

## CASE REPORT

# Atypical presentation of atypical mycobacteria in atypical diabetes

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## Abstract

A 45-year-old, non-obese male presented with low-grade, remittent fever and a fluctuant swelling over the posterior aspect of his lower left flank. Laboratory tests revealed leukocytosis, raised ESR, hyperglycemia and raised HbA1C levels. Light microscopy of Ziehl–Neelsen-stained pus sample revealed numerous acid-fast bacilli. After 72 h of incubating aspirated pus in Löwenstein–Jensen media, non-pigmented, cream-colored colonies were observed, suggestive of rapid-growing atypical forms of mycobacteria. Polymerase chain reaction of isolated bacteria identified *Mycobacterium chelonae* as causative organism. Abdominal skiagram revealed extensive pancreatic intraductal calcifications suggestive of fibrocalculous pancreatic diabetes and lumbar vertebral body destruction with evidence of paravertebral abscess. The patient was prescribed a split-mixed insulin regimen, clarithromycin and ciprofloxacin with complete resolution of the subcutaneous abscess at 6 months. Diabetic patients are prone to infections. Mycobacteria, especially atypical ones, involving the spine and subcutaneous tissues have rarely been reported.

## INTRODUCTION

Diabetic patients are prone to infections involving the skin and subcutaneous tissues. Poor glycemic control with sustained hyperglycemia predisposes these individuals to increased risk of infections. In developing countries, often infections are the initial presentations of patients previously undiagnosed with diabetes. Atherosclerotic vascular disease, sensory neuropathy and hyperglycemia lead to abnormalities of microcirculation, leukocyte adherence, chemotaxis and phagocytosis [1–3], substantially increasing the risk of infections. Cutaneous infections commonly found at presentation include candidiasis, furunculosis, carbuncles, styes, erythrasma, malignant otitis externa, necrotizing fasciitis, dermatophytosis and mucormycosis. Organisms frequently isolated from bacterial infections include *Staphylococcus*

*aureus*, group A streptococcus, pseudomonas and anaerobes. Mycobacteria, especially atypical ones as causative agents, have rarely been reported. This case highlights the need for a high index of suspicion in diagnosing cutaneous forms of mycobacterial infections, especially, in endemic zones.

## CASE DISCUSSION

A 45-year-old male presented with low-grade fever and a fluctuant swelling over the posterior aspect of his lower left flank persisting for the preceding month. Fever was remittent and low grade without associated chills or rigor. He had first noticed a small swelling in left lower paravertebral area, which progressively increased in size to its present dimension (15 cm × 7 cm) (Figs 1 and 2). There was no history of local trauma to the affected

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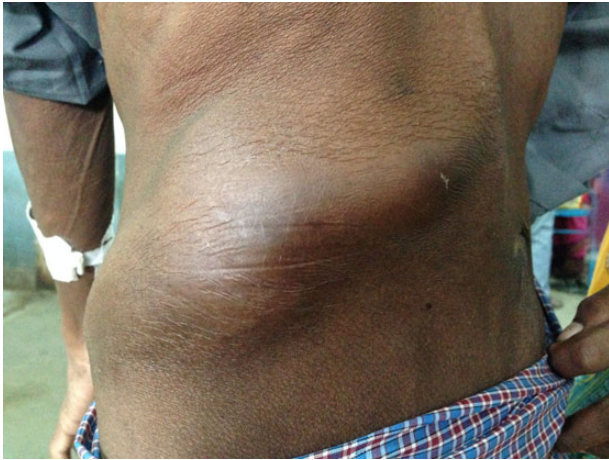


Figure 1: A fluctuant, non-tender swelling over the posterior aspect of left lower paravertebral region measuring 15 cm × 7 cm.



Figure 2: A fluctuant, non-tender swelling over the posterior aspect of left lower paravertebral region measuring 15 cm × 7 cm extending to the left flank.

area. The patient did not complain of any associated pain in the lumbar region or lower limbs. Prior to this presentation, he had never been diagnosed with diabetes or any other chronic debilitating disease. He denied using steroids, illicit drugs, alcohol or nicotine-containing products. He had had a steady sexual partner and did not travel in recent past. There was no history of diabetes in first- or second-degree relatives. Being a farmer, he was required to work outdoors for most part of the day exposed to harsh conditions. Careful questioning revealed passage of bulky, oily stools. Past history was insignificant with regard to acute emergencies requiring hospitalization. On examination, he appeared non-obese (BMI 19.4 kg/m<sup>2</sup>) with an axillary temperature of 38.1°C. A fluctuant, non-tender swelling was noted over the left lower paravertebral region. There was no evidence of acanthosis nigricans. A complete neurological evaluation failed to reveal any neurodeficit. Laboratory tests revealed leukocytosis (11 500/mm<sup>3</sup>), raised erythrocytic sedimentation rate (130 mm), fasting plasma glucose of 186 mg/dl, post prandial plasma glucose of 294 mg/dl and HbA1C levels of 11.0% (NGSP) [97 mmol/mol(IFCC)]. Pus aspirated from the swelling was inoculated simultaneously in blood agar, MacConkey agar, Löwenstein-Jensen media in duplicate (one of them covered with

