

# The Clinical Spectrum of Nodular Lymphangitis

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**N**odular lymphangitis is an easily recognized but infrequently encountered clinical entity. Patients present with ulcerated distal lesions and develop proximal subcutaneous nodules following lymphatic drainage. Potential pathogens are numerous and uncommon; bacteria, fungi, viruses, and protozoa may all be present, and a high index of suspicion may be required in order to direct the diagnostic evaluation. Careful history, biopsy, and appropriate cultures are essential in establishing the correct diagnosis and course of therapy. This article presents two separate cases of nodular lymphangitis, one in a 70-year-old woman and one in a 35-year-old man. Differential diagnosis and treatment are also discussed.

## CASE ONE PRESENTATION

A 70-year-old woman is admitted to the orthopedic service with worsening ulceration accompanied by painful, erythematous nodules over her left metacarpal phalangeal joint, wrist, and forearm for débridement and intravenous therapy.

### Patient History

The patient's medical history is significant for colon cancer resection, but she is not currently taking any medications on a regular basis. Two weeks prior to presentation, the patient developed a painful nodule of the proximal interphalangeal joint of her left hand. The patient attempted to drain the nodule with a hot sewing needle, but no purulence or fluid could be expressed. The nodule progressed to an ulceration and was accompanied by additional erythematous, painful nodules over the metacarpal phalangeal joint, wrist, and forearm (**Figure 1**).

One week after initial symptom onset, red streaking developed from the patient's left wrist to the antecubital fossa, and she presented to the emergency department where she received an unknown intravenous antibiotic drug and a course of an unknown

oral agent. She was then referred to the orthopedic service.

## Current Presentation, Diagnosis and Treatment

In the orthopedic service, the patient denies fever and any other constitutional symptoms. She also denies gardening or exposure to salt or fresh water. Based on the patient's clinical presentation, she is diagnosed with nodular lymphangitis. She is immediately admitted to the orthopedic service and undergoes débridement. Culture of the material removed at débridement grows *Mycobacterium chelonae*. An intermediate purified protein derivative placed prior to the culture results produces 5 mm of induration after 48 hours.

A 4-week oral regimen of clarithromycin (500 mg three times daily) and ciprofloxacin (750 mg twice daily) is prescribed and has little effect on the nodules. A course of amikacin dosed once daily according to renal function in combination with cefoxitin promptly resolves symptoms.

## CASE TWO PRESENTATION

A 35-year-old man presents to his primary care physician with painful, erythematous, ulcerating nodules on the fingers of both hands. A 2- by 3-cm weeping ulceration involving the distal phalanx is also evident (**Figure 2**). The nodules on the patient's hands are accompanied by smaller nodules progressing up the lymphatic channels of his right forearm (**Figure 3**).

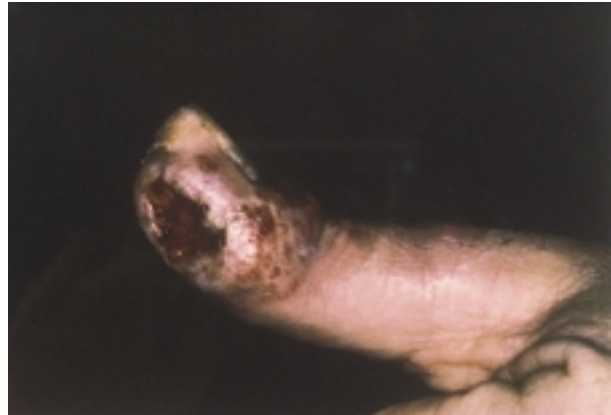
The patient is referred to a general surgeon and undergoes incision and drainage of the thumb lesion. Bacterial culture grows methicillin-resistant *Staphylococcus*

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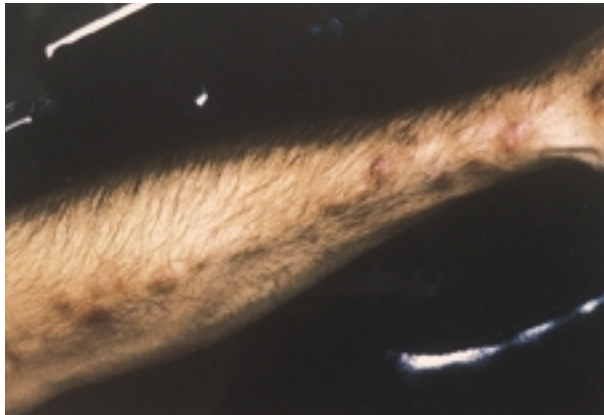
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**Figure 1.** Photograph of multiple inflammatory nodules of *Mycobacterium chelonae* in the hand of the patient in the case one presentation.



