# A Diabetic Woman with Insulin Injection Abscesses

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## ABSTRACT

A 50-year-old diabetic woman developed multiple abscesses after daily injections of subcutaneous regular human insulin. Initial cultures from the draining fluid revealed no organisms, and the patient was unresponsive to multiple courses of antibiotics including doxycycline, amoxicillin/clavulanic acid, and intravenous vancomycin and piperacillin/tazobactam. After consulting dermatology, the patient underwent punch biopsy and tissue culture. The tissue culture grew *mycobacterium fortuitum* after 22 days of incubation. The patient was diagnosed with non-tuberculous mycobacterial infection and began to improve after treatment with ciprofloxacin. Non-tuberculous mycobacteria are common in the environment, although systemic manifestations of infection are rare in healthy individuals. In this paper, we discuss the risk factors, diagnostic methods, and treatment recommendations for these types of infections.

## CASE REPORT

A 50-year-old woman with newly diagnosed type 2 diabetes mellitus began self-administering subcutaneous regular human insulin daily using a multi-dose vial. One month later, she developed multiple abscesses on her abdomen and thighs in the areas that she had injected. She reported that the lesions occasionally drained fluid, were warm to the touch and painful. Several prior cultures obtained from the draining fluid had revealed no organisms.

The lesions were unresponsive to multiple courses of oral antibiotics including sulfamethoxazole/trimethoprim, amoxicillin/clavulanic acid and doxycycline. As a result of failing outpatient antibiotics, she was subsequently hospitalized for treatment with intravenous vancomycin and piperacillin/tazobactam with minimal improvement. When she initially presented to the dermatology clinic, physical examination of the lower abdomen and bilateral thighs revealed multiple 1 cm hyperpigmented, tender, warm, indurated nodules with a surrounding border of erythema and scant serous drainage. The patient was afebrile and otherwise appeared well. Punch biopsies were obtained for histologic examination and tissue culture. Insulin obtained from the multi-dose vial was also sent for culture.

Histologic examination demonstrated granulomatous inflammation in the deep dermis and subcutis. Acid fast bacilli and Periodic acid-Schiff tissue stains were negative for organisms. PCR-pyrosequencing on formalin-fixed paraffin embedded tissue (Quest Diagnostics) was negative for isolates of acid fast bacilli. *Mycobacterium fortuitum* was isolated from tissue culture after 22 days

of incubation. No organisms were isolated from the multi-dose vial of insulin. The patient was diagnosed with a non-tuberculous mycobacterial infection. Initially, the patient was treated empirically with clarithromycin 500 mg twice daily and doxycycline 100 mg twice daily. Subsequent organism susceptibility demonstrated resistance to clarithromycin and sensitivity to doxycycline and ciprofloxacin. Clarithromycin was discontinued and ciprofloxacin initiated. The patient will require a prolonged course of antibiotics; however, she has demonstrated significant clinical improvement after 3 months of appropriate antibiotic therapy.

## FIGURES

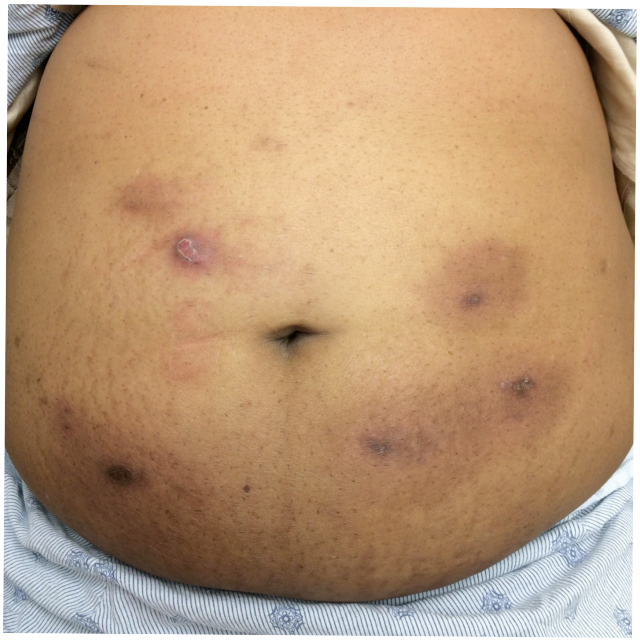

Figure 1. Initial presentation of the patient with multiple erythematous subcutaneous nodules in sites of previous insulin injections. These lesions were tender, hot and occasionally draining serous fluid.

