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Canine sporotrichosis in Rio de Janeiro, Brazil: clinical presentation, laboratory diagnosis and therapeutic response in 44 cases (1998–2003)

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A sporotichosis epidemic involving forty-four dogs in the Metropolitan area of Rio de Janeiro is described. Solitary skin lesions were noted in 18 dogs (40.9%), 2–4 such lesions were observed in 17 animals (38.6%), and nine (20.5%) animals had five or more lesions. Twenty-five (56.8%) animals had single ulcerated skin lesions on the nose and nine (20.5%) showed nasal mucosal involvement (three of which also has a skin lesion). Respiratory symptoms were observed in 17 (38.6%) dogs and were found to be the most common extracutaneous signs of infection. Anemia, leukocytosis with neutrophilia, hypoalbuminemia and hyperglobulinemia were the most frequent hematological abnormalities. Histopathological analysis of skin biopsies in most cases revealed granulomatous reactions characterized by histiocytic hyperplasia and neutrophil infiltration. Yeast-like cells were observed in seven (16.7%) of 42 dogs examined histologically. During the study, eight (18.2%) animals were lost to follow-up and three (6.8%) were submitted to euthanasia. Of the remaining 33 dogs, five (15.2%) presented spontaneous regression of the lesions, 26 (78.8%) were cured after treatment, and two (6%) continue to be treated. The present cases indicate that many dogs with sporotrichosis respond well to treatment and in a few dogs, the disease may be self-limiting.

Keywords sporotrichosis, *Sporothrix schenckii*, dogs, diagnosis, drug therapy

Introduction

Sporotrichosis, a worldwide subcutaneous mycosis caused by the dimorphic fungus *Sporothrix schenckii*, affects humans and animals. The fungus grows in moist soil rich in decaying vegetation, sphagnum moss, grass and bark of trees. Usually, *S. schenckii* is introduced via skin trauma and occasionally by animal injury. The disease develops with the formation of localized skin lesions and ascending nodular lymphangitis [1]. In cats, infection occurs both through traumatic inoculation and inhalation routes [2].

In many reports canine sporotrichosis was acquired during hunting activities with possible introduction of the organism through thorns or wood splinters [3].

Experimental susceptibility of dogs to *S. schenckii* has been demonstrated by Schenck [4], and naturally acquired disease has been described [5]. Sporotrichosis is rare in dogs and is usually characterized by multiple cutaneous and subcutaneous lesions on the head, ears

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and thorax. However, rare osteoarticular and disseminated forms have been noted in the literature [6,7]. Until the 1990s, the largest series of cases involving dogs consisted of only 12 animals [8]. Since 1998, a sporotrichosis epidemic affecting domestic pets and humans has been observed in Rio de Janeiro, Brazil [2,9,10]. The objectives of the present study were to describe the epidemiological, clinical, laboratory and therapeutic aspects of canine sporotrichosis from this epidemic.

Materials and methods

The isolation of *S. schenckii* from exudates and tissue fragments of lesions collected from the dogs potentially involved in the epidemic was used as the criterion for inclusion of the animals in the study. All dogs belonged to private owners and were treated at the Zoonosis Service of the Evandro Chagas Clinical Research Institute – Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil, between July 1998 and October 2003. The study protocol was approved by the Institutional Ethics Committee of the Center for Biological Evaluation and Care of Research Animals at Fiocruz.

The dogs were submitted for general clinical and dermatological examinations. Biological samples were collected on admission, i.e., surface secretions obtained with swabs from exudative lesions or draining tracts and punch skin biopsy specimens recovered from the border of active lesions. Tissue fragments were macerated, with a portion of each sample used for direct microscopy with 4% sodium hydroxide and another portion inoculated onto Sabouraud-dextrose agar and mycobiotic agar (Difco) to be incubated at 25°C. The macroscopic and microscopic morphologies of colonies suspected to be *S. schenckii* were studied on potato-dextrose agar (Difco) at 25°C and conversion to the yeast-like form was performed on brain heart infusion agar (Difco) at 37°C. Additionally, punch skin biopsy specimens were submitted for histopathological examination [11]. Blood samples were collected for routine serum chemistry and hematological examination.

