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ORIGINAL REPORT

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Ocular lesions in cats diagnosed with systemic sporotrichosis

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Abstract

Objectives: To describe the most common ocular lesions and demonstrate the frequency of ophthalmic involvement in a group of cats with systemic sporotrichosis.

Animals Studied: Two hundred seventy-four cats diagnosed with systemic sporotrichosis. The inclusion criteria included previous positive cytopathological examination, histopathological examination, or fungal culture.

Procedures: In a prospective case–control study, 274 cats diagnosed with systemic sporotrichosis underwent ophthalmic evaluation and received treatment for systemic sporotrichosis. Of these animals, 63 had ocular abnormalities which were recorded, and conjunctivitis was scored from 0 to 5. Diagnostic techniques utilized included fungal culture, as well as cytopathological (10 eyes; 10 cats), and histopathological examination of the palpebral conjunctiva and eyes (2 eyes).

Results: Cytopathological and histopathological examination of the conjunctiva, as well as fungal culture, proved to be important tests for the detection of *Sporothrix sp*. Five cats without the evidence of ophthalmic abnormalities also had a positive fungal culture. The identified ocular lesions in animals with systemic sporotrichosis included increased serous discharge (79 eyes; 53 cats), blepharoconjunctivitis (33 eyes; 25 cats), conjunctivitis (39 eyes, 20 cats), blepharitis (9 eyes; 8 cats), uveitis (5 eyes; 3 cats), and Florida keratopathy-like lesions (2 eyes; 1 cat).

Conclusion: Sporotrichosis should be considered a differential diagnosis for conjunctivitis and blepharoconjunctivitis, especially in endemic areas. Fungal culture and cytopathology of ocular discharge and histopathological examinations of the conjunctiva are important for the diagnosis of ophthalmic sporotrichosis, although not all cats underwent laboratory testing in this study. Ocular discharge could be a source of contagion transmission.

KEYWORDS

blepharitis, conjunctival swabs, conjunctivitis, feline blepharoconjunctivitis, fungal culture, sporotrichosis

1 | INTRODUCTION

Sporotrichosis is a subcutaneous mycosis caused by dimorphic fungi of the genus *Sporothrix* spp.[1] Currently, at least six clinically important species comprise the *Sporothrix schenkii* Complex.[2] In Brazil, the most important species is the *Sporothrix* brasiliensis[3,4,5,6]. This fungal complex has been isolated from a large variety of living organisms, including seaweed, insects, birds, reptiles, iguanas, camels, chimpanzees, dogs, armadillos, cattle, horses, donkeys, rodents, and humans.[4] However, the domestic cat (*Felis catus*) is the most susceptible species and is the primary cause of transmission in urban outbreaks.[3] Feline disease typically occurs from contamination of cutaneous wounds, especially bites and scratches from fights with other cats, with fungal propagules (usually spores) from organic matter or exudate, secretions, and aerosols.[5] The disease is zoonotic, and human sporotrichosis has been documented by contact with infected cats after bites and scratches or exudate contamination, and rarely with contaminated plants.[4,7] Human cases are usually lymphocutaneus, whereas cats mainly develop disseminated cutaneous disease. However, feline sporotrichosis can also cause extracutaneous manifestations such as respiratory or ocular disease and systemic signs such as lethargy and anorexia principally in immunocompromised animals.[4]

The primary ophthalmic manifestation of sporotrichosis in both cats and humans is granulomatous conjunctivitis, which has been poorly characterized to date.[8–11] Nevertheless, in most cases, dermatologic and respiratory manifestations are very severe, overlapping the more discrete ocular signs, the latter of which may become a lower treatment priority in some clinical situations. The main purpose of this study is to characterize the ocular lesions caused by sporotrichosis in cats with cutaneous lesions. Providing a clear clinical characterization of the ophthalmic manifestations of sporotrichosis will contribute to a better understanding of the disease pathogenesis and introduce the disease as an important differential diagnosis for conjunctivitis in cats living in endemic areas, something that is currently lacking in the literature. Additionally, knowing the spectrum of ophthalmic manifestations may result in better recognition of ophthalmic disease and improve directed treatment.

2 | MATERIALS AND METHODS

2.1 | Data collection and animal selection

This study was conducted at the Pontifical Catholic University of Paraná (PUCPR) and at the Federal University of Paraná (UFPR), between 2019 and 2020. The patients were seen at PUCPR. To assess the clinical and epidemiological profile of the studied population, a standard form was designed to record individual information of each cat with systemic sporotrichosis. Standardized questions consisted of sex, breed, reproductive status, habitat, possible contacting animals, affected owners, previous treatments, and examinations. All procedures performed in the study were in accordance with the ARVO Statement for Use of Animals in Ophthalmic Vision and Research. PUCPR's Research Ethics Committee (CEUA-PUCPR) approved the investigation under certificate #02060.

In a prospective case–control study, cats with ulcerative or nodular skin lesions, conjunctivitis, and nodules on the nasal bridge were forwarded by the zoonosis control center of the Curitiba to the attendant service for sporotrichosis at the veterinary school clinic of PUCPR. Only cats with a diagnosis of systemic sporotrichosis were included in the study, regardless of sex, breed, or age group. The inclusion criteria included a positive result for sporotrichosis on cytology, histopathology, and/or fungal culture from dermatologic or nasal lesions concomitantly with eye injuries, or from ophthalmic lesions alone. During the investigation period, 274 cats with systemic sporotrichosis were evaluated. The diagnosis was achieved after association of the following factors: anamnesis, clinical examination, visualization of fungal yeasts in the cytological or histopathological examination, and isolation and microbiological identification of *Sporothrix* spp. in a specific fungal culture medium. Sample collection was either of exudate from skin lesions by swab (for the fungal culture and cytological examination) or imprint (for the cytological examination) and a skin biopsy of nodular lesions (for the histopathological examination). Cats with ocular or respiratory injuries without dermatologic lesions were tested by conjunctival or nasal swabs, or histopathological examination (palpebral conjunctiva), to confirm the diagnosis of ocular and respiratory sporotrichosis.

