

# Drug resistant pulmonary tuberculosis mimicking a flu-like syndrome in an elderly man: an atypical case report

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## SUMMARY

Despite remarkable reductions in its incidence and mortality, tuberculosis (TB) continues to be a major health burden globally. Pulmonary TB occasionally challenges physicians, either due to TB's ability to mimic many different conditions or because of the increasing number of drug-resistant *Mycobacterium*

*tuberculosis* isolates. Here we present a case of pulmonary TB with both characteristics and a brief review of the relevant literature.

**Keywords:** tuberculosis; atypical; lower respiratory infection; treatment resistance.

## INTRODUCTION

Tuberculosis (TB) is a major health burden worldwide and is often underestimated, especially in the developed countries [1]. Its ability to mimic a great spectrum of diseases, combined with the increased number of drug-resistant strains reported, pose a threat against the effort to inhibit TB's burden. The purpose of this report is to present a case of pulmonary TB with an atypical presentation and a drug-resistant isolate, and to present a brief review of the relevant literature.

## CASE REPORT

A 73-year-old Caucasian male was referred to the Department of Pulmonary Medicine of the Saint George General Hospital of Chania, Crete, with

a 2-week history of fever, fatigue and cough and symptoms of an acute lower respiratory tract infection (LRTI). His past medical history included a colectomy due to colon cancer 4 years earlier. There was no family history of pulmonary or extrapulmonary TB. He was also an ex-smoker of approximately 30 pack-years.

On presentation, the patient was febrile while all other vital signs were within normal range. His chest X-ray revealed bilateral infiltrative processes, mainly in the left lower lung region (Figures 1 and 2). The patient was admitted and received a 10-day oral empirical antibiotic treatment with cefuroxime axetil 500 mg and claritromycin 500 mg twice daily.

After not responding to the antibiotics, the investigation was broadened. Additional tests for autoimmune diseases, atypical respiratory pathogens and metastatic cancer were negative. A chest computed tomography was performed, which revealed bilateral multiple sized nodular lesions (Figure 3), one of which was biopsied using a CT-guided fine needle aspiration (FNA) biopsy. Bronchoscopy revealed no endobronchial

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**Figure 1** - Chest X RAY showing bilateral infiltrates.



**Figure 2** - Chest X RAY showing bilateral infiltrates.



**Figure 3** - Computed Tomography thoracic scan disclosing bilateral nodular lesions.

findings and his pulmonary functional tests were within normal range. The tuberculin skin test reaction resulted in an induration of 15 mm.

The results of the Ziehl-Neelsen stain of sputum and bronchial washing were negative for acid-fast bacilli.

The biopsy, on the other hand, revealed granulomatous inflammation with caseation. The diagnosis of pulmonary TB was confirmed by a positive culture of bronchial washing sample.

The patient initially received treatment with isoniazid (INH), rifampin (RIF), pyrazinamide (PZA) and ethambutol (EMB). The susceptibility results indicated resistance of the isolate to INH and streptomycin (SM) and so the regimen was altered to RIF, EMB and PZA. After 9 months of treatment, the patient developed optic neuritis and thus the regimen was once again altered to RIF, PZA and moxifloxacin, in order to complete a 12-month treatment. The patient gradually improved to full recovery and has showed no signs of relapse to date.

## ■ DISCUSSION

Despite the remarkable reduction in terms of incidence and mortality, TB remains a great global health burden and constitutes, next to HIV, the second most common cause of infectious-related death [1]. It is estimated that more than a third of the world's population is infected with TB [2]. In 2014, according to the World Health Organization (WHO), 9.6 million new cases of TB and 1.5 million TB-related deaths occurred worldwide [1]. There is a great variation of the epidemiology around the globe, with the highest burden, in terms of absolute numbers, being observed in India, China, sub-Saharan Africa and Indonesia [1]. Tuberculosis is highly associated with socioeconomic factors, in terms of both becoming infected and developing the disease. Highly indicative of this is the example of TB burden in Europe, which rapidly declined from the 19<sup>th</sup> to the 20<sup>th</sup> century, long before the development of effective treatment or vaccination.

It was not only attributed to the isolation of patients in sanatoriums, but to the socioeconomic development, better hygienic and nutritional conditions as well. In addition to incidence, low socioeconomic status in developing countries af-

fects mortality rates, as patients often don't get access to diagnostic or treatment services [3-5].

Although the vast majority of TB cases concern the developing countries, the burden in the developed countries has been magnified because of HIV, increasingly drug-resistant TB isolates and migrating populations from endemic regions [1, 6-10]. HIV-infected patients are at increased risk of primary and reactivated TB, and of higher mortality rates, especially in patients not receiving antiretroviral therapy [6-8]. It is thus no surprise, that 27% of the reported deaths from TB and 12% of the reported new cases in 2014 concerned HIV-positive patients [1].

It was not long after the use of the first antitubercular agent, streptomycin, that drug-resistance was noted, more than 70 years ago [11]. This subsequently led to the principle of multidrug regimens for the treatment of TB, soon after [12]. Nowadays, TB caused by isolates resistant to one of the first line antitubercular [isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), ethambutol (EMB), streptomycin (SM)] is defined as "drug-resistant TB". The term "multidrug-resistant TB" (MDR-TB) defines isolates resistant to INH and RIF and "extensively drug-resistant TB" (XDR-TB) refers to resistance to any fluoroquinolone and at least one aminoglycoside or capreomycin, in addition to MDR [13].

Surveys from around the globe indicate that drug-resistant TB is a major threat in the war against the disease, and, as improved drug susceptibility testing is being implemented, this will be even more obvious [1, 2, 13-15]. According to the Global Tuberculosis Report of 2015, by the WHO, 480000 new cases and 190000 deaths from MDR-TB occurred in 2014. Of the reported MDR-TB cases, an estimated 10% had XDR-TB [1]. The greatest risk factor for the development of drug-resistance is inadequate treatment due to either prescribing errors, lack of susceptibility testing or poor compliance [16].

In our case as well, drug-resistance was an issue, as our patient tested positive for an isolate resistant to INH and SM, although drug resistance is reported to be less common in older individuals [17, 18]. It is noteworthy that our patient didn't have any prior TB history, nor did he report contact with a drug-resistant patient, two known risk factors for drug-resistant strains [13]. Social deprivation of our patient due to the financial crisis in

Greece and significant reductions of his pension during the last years could be an important risk factor for tuberculosis infection. In alignment with this an interesting epidemiologic study by Ponticello et al., reported a significantly increase incidence of tuberculosis in a deprived Italian population [19].

It is reasonable to assume, that timely susceptibility testing and appropriate regimen alterations favoured the positive outcome in our case. In all patients, sputum should be collected, before initiating treatment, for culture and susceptibility testing.

TB is a multisystem disease that is known for its ability to mimic symptoms of many other conditions. This leads, in many cases, to delayed diagnosis and incorrect initial treatment with destructive impacts in terms of controlling the spread of the disease and preventing the development of drug-resistant strains [20-22]. As reported in studies, atypical symptoms and incorrect initial diagnosis are more common in elderly patients [23]. In our case, the patient was initially diagnosed incorrectly as LRTI and treated with empirical antibiotics, mainly because of the atypical radiographic features and the non suggestive history or demographic data. Increased awareness for TB by all clinicians is essential, especially in cases of uncertain diagnosis.

## ■ CONCLUSION

To limit the burden of TB furthermore, awareness of physicians needs to be enhanced. TB should be considered in any uncertain diagnosis and every positive culture for TB needs to undergo a susceptibility test.

**Conflict of interest.** The authors have no conflicts of interest to disclose.

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