

Mycobacterium haemophilum Skin Infection in the Setting of Systemic Lupus Erythematosus and Multiple Drug Allergies

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A 52-year-old female presented to her rheumatologist with a rash and tender skin nodules involving all four extremities. She had painful, inflamed, nodular skin lesions in the proximal interphalangeal joints of the second and third fingers on her right hand; the lesions extended proximally. Her left arm and both thighs also became involved. The patient had long-standing systemic lupus erythematosus (SLE) treated with immunosuppressants (short courses of azathioprine, cyclophosphamide, mycophenolate mofetil and belimumab, and long-term corticosteroids) as well as hypertension, hyperlipidemia, depression and non-alcoholic steatohepatitis.

Shortly before the rash developed, she swam in a hotel pool with “dirty water.” This played a limited role in suspecting a nontuberculous mycobacterial (NTM) infection.

On examination, she was found to have patches of erythema associated with erythematous, mildly tender, nodular lesions on both arms near the elbows. The lesions on her thighs included plaques and nodules that were erythematous and desquamating. Her rheumatologist initially entertained a diagnosis of vasculitis and increased her methylprednisolone dose. This resulted in reduced swelling of her hand, although new lesions continued to appear. A biopsy of the right forearm revealed subcutaneous granulomatous inflammation with acid-fast bacilli (AFB) noted on AFB stain. Repeat biopsies were sent for mycobacterial culture, and treatment was withheld until the organism was identified and the susceptibilities confirmed. Final cultures were positive for *Mycobacterium haemophilum* suscep-

tible to clarithromycin, rifampin, trimethoprim/sulfamethoxazole (TMP/SMX), amikacin, linezolid, ciprofloxacin, doxycycline and minocycline.

Initially, the patient was treated with clarithromycin and rifampin for one week. Treatment was switched to azithromycin and rifabutin because of a significant interaction between rifampin and methylprednisolone, which led to adrenal crisis requiring hospitalization, and because of significant nausea and vomiting from the clarithromycin. After three weeks, amikacin IV five times weekly was added because of unclear response to two-drug therapy. This three-drug regimen was continued for six weeks, after which the amikacin was stopped because of ototoxicity. Two months later, because of continued concerns about poor response to therapy, doxycycline was added to her program of azithromycin and rifabutin. Doxycycline was discontinued after one week because of concerns it had caused the patient's SLE to flare.

The patient was seen in follow-up by both an infectious disease specialist and a dermatologist, and slow-but-significant reduction in her skin lesions was noted. The lesions became less confluent and lighter in color. At her most recent follow-up, the patient had completed 12 months of therapy; an additional six months or more is tentatively planned.

Discussion

Mycobacterium haemophilum is an acid-fast bacillus that is known to cause skin and joint infections in immunocompromised patients.^{1,2} It is slow-growing and can be difficult to isolate because of its requirements for media containing fer-

ric ions and incubation at 30°C.³⁻⁵ It is the second most common cause of cervical lymphadenitis in children and occasionally causes lymphadenitis in adults. Skin and joint infection have been described in patients with cellular immunodeficiency including HIV infection, immunosuppression after organ transplant, and who are taking antirheumatic drugs; they also have been described in patients who have undergone chemotherapy treatment for malignancy.⁶⁻¹⁰

It is believed that immunocompromised patients are at risk because of difficulty with granuloma formation from impaired cell-mediated immunity.^{11,12} Therefore, *M. haemophilum* should be included in the differential for such patients who present with cutaneous lesions, particularly nodules around joints. Classically, the infection presents with skin lesions that initially start as nodules or tender erythematous papules that progress to painful ulcers. Other reports have described the presence of cysts, scales and plaques.^{11,13,14} These skin findings are usually on the extremities in close proximity to joints; this is believed to be caused by the organism's low-temperature requirements for growth. Less commonly, infection of the bone, lungs, blood or lymphatics has been reported.^{11, 13-15}

Currently, there are no specific guidelines for treating *M. haemophilum*. Cervical lymphadenitis can usually be treated with surgical excision alone. Susceptibility data should be used cautiously when creating a treatment program since there is no standardized testing methodology. Skin, soft-tissue and disseminated infection are usually treated with a multidrug regimen for varying durations. Successful regimens have included combinations of

ciprofloxacin, clarithromycin or azithromycin, rifampin or rifabutin, TMP/SMX, tetracycline and an aminoglycoside (usually amikacin).¹¹ In this case, although the organism was drug-susceptible, treating this patient was difficult because of drug interactions and the patient's extensive drug-allergy history, which included TMP/SMX, ciprofloxacin, tetracycline, cephalexin and clindamycin.

Previous reports have stressed the importance of discontinuing immunosuppression along with antibiotic therapy for cure of disseminated *M. haemophilum* infection.¹¹ However, in some instances, this is not feasible.

The diagnosis and treatment of *M. haemophilum* infection were challenging in this case. Skin biopsies are often critical for diagnosis of NTM and other atypical infections in immunosuppressed patients who present with new skin lesions. In this case, they were diagnostic. The case also illustrates that clinical

improvement can occur with long-term combination antimicrobial therapy when complete cessation of steroids is not possible. **MM**

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