

Neither Neoplasia Nor Tuberculosis, but *Francisella*

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Tularaemia is an emerging anthrozoosis transmitted by contact with infected animals and through arthropod bites, inhalation, or ingestion. We describe a pulmonary nodule suggesting cancer in a 70-year-old man. Histological analysis excluded neoplasia, and bacteriological culture excluded tuberculosis. Serological testing and PCR *Francisella* were positive for this hunter patient, then treated by ciprofloxacin with a favourable outcome.

Keywords. *Francisella tularensis*; pulmonary nodule; 16S rRNA sequencing.

INTRODUCTION

Tularaemia, caused by the Gram-negative coccobacillus *Francisella tularensis*, is an anthrozoosis with high incidence in the northern hemisphere. This highly virulent and infectious bacterium has been characterized in the beginning of the 20th century. *Francisella tularensis* is transmitted by arthropod bites, direct contact with infected animals, their contaminated tissues and fluids, or by direct ingestion and inhalation. Therefore, this bacterium is potentially a bioterrorism agent. The clinical outcomes of this disease are the most often ulceroglandular, typhoidal, and rarely oculoglandular, oropharyngeal, and pneumonic forms [1, 2]. Here, we report the case of an immunocompetent patient with pneumonic form of tularemia.

CASE PRESENTATION

A 70-year-old businessman was referred due to an unusual ashenia, without weight loss and fever. This patient being a former smoker, a thoracic X-ray was performed and showed a mass

in the upper right lung lobe. This mass, confirmed by tomography (Figure 1), measured 35 mm, and was associated with lymphadenopathy of Baret lodge. A PET-CT scanner revealed accumulation of FDG on these lesions. Bronchial fibroscopy failed to reveal any abnormality. Mediastinoscopy was performed and the biopsy revealed necrosis and giant cells. Due to high suspicion of malignancy, a right segmentectomy with lymph nodes dissection was then performed. The histological analysis revealed a necrotic granuloma without malignant cells suggesting tuberculosis (Figure 2). Using direct evidence (Acid-Fast Bacilli smear) and bacterial culture on surgical specimen and sputum, the diagnosis of tuberculosis was finally excluded and the patient was admitted in the Department of Infectious Diseases to explore this granulomatosis.

On admission, the patient was globally healthy but complained of a slight cough without fever. The physical examination was normal. The leukocyte count was also normal and CRP was negative. Tuberculin skin test was negative. Tumor markers and autoantibodies for autoimmune diseases were negative. To complete the infectious workup behind this necrosis granulomatosis, serological assays were performed. Viral serologies for human immunodeficiency virus, hepatitis B virus, hepatitis C virus, Epstein-Barr virus, cytomegalovirus were negative. Serological testing for *Bartonella quintana* and *Francisella tularensis* were positive by immunofluorescence assay with IgG titer

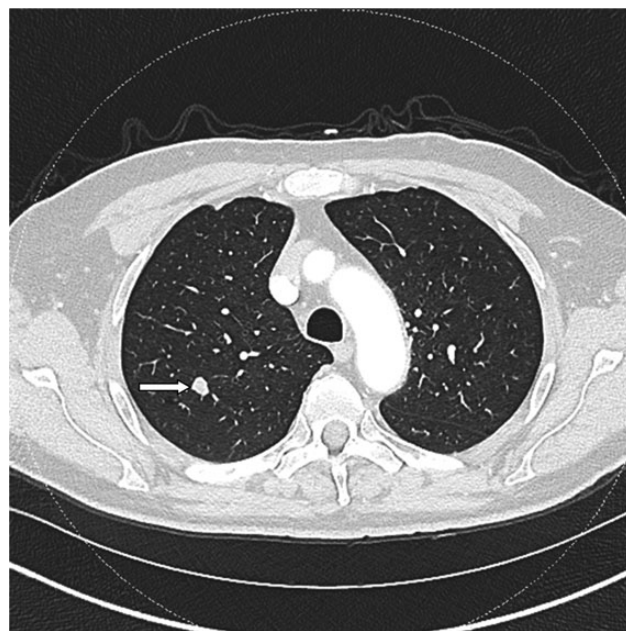


Figure 1. Scanner showing a nodule in the upper right lung lobe (arrow)

