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Lung cancer, brucellosis and tuberculosis: remarkable togetherness

Muhammed Emin Akkoyunlu¹, Yasemin Akkoyunlu^{2*}, Ismail Necati Hakyemez³, Fatma Erboy⁴, Gulhan Arvas⁵, Turan Aslan⁶

¹Bezmalem Vakif University, Department of Chest Diseases, Istanbul, Turkey

²Bezmalem Vakif University, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey

³Bursa Educational and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Bursa, Turkey

⁴Bulent Ecevit University, Department of Chest Diseases, Zonguldak, Turkey

⁵100. Yil University, Department of Microbiology, Van, Turkey

⁶Bezmalem Vakif University, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey

PEER REVIEW

Peer reviewer

Dr. Hayrettin Akdeniiz, Professor, Department of Infectious Diseases and Clinical Microbiology, Medical Faculty of Abant İzzet Baysal University (AIBU), Gököy campus, 14280, Bolu, Türkiye.

Tel: +905364846962

Fax: +903742534559

E-mail: akdenizhayret@hotmail.com

Comments

This is a good study in which the authors evaluated the togetherness of lung cancer, tuberculosis and brucellosis and pointed to the diagnostic difficulties in such cases, especially in endemic areas for brucellosis and tuberculosis.

Details on Page 330

ABSTRACT

A 68 years old male farmer referred with cough, expectorating sputum, intermittent fever, night sweats, fatigue and anorexia persisting for two weeks. There was a history of 80 packs each year of smoking and he was still an active smoker. Pneumonectomy was performed because of pulmonary epidermoid cancer and he received chemotherapy. He was diagnosed lung tuberculosis and using anti-tuberculous treatment for 4 months. He had a weight loss of 8 kg in last month. His body temperature was 38.5 °C. Heart rate was 100/min. ESR was 51mm/h and CRP was 5.6 mg/dL. There was no proliferation in blood and sputum cultures. Three sputum specimens were examined and AFB wasn't detected. Fibronodular infiltration was seen in right lower zone of chest X-ray. In thorax CT, fibronodular densities were seen in lower lobe anterior and posterior segments. *Brucella melitensis* was isolated in blood culture. Second bronchoscopy was performed with suspect of brucellosis pneumonia. Brucella tube agglutination test was positive at titer 1/320 in the bronchial lavage fluid and 1/640 in concurrent serum sample. In cases with chronic cough or pneumonia which is irresponsive to nonspecific antibiotherapy, respiratory brucellosis must be remembered in endemic areas.

KEYWORDS

Tuberculosis, Brucellosis, Lung cancer

1. Introduction

Brucellosis is a systemic zoonotic disease that rarely involves lungs. Brucellosis remains endemic in many developing countries and in rural areas of many developed countries all around the world. The organism is a Gram negative coccobacilli and transmission can occur by direct contact with contaminated animals, ingestion of infected

products and inhalation of infectious aerosol particles^[1,2]. Respiratory symptoms are seen in 1%–5% of patients^[3,4]. Pulmonary involvement is detected in less than 50% of patients having respiratory symptoms. Flu-like disease, interstitial pneumonia, granulomas and solitary nodules, pleural effusion, empyema, lobar pneumonia, abscess, hilar and paratracheal lymphadenopathy and even pneumothorax have been reported. This wide range of

*Corresponding author: Dr. Yasemin Akkoyunlu, Bezmalem Vakif University, Department of Infectious Diseases and Clinical Microbiology, Vatan Cad. 34093 Fatih, Istanbul, Turkey.

Tel: +90 530 143 65 55

E-mail: yaseminakkoyunlu@gmail.com

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pulmonary involvement of brucellosis causes confusion in differential diagnosis with many other diseases[4]. Therefore, in reports about pulmonary brucellosis, attention was paid especially on the difficulties in differential diagnosis.

Serological tests such as Rose Bengal, Wright agglutination and ELISA can be used for diagnosis whereas in patients with suspicion of pulmonary brucellosis, culture of blood, sputum and lung tissue must be performed with lengthy incubation period[1].