**Figure 2.** Photograph of an ulcerated primary lesion of *Sporothrix schenckii* on the thumb of the patient in the case two presentation.



**Figure 3.** Photograph of the proximal extension of small nodules following the lymphatic drainage of the patient's right forearm.

*aureus*, and the patient is given a 7-day course of trimethoprim-sulfamethoxazole.

Throughout the next 6 weeks, the patient's initial thumb wound does not heal and additional painful nodules extend proximally to the axilla. Referral to an infectious diseases specialist reveals a history of topiary assembly with sphagnum moss. A surface culture for fungi is negative.

An empiric course of itraconazole (400 mg/day) results in resolution of the ulceration in 2 weeks and more gradual improvement in the proximal nodules. Symptoms resolve in 8 weeks (9 weeks after initial presentation).

#### DISCUSSION

As previously mentioned, fungi, bacteria, viruses,

and protozoa are all potential pathogens involved with nodular lymphangitis (Table 1).

#### Fungi

The most common cause for nodular lymphangitis is *Sporothrix schenckii*. The lesions of sporotrichosis are pathognomonic for nodular lymphangitis and lend the designation *sporotrichoid* to the proximal extension pattern of nodules along the lymphatics from a distal primary lesion.

A history of exposure to wood splinters, thorns, or sphagnum moss is typically found.<sup>1</sup> Few organisms are present in the skin and the yeast forms are often not detected on histologic examination. Fungal culture, however, is considered diagnostic of infection. No serologic tests are reliable for this infection.

Treatment of sporotrichosis has evolved from potassium iodide and amphotericin B to the new azole antifungals with itraconazole being used most effectively.<sup>2</sup> Antifungal therapy should extend beyond lesion resolution because relapse has been shown to occur. Treatment courses of 6 months or longer are not unusual. If routine antibiotic therapy yields no improvement, as in the second case presentation, then biopsy or débridement is considered.

The endemic fungi *Histoplasma*, *Coccidioides*, and *Blastomyces* and the opportunistic fungus *Cryptococcus neoformans* have been described as infrequent causes of nodular lymphangitis.<sup>3-6</sup> Diagnosis is based on the culture results from the lesions and appropriate exposure history: for example, the Southwestern desert for *Coccidioides* and the Ohio and Mississippi River basins for *Histoplasma*. Amphotericin B is active against all of these fungi, but the new azole antifungals have also shown excellent activity.

**Bacteria**

**Mycobacterium.** The most common bacterial cause of chronic lymphangitis is *Mycobacterium marinum*, a photochromogenic mycobacterium found in fresh and salt water.<sup>7</sup> History usually demonstrates an injury in an aquatic environment, and acid fast culture at 30° to 32°C is necessary for diagnosis. A number of antibiotics have been used successfully in treatment, and macrolide clarithromycin has proven to be the most effective both in vitro and in vivo.<sup>8,9</sup>

*Mycobacterium chelonae* and *Mycobacterium fortuitum* are rapidly growing mycobacteria that can produce nodular lymphangitis. As demonstrated in the first case presentation, a history of trauma is usually followed by nonhealing ulcerative lesions that fail to respond to antimicrobial therapy. When cultured for acid fast bacilli, these organisms can be grown in 5 to 7 days from the ulcerated areas or from the time of débridement. Treatment of *M. chelonae* and *M. fortuitum* is less effective than treatment for *M. marinum* and is best directed by antimicrobial susceptibilities. Clarithromycin and the quinolones, which can be given orally, and amikacin and cefoxitin, which require intravenous administration, have proven effective.<sup>10</sup>

The primary pulmonary pathogens, *Mycobacterium tuberculosis* and *Mycobacterium kansasii*, are rare causes of nodular lymphangitis that may develop as a result of dissemination or by direct inoculation.<sup>11</sup>

**Nocardia.** *Nocardia asteroides* and *Nocardia brasiliensis* have been isolated in cases of nodular lymphangitis.<sup>12,13</sup> Trauma and soil contact are common factors preceding the appearance of the primary lesion. Diagnosis can be made by the appearance of branching gram-positive rods on Gram's stain, which are also acid fast when stained by the modified Ziehl-Neelsen stain. *Nocardia* may take days to weeks to grow on routine media and the laboratory should be advised not to discard the cultures for 4 to 6 weeks in suspected cases. Antimicrobial therapy with trimethoprim-sulfamethoxazole or sulfonamides is highly effective.

