

Uncommon aetiology of lymphadenopathy in a healthy child: a sporotrichosis case with painless lymphadenopathy

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SUMMARY

A 6-year-old boy was referred to the paediatric infectious disease clinic with a 2-month history of enlarged, erythematous, painless cervical lymph nodes. He initially presented to his paediatrician with a painless lesion. At that time, he was treated empirically with clindamycin and azithromycin due to a history of cat exposure. Despite treatment, the lesion evolved into a non-healing linear ulcer with painless, ascending cervical lymphadenopathy. Serologies were negative for *Bartonella henselae* antibodies. Additional laboratory studies revealed eosinophilia and negative *Toxoplasma gondii* antibodies. After no improvement following a course of trimethoprim–sulfamethoxazole, further questioning revealed that the patient had fallen into a haystack 1 month before the initial cervical lesion. The patient's parents opted to treat the infection empirically for sporotrichosis with itraconazole rather than undergo lymph node biopsy. At the 2-week follow-up, his lymphadenopathy had resolved and had returned to baseline activity.

BACKGROUND

Sporotrichosis is a chronic granulomatous infection caused by the dimorphic fungus *Sporothrix schenckii sensu lato*.¹ It is first described by Schenck in 1898.² Sporotrichosis is reported as a worldwide prevalent yet occurs most frequently in Central and South American countries, such as Mexico,^{3–6} Brazil,^{4–8} Australia,⁵ Peru,^{4 5 9 10} Colombia⁵ and Venezuela,^{4 5 11} in Asian countries, including China,^{4 5 12 13} India,^{4 5 14} and Japan.^{4 5 15}

S. schenckii was thought to be the only pathogen of sporotrichosis in earlier studies.⁴ Recently, six other genotypes have been identified due to advanced genotyping technology. In the light of the latest development, *S. schenckii* was renamed as *S. schenckii sensu stricto*; while the other genotypes are named as *Sporothrix globosa*, *Sporothrix brasiliensis*, *Sporothrix luriei*, *Sporothrix mexicana*, *Sporothrix pallida* and *Sporothrix chilensis*. All genotypes are categorised under *S. schenckii sensu lato*.^{4 5 16–18}

Individuals usually contract sporotrichosis via soil contaminated with fungal conidia, which is often associated with sphagnum moss, rose bushes, decaying vegetative matter and hay.^{1 19 20} The fungus usually enters the skin through a small cut or scrape, but rare cases of sporotrichosis have been associated with scratches or bites from animals.^{19 20} There are four main sporotrichosis clinical presentations: lymphocutaneous, fixed cutaneous, multifocal or disseminated cutaneous and extracutaneous.

The lymphocutaneous form is the most common clinical presentation with 80% of the cases and is characterised by ulcerated nodules in a linear distribution on the limbs.^{19 21–23} The lesions are granulomatous, ulcerous and painful.²³ Spontaneous regression is extremely rare, and majority of the patients need treatment.²⁴ Thus, it is crucial to diagnose sporotrichosis to treat patients, because patients without treatment might develop disseminated or extracutaneous disease.^{24–26}

Clinical suspicion is the key for early diagnosis.^{24 27–29} Hence, patient's history and physical examination have a crucial role for diagnosis and initiating the treatment in the absence of lymph node biopsy due to lack of consent or assent as in this case. It is essential to be flexible as a diagnostician when a patient does not improve under evidence-based medicine-driven management. This report describes the management of a child with a rare infectious process, which prompted treatment based on clinical suspicion.

