


Patient on Immunomodulatory Therapy Experiencing Joint Pain and Skin Lesions: A Case Report

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Abstract

A woman in her late fifties was admitted to the Family Medicine Inpatient Service directly from Rheumatology clinic for polyarticular pain and erythema with concern for infection. She was taking immunosuppressant medications for a history of multiple autoimmune diseases. Examination showed increasing erythema and tenderness on the upper and lower extremity joints. Histologic evaluation, surgical evaluation, and cultures were consistent with *Mycobacterium haemophilum* infection. *Mycobacterium haemophilum* is an uncommon opportunistic infection that usually affects immunocompromised patients. The patient was treated with a multi-drug antibiotic regimen for several months due to drug resistance. Although this opportunistic infection is not common it should be considered in the differential of immunocompromised patients with skin and articular symptoms. Treatment outcomes are usually favorable if it caught earlier in the course.

Keywords

Mycobacterium haemophilum, immunosuppressed, arthralgia, rheumatologic disease, cutaneous lesions

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Case Presentation

A 59-year-old woman was seen at a Rheumatology appointment for a several month history of increasing pain and discomfort of her right elbow, right wrist and right ankle. The patient had a past medical history significant for spondyloarthritis taking daily prednisone and methotrexate, Ehlers-Danlos syndrome, Von Willebrand's disease, Crohn's disease taking ustekinumab (Stelara), and osteopenia secondary to postmenopausal status. She was followed by multiple specialties including Pain Medicine and Rheumatology. Notably, she was also being seen by Orthopedics for several months of right hand and wrist pain and a femoral head insufficiency fracture with non-operative management. Bacterial cultures and fungal cultures were obtained from the right hand at the time of her initial discomfort complaints but no acid-fast or mycobacterium cultures were done. Just prior to her rheumatology appointment she had seen dermatology for recent onset skin lesions who took biopsies due to concern for herpes simplex virus (HSV).

The patient's rheumatologist suspected joint infections potentially complicated by systemic infection so sent her for

admission. The patient denied any new neurologic symptoms such as headache, vision changes, changes in sensation, or motor weakness. She also denied any fever, chills, chest pain, shortness of breath, and palpitations, though she did report recent skin lesions on her gluteal cleft as well as her right forearm with some increasing red discolorations. On exam the patient was afebrile, normotensive, and saturating well with normal heart and respiratory rates. There was notable tenderness on her right hand and wrist with intact range of motion. The right elbow was swollen and tender to palpation but range of motion was also intact. The right ankle and foot had significant swelling erythema with limited range of motion secondary to pain. The patient did have subcutaneous ulcers, without vesicles, on her right upper thigh and gluteal cleft region. She also had red nodules that were firm and non-blanchable

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located on her upper and lower extremities near the affected joints that varied in size from a 0.5 to 2 cm.

Initial labs were notable for a mild leukocytosis of 14.6 with neutrophil predominance of 12.8, an elevated ESR of 29, CRP of 17.5, a slightly elevated lactate of 2.3, and anti-CCP 84.6. Her creatinine and liver enzymes were normal. A SARS-coronavirus-2 swab was negative/undetectable. An infectious workup was completed including blood cultures for fungal, bacteria aerobes and anaerobes, acid-fast smear, and mycobacterial cultures. Acid-fast stain was positive and cultures initially negative. Orthopedics and infectious disease consultations were done for evaluation of possible septic joints. After discussion, it was felt the best next step was to do joint aspiration cell sampling and cultures. Ankle cell sampling showed findings consistent with inflammatory changes, while the wrist demonstrated significantly increased nucleated cells with 24% neutrophil predominance consistent with an infection. At that time, it was felt that the wrist was going to be more diagnostic, and orthopedics performed wrist irrigation and debridement, where she was found to have chronic inflammatory lesions and necrotizing granulomas. Results were consistent with blood sampling: positive acid-fast stain with initial negative cultures that eventually grew *Mycobacterium haemophilum*.

On admission the patient was started on a broad regimen including vancomycin, ceftriaxone, Bactrim for PCP prophylaxis, and Valtrex to cover for possible HSV infection of the buttock wounds. After acid-fast stains were positive for mycobacteria, the patient was transitioned to azithromycin 500 mg daily, ciprofloxacin 500 mg b.i.d., rifampin 600 mg daily, and amikacin 800 mg IV Monday, Wednesday, Friday.

Discussion

Mycobacterium haemophilum was first described in 1978 as causing skin infections in immunocompromised patients.¹ *Mycobacterium haemophilum* is part of the sub group of non-tuberculosis mycobacteria that usually only affect immunocompromised patients and presents primarily with skin lesions and arthropathies.² Previous studies show lower temperature water sources, from tap to sea water, and damaged skin, are the likely sources of infection though other etiologies, such as via tattoos, have been described.³⁻⁵

The clinical presentations of *Mycobacterium haemophilum* vary but it may involve the cutaneous, musculoskeletal, pulmonary, ocular, or dermatologic systems. Skin lesions usually affect immunocompromised patients, like those with HIV, or patients who are immunosuppressed from medications. Skin manifestations can be localized or systemic and typically present as erythematous papules, plaques, nodules, necrotic abscesses, or chronic ulcers. They are usually found on the extremities and over joints. The evolution of skin lesions is often papule to pustule and may eventually evolve into a deep ulcer.^{3,6} Patients

sometimes can suffer from polymyositis; however, this is rare.⁷ Others suffer pulmonary complications, most commonly pneumonitis, with secondary systemic infections.⁸ Ophthalmological manifestations, from conjunctivitis to ulcers, may also occur, are difficult to treat, and will sometimes develop into corneal ulcers/perforations.⁹ In immunocompetent patients clinical presentations have been variable though cutaneous symptoms are common. However, presenting evaluations with findings of localized lymphadenitis or pulmonary infections have also been described.²

