Sporotrichosis

Rose Handler's Disease

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Importance

Sporotrichosis is caused by members of the fungal genus *Sporothrix*, which normally grow as saprophytes in the environment, and may be present on vegetation and in organic debris and soil. When fungal spores are accidentally inoculated into the skin (most often via sharp pieces of vegetation), some species of *Sporothrix* transform from filamentous molds into yeasts, and proliferate. In most cases, these organisms remain confined to the skin and lymphatics, causing relatively superficial lesions such as erythematous nodules, ulcers and plaques. Without treatment, these lesions may persist for months or years, or even indefinitely. Uncommonly, the organisms invade deeper tissues, including bone, joints and various internal organs, or disseminate widely in the skin. Disseminated infections, including rare instances of pulmonary sporotrichosis from inhaled organisms, can be life-threatening.

While sporotrichosis can affect a wide variety of mammals, including humans, this disease is a particular concern in cats. Most mammals have only small numbers of organisms in sporotrichosis lesions, and transmission to other animals or people is unusual. However, these yeasts are often abundant in the lesions of cats. In 2002-2003, an epidemic of sporotrichosis emerged among free-roaming cats in impoverished urban areas of Rio de Janeiro, Brazil. The organism continues to spread between cats in this area, with several thousand cases reported as of 2017. Infected cats have also transmitted sporotrichosis to more than 4000 people and over a hundred dogs. Recently, feline epidemics have emerged in other resource-poor urban centers in southern Brazil.

Etiology

At one time, sporotrichosis was thought to be caused by a single organism called *Sporothrix schenckii*, a fungus in the family Ophiostomataceae. However, *S. schenckii* is now known to contain several individual species, and it has been renamed the *Sporothrix schenckii* complex, or *S. schenckii sensu lato* (*S. schenckii s.l.*). Members of the genus *Sporothrix* normally grow as saprophytic molds in the environment, but some species can proliferate as yeasts in the tissues of humans and/or animals. These organisms also grow as yeasts in culture at 35-37ºC.

Three members of the *Sporothrix schenckii* complex, *S. schenckii sensu stricto* (*S. schenckii s.s.*), *S. brasiliensis* and *S. globosa*, appear to be responsible for most clinical cases in humans and animals. Other species including *S. luriei* (formerly *S. schenckii* var. *luriei*), *S. mexicana* and *S. pallida* (formerly *S. pallida*, *S. albicans* and *S. nivea*), have also caused a few cases. *S. luriei*, which may be highly virulent, is also considered to belong to the *S. schenckii* complex. *S. mexicana* and *S. pallida* have caused only rare opportunistic infections, and are thought to be environmental organisms of low virulence. Some authors place these two species in the *S. schenckii* complex, while others put them in the *S. pallida* complex, together with various organisms that have never been found in a clinical case (e.g., *S. stylites*, *S. humicola*) and the proposed species *S. chilensis*, which was isolated from a case of onychomycosis. There are also many other species of *Sporothrix*, which grow as environmental organisms (e.g., *S. splendens*, *S. narcissi*), belong to various complexes (e.g., the *S. candida* complex, the *S. inflata* complex) and have never been identified as pathogens.

Species Affected

Sporotrichosis has been reported in most domesticated mammals including cats, dogs, cattle, goats, swine, horses, mules, donkeys and camels, and diverse free-living or captive wildlife, such as rats (*Rattus norvegicus*), non-human primates, foxes, dolphins and armadillos (*Dasypus novemcinctus)*. Experimental infections have been established in additional species such as mice, hamsters, guinea pigs and rabbits. Most or all mammals might be susceptible to some extent.

Textbook descriptions of sporotrichosis also list birds among the species affected by this disease. However, there do not seem to be any recent published descriptions of sporotrichosis in any avian species.

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Two reports suggest that *S. schenckii s.l.* might affect reptiles, although there is currently no definitive evidence for a causative role. This organism was one of the fungi isolated from skin lesions in free-living dusky pigmy rattlesnakes (*Sistrurus miliarius barbouri*). Fungal hyphae, rather than yeasts, were visible in these lesions. *S. schenckii s.l.* was also found in mixed mycotic pneumonia in green turtles (*Chelonia mydas*), together with *Paecilomyces* sp.

