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Case report

Mycobacterium szulgai pulmonary infection in a woman with anorexia nervosa

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ABSTRACT

A 40-year-old woman with severe anorexia nervosa was found to have a bilateral pulmonary infection with rare atypical mycobacterium *Mycobacterium szulgai.* Of note, she had no preexisting structural lung disease or history of tuberculosis, smoking, or HIV. Current data suggest that both impaired cell-mediated immunity and altered respiratory mechanics are risk factors for mycobacterial infection in patients with anorexia nervosa.

Introduction

Mycobacterium szulgai is a rare, slow-growing non-tuberculous mycobacterium (NTM) that typically causes pulmonary infection. Here we describe the first case of anorexia nervosa complicated by *M. szulgai* pulmonary infection in the United States.

Case report

A 40-year-old Caucasian woman with 22-year history of anorexia nervosa was brought to a community hospital after being found unresponsive at home. She was generally well until three months prior to admission, when she developed progressive weight loss, fatigue and weakness that limited her ability to walk. Two weeks prior to presentation, she developed a dry cough. She had no dyspnea, hemoptysis, pleuritic chest pain, fevers, chills or night sweats, nausea, vomiting or diarrhea, arthralgias, or rashes.

She was noted to be hypothermic, hypotensive, and tachycardic on arrival. She was cachectic on exam, weighing 43 kg with body mass index (BMI) of 16.8. Chest x-ray and computed tomography (CT) of the chest revealed bilateral thick-walled upper lobe cavitary lesions (see image below). She was started on broad-spectrum antibiotics with vancomycin, piperacillin-tazobactam and levofloxacin for septic shock. She was placed on airborne isolation and a bronchoscopy was performed. A bronchoalveolar lavage (BAL) specimen revealed 4+ acid fast bacilli (AFB) on auramine-rhodamine stain. Empiric anti-tuberculosis therapy with rifampin, isoniazid, pyrazinamide, ethambutol and pyridoxine was initiated. She developed progressive respiratory failure six days later, requiring intubation and mechanical ventilatory support, and was subsequently transferred to our hospital for further care.

At our institution, azithromycin was added to treat for the possibility of NTM infection. Laboratory studies were notable for: white blood cell (WBC) count 15.7 K/mcL, absolute lymphocyte count 330/mcL, hemoglobin 9.4 g/dL, platelets 60 K/mcL, and non-reactive human immunodeficiency virus (HIV) antigen/antibody test. Immunologic tests included normal total immunoglobulin G (IgG) 1079 mg/dL (700–1600). AFB blood cultures were negative. QuantiFERON®-TB gold (QIAGEN®, Germantown, MD) was indeterminate as the patient's mitogen response was <0.5IU/mL [1]. DNA probes for *M. tuberculosis* complex, *M. avium* complex and *M. kansasii* were negative, and the organism was speciated as *M. szulgai* at 28 days. Pyrazinamide and azithromycin were discontinued. She subsequently developed elevated AST on rifampin, isoniazid and ethambutol. After consultation with National Jewish, the patient was switched to moxifloxacin, ethambutol and rifabutin. She was discharged to an acute rehabilitation facility after 65 days of hospitalization, weighing 27 kg (BMI 10.5).

At a subsequent outpatient infectious disease clinic visit, the patient had gained 6 kg but had developed a drug rash. AFB culture susceptibilities returned and the isolate was found to be resistant to ciprofloxacin and rifampin (Table 1). The patient was then started on clarithromycin and amikacin but was unable to tolerate that regimen. Therapy was changed by an outpatient provider to isoniazid, rifabutin, and pyrazinamide due to limited options

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Table 1
Antibiotic susceptibilities of *M. szulgai* isolate.

Antibiotic	MIC	Interpretation
Amikacin	2	Sensitive
Ciprofloxacin	8	Resistant
Clarithromycin	.5	Sensitive
Ethambutol	4	Sensitive
Ethionamide	5	
Isoniazid	1	
Linezolid	8	Sensitive
Moxifloxacin	2	Sensitive
Rifampin	8	Resistant
Rifabutin	2	Sensitive
Streptomycin	8	
Trimethoprim/sulfamethoxazole	1/19	Sensitive

CT image of the chest taken after 6 weeks of NTM therapy showing persistent large bilateral upper lobe cavitary disease, left greater than right, with some thinning of both walls and decreased adjacent consolidation. There is also decrease in areas of airway centered nodularity with scattered residual areas in all 5 lobes.

secondary to adverse reactions. Her course was then complicated by drug-induced dermatological skin eruption and hepatotoxicity, the latter of which required readmission and cessation of therapy. Her weight increased to 29 kg with nasogastric feeds and she was transferred to an eating disorders unit at a psychiatric hospital. She was subsequently lost to follow-up.