2.2 | Clinical classification of cutaneous and ophthalmic abnormalities

All cats underwent detailed clinical examination. Cutaneous lesions were classified as (1) fixed cutaneous (a single lesion, generally restricted to the fungal inoculation point), (2) lymphocutaneous (skin lesions were contiguous to the lymphatic pathway and associated with lymphangitis and regional lymphadenitis), or (3) disseminated cutaneous (multifocal or generalized ulcerative-gummy lesions). Ophthalmic and respiratory abnormalities were considered extracutaneous lesions, recorded following the airway examination, which sought to observe the

presence of nodules or tumors on the nasal bridge, facial deformity, nodules in the nasal cavity, abnormal respiratory sounds, increased serous ocular discharge, sneezing, dyspnea, and tachypnea. In addition, all selected cats underwent ophthalmic evaluation, with neuro-ophthalmic evaluation through direct and consensual pupillary light reflex, dazzle reflex, and menace response performed with a 3.5 V Finoff transilluminator with a halogen lamp (Welch Allyn®, Skaneateles Falls). Slit-lamp evaluation (Hawk-Eye, Dioptrix,) and corneal staining with fluorescein and lissamine green strips (Drogavet), tonometry using the Tono-pen tonometer (Mentor Ophthalmics Inc, Norwell), and funduscopy by indirect ophthalmoscopy (Welch Allyn®, Skaneateles Falls,) after pharmacological mydriasis with 1% tropicamide (Mydriacyl®, Novartis®,) were also performed.

Any lesion of the eyes or adnexa was considered as an ophthalmic disease. The signs of conjunctivitis were conjunctival hyperemia (mild, moderate, or severe), chemosis, presence of conjunctival granuloma with or without increased serous ocular discharge, and the presence of lymphoid follicles. Conjunctivitis with or without blepharitis (blepharoconjunctivitis) was staged from 0 to 5 according to HARTMANN et al. (2010)[12] (Table 1).

2.3 | Diagnostic testing

Samples were collected from the inferior conjunctival fornix of the left eye of the twenty animals (10 with ocular abnormalities and 10 without ocular lesions) using conjunctival swabs for cytological examination. After collection, the sample was distributed on a glass slide, stained by the Romanowski method with rapid Panoptico (Laborclin), and analyzed under an optical microscope with 40X and 100X objectives for yeast counting and evaluation of the inflammatory infiltrate.

A second swab of the left eye was collected from the same animals (10 with ocular abnormalities, and 10 without ocular abnormalities) for fungal culture. Swab material was incubated in Sabouraud dextrose agar with chloramphenicol (0.05 g/L) for 5 to 7 days at 25°C to visualize the mycelial phase, followed by incubation in brain-heart infusion agar at 37°C to identify the yeasts. Identification of the mycelial phase was determined by the color change of the colonies and the observation of this phase under optical microscopy using the acetate tape prep method and staining with cotton-blue lactophenol. Diagnosis was confirmed by observing septate hyphae with small ovoid conidia in a 100X objective lens.[13] A small number of animals was selected from the cytological examination and fungal culture because of the difficult handling of the sick cats and staff training.

Among those 10 animals tested with ocular abnormalities, 2 animals with a conjunctivitis score of 4/5 were subjected to an incisional biopsy. Using a 2 mm biopsy punch, the right lower palpebral conjunctiva was collected following an intramuscular injection of dexmedetomidine (10 mcg/kg), ketamine (3 mg/kg), methadone (0.3 mg/kg), and midazolam (0.15 mg/kg) in the semi-tendinous muscle of the right thigh. Two other animals with a score of 4 were submitted to bilateral *postmortem* enucleation, with biopsy material stored in 10% formalin, embedded in paraffin, and then submitted to serial sections of 5 μm with a microtome. The slides were stained with periodic acid-Schiff stain (PAS) and hematoxylin–eosin (H&E)[14] and evaluated by optical microscopy using 40X and 100X objectives. Unfortunately, not all of the cats with ocular abnormalities were tested by laboratory techniques due to financial constraints.

2.4 | Treatment

All cats with a definitive systemic sporotrichosis diagnosis were treated with oral itraconazole every 24 h at a dose of 50 mg/animal in cats weighing 1–3 kg or 100 mg/animal

TABLE 1 Staging of sporotrichotic granulomatous conjunctivitis/ blepharoconjunctivitis by global score

Score	Conjunctivitis/ blepharoconjunctivitis classification
0	No signs of conjunctivitis
1	Mild conjunctival hyperemia associated with mild chemosis with or without epiphora
2	Moderate conjunctival hyperemia and chemosis, with or without epiphora
3	Conjunctival hyperemia and intense chemosis, with the onset of nodular or granulomatous appearance with or without epiphora
4	Intense conjunctival hyperemia and chemosis, with an appearance of a clear nodular or conjunctival granuloma with or without epiphora or association with lymphoid follicles
5	Severe conjunctivitis with tumoral appearance and eyelid margin deformation

Note: Adapted from Hartmann et al. (2010)[12]

in cats weighing >3 kg and oral potassium iodide at a dose of 2.5–5 mg/kg every 24 h. Animals diagnosed with severe conjunctivitis (scored 4–5), received in addition to previous treatments a single application of 0.5 ml intralesional amphotericin b at a concentration of 5 mg/mL by insulin needle under the same sedation protocol as used for biopsy.