Zoonotic potential

S. schenckii s.s., *S. brasiliensis* and *S. globosa* have been found in most human clinical cases. *S. luriei*, *S. mexicana* and *S. pallida* have been described rarely.

Geographic Distribution

Members of the *S. schenckii* complex are found worldwide, although clinical cases seem to be more common where high humidity and temperatures promote fungal growth. In North America, this disease occurs most often in southern coastal regions and river valleys.

Individual species of *Sporothrix* seem to differ in their distribution. *S. globosa* and *S. schenckii s.s.* have been reported from a number of locations in both Eastern and Western Hemispheres. *S. brasiliensis* seems to be restricted to Latin America. As of 2017, it has been described only in Brazil, where it is responsible for an ongoing epidemic in cats, people and other species. *S. mexicana* has, to date, been documented in Latin America (Mexico), Africa and Australia. One clinical case was reported in Europe (Portugal), but this person had also traveled to Malaysia.

Transmission

Members of the genus *Sporothrix* normally grow as molds in the environment, where they can be found in/ on soil, wood, vegetation and organic debris. Most clinical cases result from contact between broken skin and fungal spores, especially when they are inoculated in penetrating wounds from items such as wood splinters, sphagnum moss, thorns or hay. Bites, scratches and pecks from a variety of animals and birds can also inoculate the organism into wounds. Some of these animals are infected, but others are only temporarily contaminated by organisms from the environment. Insect stings were associated with a few cases. Laboratory-acquired infections can result from direct contact with *S. schenckii s.l.* in fungal cultures or tissues. Rarely, inhalation can result in the pulmonary form of the disease.

Sporotrichosis is most likely to be contagious in cats, as their skin lesions often contain large numbers of yeasts. In addition to being transmitted through cuts and abrasions, these organisms seem to be able to enter the body through minimally damaged skin (including skin that appears undamaged), possibly due to their abundance. They can be found in the mouth and nasal cavity and on the nails of infected cats, facilitating transmission in bites and scratches. *S. schenckii s.l.* has also been detected in the feces of some cats. *S. brasiliensis* is reported to be fairly common in the testes of intact male cats. Other host species could also spread sporotrichosis from discharging lesions; however, the organisms are usually very sparse and transmission is much less likely. One instance of person-to-person transmission has been documented. In this case, the organism was transmitted from a lesion on a mother's arm to her child's face after frequent close contact. A probable transplant-associated infection was reported in a lung transplant patient. Once *S. schenckii s.l.* enters the environment, it can survive for long periods, or indefinitely if it finds a suitable environment in which to proliferate.

Disinfection

S. schenckii s.l. is susceptible to a variety of disinfectants including 1% sodium hypochlorite, iodine, phenolics, 70% ethanol, accelerated hydrogen peroxide (6,000 ppm) and formaldehyde. Chlorhexidine also has antifungal activity. *S. schenckii s.l.* can be inactivated by moist heat of 121°C for 15 minutes or longer.

Infections in Animals

Incubation Period

The incubation period in animals is probably similar to humans, whose clinical signs develop several days to 3 months after exposure. In experimentally infected mice and hamsters, erythema and swelling appeared within a week of inoculation, and small nodular lesions were first detected in approximately one week, becoming more apparent over the next few weeks.

Clinical Signs

Three forms of sporotrichosis –lymphocutaneous, cutaneous, and disseminated – are recognized in animals. In the lymphocutaneous form, one or more firm nodules develop first at the inoculation site, then spread along the lymphatics as a chain of nodules. These lesions and the regional lymph nodes may ulcerate, crust and drain a purulent, thick brownish-red or serohemorrhagic exudate. The lymphatics may concurrently become thickened, hard and cordlike. Systemic illness is usually absent at first, but chronically affected animals may eventually become febrile, depressed and inappetent. Similar lesions occur in the cutaneous form, but they remain localized to one area. They can include nodules; verrucous lesions with well-demarcated, alopecic areas covered with small scales and bordered by microabscesses; ulcerated plaques with raised borders; and lesions that appear as localized granulomas. Lesions that heal may recur. While many infections remain limited to the skin and subcutaneous tissues, *S. schenckii s.l.* can disseminate to deeper tissues or organs, such as the lungs, bone, liver, spleen, kidneys, testes, gastrointestinal tract and central nervous system (CNS). The most common presentations of sporotrichosis may differ between animal hosts.

