

## *Mycobacterium neoaurum* bacteremia in a hemodialysis patient

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Bacteremia due to *Mycobacterium neoaurum*, a rapidly growing mycobacterium, is described in a diabetic woman on hemodialysis. This is the first reported case of *M neoaurum* bacteremia in Canada. The organism initially grew on standard BacT/Alert SA aerobic blood cultures, and was subsequently positively identified using 16S rRNA sequence analysis. The present case serves to reinforce the need for a high index of clinical suspicion of infections caused by unusual microorganisms in the context of an immunocompromised host.

**Key Words:** 16S rRNA sequencing; Hemodialysis infection; *Mycobacterium neoaurum*

### Bactériémie à *Mycobacterium neoaurum* chez une patiente traitée en hémodialyse

Voici un cas de bactériémie à *Mycobacterium neoaurum*, une mycobactérie à croissance rapide, chez une femme diabétique traitée en hémodialyse. Il s'agit du premier cas déclaré de bactériémie à *M. neoaurum* au Canada. Le germe s'est d'abord développé sur des hémocultures standard BacT/Alert en aérobiose, puis sa présence a été confirmée par l'analyse de séquence de l'ARN ribosomique 16S. Le présent exposé de cas vient renforcer la nécessité d'un indice élevé de suspicion clinique à l'égard d'infections causées par des germes inhabituels chez des hôtes immunodéprimés.

The present report describes a case of *Mycobacterium neoaurum* bacteremia and arteriovenous shunt infection in a hemodialysis patient. *M neoaurum*, a member of the *Mycobacterium parafortuitum* complex, belongs to the group of rapidly growing environmental mycobacteria that are responsible for a broad spectrum of illnesses, including surgical wound and catheter infections, and disseminated cutaneous and pulmonary diseases (1). To our knowledge, this is the first case of infection due to *M neoaurum* reported in the Canadian literature.

### CASE PRESENTATION

A 40-year-old woman with type 2 diabetes mellitus, end stage renal disease and hepatitis C presented with a two-month history of intermittent fevers, chills and malaise, and a weight loss of 6 kg. Additional complaints included episodes of pleuritic left-sided chest pain associated with shortness of breath and a dry cough. She had been receiving hemodialysis for one year, and for the previous nine months was dialyzed via a left arm fistula that included a 5 cm long, 6 mm diameter piece of interpositioned polytetra-fluoroethylene graft. Initial physical examination did not reveal a focus of infection. Investigations

that had been obtained after one month of symptoms included a normal chest x-ray and two peripheral blood cultures drawn on May 3 and 8, 2001 on routine media (BacT/Alert SA aerobic medium using BacT/Alert (bio Merieux, France) Classic blood culture continuous monitoring system with no growth. On June 2, she was reassessed and repeat blood cultures were obtained from a peripheral site and from the fistula. These were incubated in BacT/Alert SA aerobic medium and both became positive after seven days. The initial Gram stain of the culture medium was negative, but the acridine orange stain revealed numerous rods. Subsequent Kinyoun stain confirmed the presence of acid-fast bacilli (AFB).

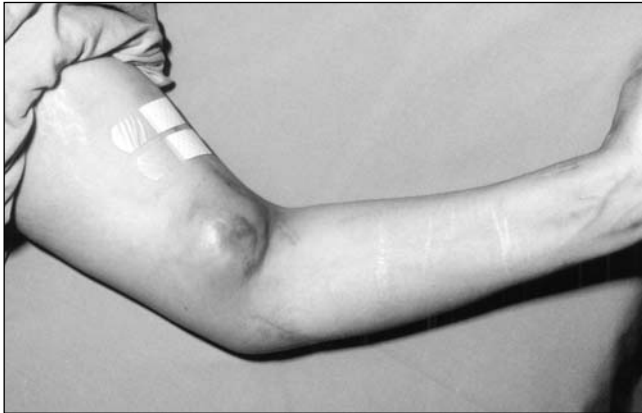
The patient was admitted to hospital on June 9, 2001 following the report of the positive blood culture. She had ongoing complaints of intermittent fever and shortness of breath, but was afebrile on admission and physical examination again showed no localizing findings. The peripheral leukocyte count was  $11.2 \times 10^9$  with 89% neutrophils. A repeat chest x-ray was unremarkable. Antimicrobial agents were held pending susceptibility testing of the organism. On June 11, the patient developed left arm tenderness and enlargement of the fistula (Figure 1). An ultrasound of her arteriovenous fistula revealed