According to the availability of antifungal drugs provided free of charge by our research center, dogs were assigned to one of the following therapeutic regimens: 5–10 mg/kg itraconazole [2.25–4.5 mg/lb], by mouth every 24 h or 5–10 mg/kg ketoconazole [2.25–4.5 mg/lb], by mouth every 24 h. The owners orally administered all drugs at home. After complete healing of the lesions, the dogs were clinically re-evaluated, the treatment was discontinued and an annual follow-up check was recommended.

Results

During the study period, sporotrichosis was diagnosed in 44 dogs. The animals came from the city of Rio de Janeiro and neighboring municipalities. Twenty-three (52.3%) dogs were males and 21 (47.7%) were females, including one that was pregnant. Ages ranged from 6 months to 12 years (median = 4 years). Twenty-three (52.3%) dogs were mongrels, 14 (31.8%) were of the Toy breed (poodle and miniature pincher), 4 (9.1%) were German shepherds and 3 (6.8%) were of other breeds (Dalmatinas, Cocker Spaniels, Labrador retrivers). Thirty-seven (84.1%) dogs and 15 of their respective owners with sporotrichosis had contact with cats with confirmed sporotrichosis. An unrelated traumatic injury preceding the symptoms was reported for 2 (4.5%) dogs, and no suggestive epidemiological history was obtained for 5 (11.4%).

The duration of dermatological lesions ranged from 2 to 48 weeks (median = 6 weeks), with ulcers and nodules being the most common skin lesions. The firm subcutaneous nodules slowly softened, generally draining purulent or seropurulent material and progressing to form exudative ulcers with slightly elevated well-defined borders and a granulomatous fundus.

Solitary skin lesions were noted in 18 dogs (40.9%), 2–4 such lesions were observed in 17 (38.6%) animals, and 9 (20.5%) animals had 5 or more lesions (Fig. 1). The skin lesions were most frequently observed on the nose ($n = 25$, 56.8%), followed by the forelimbs ($n = 13$, 29.5%). Nasal mucosal involvement was observed in 9 (20.5%) animals (3 of which also showed a single skin lesion) and was the only affected site in 3 (6.8%) cases (Fig. 2).

Three (6.8%) dogs presented lymphangitis (Fig. 3) and 19 (43.2%) had regional lymphadenitis.

Fig. 1 Photograph of a dog with multiple skin lesions on the hind limbs, on the flank and on the head.

Fig. 2 Photograph of a dog with skin ulcers on the nose and destruction of the nostrils.

While thirty-eight (86.4%) dogs were in good general health, 13 of them had extracutaneous symptoms of sporotrichosis. The extractuaneous signs observed in a total of 18 (40.9%) of the dogs are shown, in order of increasing frequency, in Fig. 4.

While *S. schenckii* was isolated from all 44 dogs, it was recovered from exudate specimens of 25 of the 33 dogs (75.8%) from which they were collected. Far higher rates of isolation of the etiologic agent were observed with tissue fragments, i.e., 41/42 or 97.6% of samples. Swabs used to obtain material from the surfaces of nasal and oral lesions were positive for *S. schenckii* in 7/12 (58.3%) and 1/10 (10%) dogs, respectively. Direct microscopy of wet mounts of secretions and tissue fragments collected from the lesions and prepared with 4% sodium hydroxide revealed small round to oval yeast-like elements in 6 (13.6%) of the 44 samples tested.

Fig. 3 Photograph of a dog with nodular lymphangitis on the hind limbs.

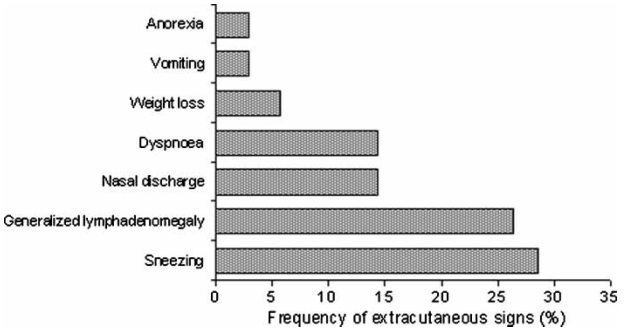

Fig. 4 Frequency of extracutaneous clinical signs in 18 dogs with sporotrichosis.

Histopathological examination of the skin biopsies specimens from 42 dogs revealed a chronic inflammatory process in all of them and granuloma formation in 19 (45.2%) animals. The fungus was visualized in tissue specimens in 16.7% of cases ($n=7$) but no asteroid bodies were observed.