Equidae

In horses and mules, sporotrichosis occurs most often on the lower limbs. The lymphocutaneous form is most common, and the affected limb may swell due to lymphatic stasis. The regional lymph nodes are rarely involved in horses, and disseminated disease has not been reported.

Cats

In cats, clinical sporotrichosis varies from single lesions that regress spontaneously to fatal disseminated systemic disease. The initial lesions can occur anywhere, but tend to develop on the distal extremities, base of the tail, or head. They may begin as small, draining puncture wounds that resemble wound abscesses/ cellulitis, before developing into more characteristic sporotrichosis lesions. Some ulcers may cavitate, exposing large areas of underlying muscle and bone. Although the organisms can spread along the lymphatics, these vessels may not be obviously involved in cats. Cats can also spread *S. schenckii s.l.* to other parts of the body by grooming. Mucosal involvement is reported to be common, especially in the respiratory tract, with signs that may include sneezing, nasal discharge and dyspnea. Weight loss, anorexia, fever and depression can be seen if internal organs are affected or skin lesions are extensive, and some cases are fatal.

Dogs

In dogs, sporotrichosis is typically a localized multinodular disease. The lesions often occur on the trunk and head, but they may also be present on the limbs. Cording of the lymphatics may be evident. Some dogs have had bone, joint, liver or lung involvement, with or without skin lesions at the time of presentation. Disseminated disease seems to be uncommon in most reports; however, dogs that lived with infected cats in Brazil sometimes had respiratory signs and/or skin lesions at multiple sites, possibly from being repeatedly exposed to the organism.

Post Mortem Lesions

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Granulomatous nodules are typically present in the skin, often in chains along lymphatic vessels. Exudation, ulceration, cavitation, crusting, scabbing or scarring may be seen. The affected lymphatics are usually thickened and cordlike, and some limbs may be edematous. Histopathology may reveal diffuse or nodular dermatitis, which can be suppurative, pyogranulomatous or granulomatous. Well-formed granulomas seem to be less common that poorly formed granulomas in cats. Most necropsies in this species reveal evidence of lymph node involvement, and small numbers of organisms may be found in internal organs

Diagnostic Tests

Sporotrichosis is usually diagnosed by fungal culture of lesions or exudates. *S. schenckii s.l.* will grow on various fungal media, including Sabouraud's dextrose agar, as well as on enriched media such as blood or chocolate agar. It appears as a mold at room temperature, but as smooth yeast colonies on blood agar at 35-37°C. Colonies usually become visible within 8 days, but some may take up to 4 weeks to appear. Occasionally, there may be strains, usually associated only with cutaneous infections, that do not grow well at temperatures as high as 35-37°C. Individual species within the *S. schenckii* complex can be distinguished by molecular techniques such as PCR. Morphological analysis of conidia, biochemical characteristics and growth at 37°C can also be used; however, several groups have noted that they misidentified some field isolates by using phenotypic characteristics alone. Some PCR assays are being investigated for use directly with tissue samples.

Cytology may reveal the characteristic round to cigar-shaped (sometimes budding) pleomorphic yeasts in exudates and skin or tissue biopsies. The organisms are usually abundant in lesions from cats. They are typically rare in other species, and in many cases, they are not detected during visual examination. Occasionally, yeasts can be found only by culture even in cats. Hematoxylin and eosin, or Romanowsky-type stains (e.g., DiffQuik, Wright's or Giemsa) are generally used for microscopic examination in veterinary medicine. Special stains such as Gomorimethenamine silver or periodic acid-Schiff stains can enhance fungal detection in tissues. With conventional staining methods, *S. schenckii s.l.* must be distinguished from other yeasts such as *Candida* spp., *Histoplasma capsulatum* and *Trichosporon* spp., and from the protozoal parasite *Leishmania.* Immunofluorescent or immunohistochemical staining may be helpful in revealing small numbers of organisms.