Tuberculosis, lung cancer and brucellosis have nonspecific symptoms. This causes difficulty in differential diagnosis. Increasing incidence of tuberculosis and lung cancer, brucellosis is also endemic in our region that makes it more possible for the togetherness of these three diseases. In patients with nonspecific symptoms and crucial diagnosis, brucellosis should be remembered.

2. Case report

A 68 years old male farmer referred with cough, expectorating sputum, intermittent fever, headache, vertigo, night sweats, hemoptysis, fatigue and anorexia persisting for approximately last 2 months. He had a weight loss of 12 kg in the last 2 months. There was a past history of 80 packs each year of smoking and he was still an active smoker. Pneumonectomy was performed because of pulmonary epidermoid cancer and he had received 2 regimens of chemotherapy (cisplatin/gemzaar). His body temperature was 37.5°C. Auscultation of thorax revealed rales in right lower zone of thorax. Erythrocyte sedimentation rate (ESR) was 62 mm/h and C reactive protein (CRP) was 2.6 mg/dL.

The patient was hospitalized to investigate the etiology of fever and hemoptysis. Oral cefuroxime axetil 500 mg bid was given. In sputum examination, acid fast bacilli (AFB) was detected. Then antituberculous treatment was started with isoniazid, rifampin, etambutol and pyrazinamide. Later, the patient was transferred to tuberculosis dispensary.

At the end of the 2nd month of anti-tuberculosis treatment, we decided to continue the treatment with isoniazid and rifampin because the patient was detected to be sensitive to all these drugs and also radiologic improvement was detected.

In the 4th month of anti-tuberculous treatment, the patient presented with deteriorated symptoms approximately for 2 weeks. He had cough, sputum, fatigue and night sweats. He had a weight loss of 8 kg in the last month. Body temperature was 38.5°C. Heart rate was 100/min, and respiratory rate was 26/min. Hemoglobin was 11.1 g/dL,

white blood cell count 8900/mm³, platelet 124000/mm³, ESR 51 mm/h and CRP 5.6 mg/dL. There was no proliferation in blood and sputum culture. Three sputum specimens were examined and AFB wasn't detected.

Sulbactam ampicilline is started with the working diagnosis of pneumonia. On the 4th day of treatment, the fever was still continuing. Fibronodular infiltration was seen in right lower zone of chest X-ray (Figure 1).

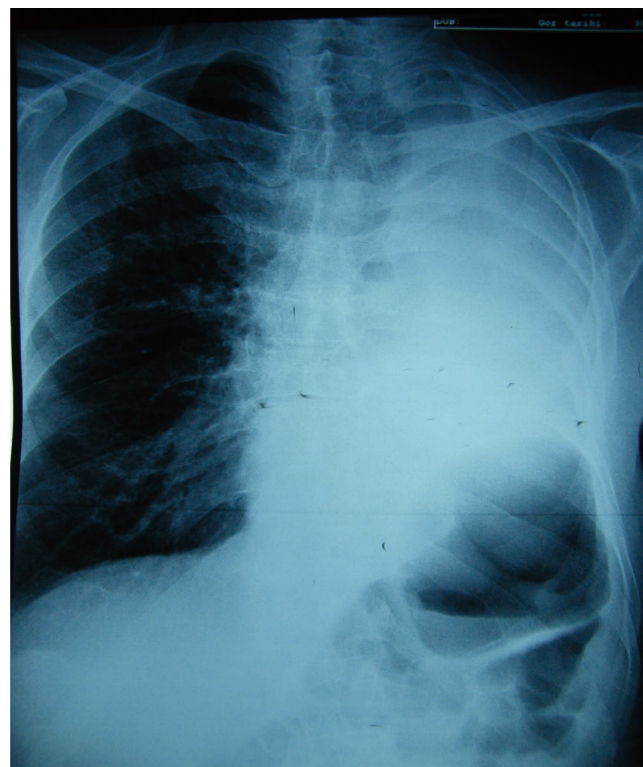


Figure 1. Fibronodular infiltration at right lower zone on chest X-ray.

In thorax CT, fibronodular densities were especially seen in lower lobe anterior and posterior segments (Figure 2). Bronchoscopy was performed. AFB were not detected in bronchial lavage, and no malignant cells were found. The mucosal biopsy taken during bronchoscopy only revealed signs of inflammation. There was no growth in the bacteriological culture of bronchial lavage fluid.

