Mycobacterium haemophilum infection in a seronegative rheumatoid arthritis patient on anti-TNFα therapy: Should we start screening for nontuberculous mycobacteria in immunosuppressed patients?

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BACKGROUND

- Mycobacterium haemophilum was first described in 1978 as a pathogen causing skin infections most frequently in immunocompromised patients, which may explain its predilection for growth in 30°C to 35ºC temperatures and its tendency to cause skin and joint disease.
- It is a non-tuberculous mycobacteria (NTM) that can cause either localized or disseminated cutaneous lesions that present as painful, erythematous, and ulcerative skin nodules.
- It is more difficult to isolate than other NTM and requires a heme-supplemented culture medium for optimal growth.
- M. haemophilum is recognized in adult persons who are severely immunosuppressed such as in HIV, lymphoma following treatment, and those on immunosuppressive therapy after organ transplant.
- Patients with autoimmune conditions such as RA treated with anti-TNFα biologics such as infliximab, etanercept and adalimumab are at risk for NTM or other granulomatous disease.
- Here we present a case of disseminated M. haemophilum in a 77-year-old man with seronegative rheumatoid arthritis on infliximab and methotrexate.

CASE DESCRIPTION

- A 77-year-old man with a history of seronegative rheumatoid arthritis, CPPD arthritis, osteoarthritis, and pulmonary hypertension, whose symptoms had been previously well controlled on infliximab and methotrexate for 20 years, presented with a 2-month history of scaly, pruritic, and mildly tender erythematous nodule on his posterior left forearm, dorsum of left wrist and later left lower extremity unresponsive to topical agents and antibiotics.
- He lives in southwestern USA for half a year and the remaining half in the northwestern region. He denied history of smoking, alcohol use, IV drug use, exposure to TB, armadillo, fevers, chills, night sweats, or weight changes.
- On physical exam he had hand synovial changes consistent longstanding rheumatoid arthritis. An ~2-3 cm scaly erythematous nodule was noted on his left hand dorsum and left forearm. XR of his hands and knees were notable for his known degenerative joint disease.
- Lab studies including QuantiFERON-TB Gold, HCV, CBC, BMP, LFT, and CXR were all unremarkable. He denied HIV risk factors and declined testing.
- Biopsy of the hand lesion demonstrated deep dermal inflammation with a granulomatous component and associated fibrosis, positive Fite's Acid Fast stain for mycobacteria, NTB mycobacterial positive PCR testing, negative MTB complex and negative fungus and other bacteria.
- His infliximab was discontinued and he was continued on methotrexate, sulfasalazine and low dose prednisone.
- He was started on triple antibiotic therapy with clarithromycin, moxifloxacin, and rifampin with anticipated 6-18 months of therapy.

CLINICAL & DIAGNOSTIC IMAGES

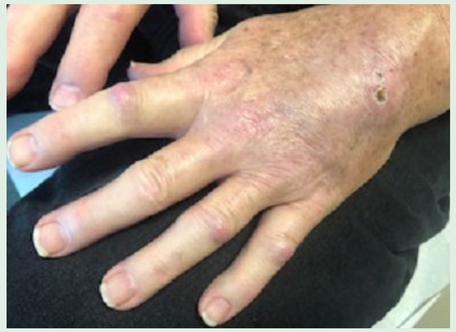

Figure 1: Painless erythematous skin papules on the patient's hand

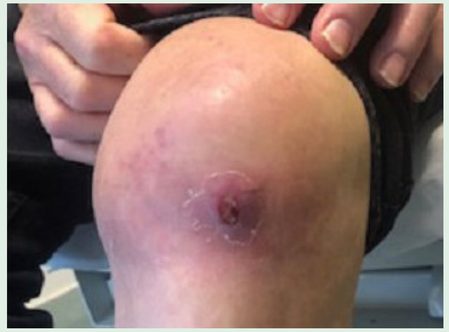

Figure 2: Evolution of papules into painful ulcerations on the patient's knee

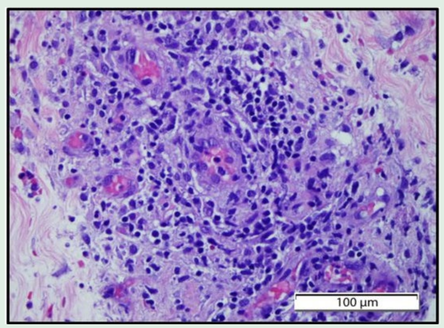

Figure 3: Representative skin biopsy with neutrophilic and granulomatous inflammation (not from the patient)

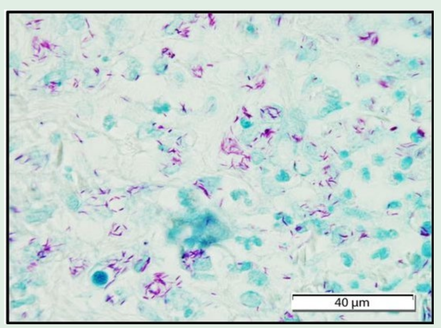

Figure 4: Representative acid-fast stain with numerous mycobacterial bacilli (not from the patient)

DISCUSSION

- The incidence and prevalence of NTM infection in patients with autoimmune disease treated with anti-TNFα is unclear.
- To date, emphases has been placed on TB prevention in patients treated with these therapies but little is known about the frequencies of NTM infections in such patients.
- There should be a high index of suspicion for M. haemophilum or other NTM skin infections when a patient on TNFα inhibitor therapy presents with unexplained localized or disseminated skin lesions.
- Once a diagnosis is made, treatment and duration of therapy becomes challenging as there are currently no standardized guidelines for optimal management of patients infected with M. haemophilum.
- This case highlights the known risks of opportunistic infections in patients with autoimmune diseases who are treated with TNFα inhibitors, but also raises the question as to whether to consider screening for such infections in at-risk patients on these therapies.
- Furthermore, epidemiologic studies may be warranted on an ongoing basis in the future to better understand the magnitude of this problem in order to develop an appropriate approach to the management of these patients.

REFERENCES

1. Wallis RS, Broder MS, Wong JY, Hanson ME, Beenhouwer DO. Gran-ulomatous infectious diseases associated with tumor necrosis factor antagonists. Clin Infect Dis 2004; 38:1261–5 (erratum: Clin Infect Dis 2004; 39:1254–5).
2. Collins CS, Terrell C, Mueller P. Disseminated Mycobacterium haemophilum infection in a 72-year-old patient with rheumatoid arthritis on infliximab. BMJ Case Rep. 2013 Mar 15;2013. pii: bcr2012008034. doi: 10.1136/bcr-2012-008034. PubMed PMID: 23505273; PubMed Central PMCID: PMC3618757.
3. Winthrop KL, Chang E, Yamashita S, Iademarco MF, LoBue PA. Nontuberculousmycobacteria infections and anti-tumor necrosis factor-alpha therapy. EmergInfect Dis. 2009 Oct;15(10):1556-61. doi: 10.3201/eid1510.090310. Review. PubMed PMID: 19861045; PubMed Central PMCID: PMC2866401.
4. Winthrop KL, Yamashita S, Beekmann SE, Polgreen PM; Infectious DiseasesSociety of America Emerging Infections Network. Mycobacterial and other seriousinfections in patients receiving anti-tumor necrosis factor and other newlyapproved biologic therapies: case finding through the Emerging InfectionsNetwork. Clin Infect Dis. 2008 Jun 1;46(11):1738-40. doi: 10.1086/587989. PubMed PMID: 18419421.

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