2.5 | Statistical analyzes

Descriptive statistics were performed with StatView (SAS Institute,). Specificity, predictive value, and sensitivity calculations were performed using GraphpadQuickCalcs statistical software (Graphpad Software Inc.,).

3 | RESULTS

Between 2018 and 2020, 274 cats with sporotrichosis were evaluated at SVC-PUCPR for ophthalmic signs. Of these, seven animals (2.55%) were Siamese, three (1.09%) were Persian, and 264 (96.35%) were mixed breed. Two hundred and twenty-one (80.65%) were males and 53 (19.35%) were females. One hundred and eighty-three cats (66.79%) were intact and 91 (33.21%) were spayed or neutered. The mean age of the population was 34.02 months, with a minimum age of three and a maximum of 156 months.

Ophthalmic lesions were found in 63 out of 274 cats (22.99%) definitively diagnosed with systemic sporotrichosis. Among those cats diagnosed with ophthalmic signs, 62 (98.41%) were mixed breed and one cat (1.59%) was a Persian. Forty-three (68.25%) were males and 20 (31.75%) were females, 10 cats (15.87%) were spayed or neutered, and 53 (84.13%) were intact. The average age was 27.32 ± 15.82 months, with a minimum age of 3 months and a maximum of 144 months.

Disseminated cutaneous sporotrichoses were identified in 211 animals (77.01%). Forty-four cats (16.06%) had focal cutaneous lesions, five cats (1.82%) had lymphocutaneous disease, and 148 (54.01%) had extracutaneous lesions (respiratory or ophthalmic). Among cats with ophthalmic lesions, disseminated sporotrichosis was documented in 60 animals (95.24%), and 61 animals (96.83%) had respiratory signs compared with only two (3.17%) with exclusively ophthalmic abnormalities. Ophthalmic lesions included increased serous ocular discharge in 53 animals (84.13%; 79 eyes) of which 27 had unilateral signs (50.94%) and 26 had bilateral signs (49.06%), blepharoconjunctivitis in 25 (39.68%; 33 eyes) of which 17 had unilateral signs (68%) and 8 had bilateral signs (32%), conjunctivitis in 20 animals (31.74%; 39 eyes) of which 11 had unilateral signs (55%), and 9 had bilateral signs (45%), blepharitis without conjunctivitis in 8 animals (12.70%; 9 eyes) of which 7 had unilateral signs (87.5%) and one had bilateral signs (12.5%), uveitis in 3 animals (4.76%; 5 eyes) one with unilateral signs (33.33%), and 2 with bilateral signs (66.66%) and Florida keratopathy-like lesions in one cat (1.59%; 2 eyes) with bilateral signs. (Table 2). Animals with uveitis had a diffuse corneal edema (severe), an absent menace response, and two animals were FeLV positive. Conjunctivitis and blepharoconjunctivitis were classified by score according to Table 3 and illustrated in Figure 1.

Of the 63 animals, 47 (74.60%) had clinical improvement with any of the proposed treatments. Twenty-two animals (34.92%) received an intralesional amphotericin injection. All animals with blepharoconjunctivitis or conjunctivitis that showed skin improvement during the treatment also showed improvement in ophthalmic lesions (Figure 2).

Not all cats had laboratory testing of ophthalmic tissues for sporotrichosis, but in all samples collected from the conjunctiva of cats that were diagnosed with sporotrichosis and had ocular involvement had a positive fungal culture. Five conjunctival swabs of the ocular discharge in 10 affected cats (50%) were positive for sporotrichosis on cytology (Patients 01, 10, 14, 19, 63; Table 2) (Figure 3). Of the 10 cats without ocular lesions, 5 (50%) of the samples collected had a positive fungal culture and one sample (10%) had a positive cytological examination. Histologically, the organisms appeared as small, pink, ovoid, or dot-like yeasts in periodic acid-Schiff stain (PAS), lying in vacuoles often grouped within macrophages, but were also detected free in the conjunctival parenchyma. Numerous yeasts were identified in the palpebral conjunctival samples from all evaluated animals (Patients 09, 14, and 63; Table 2) (Figure 3), whereas fungal organisms were not detected in other ocular structures.

Animals with a positive fungal culture demonstrated a high conjunctival cytological specificity (100%, with a confidence interval between 47.82% and 100%) but a low sensitivity (40%, with a confidence interval between 16.34% and 67.71%) for sporotrichosis. Consequently, the positive predictive value was 100% and the negative value was 35.71% with a confidence interval between 26.87% and 45.65% ($p < .05$).

