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Case report

Mycobacterium neoaurum line-related bacteremia with pulmonary involvement: Case report and review of literature

Saqib Walayat, Talha Awwal, Moni Roy, Sharjeel Ahmad

University of Illinois, 219 E. Illinois Ave, Peoria, IL 61603, United States

A B S T R A C T

Mycobacterium neoaurum is a rapidly growing non-tuberculous mycobacterium which is ubiquitous in nature. While it can cause line related infections in immunocompromised host, case reports of urinary tract infections, cutaneous infections, pulmonary infections, and meningoencephalitis have also been reported. We report the first case of *Mycobacterium neoaurum* line related bacteremia with concomitant pulmonary involvement. Our patient responded well to a nine week course of antimicrobials after removal of infected central line.

Introduction

Rapidly growing non-tuberculous mycobacteria (NTM) are usually defined as mycobacteria which grow within one week on culture media. They comprise a diverse group of naturally found microorganisms associated with a wide array of infections including soft tissue infections, keratitis, endocarditis, pneumonia, and catheter related bloodstream infections [1]. While tuberculosis is on a decline, the prevalence of rapidly growing non-tuberculosis mycobacteria (NTM) is reportedly on the rise all over the world [2,3]. This rise is postulated to be due to various environmental and host factors such as global warming, increased humidity, use of immunomodulator drugs, and an increase in immunocompromised population [1,3,4]. *Mycobacterium fortuitum*, *Mycobacterium chelnoae* and *Mycobacterium abscessus* account for most common rapidly growing NTM [1]. Among these *M. fortuitum* and *M. chelonae* are notorious for catheter related infections [5]. *Mycobacterium neoaurum* is a very rarely reported member of this group usually associated with infections in immunocompromised population [1]. It is a rapidly growing pigmented member of parafortuitium complex, first isolated from the soil in 1972 by Tsukamura and Mizuno [1,4]. It has been implicated in wide range of infections including catheter related bloodstream infections, meningoencephalitis, bacteremia, cutaneous infections, pulmonary and urinary tract infections.

Case history

A 68 year old Caucasian male initially presented to outpatient infectious disease clinic with a chief complaint of intermittent fever for 3–4 weeks. The fever was associated with chills, night sweats, nausea, headaches, and a fifteen pound unintentional weight loss. His past medical history was significant for recurrent small bowel obstruction with multiple previous abdominal surgeries, chronic watery diarrhea, factor V Leiden deficiency, recurrent urinary tract infections, MRSA infection, and type II diabetes. Patient had a trans-psoas Hickman catheter initially placed about 3 years ago for total parenteral nutrition (TPN) and hydration purposes. The catheter was replaced about 2 months ago prior to presentation due to malfunctioning and retraction issues. Vital signs included blood pressure: 98/50 mm-hg, pulse 70 beats per minute, respiratory rate of 18 per minute and temperature of 98 F. There was no focus of infection on physical examination, including the port site. He denied recent travel outside Illinois, had a pet cat at home, and used tap water for drinking. His white cell count was within normal limits, and ESR was elevated 55 (normal limit: 0–15 mm/h).

Work up including blood cultures, Quantiferon gold test, sputum for acid fast bacilli (AFB), and a trans-esophageal echocardiography (TEE) was ordered. Two sets of blood cultures 2 weeks apart were positive for *Mycobacterium neoaurum*. Work up for histoplasmosis, and human immunodeficiency virus (HIV) was unremarkable. Tagged white blood cell (WBC) scan showed increased uptake in bilateral lungs consistent with pneumonitis. Computed tomography (CT) chest was ordered due to new onset cough which showed numerous bilateral small non calcified centrilobular nodules within upper and lower lobes, consistent with pneumonitis (Fig. 1). Interferon-Gamma Release Assay (IGRA) for TB (QuantiFERON®-TB Gold In-Tube test, Qiagen, NV, Venlo, Netherlands) was also positive. Transesophageal echocardiogram (TEE) showed no vegetation or abnormalities. The Hickman catheter was removed, and catheter tip was sent for AFB cultures. A temporary right femoral central venous catheter was placed. The patient was started on intravenous (IV) cefoxitin 2 g 4 times daily, IV ciprofloxacin 500 mg twice daily, and

E-mail address: saqib.k.walayat@osfhealthcare.org (S. Walayat).