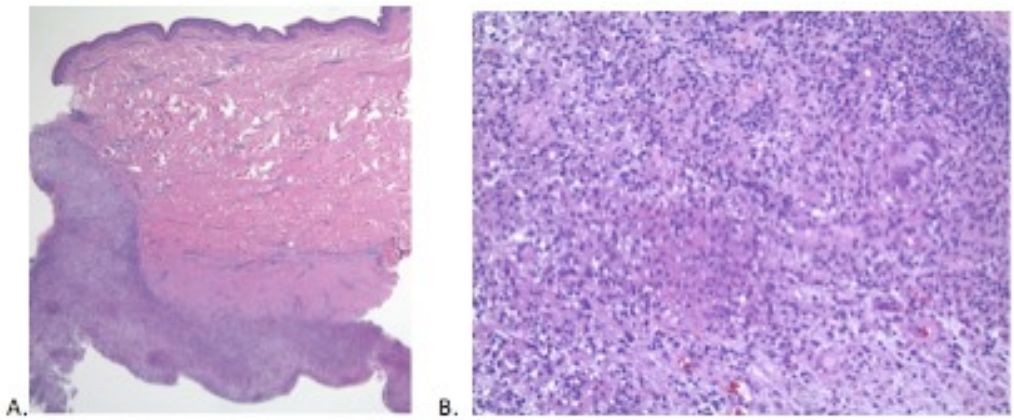


Figure 2. Scanning magnification of punch biopsy from the skin revealed deep dermal granulomatous inflammation (A). High power view shows pleomorphic inflammatory infiltrate with granuloma formation and focal necrosis (B). Special stains including acid fast bacilli and Periodic acid-Schiff were negative (not shown).

## DISCUSSION

Fast-growing, non-tuberculous mycobacteria are widespread contaminants in the environment found routinely in soil, dust and water. Skin and soft tissue mycobacterial infections are typically associated with trauma or surgical procedures, manifesting as pyogenic abscesses with local warmth, discharge and tenderness. Systemic manifestations are rare in healthy individuals.

Nosocomial etiologies of mycobacterial skin infections can arise from contaminated water sources, inadequate sterilization of surgical instruments and even contaminated disinfectants[1]. Mycobacterial skin infections have been reported in diabetic patients on insulin therapy and causative organisms include *M. abscessus, M. chelonae, M fortuitum* and *M. kansasai*[2-6]. In these cases, the route of insulin administration ranged from continuous insulin pump, injectable insulin pen systems and multi-dose vials.

Who is susceptible? There are demographic and clinical differences among patients with *M. fortuitum* compared to *M. chelonae* and *M. abscessus* cutaneous infections[7]. Patients with *M. fortuitum* infections tend to be younger, are less likely to be immunosuppressed and are more likely to have a history of preceding trauma or prior invasive surgical procedure. *M. fortuitum* is more likely to manifest as a single lesion, however the presence of a concomitant systemic comorbidity is associated with an increased risk of developing multiple lesions. The median time from onset of symptoms to microbiologic diagnosis is 86 days. This delay in diagnosis likely reflects the fact that mycobacterial cultures are not routinely performed.

Detection of mycobacterial organisms is challenging for many reasons. New techniques such as PCR on paraffin-embedded specimens are promising alternatives to culture, and may provide more rapid diagnoses[8]. In this case, making the correct diagnosis was complicated by the fact that our laboratory does not routinely test for *M. fortuitum*. We were not able to detect *M. fortuitum* from the insulin obtained directly from the multi-dose vial. This may reflect the inherent difficulty in culturing these organisms or may point to the possibility of another source of contamination (condensation on the vial top, for example).

No treatment guidelines have been established for rapidly growing mycobacterial skin infections. Susceptibility testing is recommended, however empiric treatment with dual therapy is a reasonable initial approach given the prevalence of single agent resistance. *M. fortuitum* isolates are usually susceptible to a number of oral antimicrobial agents including fluoroquinolones and sulphonamides; however, macrolide resistance can be an issue as in this case [9]. Duration of treatment should be guided by clinical response (at least 3 months typically) and occasionally, surgery for local abscess debridement when antibiotic therapy is ineffective.

With regard to best practices to prevent infection, there is little evidence to support disinfection of the skin and vial top or pen because risk of infection is negligible. In this case, our patient used new syringes and needles with each injection. However, she did not disinfect the skin or vial top. Current guidelines recommend cleaning and drying the skin prior to insulin injection; guidelines do not recommend cleansing with alcohol swabs[10].

Clinicians caring for patients with chronic “abscess-like” skin lesions in sites of injection should have a high index of suspicion for mycobacterial culprits. Adequate tissue samples should be obtained in order to appropriately culture these organisms. Additionally, PCR-based diagnostic tests should also be considered when the clinical suspicion for a mycobacterial infection is high.

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