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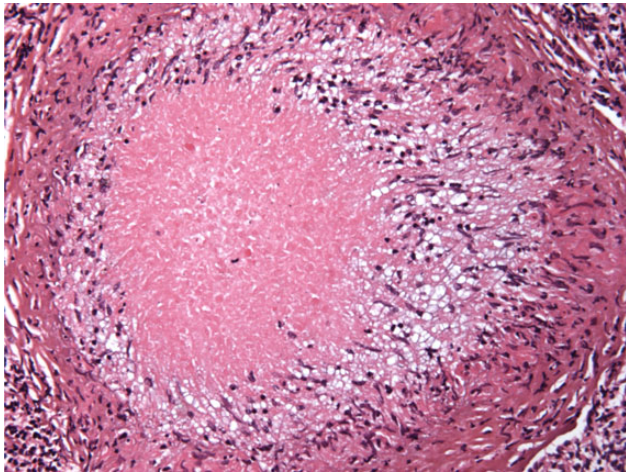


Figure 2. Tuberculoid granuloma. Eosinophil, caseous necrosis surrounded by a ring of epithelioid macrophages and some giant cells. HES×20

of 1:640 without IgM for *B. quintana* and IgG titer of 1:320, IgM titer of 1:40 for *F. tularensis*. To discriminate these two etiologies, frozen pieces of lung and adenopathy biopsies conserved at -80°C were in a second step analyzed by Polymerase Chain Reaction for *Bartonella* and *Francisella*: these two biopsies were positive for *F. tularensis* whereas *Bartonella* PCR remained negative. To understand this diagnosis of tularaemia, a strict questioning of the patient revealed he did not recall any tick bite but he was an amateur hunter. So the patient was treated with ciprofloxacin (500 mg twice a day for 15 days) and had a favourable outcome.

DISCUSSION

The pneumonic form of tularaemia results from inhalation of *F. tularensis* or in 10%-15% of ulceroglandular tularaemia cases, from blood infection [2, 3]. Clinical symptoms are not specific and radiological data are variable, showing lobar or multi-lobar infiltrates in most cases. Rarely, *F. tularensis* is associated with pleural effusions, hilar adenopathy, empyema and cavitary pneumonia [4, 5].

The outcome of respiratory tularaemia depends on two etiological subspecies agents. Infection with *F. tularensis tularensis* (type A, more frequent in USA) results in a fulminant pneumonia that was lethal at 30%-60% prior to the discovery of antibiotic therapy.

F. tularensis subspecies *holarctica* (type B, more frequent in Europe) infection leads to a moderate form of pneumonia, frequently displaying hilar adenopathy, as described in our patient [1, 2].

In a recent study based on four patients with pulmonary tularaemia, the result of the PET-CT scan suggested lung cancer, as well as on our patient [4].

Our patient was treated with ciprofloxacin 1000 mg daily divided into two doses, according to the recommendations [2]. He was admitted almost one year after the beginning of symptoms and was quite asymptomatic on admission, suggesting the role of the initial mediastinoscopy. Severe tularaemia (like in US with *F. tularensis tularensis*) often requires aminoglycosides, whereas in moderate cases and in Europe ciprofloxacin is frequently used. An alternative is doxycycline [2, 5]. Pulmonary tularaemia usually does not require surgery.

CONCLUSION

Tularaemia is a rare but probably under-diagnosed cause of pulmonary nodule first suggesting a cancer. This infection should be suspected in patients with respiratory symptoms and history of animal contact, as a differential diagnosis of pulmonary abscess and tuberculosis. Diagnosis is suspected by serological testing and confirmed if possible by PCR on a biopsy. Treatment consists in antibiotics like aminoglycosides, fluoroquinolones or tetracyclines and sometimes requires an associated surgery.

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