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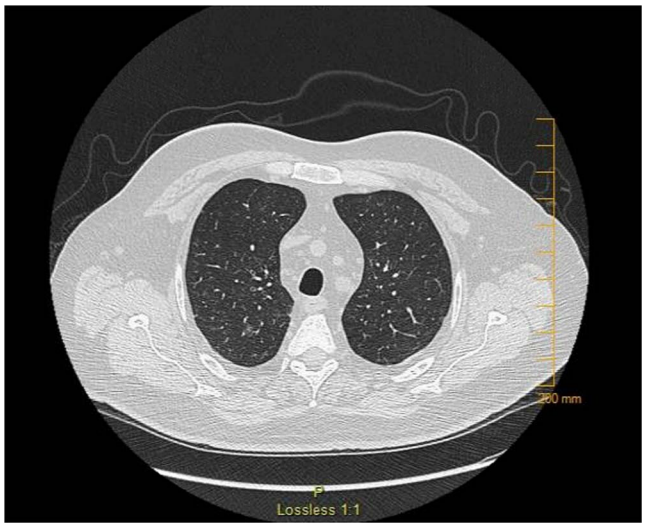

Fig. 1. CT scan showing pulmonary nodules before treatment.

oral doxycycline 100 mg twice daily. Blood cultures drawn after the initiation of anti-microbial drugs yielded no growth. Catheter tip culture showed growth of acid fast bacilli after 8 days. Culture susceptibilities showed the mycobacterium being susceptible to cefoxitin (MIC: 8 mcg/mL), imipenem (MIC < = 2 mcg/mL), ciprofloxacin (MIC: 0.25 mcg/mL), moxifloxacin (MIC < = 0.25 mcg/mL), amikacin (MIC < = 1 mcg/mL), doxycycline (MIC: 1 mcg/mL), trimethoprim-sulfamethoxazole (MIC: 0.5–9.5 mcg/mL), linezolid (MIC: 4 mcg/mL) and resistant to clarithromycin (MIC > 16 mcg/mL) and tobramycin (MIC: 16 mcg/mL).

The Hickman catheter was replaced a week after negative blood cultures. This 3-drug combination therapy was continued for 6 weeks and patient was transitioned to oral ciprofloxacin and doxycycline with plans for another 6 weeks of treatment. Treatment was stopped three weeks after transition (9 weeks total) as patient developed a diffuse macular erythematous rash on face and arms. CT chest obtained at the time of completion of treatment showed resolution of pulmonary nodules (Fig. 2). The patient was afebrile without further respiratory symptoms, fevers or chills at 6 months' follow up.

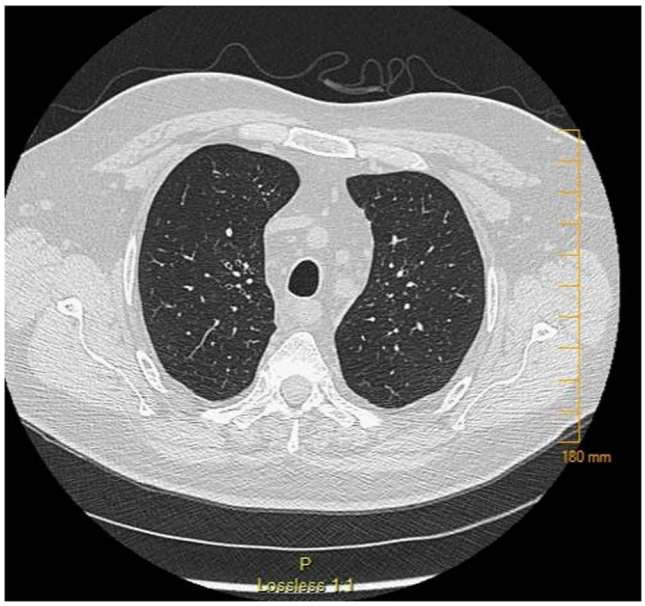

Fig 2. CT scan after treatment showing resolution of symptoms.

Discussion

Mycobacterium neoaurum is a rarely reported mycobacterium in humans which can cause a wide variety of infections but is more notorious for catheter related blood stream infection. The first case of human infection was reported in 1987 in an elderly female with cystadenocarcinoma of the ovary who had a Hickman catheter placed for TPN. Patient's Hickman catheter was left in place and her bacteremia responded to 7 weeks of gentamicin and cefoxitin [6].

Mycobacterium neoaurum is ubiquitous in nature and has been isolated from soil, rock, water and dust [7]. Review of literature showed only 21 reported cases in English literature. Patients ranged in age from 15 months to 80 years, median age being 46 years. Male to female ratio was 1:2.4. Malignancy, immunosuppression, recurrent bacterial infections, recent antimicrobials, IV drug use, prosthetic valves, diabetes mellitus, presence of foreign body like pacemaker and multiple comorbid conditions are reported to be risk factors [1,8]. Duration of bacteremia has been reported for up to 2 weeks [5].