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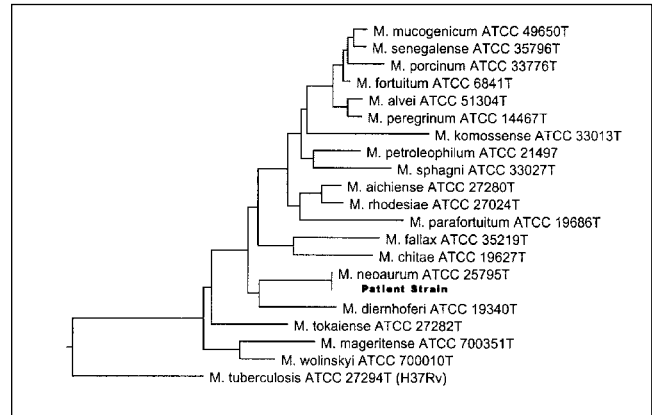


**Figure 1)** The arteriovenous fistula aneurysm in the antecubital fossa of the patient's left arm

a 4x2x2 cm aneurysm. On June 14, she was taken to the operating room for removal of the synthetic material and repair of the fistula. The graft material was submitted for AFB cultures on June 15 and became positive for AFB on July 6.

The organism was subcultured onto blood agar, chocolate agar, Lowenstein-Jensen media, Middlebrook 7H10 agar and 7H9-bovine albumin liquid media. Sequencing of the 16S rRNA gene for the identification of the organism (2) and standard biochemical tests for the characterization of mycobacteria were performed (3). Sensitivity testing of the organism was determined using E-test methodology. The organism grew at 25°C to 42°C and showed a bright orange pigment in both light and dark conditions. Relevant biochemical tests included a negative three-day and positive 14-day arylsulfatase test; positive nitrate reductase, urease, Tween 80 hydrolysis and iron uptake; tolerance to 5% sodium chloride; negative niacin; and no growth on MacConkey agar. Heat stable catalase activity was weak. Acid was produced from fructose, mannitol and inositol, but not sorbitol. While these biochemical test results did not conclusively identify our organism as *M neoaurum*, they were consistent with that identification. Partial 16S rRNA gene sequencing of this isolate from the initial blood cultures on June 12 and the tissue graft on July 12 displayed 100% identity to the type strain of *M neoaurum* ATCC 25795<sup>T</sup> sequenced at the National Reference Centre for Mycobacteriology (Figure 2). Standard methods were used for DNA extraction, 16S rRNA amplification and sequencing (3). E-test susceptibilities on June 12 revealed that the organism was sensitive to ciprofloxacin, doxycycline, rifampin and imipenem, and was resistant to isoniazid, ethambutol and clarithromycin.

The patient was started on twice daily oral ciprofloxacin 250 mg and twice daily oral doxycycline 100 mg on June 13. A transthoracic echocardiogram, performed on June 12, showed no evidence of cardiac vegetations. She remained afebrile in hospital and was discharged home six days after starting antibiotics. She received a further three-week course of the same antibiotics following discharge. Physical examination after the completion of the course of antibiotics revealed no focal findings, and there was no recurrence of symptoms. Repeat blood cultures for AFB were negative on August 1. The patient has



**Figure 2)** Phylogenetic tree based on the 5' region of the 16S rRNA gene (*Escherichia coli* bp 54-510) of the patient strain and its closest relatives. Sequences of all reference strains were determined at the National Reference Centre for Mycobacteriology, Health Canada. This tree was constructed using the Clustal method algorithm in the Megalign component of the Lasergene program version 4.01 (DNASTAR, Inc, USA). The tree was rooted using *Mycobacterium tuberculosis*, a slow-grower, as the out-group sequence. T Type strain

remained well following completion of the course of antimicrobial therapy.

## DISCUSSION

Molecular-based methodologies are increasingly taking place in diagnostic laboratories. In mycobacteriology, species identification based on conventional biochemical tests alone are time consuming (from four to eight weeks) and are quite often inaccurate or nonconfirmatory. The use of commercial DNA probes for the detection of the most commonly isolated species of mycobacteria, which include *Mycobacterium tuberculosis* complex, *Mycobacterium avium* complex, *Mycobacterium kansasii* and *Mycobacterium goodii*, has become routine in most mycobacteriology laboratories, because results are available in a few hours. However, there are more than 90 established mycobacterial species to date (4). Therefore, more advanced methods are necessary to accurately identify species. Some of the more widely used methods performed in reference laboratories for the identification of nontuberculous mycobacteria (NTM) species include 16S rRNA gene sequencing, polymerase chain reaction-restriction fragment length polymorphism of the *hsp65* gene, and high performance liquid chromatography (HPLC). As a member of the *M parafortuitum* complex, *M neoaurum* is one of the rapidly growing scotochromogenic mycobacteria and is difficult to conclusively identify based on biochemical tests alone. Consequently, the 16S rRNA sequence analysis has been the most commonly reported method for the identification of this particular mycobacterium species. In the present report, definitive identification involved 16S rRNA analysis with subsequent sequence comparison with two quality controlled databases; the National Reference Centre for Mycobacteriology database (5) and the Ribosomal Differentiation of Microorganisms database (6).