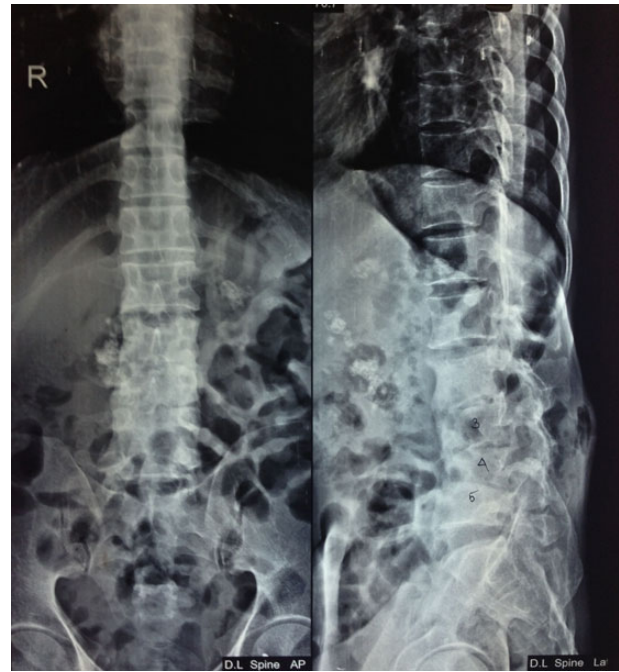


Figure 3: Erect abdominal skiagram showing linear fluffy calcifications along the pancreatic duct; destruction, collapse and wedging of third, fourth and fifth lumbar vertebral bodies, involvement of corresponding intervertebral discs, with evidence of paravertebral abscess.

black paper for scotochromogen) and Sabouraud's dextrose agar (SDA) slants. A smear prepared from the pus was stained by Ziehl-Neelsen (Z-N) stain for microscopic evaluation. Other baseline biochemical parameters remained noncontributory. In view of the absence of features suggestive of Type 2 diabetes (lean built, absence of acanthosis nigricans and a family history negative for diabetes), search for an alternative etiology was pursued. An erect abdominal skiagram revealed linear fluffy calcifications along the pancreatic duct; destruction, collapse and wedging of third, fourth and fifth lumbar vertebral bodies, involvement of corresponding intervertebral discs, with evidence of paravertebral abscess (Fig. 3). A screening magnetic resonance imaging (MRI) of lumbar spine revealed extension of the vertebral and paravertebral suppuration through the left paraspinal muscle into subcutaneous plane posteriorly. Subsequently, an ultrasound of the abdomen was remarkable for a dilated main pancreatic duct with extensive intraductal calcifications. A post-meal serum C-peptide level was estimated to be 1.1 ng/ml (cutoff 1.8 ng/ml). Pancreatic autoantibodies (anti-GAD 65 and anti-IA2) were negative. Thus, diagnosis of fibrocalculous pancreatic diabetes (FCPD) was arrived at. Light microscopy of the Z-N-stained pus sample revealed numerous acid-fast bacilli (Fig. 4). After 72 h of incubation, non-pigmented, cream-colored colonies were observed in Löwenstein-Jensen media suggestive of rapid-growing atypical forms of mycobacteria (Fig. 5). No growth was discernible in any other media, even on prolonged incubation. For the purpose of species determination, a polymerase chain reaction (PCR) of the isolated bacteria was undertaken. It identified *Mycobacterium chelonae* as the causative organism. The organism was identified using PCR-based Line Probe Assay (Hain Lifescience, Geno Type Mycobacterium CM). The whole procedure was divided into three steps: (i) DNA extraction from cultured material, (ii) a multiplex amplification with biotinylated primers and (iii) a reverse hybridization. The patient was treated with a

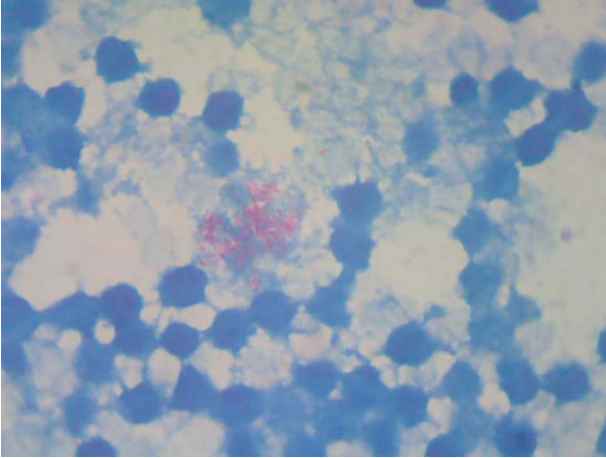


Figure 4: Light microscopy (100 $\times$  magnification) of the Z-N-stained pus sample showing numerous acid-fast bacilli.