4 | DISCUSSION

Sporotrichosis is a common fungal infection in Brazil, especially in the south and southeast regions that are the most affected by urban disease epidemics.[4] In Curitiba (State of Paraná, Brazil), since 2014, there have been a large number of sporotrichosis cases in

TABLE 2 Main clinical features and type of diagnostic test searching for sporotrichosis performed

Cat Identification	Age (months)	Sex	Breed	Reproductive status	Skin lesion	Ocular condition	Respiratory signs	Positive fungal culture	Response to treatment
Patient 01	96	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin and eye	Responsive
Patient 02	24	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 03	24	female	Mixed breed	Entire	Disseminated cutaneous	Serous discharge	Yes	Skin	Not responsive
Patient 04	48	female	Mixed breed	Entire	Disseminated cutaneous	Blepharitis and serous discharge	Yes	Skin	Responsive
Patient 05	7	female	Mixed breed	Entire	Disseminated cutaneous	Blepharitis and serous discharge	Yes	Skin	Responsive
Patient 06	36	male	Mixed breed	Neutered	None	Serous discharge	Yes	Eye and nasal discharge	Not responsive
Patient 07	24	female	Mixed breed	Entire	Disseminated cutaneous	Blepharitis and serous discharge	Yes	Skin	Responsive
Patient 08	24	male	Mixed breed	Entire	Disseminated cutaneous	Serous discharge	Yes	Skin	Not responsive
Patient 09	72	female	Mixed breed	Entire	Disseminated cutaneous	Blepharitis and serous discharge	Yes	Skin and eye	Not responsive
Patient 10	36	male	Mixed breed	Neutered	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin and eye	Responsive
Patient 11	12	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin and eye	Responsive
Patient 12	21	male	Mixed breed	Neutered	Disseminated cutaneous	Serous discharge	Yes	Skin and eye	Responsive
Patient 13	36	male	Persa	Entire	Disseminated cutaneous	Serous discharge and Florida keratopathy-like lesions	Yes	Skin and eye	Responsive
Patient 14	24	male	Mixed breed	Entire	None	Blepharoconjunctivitis and serous discharge	No	Eye	Not responsive
Patient 15	12	female	Mixed breed	Neutered	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Not responsive
Patient 16	6	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patiente 17	36	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 18	3	male	Mixed breed	Entire	Disseminated cutaneous	Uveitis	Yes	Skin	Not responsive

(Continues)

TABLE 2 (Continued)

Cat Identification	Age (months)	Sex	Breed	Reproductive status	Skin lesion	Ocular condition	Respiratory signs	Positive fungal culture	Response to treatment
Patient 19	12	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin and eye	Responsive
Patient 20	30	male	Mixed breed	Neutered	Disseminated cutaneous	Serous discharge	Yes	Skin	Responsive
Patient 21	28	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis	Yes	Skin	Responsive
Patient 22	36	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 23	34	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis	Yes	Skin	Responsive
Patient 24	32	female	Mixed breed	Entire	Disseminated cutaneous	Blepharitis, uveitis and serous discharge	Yes	Skin	Responsive
Patient 25	32	female	Mixed breed	Neutered	Disseminated cutaneous	Serous discharge	Yes	Skin	Responsive
Patient 26	36	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 27	36	female	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 28	24	female	Mixed breed	Neutered	Disseminated cutaneous	Blepharitis and serous discharge	Yes	Skin	Responsive
Patient 29	18	male	Mixed breed	Entire	Disseminated cutaneous	Serous discharge	Yes	Skin	Not responsive
Patient 30	36	male	Mixed breed	Neutered	Disseminated cutaneous	Blepharitis and serous discharge	Yes	Skin	Responsive
Patient 31	30	female	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 32	30	male	Mixed breed	Entire	Disseminated cutaneous	Blepharitis and serous discharge	Yes	Skin	Responsive
Patient 33	36	male	Mixed breed	Neutered	Disseminated cutaneous	Conjunctivitis	Yes	Skin	Responsive
Patient 34	12	male	Mixed breed	Entire	Disseminated cutaneous	Uveitis	Yes	Skin	Not responsive
Patient 35	8	female	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 36	48	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 37	48	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive

TABLE 2 (Continued)

Cat Identification	Age (months)	Sex	Breed	Reproductive status	Skin lesion	Ocular condition	Respiratory signs	Positive fungal culture	Response to treatment
Patient 38	48	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 39	18	female	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 40	18	female	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 41	24	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 42	24	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Not responsive
Patient 43	20	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis	Yes	Skin	Responsive
Patient 44	24	female	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Not responsive
Patient 45	36	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 46	36	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 47	18	female	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 48	36	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 49	8	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 50	24	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 51	36	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 52	30	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis	Yes	Skin	Not responsive
Patient 53	24	male	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 54	12	female	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis	Yes	Skin	Not responsive
Patient 55	36	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive

(Continues)

TABLE 2 (Continued)

Cat Identification	Age (months)	Sex	Breed	Reproductive status	Skin lesion	Ocular condition	Respiratory signs	Positive fungal culture	Response to treatment
Patient 56	8	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis	Yes	Skin	Responsive
Patient 57	48	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 58	24	female	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Not responsive
Patient 59	12	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 60	18	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis	Yes	Skin	Not responsive
Patient 61	12	female	Mixed breed	Entire	Disseminated cutaneous	Blepharoconjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 62	8	male	Mixed breed	Entire	Disseminated cutaneous	Conjunctivitis and serous discharge	Yes	Skin	Responsive
Patient 63	12	female	Mixed breed	Neutered	None	Conjunctivitis and serous discharge	No	Eye	Not responsive

TABLE 3 Number of eyes categorized by conjunctivitis/blepharoconjunctivitis and respective clinical scores

Score	Number of eyes
01	11 (15.27%)
02	13 (18.06%)
03	10 (13.89%)
04	22 (30.56%)
05	16 (22.22%)
Total	72

domestic cats, as well as humans, and is considered an important zoonotic disease.[15] This disease usually affects semi-domiciled cats, with street access, through injuries caused by scratches, bites, or contact with lesion exudates rich in fungal elements, especially after fights. As would be expected, sporotrichosis most often affects male non-neutered cats.[5,16] However, we cannot rule out that *Sporothrix* spp. could be an environmental contaminant in some cases, as suggested by tear culture results in the present study (15 of 20 positive cultures), especially in cats with disseminated respiratory and cutaneous conditions, representing a possibility of contagion between animals and a dermatozoonotic form of the disease.

