Case Report

Pulmonary Tuberculosis in a Patient with Cystic Fibrosis

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Abstract

Context: *Mycobacterium tuberculosis* (MTB) infection is rarely seen in cystic fibrosis (CF) patients. **Case Report:** We report a 24-year-old CF patient with fever, cough, hemoptysis, and weight loss of 1week duration prior to admission. Past sputum cultures grew methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The patient was treated with broad spectrum antibiotics based on previous culture data, but failed to improve. Chest radiograph and computed tomography (CT) chest revealed chronic collapse of the anterior subsegment of right upper lobe and multiple bilateral cavitary lesions which were worse compared to prior films. MTB was suspected and was confirmed by positive acid-fast bacilli (AFB) smears and cultures. After receiving first-line antituberculous drugs, the patient's condition markedly improved. **Conclusion:** MTB is an infrequent finding, but considered a potential pathogen in CF patients, and may lead to serious pulmonary complications if there is a delay in diagnosis and treatment.

Keywords: AFB, Cystic fibrosis, Genotyping, GeneXpert MTB/RIF assay, MTB

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Introduction

The basic defect in airway epithelial cells in cystic fibrosis (CF) leads to chronic infection with various bacterial and fungal pathogens. Despite this, *Mycobacterium tuberculosis* (MTB) is encountered rarely in CF patients and there are very few case reports of MTB infection in this population.[1-4] Most of mycobacterial infections in CF patients are secondary to nontuberculous mycobacteria (NTM) with a reported prevalence of 7-13%.[5-7]

Case Presentation

A 24-year-old Caucasian female diagnosed with CF (DF508 and G551D) at the age of 3 years was admitted to a hospital in Arkansas in November 2010 with a 2-week history of fevers (up to 101.5°F), worsening cough, coughing up blood, severe right-sided chest pain, and a 10 pound weight loss. Past sputum cultures had grown methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* and past acid-fast bacilli (AFB) cultures revealed no growth. Her forced vital capacity (FVC) and forced expiratory volume (FEV1) had dropped to 57 and 42% of predicted as compared to her baseline of 103 and 79%, respectively. On clinical examination, she was an ill-appearing thin female with increased work of breathing and bilateral coarse rhonchorous breath sounds. Vital signs revealed a temperature of 101°F, respiratory rate of 24, and pulse rate of 98. Laboratory parameters including complete blood count and basic metabolic panel were normal. Admission chest radiograph [Figure 1] and computed tomography (CT) chest [Figure 2] revealed the chronic collapse of the anterior subsegment of right upper lobe and multiple bilateral cavitary lesions that had worsened. She was started on broad spectrum antibiotics consisting of amikacin, levofloxacin, and vancomycin; without significant clinical improvement in her symptoms even after 4 weeks of treatment. Her initial AFB smears were negative, but subsequent cultures grew MTB after

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4 weeks, which was sensitive to all first-line TB drugs. Due to the culture results, the patient was initiated on a four drug anti-tuberculous regimen of isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA) that was continued for 2 months followed by 4 months of INH and RIF. The patient demonstrated clinical improvement with resolution of her submassive hemoptysis and febrile episodes along with an increase in her weight. Her subsequent AFB cultures after 2 and 6 months of treatment were negative for MTB and a radiograph of the chest [Figure 3] 7 months after the initial diagnosis showed marked clearing of the multiple bilateral cavitary lesions. Her FVC and FEV1 had improved to 85 and 58% of predicted, respectively.

Arkansas is a participant in the United States TB genotyping program that was implemented in 2004.[8] TB genotyping is a laboratory-based approach used to examine the genetic material of MTB. Specific sections of the genetic content help in distinguishing between the different strains of MTB based on the distinct genetic patterns formed by them. The isolate from our case was found to be in a genotype cluster with another case that was reported at the same time from an 87-year-old female in another county about 200 miles away. No epidemiologic links were found between the two and these were the only cases with the genotype G08667 in the national database. Laboratory cross-contamination was ruled out.