CASE PRESENTATION

A previously healthy, fully immunised 6-year-old boy presented to the paediatric infectious diseases clinic for evaluation of enlarged, erythematous, painless cervical lymph nodes (figure 1). His symptoms started 2 months ago as a painless lesion on the neck. He was initially evaluated by his paediatrician and treated empirically with clindamycin as well as azithromycin for suspicion of cat scratch disease. Laboratory results were found to be negative for *Bartonella henselae* antibodies. The lesion evolved into a non-healing linear ulcer with reddened, painless, enlarged lymph nodes ascending the neck from the initial lesion. Following the laboratory results and progressive lymphadenopathy, the boy was referred for further evaluation. The mother states that the patient has been more fatigued than usual, but has no pain or fever at the time of the visit. The patient describes interacting with numerous cats on his family's farm in eastern New Mexico. Physical examination is within normal limits aside from the small cervical lymphadenopathy on his neck along with the linear ulcerous erythematous lesion.

INVESTIGATIONS

Before referral to the infectious disease clinic, the local paediatrician ordered a serology study for *B. henselae* antibodies,³⁰ which were negative. At the time of presentation to the infectious disease clinic, antibody for serologies for *B. henselae* were



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Figure 1 Photograph of ulcerous lesion at first visit to infectious disease clinic.

repeated, and *Toxoplasma gondii*,^{30 31} as well as a complete blood count (CBC) with differential, ordered. The antibody serologies were both reported to be negative, and the CBC with differential revealed eosinophilia. The patient's parents decided not to proceed with a lymph node biopsy and agreed on treating it medically.

DIFFERENTIAL DIAGNOSIS

For acute lymphadenopathy, a differential diagnosis should include a variety of infections caused by bacteria, parasites, and fungi. *B. henselae* is typically at the top of the differential in a patient with this presentation and cat exposure history.³² However, the presence of eosinophilia, lack of response to appropriate antibiotics and repeatedly negative serology results for *B. henselae* can lead to other infectious agents to be considered.^{30 32} *Francisella tularensis* could present similarly, but the presence of painless ascending lymphadenopathy rather than painful lymphadenopathy without any exposure history made *F. tularensis* an unlikely aetiology. Infection with *Staphylococcus* and *Nocardia* sp could also be considered. Due to the history of cat exposure and the eosinophilia, also the parasite *T. gondii* should be considered, but laboratory results were negative for *T. gondii* antibodies.³¹ The considered fungal agents included *Candida albicans* and *Sporothrix* sp. Treatment with itraconazole typically cures infections of both fungi in an immunocompetent individual, but *C. albicans* typically presents as lymphadenopathy with additional oropharyngeal symptoms such as white patches on the inner cheeks, tongue, the roof of mouth or throat.³³ Also, in children, oropharyngeal *C. albicans* infections are often associated with immunocompromised states or the use of oral steroids. Autoimmune and neoplastic pathologies such as acute leukemias, lymphoma or Kawasaki disease can cause lymphadenopathy in children.³⁴ However, the labs were not consistent in this case. Also, *Sporothrix* sp are usually associated with painful ulcerous lymphadenopathy,^{23 34 35} which is not a mandatory symptom for the diagnosis of sporotrichosis. On the other hand, despite not being mandatory, a great deal of sporotrichosis cases are diagnosed with painful lymphadenopathy, and cases with painless lymphadenopathy are reported to be unusual cases in the literature.^{36 37} Few studies were found in the literature that consider it as an unusual sporotrichosis case for adolescents with painless lymphadenopathy without any other

significant symptoms.^{36 37} Hence, after ruling out other causes, and the absence of pain led us to consider the case as an unusual sporotrichosis case.

TREATMENT

The patient completed courses of clindamycin, azithromycin and trimethoprim–sulfamethoxazole with no improvement. The patient was given an empiric treatment of itraconazole 10 mg/kg/day (divided two times per day) at his follow-up visit to the infectious disease clinic. He completed an additional 2-week regimen of itraconazole following this third visit to the infectious disease clinic, since he had returned to baseline activity with resolved lymphadenopathy.

OUTCOME AND FOLLOW-UP

As previously stated, the patient returned to the clinic for the third time after 2 weeks of empiric itraconazole therapy. At that time, lymphadenopathy had resolved, and the boy returned to baseline activity. He completed an additional 2-week regimen of itraconazole with complete resolution of the lesions.