The majority of the evaluated cats in the present study had severe disseminated skin conditions with extensive ulcerous, exudative lesions often surmounted by scabs. Such lesions probably result from self-trauma and auto grooming habits with the presence of fungus in the claws and the oral cavity, in addition to dissemination via hematogenous or lymphatic routes.[17,18] The auto grooming habit of licking their limbs and then passing them over the face, possibly contributes to ophthalmic contamination by spreading the fungus over the ocular surface.[19] This may happen mainly due to the presence of cutaneous-disseminated infections with areas of extensive ulcerations and exudate on the face.

The presence of general mucosal lesions was observed in 34.9% of cats with sporotrichosis in a previous work.[18] Nonetheless, that study did not separate the mucocutaneous lesions by the tissue involved (e.g., conjunctiva). In the present study, of the 63 animals with ophthalmic involvement, at least mild signs (e.g., exclusively increased serous ocular discharge) were observed. Severe cases of granulomatous conjunctivitis and blepharoconjunctivitis were observed in 71.43% of the affected cats. Because the present study was performed by both ophthalmologists and dermatologists, more precise lesion identification was likely achieved.

A recent study described three cats with granulomatous conjunctivitis and increased serous ocular discharge secondary to sporotrichosis, without presenting systemic

FIGURE 1 Ophthalmic findings, A, Conjunctivitis score 1 (Patient 10). Note the epiphora with mild conjunctival hyperemia and chemosis. B, Conjunctivitis score 2. Marked hyperemia associated with chemosis and epiphora (Patient 10). C, Conjunctivitis score 3 is similar to a score of 2 but associated with blepharitis. Note the severe eyelid swelling and the nodular conjunctiva appearance (Patient 01). D, Conjunctivitis score 4. Note the presence of blepharitis, mainly in the lower eyelid and nasal corner, extending to part of the upper eyelid, a large amount of purulent secretion in the nasal corner and intense chemosis with granuloma formation, in addition to epiphora. Lymphoid follicles were present, denoting a conjunctival score of 4 from 3. (Patient 02). E, Conjunctivitis score 5. Note the disruption of inability to fully visualize the eyelid margin along with the tumoral appearance, compromising the assessment of the ocular surface (Patient 21)

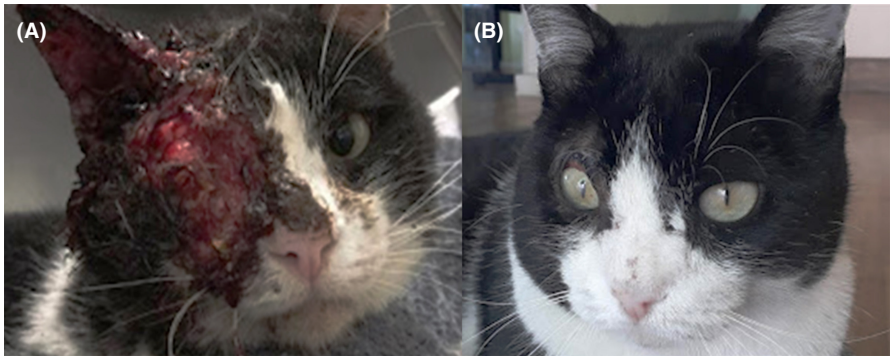

FIGURE 2 Treatment response, Evolution of ophthalmic sporotrichosis after treatment with itraconazole potassium iodide and amphotericin b. A, Blepharoconjunctivitis score 5 before treatment. B, Same animal after 6 months of treatment showing slight change to the palpebral fissure in the right eye compared with the normal left eye, including cicatricial elevation of the superior eyelid. (Patient 15)

symptoms or skin lesions.[11] In the present study, one cat had increased serous ocular discharge concomitant to a respiratory condition. However, no evidence of systemic or dermatological alterations was observed, and two cats had exclusively ophthalmic abnormalities characterized by granulomatous conjunctivitis scored 4/5.

