THE UNEXPECTED EMERGENCE OF MULTIDRUG-RESISTANT TUBERCULOSIS AFTER SEEMINGLY EFFECTIVE TREATMENT OF PULMONARY TUBERCULOSIS - SUSPECTED MIXED-STRAIN INFECTION

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Objective:

INTRODUCTION

Although known from ancient times, and despite slow incidence decline, tuberculosis still represents an important cause of morbidity and mortality. As reported by WHO, tuberculosis is the leading infectious cause of death, with almost 4000 deaths daily. This can be explained by still incompletely known host-*M. tuberculosis* interaction, drug-resistant strains spreading, and growing population of immunodeficient patients. Another cause of high tuberculosis incidence is a mixed-strain infection, a phenomenon where one individual is infected with genetically different tuberculosis strains, with different drug-susceptibility characteristics.

Here we present a case of probable mixed-strain tuberculosis.

CASE REPORT

A 67-year old patient was hospitalized due to weight loss and malaise. The patient with a history of rheumatoid arthritis initially treated with corticosteroids received adalimumab and methotrexate during the last eight years. Thoracic and abdominal CT revealed lung consolidation in the right upper lobe, hilar and mediastinal lymphadenopathy, right pleural effusion, and ascites. In laboratory tests, ESR was elevated (60 mm/h), with microcytic anemia (hemoglobin 107 g/L, MCV 74.3 fL). Quantiferon test was positive. Fiberbronchoscopy was performed twice, malignant cells were not found, epitheloid, multinuclear cells were detected. *M.tuberculosis* cultures remained negative. Pleural effusion analysis

revealed lymphocytic exudate with a high level of adenosine deaminase (49 U/ml), ascites were also lymphocytic. *M.tuberculosis* was not detected in pleural effusion or ascites. Considering all findings, empirical antituberculosis therapy (isoniazid, rifampicin, ethambutol, pyrazinamide) was initiated. The control showed total clinical improvement with weight gain, regression of right pleural effusion, ascites, and partial regression of lung consolidation. All sputa samples were culture negative. After completion of therapy, PET/CT showed discrete metabolism (SUV Max 3,2) in the remaining infiltrate/cavitation of the right upper lobe. Another sputum sample was taken and, surprisingly, grew *M. tuberculosis* that was later shown to be resistant to isoniazid, rifampicin, pyrazinamide, streptomycin, and kanamycin.

CONCLUSION

Mixed-strain tuberculosis is often overlooked and undetected but a significant cause of poor treatment outcome and tuberculosis spreading. In our case, the patient was initially, empirically, treated as drug-susceptible tuberculosis with a good clinical and radiological improvement. Six months after antituberculosis treatment multidrug-resistant tuberculosis was detected. We hypothesize that the patient probably had coinfection with drug-susceptible and drug-resistant strains. The ''unmasking'' of mixed infection is important to choose optimal therapy and to reduce drug-resistant spreading.