Gram negative coccobacilli was isolated in blood culture. The bacteria isolated with BACTEC 9120 blood culture system and the colonies were smooth, micro and round in blood and chocolate agar. By Gram stain, Gram negative coccobacilli were seen. Catalase and oxydase activity was found as positive. The colonies were assessed as *Brucella* spp. and they were grouped as *Brucella melitensis* according to their requirement to 5%–10% CO₂, urease activity, the property and duration of generating H₂S.

Second bronchoscopy and bronchial lavage were performed under the suspicion of brucellosis pneumonia, because the region is endemic for brucellosis. *Brucella* tube agglutination test was positive at titer 1/320 in the bronchial lavage fluid and 1/640 in concurrent serum

sample.

The patient was diagnosed as brucellosis pneumonitis and streptomycin 1 g/d, rifampin 600 mg/d, and doxycycline 200 mg/d was started. Rapid clinical recovery was observed.

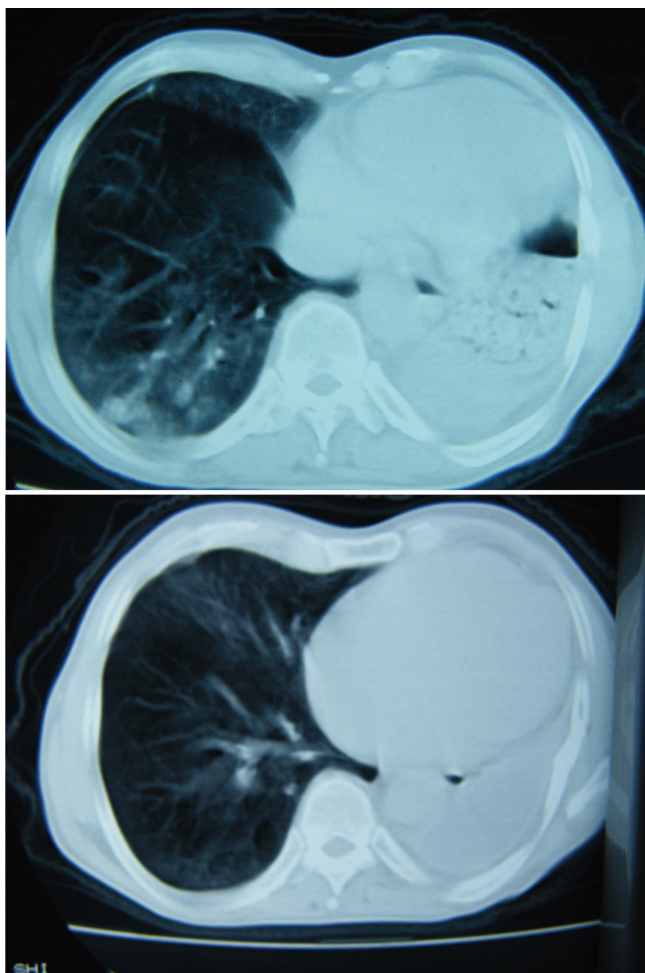


Figure 2. Fibronodular densities were especially seen in lower lobe anterior and posterior segments on thorax CT.

3. Discussion

Brucellosis is a systemic disease that rarely involves lungs. It can be detected as a chest X-ray abnormality only or a part of a subacute systemic disease. It is the second most frequent cause of fever of unknown origin. Even though brucellosis is so common, there are few reports of respiratory involvement in brucellosis, many of which are case reports. In a study from Greece, 450 patients diagnosed as brucellosis was analysed and pulmonary involvement was reported as approximately 7%^[4]. In most studies, respiratory involvement was considered as a rare focal form of brucellosis. Therefore, brucellosis is rarely remembered as a differential diagnosis in respiratory diseases.

The clinical and physical findings of pulmonary brucellosis are frequently nonspecific and chronic^[5,6]. Respiratory symptoms such as dry or productive cough and chest pain are reported in up to 14%–20% of patients^[4,6]. Due to this reason, it is hard to differentiate it from other pulmonary diseases. In our case, the additional presence of tuberculosis delayed the diagnosis of brucellosis, which has almost the same nonspecific symptoms^[6–8]. We started to suspect of brucellosis only after the proliferation of Gram negative bacilli in blood culture.