Discussion

This is the first case of anorexia nervosa complicated by *M. szulgai* pulmonary infection in the United States, and the second documented in English language literature. The first case was described by Hotta, et al. in Japan in 2003 [2]. Our patient met ATS/IDSA diagnostic criteria with chronic cough, upper lobe cavities on chest imaging, positive BAL culture, and negative DNA probe for *M. tuberculosis* complex [3]. Factors that predispose to *M. szulgai* pulmonary infection include male gender, age greater than 50, history of structural lung disease, tobacco use, pulmonary tuberculosis, and HIV [3–5]. Interestingly, our patient had none of these characteristics.

M. szulgai is a slow-growing, scotochromogenic NTM that has been isolated from snails, aquarium water, swimming pool water, and tropical fish [5]. *M. szulgai* is an unusual pathogen, and accounts for <1% of all NTM infections [4,5]. *M. szulgai* causes pulmonary infection in two-thirds of patients [4]. However, it has been reported to cause extrapulmonary infections of the skin, soft tissue, joints, and lymphatics, as well as disseminated disease in immunocompromised individuals [3,4]. Pulmonary infection with *M. szulgai* clinically and radiographically resembles infection with *M. tuberculosis* [4]. *M. szulgai* is susceptible to most antituberculosis drugs, and current guidelines for pulmonary infection recommend combination therapy with three-to-four antimycobacterial drugs until sputum cultures are negative for 12 months [3].

Defense against pulmonary mycobacterial infection requires both intact local clearance mechanisms and cell-mediated immunity [3,6,7]. Mycobacteria are phagocytosed by alveolar macrophages, which release the cytokine interleukin-12 (IL-12), activating T-lymphocytes and natural killer cells to produce interferon gamma (IFN- γ) [3,6,7]. IFN- γ signals macrophages to produce IL-1 and tumor necrosis factor-α (TNF-α), enhancing their ability to kill mycobacteria [3,6,7]. TNF-α plays a critical role in granuloma formation and maintenance [3,6,7]. Macrophages also present mycobacterial antigens on their surface that trigger T-helper (Th) cell proliferation, which further augments host response [3,6,7].

Studies of the immune systems of anorexic patients reflect altered function. Patients with anorexia have lower total WBC and absolute lymphocyte counts, with a relative lymphocytosis compared to healthy controls [8–13]. Cell-mediated immunity appears to be altered with diminished response to delayed-type hypersensitivity skin tests and low in-vitro T-lymphocyte responses to mitogens [11,9–13]. Distorted T-lymphocyte subsets are also evident [8,10,9–13]. Some studies have suggested that distorted CD4+/CD8+ ratios and altered cytokine levels normalize with weight gain, but some have not [8,10,12]. In sum, impaired T-lymphocyte activation, distorted T-lymphocyte subsets, and an imbalance of cytokines and are thought to cause an impairment in T-lymphocyte function, T to B-lymphocyte cooperation, and altered immune response to mycobacterial infection in anorexics [8,11]. Of note, our patient demonstrated low response to the QuantiFERON-TB Gold mitogen, which may have been caused by a low absolute lymphocyte count or the inability of lymphocytes to release IFN- γ [1].

Low BMI appears to be an independent risk factor for pulmonary NTM infection [6,7]. Pulmonary NTM patients are observed to have lower levels of subcutaneous fat than controls, which may be attributable to the adipokines leptin and adiponectin [6,7,14,15]. Leptin is a hormone expressed by white fat cells that regulates satiety and has immunomodulatory effects on T-lymphocyte differentiation, enhancing phagocyte function, and increasing TNF-α and IL-12 production [6,14,15]. Leptin also promotes the Th1 response with increased secretion of IFN- γ [14,15]. Patients with malnutrition and anorexia nervosa have lower levels of leptin which may lead to low IFN-γ from T-lymphocytes, predisposing to infection [6,14,15].

Anorexics may also exhibit altered respiratory anatomy and mechanics, including respiratory muscle atrophy, air trapping, hyperinflation, decreased inspiratory drive and response to chemical stimulation, and impaired ventilation and gas exchange [9,15].

In summary, *M. szulgai* is a rare NTM that typically causes pulmonary infection clinically similar to *M. tuberculosis*. Both cell-mediated immunity and respiratory mechanics are impaired in anorexic patients, which may predispose to pulmonary mycobacterial infection. Weight gain may reverse some of these defects, and progressive weight loss likely contributed to the continued decline in our patient.

CRediT authorship contribution statement

Kamini Shah: Conceptualization, Data curation, Investigation, Writing - original draft. **Jonathan Siglin:** Writing - review & editing. **Devang M. Patel:** Conceptualization, Writing - review & editing, Supervision.

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