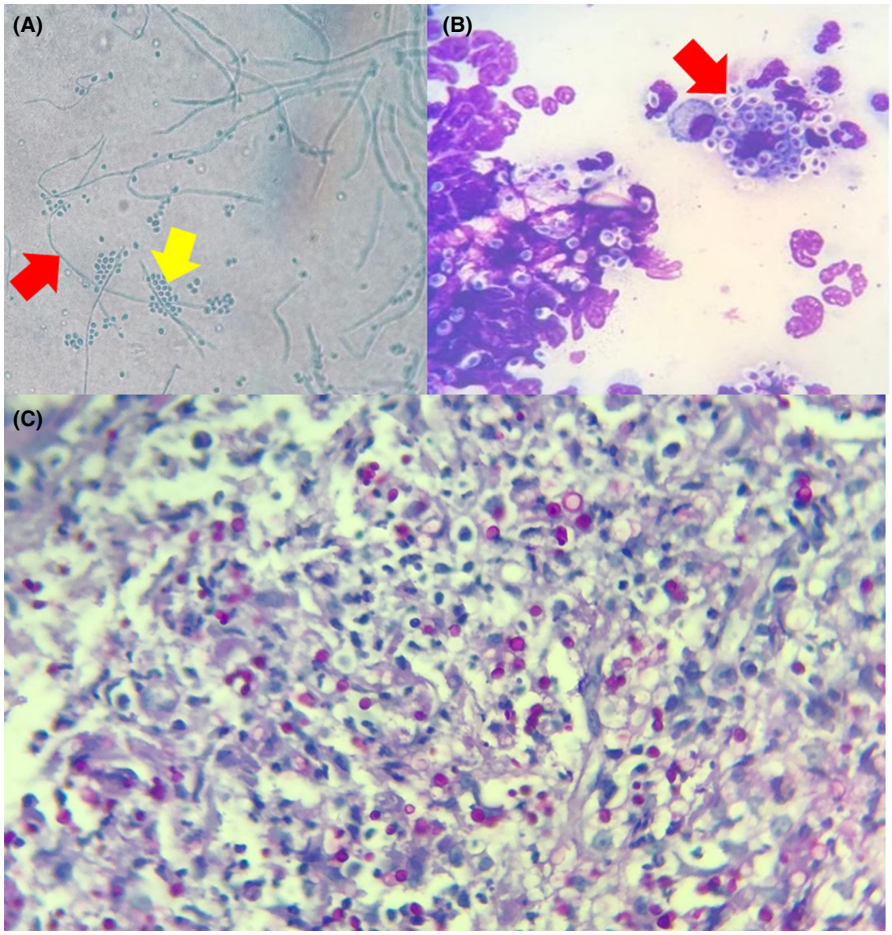

FIGURE 3 Laboratory findings, A, Microscopic image (1000X magnification) of positive fungal culture and sample staining with cotton blue lactophenol. Note hyphae (red arrow) and fungal yeasts (yellow arrow). B, Conjunctival swab cytology. Note large amounts of pleomorphic yeasts interspersed with a pyogranulomatous inflammatory infiltrate (red arrow) (1000X rapid panoptic). C, Palpebral conjunctiva histopathology. Representative photomicrography showing the presence of pyogranulomatous inflammatory infiltrate, with epithelioid macrophages and numerous small, 2–6 μm diameter, dot-like to oval yeasts consistent with Sporothrix schenckii can be observed (PAS 1000X)

Systemic signs most frequently observed in cats with sporotrichosis involve the respiratory system.[18] There appears to be an association of conjunctivitis, blepharoconjunctivitis, and increased serous ocular discharge with severe respiratory and disseminated conditions. Furthermore, the proximity of the nasal cavity with the lacrimal system and their communication through the nasolacrimal duct could also contribute to the disease spreading from the airways to the ocular adnexa. This may explain the presence of fungus in the conjunctiva of systemically infected cats without other ophthalmic signs. Increased serous ocular discharge could also be explained in most cases by the intimacy of the nasal cavity with the lacrimal system; some animals can have nodules that extend into the nasal cavity[20] and may obliterate the nasolacrimal duct causing decreased tear outflow rather than epiphora. Additionally, ocular discharge could be a contributor in system spread via transmission to the nasal cavity during self-grooming, however further studies are needed.

Conjunctivitis was the second most common ocular lesion in cats with sporotrichosis, the majority of which were severe with a score of 4/5. However, conjunctivitis has been reported to be responsive to conventional sporotrichosis treatments, such as the use of itraconazole and potassium iodide or intralesional amphotericin B injection.[21–23] Scoring conjunctivitis in a similar manner may facilitate monitoring the evolution of the severity from the beginning of the therapy, and it can help to assess its efficacy of new medications in future studies.

It is important to consider other conjunctival conditions and comorbidities that were not investigated, such as chlamydiosis or herpesvirus, which could cause lesions similar to those mentioned in the present study. Infections associated with the feline respiratory complex, such as the aforementioned viral and bacterial infections, are considered the main causes of conjunctivitis in cats.[24,25] These infections were not tested in the present work because of financial restrictions, however future molecular studies will be performed to elucidate this bias. Despite the low number of samples of ocular discharge and conjunctiva collected for laboratory examination, 22.9% of cats with systemic sporotrichosis had ocular lesions with increased serous ocular discharge, blepharoconjunctivitis, and conjunctivitis being the main lesions found. Nonetheless, the present study suggests that sporotrichosis should be considered as a cause of conjunctivitis in endemic areas.

Sporotrichosis also seems to be an important cause of blepharitis and blepharoconjunctivitis, often appearing

similar to other infectious diseases of the eyelids such as dermatophytosis and feline demodicosis, immune-mediated diseases such as pemphigus foliaceous, and neoplastic conditions such as squamous cell carcinoma.[26,27] The latter usually causes expansive, ulcerated lesions in the periocular region and over the eyelids, and may present as deforming facial lesions, potentially appearing similar to the lesions caused by sporotrichosis. Thus, histopathological analysis and fungal culture are fundamental for this differentiation.

Intraocular sporotrichosis is not a typical presentation, understandably so considering that it is a mycotic infection of implantation and its dissemination is most often through the subcutaneous and lymphatic routes, causing cellulitis, lymphangitis, and lymphadenitis, affecting the skin, eyelids, and conjunctiva. In humans, there is some evidence that sporotrichosis may be associated with endophthalmitis and posterior uveitis through the hematogenous route, however, there are no similar studies in cats.[28] Other fungal infections such as cryptococcosis reach the retina and posterior uvea through the breakdown of the blood-aqueous barrier caused by vasculitis secondary to the fungal infection.[29] However, in the present study, three animals were diagnosed with uveitis, two of which were positive for FeLV. There is evidence that retroviral infections modify the immune response and may worsen the prognosis of cats with sporotrichosis.[30] In addition to FeLV, poor care and low quality of life may contribute to immunodeficiency and thus increased risk of infections.[4,17] FeLV itself should be considered an important cause of uveitis in cats.[30,31] Few animals were tested for FeLV in the present study, and considering that histopathological evaluation did not reveal yeasts or fungal elements in the uveal tract, it is not possible to rule out other causes such as FeLV as the reason for uveitis. Additionally, eyes with uveitis had severe and diffuse corneal edema, which made the assessment of intraocular structures very difficult.