In pulmonary brucellosis, 1%–16% of chest X-ray can show abnormality, but these findings are not pathognomonic^[4,6]. The positivity in agglutination test ($\geq 1/160$), Rose Bengal test, and ELISA test can be used for diagnosis^[2,9]. Gold standard method for diagnosis is to show *Brucella* spp. proliferation in culture^[1]. The difficulty in proliferation of *Brucella* spp. in culture is another diagnostic difficulty^[4,6]. The isolation of the bacteria in culture is more difficult in pulmonary involvement because frequently there is no bacteriemia, incubation period is long and it is hard to produce *Brucella* spp. in standard culture materials. Because of this, bacteria isolation in pulmonary involvement had been rarely reported. In our patient, although proliferation was detected in the blood culture specimens, there was no proliferation in sputum and bronchial lavage cultures.

Miliary mottling has also been reported, thus raising an important issue that it can be difficult to differentiate respiratory brucellosis from tuberculosis, especially in regions where both brucellosis and tuberculosis are endemic. Furthermore, the clinical picture of both diseases can be very similar. There have been several case reports in which brucellosis was mistaken and the treatment was delayed because of tuberculosis^[10]. Therefore, unnecessary antituberculous treatment given to a patient with brucellosis becomes a serious problem^[11]. Also the improper use of streptomycin and rifampicin as a part of an unnecessary antituberculosis treatment in brucellosis patients is a risk factor for development of drug resistance. We believe in the accuracy of our tuberculosis diagnosis because of AFB detection in sputum for three times and positive tuberculosis culture of sputum. But similarly for our patient, brucellosis arose during rifampicin treatment. For brucellosis, this can be explained by drug resistance development because of monotherapy or an inadequate treatment.

In conclusion, following the diagnosis of lung cancer, pulmonary tuberculosis was found in our patient and then *Brucella* infection was detected during antituberculous treatment. According to our knowledge, togetherness of these three diseases have never been reported before.

Brucellosis is still endemic in rural areas. Especially

due to the dissemination of HIV infection, tuberculosis incidence is rising. In future, concurrent appearance of these diseases will be more possible and this will cause diagnostic difficulties. As a result, in cases with chronic cough or pneumonia which etiology is not clear and irresponsive to nonspecific antibiotherapy, respiratory brucellosis must be remembered, especially when the patient is living in endemic areas for brucellosis.

Conflict of interest statement

We declare that we have no conflict of interest.

Comments

Background

Brucellosis is a multisystemic disease involving all of the systems including respiratory system. Respiratory involvement can be seen in various forms such as pneumonia, bronchopneumonia and pleurisy. The same symptoms in pulmonary involvement cause to diagnostic difficulty in a patient known to have a lung cancer and tuberculosis.

Research frontiers

The comorbidity of tuberculosis and brucellosis is possible in some conditions such as spondylitis and paravertebral abscess. Similarly, some diagnostic difficulties may be seen in pleurisy cases, cervical or axillary lymphadenitis cases, scrofuloderma cases or in renal involvement.

Related reports

In such a case by Karahocagil *et al.* with pleural effusion first considered as tuberculous pleurisy due to lymphocytic predominance and elevated level of pleural adenosine deaminase, this case was later diagnosed as brucellar pleurisy with positive serologic and microbiologic test results.

Innovations & breakthroughs

Togetherness of lung cancer, tuberculosis and brucellosis is a quite rare condition and this study has showed such a togetherness and drew the attention to the diagnostic difficulty in such a condition.

Applications

It is significant to show the togetherness of tuberculosis and brucellosis in such a patient with lung cancer and

draw an attention to the diagnostic difficulties in the same patient. Although the medical treatment of both infections is similar and includes a few common drugs, improper or inefficient treatments may cause to another important problem, namely drug resistance.

Peer review

This is a good study in which the authors evaluated the togetherness of lung cancer, tuberculosis and brucellosis and pointed to the diagnostic difficulties in such cases, especially in endemic areas for brucellosis and tuberculosis.

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