Figure 5: After 72 h of incubating aspirated pus in Löwenstein-Jensen media, non-pigmented, cream-colored colonies were observed suggestive of rapid-growing atypical forms of mycobacteria.

split-mixed insulin regimen comprising of Neutral Protamine Hagedorn and rapid-acting insulin analogs. He was immobilized initially and later encouraged to use an external lumbar brace to facilitate mobilization. Clarithromycin (500 mg b.i.d) and ciprofloxacin were prescribed following *in vitro* susceptibility tests for a total of 6 months. Pancreatic enzyme supplementations were given in view of exocrine pancreatic insufficiency and resultant malabsorption. After 1 month following presentation, near-complete resolution of subcutaneous abscess was observed (Fig. 6). On follow-up at 1 year, the patient remained asymptomatic with a documented weight gain of 6 kg since the initial



Figure 6: Follow-up at 1 month after presentation shows near-complete resolution of subcutaneous abscess.

presentation. He exhibited satisfactory glycemic control, and his vertebral lesions showed signs of completed osseous healing, a minimal lumbar kyphosis (15 $^\circ$ ) and without any evidence of spinal instability or neurodeficit.

## DISCUSSION

In the developing world, where uniform and comprehensive healthcare facilities are far from reality, lack of health-related awareness and poor hygiene contribute to a growing burden of infectious diseases. A reduced T-cell response, neutrophil dysfunction, diminished humoral immunity and decreased production of inflammatory cytokines [interleukin (IL) 1 and IL-6] in response to lipopolysaccharide stimulation make diabetic patients susceptible to infections [4, 5]. Often, recurrent infections of skin and/or subcutaneous tissues are found to be the presenting feature of patients previously unknown to be diabetic. The infected diabetic foot bears a testimony to the same.

Non-tuberculous mycobacteria (NTM) are being increasingly recognized as important pathogens in the modern era. Ubiquitously found in the environment, human infections with NTM arise from unidentified environmental sources rather than human to human transmission. NTMs are classified as rapid growers (mature growth within 3–7 days) or slow growers (mature growth in 2–3 weeks) [6]. *M. chelonae* is a rapid-growing NTM belonging to Runyon group IV [7]. While cellulitis, granulomatous nodules, ulcers and localized abscesses are typical of immunocompetent patients, disseminated infection is more likely in the immunosuppressed [8]. Extracutaneous lesions include endocarditis, osteomyelitis, keratitis and catheter-related infections. NTMs including *M. chelonae* are resistant to usual antituberculous therapy. A combination of prolonged therapy with antimicrobials and debridement (when indicated) remains widely practiced [9]. *M. chelonae* may be susceptible to clarithromycin and ciprofloxacin. However, a combination of two antimicrobial agents showing adequate *in vitro* susceptibility is preferred, to avoid development of resistance [10]. Whenever feasible, a macrolide is considered in the regimen. In case of infections resistant to therapy against common pathogens, etiological diagnosis should be reviewed, taking NTMs into consideration. Not infrequently, NTMs have been isolated from insulin injection-site abscesses and nodular skin

lesions in diabetics. The skin infections are commonly due to *M. abscessus*, *M. chelonae*, *M. fortuitum* and *M. kansasii* [10]. It is of utmost importance to keep in mind the potential possibility of infection with NTMs when standard antibiotic therapy remains unyielding. Mycobacteria, especially atypical ones, involving the spine and subcutaneous tissues have rarely been reported.

Moreover, atypical mycobacterial infection as a first presentation of FCPD, an atypical form of diabetes restricted to tropical regions of the world, has been rarely reported in the world literature.

This case also serves as a reminder to the treating physician, of the rare atypical presentations of atypical mycobacteria in susceptible individuals like diabetics.

### CONFLICTS OF INTEREST STATEMENT

None declared.

### FUNDING

This case study received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

### ETHICAL APPROVAL

Approval not required.

### CONSENT

Consent was obtained.

### GUARANTOR

P.P.C. and S.N.B. are guarantors of this article.

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