Retinal and optic nerve abnormalities such as chorioretinitis and optic neuritis may be associated with fungal infections such as cryptococcosis, blastomycosis, and histoplasmosis.[29,32–34] In humans, there are reports that sporotrichosis can also be related to similar clinical presentations, especially in immunocompromised patients.[35] In the present study, these alterations were not evident in cats with sporotrichosis, although ophthalmoscopic evaluation was impaired due to severe blepharoconjunctivitis and corneal edema caused by uveitis. It is possible that in cats, *Sporothrix* spp. does not have tropism for choroid, retina, or optic nerve, or that infections within these tissues were subclinical.

Cytological examination and fungal culture are easy and inexpensive diagnostic tests for conjunctival sporotrichosis. Cytology demonstrated high specificity and low sensitivity compared to fungal culture for conjunctival sporotrichosis, with a high positive predictive value. Thus, although the visualization of *Sporothrix* spp. pleomorphic yeasts in the cytological examination of the conjunctiva are not common, its occurrence allows the presumptive diagnosis of ophthalmic sporotrichosis and helps direct therapy by ruling out other fungal infections such as cryptococcosis and histoplasmosis as differential diagnoses. Exfoliative cytology of the palpebral conjunctiva, commonly used for conjunctivitis diagnosis,[11] could increase the sensitivity of the diagnosis, but this method was not used due in this investigation to the difficulty handling sick animals for collection of these samples using the cytological brush. Compared with cytology, all samples collected from animals with ophthalmic conditions had a positive fungal culture, suggesting that culture is a very reliable test in the presence of ocular abnormalities, and has been recommended as the gold standard for sporotrichosis diagnosis.[13]

Limitations of the study include the low number of histopathological examinations, which were limited due to budget constraints and the difficulty of managing the anesthetic team to monitor patients. Biomolecular tests were not performed for the same reason. Some of these hospital visits were expensive and required a multidisciplinary approach. Future studies should broaden the data on histopathologic and biomolecular analyses.

Ophthalmic sporotrichosis is a neglected disease that has little representation in the literature despite its prevalence in some endemic areas. Sporotrichosis should be investigated mainly when there is evidence of a disseminated respiratory or cutaneous disease and should be part of the differential diagnosis of conjunctivitis and blepharoconjunctivitis, especially in endemic regions. Fungal culture is recommended as the main diagnostic tool, with cytological and histologic evaluation secondarily. In addition, *Sporothrix* spp. can be found in the conjunctiva of cats with sporotrichosis with and without the presence of ophthalmic abnormalities, raising concern of both environmental contamination but also that ocular secretion could be a source of contagion and disease transmission.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding this study.