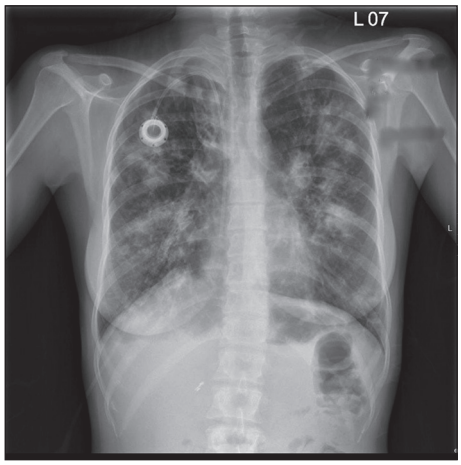

Figure 1: Chest radiograph of patient

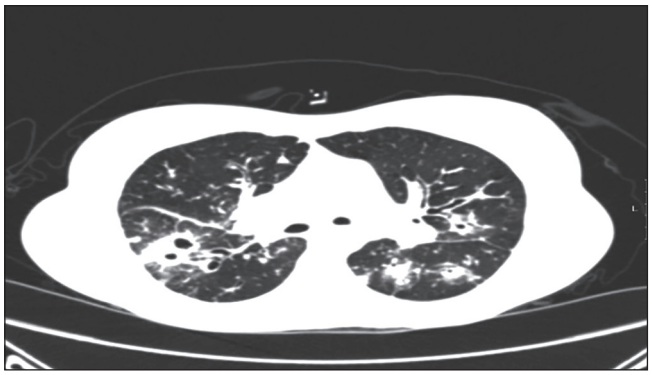

Figure 2: Computed tomography (CT) scan of patient

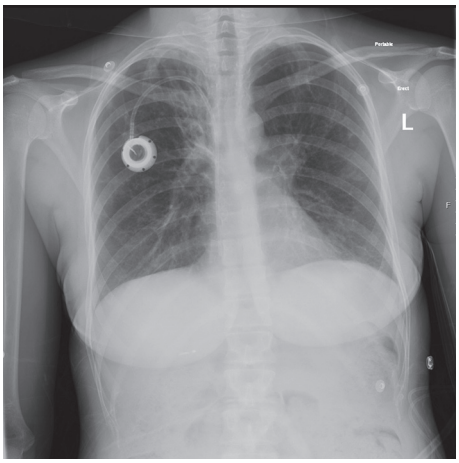

Figure 3: Follow-up chest radiograph of patient

Discussion

CF is a life-threatening autosomal recessive genetic disorder that primarily affects the lungs and digestive system. Risk factors such as chronic pulmonary disease, diabetes mellitus, malnutrition, steroid treatment, ethnic origin, and geographic location predispose CF patients to MTB infection.[3,9] During the past years, it has been appreciated that CF patients may become infected with MTB. MTB is an infrequent finding but considered a potential pathogen in CF and may lead to serious pulmonary complications, if left untreated.[2,10] In fact, previous prospective studies revealed the frequency of MTB infection in CF patients to be three out of 226 CF patients in the study by Smith *et al.*,[2] and one out of 54 patients in the study by Hjelte *et al.*[4] A recent study by Manika *et al.*,[9] reported a case of multidrug resistant (MDR) MTB in an adult patient with CF initially misdiagnosed as exacerbation of *P. aeruginosa* infection.

Possible reasons for the rarity of MTB infection in CF are still under investigation, and the exact pathogenesis remains unclear. Several pathways have been suggested which points to a genetic component of the disease or a defect in enzyme activity. It was noted in one study that carriers of this recessive gene are resistant to MTB infection, which is attributed to the production of excessive amounts of hyaluronic acid in these individuals.[11] Another possible explanation is the diminished activity of arylsulfatase, a lysosomal enzyme, in CF patients compared to normal population. Reduction in the activity of this enzyme by decreasing the availability of sulfate may have evolved as a mechanism to confer protection against MTB proliferation in CF patients.[12,13]

The low frequency of MTB diagnosis in CF may also be explained by the difficulty in the detection of mycobacterial infection both clinically and radiologically.[2,9] The difficulty in diagnosis can be due to the patient's long standing pulmonary symptoms (like chronic cough), frequent NTM infections, preexisting lung structural abnormalities (like cavities and bronchiectasis), and extensive radiographic abnormalities.[2] In most cases, the diagnosis of MTB infection in CF patients is based on a combination of clinical, radiographic, and bacteriological findings. Moreover, a clinical suspicion of MTB must be heightened in CF patients who deteriorate for unknown reasons or NTM infection that does not resolve despite adequate treatment.[10] The diagnosis of MTB is established by a combination of tuberculin skin test, interferon gamma release assays (IGRA), AFB sputum smear examination, GeneXpert MTB/RIF assay (Cepheid Inc.), and culture.[14]

Standard therapeutic regimen for MTB infection consists of at least four first line anti-TB agents (INH, RIF, PZA, and EMB), divided into 2 months of initial intensive phase followed by a 4-month course of RIF and INH in the continuation phase.[15] In CF patients with pulmonary MTB infection, treatment is complicated by the presence of live bacilli in alveolar macrophages that continuously replicate and become resistant when short-term therapy is stopped, thus longer duration of treatment might be necessary.[2] Patients diagnosed with lung cavitation on initial chest X-ray and positive cultures at completion of 2 months of the initial phase of therapy have a higher relapse rate, are more susceptible to drug resistance and require longer duration of the continuous phase of treatment (from 4 to 7 months).[16,17] The duration of therapy depends on the drugs used, the drug susceptibility test results of the isolate, and the patient's response to therapy.[16]

In summary, MTB is a rare but potential pathogen in CF. The diagnosis should be considered in CF patients with nonresolving and progressive respiratory symptoms despite adequate therapy for other common infections like *Pseudomonas* and NTM. Treatment of MTB infection in CF patients follows the standard therapeutic regimen of TB, but may require modification in the duration and choice of anti-TB agents depending on the patient's response to therapy.

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