**Francisella.** The development of painful ulcers and adenopathy within 1 week of arthropod bites or contact with small mammals is demonstrated in the ulceroglandular form of tularemia caused by *Francisella tularensis*.<sup>14</sup> The lesions are usually accompanied by significant constitutional symptoms including fever, chills, myalgias, and anorexia. *Francisella* is potentially dangerous to laboratory personnel, and the diagnosis is usually made by serologic means. Both enzyme-linked immunosorbent assay and micro agglutination are useful. Streptomycin is the drug of choice for tularemia; gentamicin is an acceptable alternative.<sup>15</sup>

**Table 1.** Potential Pathogens in Chronic Nodular Lymphangitis

Pathogen	Common Exposures
<b>Fungi</b>	
<i>Sporothrix schenckii</i>	Gardening
<i>Blastomyces dermatitidis</i>	Gardening
<i>Coccidioides immitis</i>	Southwestern desert
<i>Cryptococcus neoformans</i>	Southwestern desert
<i>Histoplasma capsulatum</i>	Ohio and Mississippi river basins
<b>Bacteria</b>	
<i>Mycobacterium marinum</i>	Water or soil
<i>Mycobacterium chelonae</i>	Water or soil
<i>Mycobacterium fortuitum</i>	Water or soil
<i>Mycobacterium kansasii</i>	Human transmission
<i>Mycobacterium tuberculosis</i>	Human transmission
<i>Nocardia brasiliensis</i>	Soil
<i>Nocardia asteroides</i>	Soil
<i>Francisella tularensis</i>	Animal or arthropod
<i>Bacillus anthracis</i>	Animal
<b>Viruses</b>	
Cowpox	Cattle
Orf	Sheep
<b>Protozoa</b>	
<i>Leishmania braziliensis</i>	Sandflies
<i>Leishmania major</i>	Sandflies

**Bacillus.** *Bacillus anthracis* can also cause nodular lymphangitis: a pruritic papule that rapidly progresses to ulceration and necrosis after exposure to cattle, sheep, or goats or their hides is characteristic of the cutaneous form of anthrax. Local lymphangitis and lymphadenopathy occur and systemic symptoms can progress. The gram-positive bacilli are easily seen on smear, and cultures should be handled with caution by laboratory personnel. Careful handling of industrial products has reduced the risk of cutaneous anthrax. Treatment with penicillin, erythromycin, or tetracycline is effective in reducing the severity of systemic symptoms.<sup>16</sup>

**Staphylococcus and Streptococcus.** Common bacterial pathogens staphylococci and streptococci have been included in this differential diagnosis.<sup>17</sup> Infection with these organisms produces acute symptoms, rapidly responds to antimicrobial therapy, and does not present a diagnostic dilemma.

### Viruses

Two viral pathogens can produce nodular lymphangitis. Vaccinia (cowpox) and the related parapoxvirus (orf [a sheep virus]) produce vesicular lesions that progress to granulomatous nodules that may take weeks to heal.<sup>18</sup> Infection is self-limited and a history of contact with the animal or its products is usually present.

### Protozoa

Outside of the United States, cutaneous leishmaniasis is a common cause of nodular lymphangitis.<sup>19</sup> Both *Leishmania braziliensis* (New world) and *Leishmania major* (Old world) species produce cutaneous disease following the bite of sand flies. In general, the cutaneous leishmaniasis demonstrates single lesions. The nodular lesion may ulcerate and be followed by satellite lesions. Pain is mild and systemic symptoms are uncommon in this limited form. The amastigotes are identified from Giemsa-stained biopsy specimens or aspirates from the border of the lesion. Swabs from the surface of the ulcer are not specific. Treatment of leishmaniasis is difficult, with pentavalent antimonial drugs being used most widely. Allopurinol has been shown to be an effective alternative in cases of American cutaneous leishmaniasis.<sup>20</sup>

### SUMMARY

A careful history is essential to determine the specific testing needed to identify the unusual pathogens involved with nodular lymphangitis. In many cases, patients have already received courses of antibiotics and some patients may have undergone biopsy or débridement before appropriate studies are conducted. These treatments can often alter the initial appearance of the lesion or lead to bacterial superinfection. Fortunately, few cases progress to serious systemic disease. Even with specific therapy, however, many of these infections are slow to respond and treatment courses often extend for months.

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