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REFERENCES

1. De Lima Barros MB, de Oliveira SA, Galhardo MC, et al. Sporotrichosis with widespread cutaneous lesions: report of 24 cases related to transmission by domestic cats in Rio de Janeiro, Brazil. *Int J Dermatol*. 2003;42(9):677-681.
2. Marimon R, Cano J, Gené J, Sutton DA, Kawasaki M, Guarro J. Sporothrix brasiliensis, S. globosa, and S. mexicana, three new sporothrix species of clinical interest. *J Clin Microbiol*. 2007;45(10):3198-3206.
3. Gremião IDF, Miranda LHM, Reis EG, Rodrigues AM, Pereira SA. Zoonotic epidemic of sporotrichosis: cat to human transmission. *PLoS Pathog*. 2017;13(1):e1006077.
4. Schubach A, de Lima Barros MB, Wanke B. Epidemic sporotrichosis. *Curr Opin Infect Dis*. 2008;21(2):129-133.
5. Madrid IM, Mattei A, Martins A, Nobre M, Meireles M. Feline sporotrichosis in the southern region of rio grande do sul, Brazil: clinical, zoonotic, and therapeutic aspects. *Zoonoses Public Health*. 2010;57(2):151-154.
6. Rodrigues AM, de Melo TM, de Hoog GS, et al. Phylogenetic analysis reveals a high prevalence of Sporothrix brasiliensis in feline sporotrichosis outbreaks. *PLoS Neglect Trop d*. 2013;7(6):e2281.
7. Lopes-Bezerra LM, Mora-Montes HM, Zhang Y, et al. Sporotrichosis between 1898 and 2017: the evolution of knowledge on a changeable disease and emerging etiological agents. *Med Mycol*. 2018;56:S126-S143.
8. Schubach A, Barros MBDL, Schubach TMP, et al. Primary conjunctival sporotrichosis. *Cornea*. 2005;24(4):491-493.
9. Da Silva DT, Pereira SA, Gremião IDF, et al. Esporotricose conjuntival felina. *Acta Sci Vet*. 2008;36(2):181-184.
10. Yamagata JPM, Rudolph FB, Nobre MCL, et al. Ocular sporotrichosis: a frequently misdiagnosed cause of granulomatous conjunctivitis in epidemic areas. *Am J Ophthalmol Case Rep*. 2017;8:35-38.
11. Spinelli TP, Bezerra LM, de Souza BO, Rocha A, Neto JE, Sá FB. Primary conjunctival sporotrichosis in three cats from northeastern Brazil. *Vet Ophthalmol*. 2021;24(2):209-215.
12. Hartmann AD, Hawley J, Werckenthin C, Lappin MR, Hartmann K. Detection of bacterial and viral organisms from the conjunctiva of cats with conjunctivitis and upper respiratory tract disease. *J Feline Med Surg*. 2010;12(10):775-782.
13. Dixon DM, Salkin IF, Duncan RA, et al. Isolation and characterization of Sporothrix schenckii from clinical and environmental sources associated with the largest US epidemic of sporotrichosis. *J Clin Microbiol*. 1991;29(6):1106-1113.
14. De Lima Barros MB, de Almeida PR, Schubach AO. Sporothrix schenckii and sporotrichosis. *Clin Microbiol Rev*. 2011;24(4):633-654.
15. Runcos LHE, Braga KF, Ribeiro SS, Monti FS, Chi KD, Farias MR. Aspectos epidemiológicos da esporotricose felina no município de Curitiba, estado do Paraná, Brasil, entre 2014 e 2016. *Revista MV&Z*. 2017;15(3):90.
16. Montenegro H, Rodrigues AM, Dias MAG, da Silva EA, Bernardi F, de Camargo ZP. Feline sporotrichosis due to Sporothrix brasiliensis: an emerging animal infection in São Paulo. *Brazil BMC Vet Res*. 2014;10(1):1-11.
17. Gremião IDF, da Rocha EMDS, Montenegro H, et al. Guideline for the management of feline sporotrichosis caused by Sporothrix brasiliensis and literature revision. *Braz J Microbiol*. 2021;52(1):107-124.
18. Schubach TM, Schubach A, Okamoto T, et al. Evaluation of an epidemic of sporotrichosis in cats: 347 cases (1998–2001). *J Am Vet Med Assoc*. 2004;224(10):1623-1629.
19. Eckstein RA, Hart BL. The organization and control of grooming in cats. *Applied Animal Behaviour Science*. 2000;68(2):131-140.
20. Schubach TMP, Schubach A, Dos Reis RS, et al. Sporothrix schenckii isolated from domestic cats with and without sporotrichosis in Rio de Janeiro. *Brazil Mycopathol*. 2002;153(2):83-86.
21. Gremião IDF, Schubach TMP, Pereira SA, Rodrigues AM, Chaves AR, Barros MB. Intralesional amphotericin B in a cat with refractory localized sporotrichosis. *J Feline Med Surg*. 2009;11(8):720-723.
22. Carvalho BW, Pereira SA, Figueiredo ABF, et al. Sodium iodide: an alternative treatment option for feline sporotrichosis? *Acta Sci Vet*. 2018;46(1):7.
23. De Souza EW, de Moraes BC, Pereira SA, et al. Clinical features, fungal load, coinfections, histological skin changes, and itraconazole treatment response of cats with sporotrichosis caused by Sporothrix brasiliensis. *Sci Rep-UK*. 2018;8(1):9074.
24. Cai Y, Fukushi H, Koyasu S, Kuroda E, Yamaguchi T, Hirai K. An etiological investigation of domestic cats with conjunctivitis and upper respiratory tract disease in Japan. *J Vet Med Sci*. 2002;64(3):215-219.
25. Baumworcel N, Soares AMB, Silva SB, Almeida NKO, Castro TXD. Correlation between clinical signs of feline conjunctivitis and molecular detection of felid herpesvirus-1, feline calicivirus, chlamydophila felis, and mycoplasma felis in cats from shelters in Rio de Janeiro. *Braz J Vet Res Anim Sci(Online)*. 2017;54(1):18-26.
26. Gelatt KN. *Veterinary Ophthalmology*. John Wiley & Sons; 2013:1476-1483.
27. Tham HL, Linder KE, Olivry T. Deep pemphigus (pemphigus vulgaris, pemphigus vegetans and paraneoplastic pemphigus) in dogs, cats and horses: a comprehensive review. *BMC Vet Res*. 2020;16(1):1-25.
28. Soto MCR. Differences in clinical ocular outcomes between exogenous and endogenous endophthalmitis caused by Sporothrix: a systematic review of published literature. *Brit J Ophthalmol*. 2018;102(7):977-982.
29. Wong BJ, Rao NA, Ameri H. Optical coherence tomography imaging of presumed Cryptococcus neoformans infection localized to the retina. *J of Curr Ophthalmol*. 2019;31(3):353-356.
30. De Miranda LHM, Meli M, Conceição-Silva F, et al. Co-infection with feline retrovirus is related to changes in immunological parameters of cats with sporotrichosis. *PloS One*. 2018;13(11):e0207644.
31. Wegg ML, Jeanes EC, Pollard D, Fleming L, Dawson C. A multicenter retrospective study into endogenous causes of uveitis in cats in the United Kingdom: ninety two cases. *Vet Ophthalmol*. 2021;24:1-8.
32. Bloom JD, Hamor RE, Gerding PA Jr. Ocular blastomycosis in dogs: 73 cases, 108 eyes (1985-1993). *J Am Vet Med Assoc*. 1996;209(7):1271-1274.

33. Brömel C, Sykes JE. Epidemiology, diagnosis, and treatment of blastomycosis in dogs and cats. *Clin Tech Small an P*. 2005;20(4):233-239.
34. Ewald MM, Rankin AJ, Meekins JM, McCool ES. Disseminated histoplasmosis with ocular adnexal involvement in seven cats. *Vet Ophthalmol*. 2020;23(5):905-912.
35. Biancardi AL, Freitas DFS, Valviesse VRGDA, et al. Multifocal choroiditis in disseminated sporotrichosis in patients with HIV/AIDS. *Retin Cases Brief Rep*. 2017;11(1):67-70.

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