Serology is normally not used for diagnosis of sporotrichosis in animals. However, an ELISA that can detect antibodies to S. *schenckii* in cats was recently published.

Treatment

Various antifungal drugs, such as itraconazole, ketoconazole, amphotericin B and fluconazole, have been used to treat sporotrichosis in animals. Potassium or sodium iodide can also be employed in the cutaneous or lymphocutaneous forms. Cats are particularly sensitive to iodine, and must be watched carefully for signs of toxicity if the latter drugs are used. Itraconazole is currently considered the drug of choice in small animals, especially when cost is not a concern. It may take a few weeks to several months of treatment before the lesions resolve completely, and most authors also recommend that antifungal drugs be continued for a time (e.g., at least one month) after clinical resolution. Some studies have found differences in antimicrobial susceptibility between the fungal species in the S. *schenckii* complex, or between strains within a species. *S. brasiliensis* is reported to respond well to antifungal drugs in most cases, while *S. mexicana* is relatively resistant. Individual isolates with antifungal resistance (e.g., itraconazole resistance in *S. brasiliensis*) have been reported.

Other treatments that have been used in cutaneous sporotrichosis, either alone or in conjunction with antifungal drugs, include surgical removal, cryotherapy and thermotherapy. Thermotherapy is used more often in people, but it was successful in at least one cat with a single localized

lesion. In this technique, the skin temperature in the area of the lesion is raised to 42-43°C, twice a day, with a hot water bag, source of infrared or other method.

Control

Disease reporting

Veterinarians who encounter or suspect sporotrichosis should follow their national and/or local guidelines for disease reporting. However, *S. schenckii* complex organisms are widespread, and infections in animals are not usually reportable.

Prevention

In animals, there is no practical way to prevent the acquisition of *S. schenckii s.l.* from the environment, other than to remove materials known to be contaminated from their vicinity. Infected animals, particularly cats, should be isolated to prevent the organism from spreading. Factors thought to be important in propagating the feline epidemics in Brazil include allowing infected pets to roam, abandoning cats that become sick, and improperly disposing of the carcasses of dead cats. Keeping cats indoors during these epidemics can help protect them from becoming infected.

Morbidity and Mortality

Ongoing feline epidemics in Brazil, which are caused by *S. brasiliensis*, have affected several thousand cats since the late 1990s. These epidemics have occurred in impoverished urban centers where health- and veterinary care are inadequate and cats are often allowed to roam freely. Ongoing outbreaks have been reported in Rio de Janeiro, Brazil since 2002/ 2003, but similar outbreaks have recently been seen in other resource-poor urban centers in southern Brazil. The organism is thought to be spread mainly by direct contact during cat fights and other interactions. *S. brasiliensis* has also affected dogs that are in contact with infected cats, though in smaller numbers: one group documented 3800 feline and 120 canine cases in Rio de Janeiro between 1998 and 2011.

Outside Brazil, sporotrichosis tends to occur sporadically, in individual animals. Various species in the *S. schenckii* complex may be involved. For example, most feline cases in Malaysia seem to be caused by *S. schenckii sensu stricto*. In dogs, sporotrichosis tends to be seen in hunting animals or other dogs that are frequently exposed to thorns and splinters. In cats, this disease occurs most often in sexually intact males allowed to roam; however, cases have been reported even in indoor cats exposed only to houseplants and potting soil. There is no obvious association with immunosuppression in cats, and several reports could find no links to infection by feline immunodeficiency virus (FIV) or feline leukemia virus (FeLV). However, treatment with immunosuppressive drugs, such as prednisolone, can worsen sporotrichosis in all species.

Cats seem to be particularly susceptible to serious complications from sporotrichosis. Approximately half of all experimentally infected, healthy cats were reported to develop disseminated disease, a form that is usually fatal without treatment. Studies from Brazil suggest that significant respiratory involvement is associated with a poorer prognosis. Fatalities are rare in horses, which usually have only skin lesions.

Infections in Humans

Incubation Period

In humans, the incubation period ranges from several days to 3 months. Most infections become apparent in approximately 1-3 weeks.