**TABLE 1**  
**Characteristics of *Mycobacterium neoaurum* infections**

Case	Reference	Year	Country	Age	Sex	Underlying medical disease	Immuno-compromised	Catheter	Reason for catheter	Total WCC/L	Antibiotics	Removal of catheter	Outcome
1	7	1994	Australia	17	M	ALL	Yes	Yes	BMT	0.1×10 <sup>9</sup>	Ticarillin, clavulanate, tobramycin	Yes	Cure
2	8	1988	Australia	53	F	Cystoadenocarcinoma	Yes	Yes	TPN	N/A	Cefoxitin, gentamicin	No	Cure
3	9	2000	USA	54	M	DM, hypertension, renal failure	Yes	Yes (peritoneal)	CAPD	3.62×10 <sup>9</sup>	Cefoxitin, ethambutol, rifampin, clarithromycin	Yes	Cure
4	10	2000	China	9	F	ALL	Yes	Yes	Chemotherapy	1.9×10 <sup>9</sup>	Ceftazidime, amikacin	Yes	Cure
5	11	1999	USA	46	M	Primary pulmonary hypertension	No	Yes	Prostacycline infusion	4.7×10 <sup>9</sup>	None	Yes	Cure
6	11	N/S	USA	N/S	M	Intravenous drug user	No	No	N/A	N/S	Piperacillin, gentamicin	N/A	Cure
7	12	2000	Italy	62	F	Recurrent UTI	No	No	N/A	N/A	Vancomycin, streptomycin	N/A	Cure
8	Present article	2001	Canada	40	F	DM, renal failure	Yes	Yes	Hemodialysis	11.2×10 <sup>9</sup>	Ciprofloxacin, doxycycline	Yes	Cure

ALL Acute lymphocytic leukemia; BMT Bone marrow transplant; CAPD Continuous ambulatory peritoneal dialysis; DM Diabetes mellitus; F Female; M Male; N/A Not available; NS Not stated; TPN Total parenteral nutrition; UTI Urinary tract infection; WCC/L White cell count per litre

A review of *M neoaurum* human infections reveals only seven reported cases in the English literature (Table 1) (7-12). Observations among all reports include the clinical presentation consisting of nonspecific symptoms. The patients ranged in age from nine to 62 years, three of the cases were women, and four of the seven patients were immunocompromised. Five patients had catheters (four intravascular, one peritoneal) in place, and, in the course of treatment, all but one of the catheters were removed. Six of the seven patients received antibiotic therapy, and all seven patients were cured. The characteristics of these cases suggest a low pathogenicity and only moderate morbidity with a *M neoaurum* infection. The presentation of disease in our patient was in keeping with the other reported cases. Our patient presented with weight loss, fevers and chills, with no localizing signs or symptoms on initial physical examination. The sensitivity profile of this strain was also consistent with those reported previously (7). The patient was treated using a combination of surgical and pharmacological therapy. Given the paucity of cases reported in the literature, there are no specific treatment guidelines for *M neoaurum*. However, both the American Thoracic Society and the National Committee for Clinical Laboratory Standards (NCCLS) recommend susceptibility testing of clinically significant isolates of rapidly growing

mycobacteria, and subsequent treatment with the appropriate antimicrobial agent (13-15). There exists a lack of standardization of methodology for the performance of antimycobacterial susceptibility of most NTM species (16), and, therefore, large multicentre trials are required to establish good correlation between laboratory findings and patient outcomes. Select well-established NTM species have consistently shown predictable antimicrobial susceptibility patterns, while newly characterized or rare species lack such patterns, largely due to a lack of abundance of isolates. There have been successful cases reported with monotherapy for the treatment of the rapidly growing mycobacterium, but in many cases, dual therapy is required. In addition, guidelines suggest that the removal of foreign bodies (eg, catheters) is important for clinical recovery (13). While surgery alone may have resulted in a cure, we used a combination of surgical and pharmacological approaches to eliminate bacteremia and to resolve the graft infection.

The original source of the organism in our patient is not known. However, we speculate that transient bacteremia from a break in the skin or the gastrointestinal tract may have led to 'seeding' of the graft. This hypothesis is consistent with her clinical presentation and the ongoing bacteremia, suggestive of an endovascular infection.

*M neoaurum* is an environmental organism that was first isolated from soil in 1972 and has since been isolated from multiple other environmental sites, including dust and water (17). Many environmental species of mycobacterium have been described to cause infections in immunocompromised as well as immunocompetent hosts. In the context of immunocompromised hosts, it is important to consider atypical mycobacterial species as potential infecting organisms, noting that infection must be differentiated from colonization. If infection with a clinically significant mycobacterial species is suspected (eg, isolates from blood, sterile body fluids, tissues or multiple isolates from sputum) (15), accurate identification using 16S rRNA sequencing or HPLC by a reference laboratory should be performed. In addition, as recommended in the NCCLS guidelines (3,14,15), specific antimicrobial agents and concentrations should be tested against rapidly growing mycobacterium. This information is essential to guide optimal therapy.

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