DISCUSSION

Despite worldwide distribution, most reported sporotrichosis cases are from Central and South America countries,²⁶ Asia countries and Australia.^{4 5} It is hard to determine the number of US citizens affected by *Sporothrix* sp because it is not under national surveillance due to its rarity. However, in the USA, this fungus has been associated with outbreaks in New Mexico, Missouri, Oklahoma and Texas.^{35 38–40} One-half of documented cases present in adults 30–40 years of age, while 30% of cases present in children 5–15 years. Lymphocutaneous infection is the most common form of the infection, especially in children, where the site of infection slowly progresses from a single lesion to a non-healing ulcer.^{3 41}

There are currently no serologic tests available to aid in diagnosis except for one test that was developed in Brazil.⁴² The golden standard confirmation test for *Sporothrix* sp is fungal cultures. Material from cutaneous lesions can be plated by samples collected via aspiration or scraping. It takes between 1 and 4 weeks to get results back from culture, so treatment is often not delayed in suspected infections.²⁶ Histopathology for *Sporothrix* sp is identified by granulomatous inflammation with occasional eosinophilia and asteroid bodies.^{3 41}

According to current clinical practice guidelines, itraconazole 200 mg orally daily for lymphocutaneous sporotrichosis is recommended for a total of 3–6 months.⁴³ However, cutaneous sporotrichosis can be cured in adults after periods of 15 days with a minimum total dose of 3.1 g. If adequate therapy is given, including the minimum total dose of 3.1 g, relapses are not known to occur.⁴⁴ There are no studies that suggest a similar treatment course in children would not cure cutaneous sporotrichosis in children. Prognosis is typically good, and full recovery is expected in immunocompetent individuals. The duration of treatment is dependent on the severity of the infection. As expected, lymphocutaneous infections do not require intensive medical treatment as systemic infections. However, it is rare for lymphocutaneous sporotrichosis to resolve spontaneously without adequate medical treatment.^{26 44}

In our case, we did not obtain a lymph node biopsy and, therefore, are not able to definitively say the patient had sporotrichosis. However, the patient responded to empiric treatment with itraconazole when previously had failed three rounds of antibiotics. The patient did receive 1 month of antifungal therapy, compared with

the recommended 3–6 months, but he did receive more than the minimum total dose of 3.1 g. It is imperative to pursue other infectious aetiologies after the patient did not respond to treatment to antibiotics covering gram-positive and gram-negative bacteria, including azithromycin, which is the empiric treatment of cat scratch disease. Serologies for *B. henselae* and *T. gondii*, which were ordered to the history of cat exposure, were both negative while the CBC with differential revealed eosinophilia. Eosinophilia is typically not only associated with parasitic infections, but is also associated with fungal infections as previous cases of sporotrichosis.^{41–44} By process of elimination, sporotrichosis best explains the patient's symptoms, and this case emphasises the importance of chasing uncommon diagnoses when common management does not improve patients' symptoms.

Although the gold standard for diagnosis of *Sporothrix* infections is fungal culture, occasionally, it is challenging to get consent for a lymph node biopsy from the parents due to cultural, religious or other factors.⁴⁵ To tackle such barriers, clinical suspicion could play a key role in diagnosis. Thus, an empiric antifungal therapy due to clinical suspicion could save time and can lead to earlier diagnosis to prevent disseminated disease.^{19–23–25}

Learning points

- ▶ This is a common presentation of an uncommon pathogen. In children, isolated lymphocutaneous presentation is the most common.
- ▶ A clinical diagnosis of sporotrichosis may be considered if standard treatment resolves symptoms, even without a definitive lymph node biopsy, primarily if more common infectious agents have been determined to be an unlikely explanation of symptoms.
- ▶ Although more common in adults, sporotrichosis can be acquired in children who live in endemic areas and are exposed to known risk factors.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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