Mycobacterium neoaurum is extremely hydrophobic and also has the ability to form biofilms, both of which contribute to its ability to cause line related infections [8]. It has the ability to survive at extreme temperatures as well as low pH and low nutrition states. The organism is reported to be resistant to common disinfectants [3]. While Hickman catheters are the most common lines that are infected as seen from our data, it could virtually involve any foreign body including PICC lines, pacemakers, prosthetic valves and AV fistulas. The first pure pulmonary infection was reported in 2006 which was thought to be related to chronic steroids and aspiration [9], while first CNS infection was reported in 2004 in an elderly female with rapidly progressive dementia [10]. However, the evidence of CNS infection was later thought to be contamination rather than true infection [11]. In case of our patient, pulmonary involvement likely occurred due to hematogenous seeding.

Most patients with catheter related infections had no evidence of infection at the catheter site [1]. Fever is almost universal at presentation except in cases of localized infections [5]. Omoryui et al. reported a case of *M. neoaurum* related hand infection in an immunocompetent patient who presented with non-healing ulcer of the hand. Their patient did not have any systemic signs of infection and inflammatory markers including WBC, ESR and CRP all were normal [12]. The source was thought to be most likely sea water exposure in that case. Earlier, Tsukamura and Mizuno also had originally isolated the organism from sea water in addition to soil. Another interesting case of skin involvement was found in a patient when *Mycobacterium neoaurum* was reported to cause alopecia in an immuncompetent host [13].

M. neoaurum is usually isolated from routine aerobic blood cultures. It forms smooth, round, yellow,-orange, schotochromogenic colonies in about 5 days on Lowenstein-Jensen agar at 25–35 °C. This helps to differentiate it from other rapid growing mycobacteria such as *M. fortuitum* and *M. chelonae* that produce non-chromogenic colonies [5]. This organism can take up to 5 days to grow, slightly longer than other rapid growing mycobacteria, and can be missed if the samples are discarded after 3–4 days [6]. 16s-rDNA sequence analysis is one of the most reliable methods for detection of this organism making it possible to have the diagnosis in as little as one day [6]. This could be useful especially in situations where there is difficulty in identifying the mycobacteria using conventional methods [1].

While there are no guidelines for treatment of infection with *M. neoaurum*, dual antimicrobial therapy is usually recommended to avoid antimicrobial resistance [6]. The American Thoracic Society recommends in-vitro susceptibility testing for rapidly growing mycobacteria [14].

Out of the twelve reported cases of CLABSI due to *M. neoaurum*, ten underwent catheter removal and antibacterial therapy, while one underwent just catheter removal [20] and another just underwent antimicrobial therapy without catheter removal [6]. A wide variety of

antimicrobials have been used including aminoglycosides, macrolides, fluoroquinolones, tetracyclines, cephalosporins, vancomycin, meropenem, linezolid, rifampin and ethambutol. There are no recommendations regarding duration of treatment or drug combinations but mostly 2–4 agents have been reported to be used. Duration of treatment also varied from 3 weeks to 4 months. Brown-Elliot et al. reviewed drug susceptibilities and reported most of the isolates to be susceptible to amikacin (46/46), cefoxitin (46/46), tobramycin (46/46), ciprofloxacin (46/46), doxycycline (21/21), gatifloxicin (38/38), imipenem (46/46), linezolid (46/46), moxifloxacin (23/23), sulfamethoxazole (20/20), tigecycline (22/22), and trimethoprim-sulfamethoxazole (45/45). There is some evidence of resistance to clarithromcyin suggesting the presence of inducible *erm* gene which is also thought to contribute to macrolide resistance in other species including tuberculosis [1,15]. Our case also showed similar findings with the organism being susceptible to cefoxitin, imipenem, ciprofloxacin, moxifloxacin, amikacin, doxycycline, TMP-SMX, linezolid, tigecycline and resistant to clarithromycin and tobramycin. Nineteen of the twenty one reported infected patients received antimicrobial therapy and all were cured except who was lost to follow up [8] and one possible fatality due to *M. neoaurum* involving the brain [22]. All the patients who were prescribed anti microbials responded to the drugs. Treatment was well tolerated and no relapse has been reported to date.

In our case, the patient had multiple comorbid conditions including TPN dependence, multiple abdominal surgeries, short bowel syndrome, and history of recurrent hospitalizations secondary to multiple infections and dehydration. Our patient also had a history of exposure to multiple infections, and a history of exposure to multiple antibacterial agents. All these could have put him at risk for infection. The American Thoracic Society has suggested a diagnostic criteria requiring clinical, radiographic and microbiologic evidence for non-tuberculosis mycobacterial lung disease. Our patient did have symptoms of fevers, night sweats and cough as well as radiographic evidence of multiple lesions which resolved after treatment making it most likely that his lung infection was also due to the NTM [14].

In conclusion, rapidly growing non-tuberculous mycobacteria such as *Mycobacterium neoaurum* are being increasingly recognized as an important human pathogen. Testing for these organisms should be considered in patients presenting with fever of unknown origin especially in immunocompromised settings or patients who have foreign bodies such as Hickman catheter present.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.idcr.2018.01.004.

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