Fig. 5 shows the frequency of hematological abnormalities in 42 dogs with complete blood counts.

Routine biochemical examination was performed on 34 dogs. A high concentration of total plasma protein (range 5.4–7.1 g/dl) was observed in 11 (32.4%) dogs, hypoalbuminemia (<2.6 g/dl) in 21 (61.8%), and hyperglobulinemia (>4.4 g/dl) in 18 (52.9%). Other biochemical abnormalities included high serum alkaline phosphatase activity (>156 U/l) in 4 (11.8%) animals, high serum alanine aminotransferase (>80 U/l) in 3 (8.8%), and high serum aspartate aminotransferase (>40 U/l) in 2 (5.9%).

During the study, 8 animals were lost to follow-up and 3 were euthanized upon request of the owner. Of the remaining 33 dogs, 5 (15.2%) presented spontaneous regression of the lesions, 26 (78.8%) were cured after treatment, and 2 (6%) continue to be treated. One was treated for 11 months with itraconazole, received no drug for a period of two months due to the inability to obtain this antifungal agent, and then was started on ketoconazole for an additional 3 months. The second dog was treated for 17 months with ketoa and then switched, without interruption, to itraconazole, for an additional 4 months.

Of the 26 dogs that completed treatment, 22 (84.6%) received only one therapeutic regimen, i.e., 8 (36.3%) with itraconazole and 14 (63.7%) with ketoconazole. The other 4 dogs were either switched from itraconazole to ketoconazole, or visa versa, due to unavailability to the compound in the pharmacy. Two dogs sustained a period of two months without any therapy.

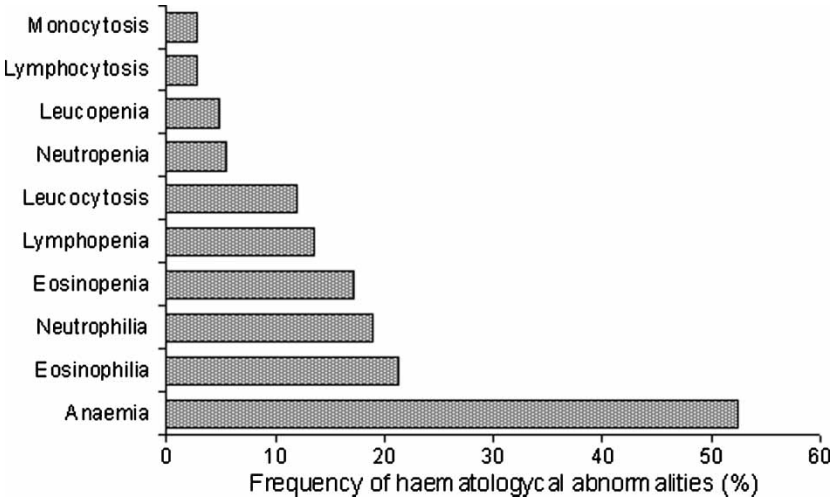

Fig. 5 Frequency hematological abnormalities in 42 dogs with sporotrichosis.

Duration of treatment ranged from 2 to 5 months (median = 2.5 months) with itraconazole, 2 to 15 months (median = 3.5 months) with ketoconazole, and from 5 to 10 months (median = 9 months) for dogs treated with two consecutive regimens. Adverse effects were observed in 3 (16.7%) dogs that received itraconazole, i.e., 2 animals developed anorexia, vomiting, diarrhea and elevated hepatic enzyme levels, and one developed vasculitis of the face. One pregnant female dog in poor general health with multiple lesions and destruction of the nostrils aborted one week after the beginning of itraconazole treatment. Treatment was continued but the animal was lost to follow-up after 4 months. However the drug had caused by this time partial regression of the lesions. She was seen 8 months later due to the reactivation of her lesions.

Discussion

In the present study, naturally acquired sporotrichosis resulting from an epidemic outbreak in Rio de Janeiro was diagnosed in 44 dogs over a period of 5 years. Present knowledge about canine sporotrichosis is derived from a few reports of isolated cases. The large number of dogs with sporotrichosis observed in this epidemic might be attributed to cats acting as the main source of infection [2,10]. In the present study, sporotrichosis in cats preceded its occurrence among their owners and dogs with which they had contact. The number of case may actually be an underestimate due in part to the fact that their owners sought specialized care at reference centers. In addition, the majority of infected dogs probably didn't have systemic manifestations, and cutaneous lesions may have resolved without treatment.