Mycobacterium haemophilum typically produce necrotic lesions and histologic examination show granulomatous/inflammatory reactions with necrotic foci. If a PPD is performed it may give an intermediate result. Cultures may not result until 8 weeks, and it is recommended that a PCR and/or acid-fast evaluation for mycobacteria be performed if suspicion is high. If testing suggests mycobacteria, antibiotic prophylactic coverage of multiple mycobacterial species is recommended until a culture based focused regimen can be prescribed.^{2,10}

Antimicrobial therapy for these infections has varied dependent on the patient type/infection and increasing antibiotic resistance. Currently, triple antibiotic therapy is usually advised as gene mutations promoting resistance are common. A common regimen would include a fluoroquinolone like ciprofloxacin, rifamycin (rifampine), and a macrolide. Treatment duration lasts for several months and in some cases going as long as 2 years. Amikacin is sometimes added for severe infection but is usually discontinued after a few weeks. Due to the long treatment course it is beneficial for the patient to acquire a central line or port for multi week IV treatments.^{2,11,12} Given the complexity and prolonged course, consultation with Infectious Disease is advised.

In our case, the patient continues treatment for her systemic *Mycobacterium haemophilum* infection. She has had multiple positive cultures for mycobacterium hemophilia despite several months of treatment. She is currently followed by Infectious Disease as well as Orthopedics specifically for her hand/elbow pain and discomfort. Her symptomatology and clinical course continue to improve, and she is expected to recover.

Conclusion

Mycobacterium haemophilum is an opportunistic infection that often presents with cutaneous symptoms such as pustules that may transition to painful ulcers, as well as joint pain. Other, less common, potential presentations include muscle pain/necrosis, pulmonary symptoms, ocular manifestations, and systemic multi-system involvement. These infections usually affect the immunocompromised such as those with HIV, or those with drug-induced immunosuppressed states such as this case.

Our patient's course demonstrates the importance of considering a wide differential in the evaluation of an immunocompromised or immunosuppressed patient presenting with new onset joint pain, especially when cutaneous lesions are present. Additionally, initial cultures were collected but no mycobacterium culture or stain was taken, highlighting the need to consider *Mycobacteria* specific testing in this patient population. In particular, acid-fast stain and more targeted testing such as PCR is needed if suspicion is high due to cultures taking up to 8 weeks to result. Surgical evaluation/intervention may also be helpful showing histologic changes consistent with the infection. A prolonged multidrug regimen is needed due to antibiotic resistance, but outcomes for these infections are usually good when diagnosed early.



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References

1. Sompolsky D, Lagziel A, Naveh D, Yankilevitz T. *Mycobacterium haemophilum* sp. nov., a new pathogen of humans. *Int J Syst Evol Microbiol*. 1978;28:67-75.
2. Lindeboom JA, van Coppentraet LEB, van Soolingen D, Prins JM, Kuijper EJ. Clinical manifestations, diagnosis, and treatment of *Mycobacterium haemophilum* infections. *Clin Microbiol Rev*. 2011;24:701-717.
3. Falkinham III JO. Surrounded by mycobacteria: nontuberculous mycobacteria in the human environment. *J Appl Microbiol*. 2009;107:356-367.
4. Kay MK, Perti TR, Duchin JS. Tattoo-associated *Mycobacterium haemophilum* skin infection in immunocompetent adult, 2009. *Emerg Infect Dis*. 2011;17:1734.
5. Smith S, Taylor GD, Fanning EA. Chronic cutaneous *Mycobacterium haemophilum* infection acquired from coral injury. *Clin Infect Dis*. 2003;37:e100-e101.
6. Geisler WM, Harrington RD, Wallis CK, Harnisch JP, Liles WC. Broad spectrum of dermatologic manifestations caused by *Mycobacterium haemophilum* infection. *Arch Dermatol*. 2002;138:229-230.
7. Jang E-Y, Lee S-O, Choi S-H, et al. Case of pyomyositis due to *Mycobacterium haemophilum* in a renal transplant recipient. *J Clin Microbiol*. 2007;45:3847-3849.
8. Lindeboom JA, Prins JM, Bruijnesteijn van Coppentraet ES, Lindeboom R, Kuijper EJ. Cervicofacial lymphadenitis in children caused by *Mycobacterium haemophilum*. *Clin Infect Dis*. 2005;41:1569-1575.
9. Millar MJ, Bulliard C, Balachandran C, Maloof AJ. *Mycobacterium haemophilum* infection presenting as filamentary keratopathy in an immunocompromised adult. *Cornea*. 2007;26:764-766.
10. van Coppentraet LSB, Smit VT, Templeton KE, Claas EC, Kuijper EJ. Application of real-time PCR to recognize atypical mycobacteria in archival skin biopsies: high prevalence of *Mycobacterium haemophilum*. *Diagn Mol Pathol*. 2007;16:81-86.
11. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med*. 2007;175:367-416.
12. Tyner HL, Wilson JW. Fifteen-year clinical experience with *Mycobacterium haemophilum* at the Mayo Clinic: a case series. *J Clin Tuberc Other Mycobact Dis*. 2017;8:26-32.