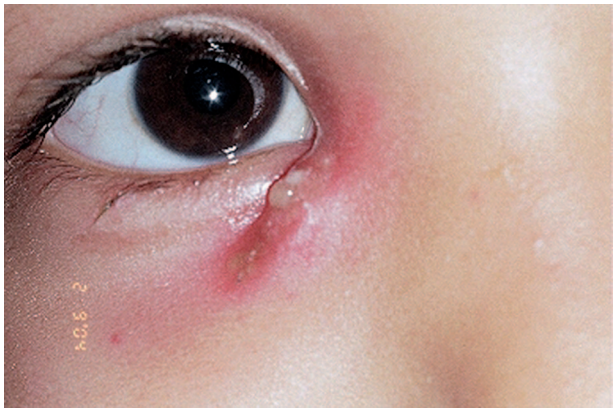

FIGURE 4. Sporotrichosis presenting as dacryocystitis.

DISCUSSION

Sporotrichosis in childhood has been considered to be rare, possibly because of the lower exposure to objects that permit introduction of the fungus into the skin.[8] Except for Peru where 60% of the cases involve children, adults account for the main proportion of cases in most endemic areas.[1,4,13]

The first 2 cases of human sporotrichosis related to contact with sick cats were diagnosed at IPEC between 1994 and 1997. After 1998, the number of cases showed an extraordinary increase, reaching 755 in December 2004. Although the frequency of patients younger than 15 years has been low compared with the total number of patients seen (11%), this is the largest series of childhood sporotrichosis with zoonotic transmission. The profile of the disease in our patients follows the pattern observed in adults (ie, a predominance of females and of the cutaneous-lymphatic form). Other series have indicated a predominance of school age boys, probably because of the preference of this age and gender for outside activities.[14–16]

In contrast to the present study, the fixed cutaneous form has been the most frequent in the pediatric group in most endemic areas.[4,17,18] It is possible that the route of transmission influences these clinical manifestations.

Similar to other reports,[4] more than half the children did not remember any injury. Because the lesions of cats are rich in parasites,[10] transmission of the disease may occur even when the skin is intact, a fact that is more evident in patients with lesions on the face. According to Da Rosa,[1] the thin and delicate skin of the face of children may favor the development of lesions even in the absence of trauma. Another hypothesis is that small injuries resulting from playing with may go unnoticed but are sufficient to facilitate inoculation of the fungus.

In the present population, sporotrichosis lesions were identified at unusual sites such as the conjunctiva and nasal mucosa. Self-inoculation or contact with a cat close to the face may have facilitated these forms of the disease. Erythema nodosum and arthralgia might be manifestations of hypersensitivity to repeated exposure to the fungus as suggested by Gutierrez Galhardo et al.[19]

The lesion pleomorphism observed emphasizes the importance of a differential diagnosis, especially with impetigo, bacterial abscess and leishmaniasis. On the basis of the present results and the findings reported by other investigators[18,20] sporotrichosis should be included in the differential diagnosis of localized, papular, crusty, papuloulcerative or nodular lesions that do not respond to antibiotic therapy.

The fact that more than 30% of the patients had a positive Montenegro skin test indicates the possibility of cross-reactivity or previous contact with leishmania. Overlapping areas of the 2 diseases in this region of Rio de Janeiro has been demonstrated in a previous study on this epidemic.[21]

Potassium iodide has been used for many years as the first-choice treatment of sporotrichosis and continues to be the treatment of choice in developing countries. In the present series, treatment was provided free of charge to all patients and the response to treatment with itraconazole was satisfactory, with no significant adverse effects being reported.

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