The clinical aspect and location of the skin lesions were similar to those described by other investigators in that the age of the animals ranged from 6 months to 12 years and lesions were preferentially located on the head [3]. The cutaneous lymphatic form was only observed in 3 dogs, in agreement with other investigators who reported cases of canine sporotrichosis without apparent lymphatic involvement [7,8,12]. Although the cutaneous lymphatic form is the most frequent clinical presentation in humans, the same does not apply to cats [2] and, possibly, as noted in this investigation, to dogs.

The skin of the nose was affected in 25 (56.8%) cases and nasal mucosal involvement was observed in 9 (20.5%), with isolated mucosal lesions being detected in 3 (6.8%) cases. Although Moriello *et al*. [7] described a dog with nasal and cutaneous lymphatic sporotrichosis, we did not find any report in the literature regarding primary mucosal involvement in dogs. It is likely that the habit of dogs to sniff their environment is related to acquisition of the fungus through the nose. The presence of cats in the homes of humans and dogs with sporotrichosis was observed in 82.9% of cases in this investigation [10]. Since *S. schenckii* was isolated from the mouth and nails of cats with sporotrichosis acquired in this epidemic [13,14], the high frequency of lesions on the muzzle of dogs may be explained by injuries caused by cats that inhabit the same household environments. In the present study, *S. schenckii* was isolated from swabs used to collect samples from the surfaces of lesions located on the nasal mucosa of 7 dogs and on the oral mucosa of an 8th dog. However, the fungus was not isolated from oral swabs collected from dogs without mucosal lesions.

The diagnosis of sporotrichosis is usually made by isolating *S. schenckii* from aspirated material, swabs or biopsy specimens obtained from active lesions. Occasionally, the diagnosis is obtained by the demonstration of suggestive fungal elements in histological sections. In the present study, rare yeast-like forms were observed in 16.7% of histological sections, a finding similar to that reported in other studies [7]. Granuloma formation was observed in 45.2% of cases, similar to what was observed in humans cases in this epidemic [10]. One should include *Cryptococcus neoformans*, *Histoplasma capsulatum*, and *Blastomyces dermatitidis* in the differential diagnosis,when examining these types of specimens. Protozoans similar in size and shape, such as *Leishmania* spp., *Toxoplasma gondii*, *Neospora*, and *Sarcocystis*, can also be confused upon the examination of HE-stained histopathological sections. However, the definitive diagnosis of sporotrichosis requires the isolation and identification of the fungus in culture.

The hematological and biochemical alterations observed were nonspecific and consistent with infectious diseases, similar to observations made in cats with sporotrichosis [2].

Although there are no reports in the literature regarding spontaneous cure in dogs, this event was observed in 5 animals which remained lesion-free for 1–4 years on follow-up examinations. In addition to the similarity of ulcerated and histopathological lesions between sporotrichosis and American cutaneous leishmaniasis, spontaneous cure can be an additional confounding factor in the differential diagnosis between these two endemic diseases when the identity of the etiologic agent has not been established [15]. The criteria used for treatment discontinuation was complete healing of the lesions, with clinical cure observed with both antifungal regimens. Other investigators reported success with the use of iodine, ketoconazole and itraconazole [7,12,16].

The present results suggest that sporotrichosis in dogs has a good prognosis and is easily treated, in contrast to cats in which the disease is usually severe, often systemic and difficult to treat [2]. In the case of the pregnant dog, it is possible that the animal's nutritional status and her pregnancy contributed to the aggravation of sporotrichosis.

Adverse effects of itraconazole treatment such as anorexia, vomiting, diarrhea and elevated hepatic enzyme levels were observed in 2 cases. The development of vasculitis as a result of intraconazole therapy has been reported by other authors [7,17,18].

Some investigators suggest that cats are the most important vector in the transmission of sporotrichosis [1,3,19]. Dogs are probably not directly involved in the transmission of sporotrichosis in view of the scarcity of viable fungal elements in lesions and the absence of *S. schenckii* in the oral cavity. In addition, there were no reports of human cases associated with transmission from dogs in this epidemic in Rio de Janeiro [10]. However, as with other infectious diseases, dogs with sporotrichosis should be handled with care since we cannot to determine their potential public health risk.

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