Clinical Signs

Cutaneous and ocular sporotrichosis

Most cases of sporotrichosis in people only involve the skin and subcutaneous tissues. Lesions can occur anywhere, but the extremities, especially the hands or arms, are often involved in adults. The face is frequently affected in children.

Lymphocutaneous sporotrichosis is most common form in humans. It typically begins as one or more erythematous papules at the inoculation site, which develop into pustules, and then into slowly expanding subcutaneous nodules. The infection spreads along the lymphatics, forming a chain of subcutaneous nodules, which can become necrotic or plaque-like, may ulcerate, and may produce gray or yellowish pustular exudate. Intact nodules are not usually tender unless they become secondarily infected by bacteria. The affected lymphatic vessels also become firm, thickened, and cordlike. Lymph nodes are usually unaffected in people.

In the fixed cutaneous form, the skin lesions do not spread via the lymphatics, but remain localized to one site. Atypical cutaneous cases, which mimic various skin diseases, have been reported occasionally. In patients who are immunosuppressed, inflammation may be reduced. Localized cutaneous lesions in multiple areas can represent either dissemination of organisms through the blood, or cutaneous inoculation at more than one site. A common reason for the latter is ongoing interactions with infected household cats.

Around the eye, the most common pattern is skin lesions on the eyelids and occasionally the eyebrows, typically as the lymphocutaneous form, with regional lymphadenopathy. Conjunctival involvement, which is uncommon, appears as a granulomatous lesion with hyperemia, edema and ocular secretions, with or without enlargement of the regional lymph nodes. Acute dacrocystitis, which is rare, is characterized by localized redness, edema and painful induration around the lacrimal gland. It can occur alone, or in combination with other ocular lesions. Endophthalmitis is a very rare presentation, but it has been reported in immunosuppressed (HIV-infected) individuals. Opportunistic infectious keratitis (*S. pallida*) occurred in one corneal transplant patient who was using prednisolone eye

drops. Severe and/or chronic complications are possible with the involvement of structures around the eye.

General health is not usually affected in the lymphocutaneous and fixed cutaneous forms. Although some localized cutaneous lesions may regress without treatment, untreated skin lesions often persist for months or years, or even indefinitely. Recrudescence is also possible. Asymptomatic infections may occur in some people who work with plants.

Mucosal involvement

Mucosal lesions are uncommon, but they have been reported at various sites in the respiratory tract and oral cavity, including the nasal mucosa, sinuses, pharynx, trachea and palate. The lungs were involved in some cases, but not others. Mucosal lesions may be verrucous, granulomatous or ulcerated, and bloody secretions may drain from the nose. The regional lymph nodes can be enlarged.

Disseminated sporotrichosis

Disseminated sporotrichosis usually occurs when organisms spread internally from skin lesions, either locally or through the blood to distant sites. However, disseminated disease can be seen occasionally without cutaneous signs, or after the skin lesions have healed. The bones and joints are affected most often (frequently at a single site if the patient is immunocompetent), but many other organs including the meninges (meningitis), peripheral nerves (neuropathy), kidneys, liver, lung, spleen, intestines, genitalia and mucous membranes can also be involved. Widespread cutaneous lesions are also considered to be a form of disseminated disease. Sporotrichosis affecting the CNS (meningitis), which seems to occur mainly in immunosuppressed people, is often fatal.

Pulmonary sporotrichosis

Pulmonary involvement can be an aspect of disseminated disease; however, it can also be an isolated syndrome caused by inhalation of the fungus. While it may be acute, it is more often chronic and resembles tuberculosis. The symptoms can include coughing, which is often productive, as well as dyspnea, pleuritic pain, hemoptysis, weight loss and fatigue. Occasional cases have been diagnosed radiologically in people without clinical signs. Some cases may be complicated by coinfection with other microorganisms. Pulmonary sporotrichosis is life-threatening and difficult to treat.

