

Introduction

The emergence of multi-drug resistant tuberculosis (MDR-TB) and its rapid progression to extremely drug-resistant tuberculosis (Pre-XDR-TB) is a global threat and is becoming a challenge to overcome due to the resistance of isoniazid, rifampin, fluoroquinolones, and other anti-TB agents. In the US, MDR-TB (resistance against isoniazid and rifampin) comprises only 1.0-1.5% of all TB cases, however the global mortality rate is 40% for MDR-TB and 60% for Pre-XDR-TB/XDR-TB. We report a case of a South-Asian immigrant with Pre-XDR-TB who, according to the Department of Health (DOH), is one of the first cases of Pre-XDR-TB in New York City.

Case

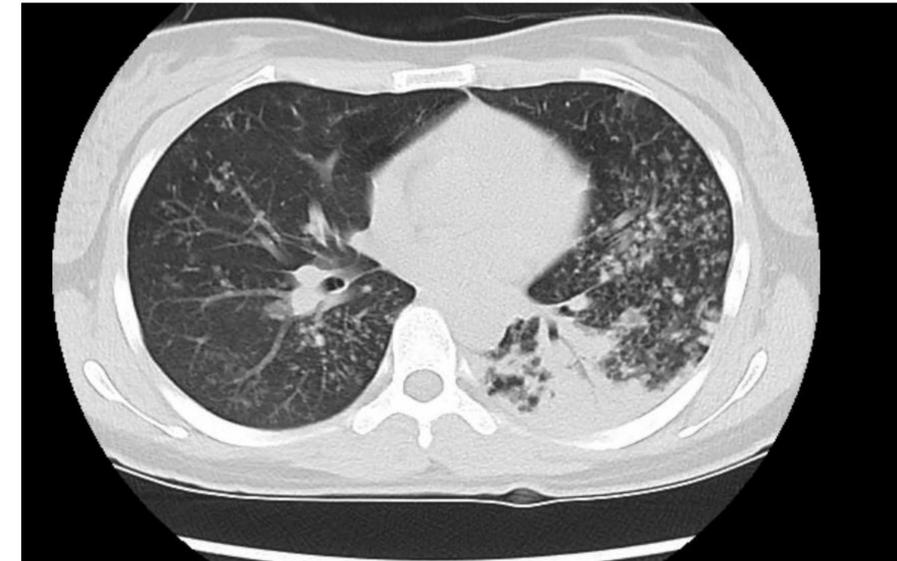
A 26-year-old female with a history of recurrent pneumonia presented with worsening cough and shortness of breath (SOB). She had a productive cough with intermittent low-grade fever, chills, fatigue, SOB, and left-sided chest pain. 2-weeks prior, she was treated for pneumonia with levofloxacin as an outpatient. In the past, she was hospitalized in India for the same symptoms and reported to have negative tuberculosis (TB) tests.

On examination, the patient was dyspneic with moderate exertion, tachycardic with SpO₂ of 94% on room air. Left-lower lobe crackles were heard. Labs revealed microcytic anemia and the HIV test was negative. Chest x-ray showed coarse reticular nodular opacities in both lungs with left lung base infiltrate. CT of the chest with contrast (Figure 1) showed small left pleural effusion with patchy opacities, air bronchograms in the left-lower lobe, diffuse nodularity, and possible cavitation. Interferon gamma release assay was positive along with acid fast bacilli in 3 sputum specimens. MTB/RIF assay showed resistance to rifampin. DOH reported ethambutol, INH, and ofloxacin resistance and was identified as “Primary Pre-XDR-TB.” The patient was started on an expanded TB regimen. The DOH reported that the patient had a TB diagnosis a year ago and was lost to follow-up. The patient was retested negative for TB and after 14 days and was discharged safely.

References:

1. "WHO Consolidated Guidelines On Drug-Resistant Tuberculosis Treatment". World Health Organization, 2019
2. Chen, J. et al " Early detection of multidrug- and pre-extensively drug-resistant tuberculosis from smear-positive sputum by direct sequencing "BMC Infectious Diseases, vol. 17, no. 1, 2017,
3. Sharma AK et al " A study on pattern of resistance to second line anti tubercular drugs among multi drug resistant tuberculosis patients." Indian J Tuberc. 2018 Jul;65(3):233-236
4. Ghajavand, H. et al "Scrutinizing the drug resistance mechanism of multi- and extensively-drug resistant Mycobacterium tuberculosis: mutations versus efflux pumps" Antimicrob Resist Infect Control 8, 70 (2019).

Figure 1



Computed tomography scan with contrast of the chest showing diffuse nodularity in a tree-in-bud configuration with patchy infiltrates in the left lower lobe.

Discussion

Tuberculosis is conventionally treated with first and some 2nd-line drugs. The concept of MDR-TB was first introduced in the 1940's and XDR/Pre-XDR-TB in 2007. According to the CDC data, there were 98 MDR-TB and 1 XDR-TB case in the US last year. Pre-XDR-TB denotes resistance to rifampicin and isoniazid in addition to at least one fluoroquinolone or one second-line injectable drug (kanamycin, amikacin, capreomycin).

Mutated target genes of antibiotics are the most common cause of MTB resistance. Rapid molecular diagnostics assays, direct sequencing of smear-positive should be used to obtain early drug sensitivity testing results. According to the 2019 WHO guidelines, initial MDR-TB treatments are separated into 3 groups which can be tailored to each patient and have been reported to have a better outcome.