Diagnostic Tests

Clinical cases in humans can be confirmed by fungal culture of exudates, tissue samples and fluids from affected sites (e.g., sputum, urine, blood, synovial fluid, cerebrospinal fluid), as in animals. Direct visual observation can also be attempted. However. *S. schenckii s.l.* is difficult to detect in lesions, exudates or fluids from people, with the exception of some immunocompromised individuals. Histopathological findings may be suggestive, although the yeasts themselves are rarely seen.

Various serological assays including agglutination tests (e.g., latex agglutination, tube agglutination), immunoprecipitation, complement fixation and ELISAs have been used as diagnostic aids in humans. ELISAs are currently used most often. Serology may be helpful in increasing the suspicion of sporotrichosis in patients without skin involvement. However, antibodies are not reliably present, and cross-reactions can occur with other organisms. A sporotrichin skin test has sometimes been employed, although some uninfected people have been sensitized to *S. schenckii s.l.* from previous exposures, while some patients with disseminated disease do not react.

Treatment

Sporotrichosis is treated with antifungal drugs. Itraconazole is currently considered the drug of choice in humans, but terbinafine, amphotericin B, fluconazole and other drugs are also used Potassium or sodium iodide may be effective in the cutaneous and lymphocutaneous forms. Some reviews and practice guidelines no longer recommend the use of ketoconazole. Thermotherapy and cryotherapy are occasionally employed, either alone (e.g., in pregnant patients with localized disease) or in conjunction with antifungal drugs. Photodynamic therapy was used, together with an antifungal drug, in one refractory case of cutaneous sporotrichosis. Debridement and repair may be necessary in some cases where the joints are involved.

Disseminated disease is more difficult to treat than cutaneous sporotrichosis, and requires long-term treatment. To prevent recurrence, lifelong therapy may be required in people with immunosuppressive conditions that cannot be reversed (e.g., transplant patients). The pulmonary form can be difficult to treat. In addition to drugs, surgical resection may be attempted if the lesions are localized to one area of the lungs.

Prevention

Protective clothing such as gloves, long-sleeved shirts and long pants can decrease the risk of infection when working with rose bushes, hay bales, wires, conifer seedlings or other plant material that can puncture the skin. Skin contact with sphagnum moss should also be avoided, as this material has been implicated in several outbreaks of sporotrichosis.

Gloves should be worn while handling or treating affected animals, particularly cats. After the gloves are removed, the hands should be washed thoroughly and disinfected with chlorhexidine, povidone iodine or another solution with antifungal activity. Controlling epidemics in cats is expected to reduce concurrent cases in humans.

Morbidity and Mortality

Sporotrichosis tends to be seen mainly in people who contact known sources of the organism, such as plant material or infected cats. However, clinical cases have been reported even in young infants who had seemingly never been exposed to the organism. Most cases of sporotrichosis are sporadic, but

outbreaks have been described. They are often linked to contaminated plant material, such as sphagnum moss, hay or wood. A few outbreaks in Africa occurred in mines, where the organism presumably grew on wooden structures in the hot, humid, underground environments. An ongoing feline epidemic in southern Brazil has caused more than 4000 zoonotic clinical cases, as of 2011. Armadillo (*Dasypus septemcinctus*) hunting has also been associated with sporotrichosis in Latin America, probably from organisms that grow on organic material in their burrows.

The most common forms of sporotrichosis in humans usually remain localized to the skin and are rarely life threatening in healthy people. However, scarring, disfigurement and bacterial superinfections are possible. Disseminated sporotrichosis, in contrast, is a serious, potentially life-threatening disease. This form of sporotrichosis is rare in healthy people; in one outbreak, it occurred in only 5 of 3000 infected miners. Disseminated disease is more common in people who are immunocompromised by conditions such as alcoholism, diabetes, cancer, AIDS or medication-associated immunosuppression. HIV-infected individuals tend to have the skin form unless their CD4+ T cell count is low.

Pulmonary sporotrichosis is a rare disease that tends to affect people who have preexisting lung diseases or are immunocompromised. It can be chronic and fatal, and may respond poorly to antifungal treatment, especially in immunosuppressed patients.

Internet Resources

Centers for Disease Control and Prevention (CDC)

Ministry of Health, Brazil

PHAC. Pathogen Safety Data Sheets

The Merck Manual

The Merck Veterinary Manual

World Health Organization

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