

Tuberculosis Can Mimic Lung Cancer: A Case Series

Tüberküloz Akciğer Kanseri Taklit Edebilir: Olgu Serisi

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Abstract

Özet

Tuberculosis can mimic all pathological considerations of the lung and can present in many various forms and appearances. Most common radiographic appearances are cavitary, fibroproductive, exudative, acinary, micro and macronodular and miliary types. Six patients (5 men; ages ranging from 38 to 74 years) who presented at our clinic during previous years were evaluated. In this case series report we discussed the consideration that, very rarely, post-primary lung tuberculosis presenting with large nodular and mass-like forms in a chest X-ray or tomography scan, can be considered as having a neoplastic pattern.

KEY WORDS: Lung cancer, mass, pulmonary tumors, tuberculosis

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Tüberküloz akciğerin hemen hemen patolojik tüm durumlarını taklit edebilir ve çok çeşitli form ve görünümde ortaya çıkabilir. En sık izlenen radyolojik görünüm kaviter, fibroproduktif, eksüdatif, asiner, makro ve mikronodüler ve milyer tiptir. Kliniğimize başvuran altı olgu (5 erkek, 38-74 yaşları arasında) değerlendirildi. Bu olgu serisi ile postprimer akciğer tüberkülozunun nadir olarak akciğer grafisi ya da tomografide kitle veya nodül görünümü gösterdiği ve neoplastik oluşumları taklit edebildiği tartışılarak hatırlatıldı.

ANAHTAR SÖZCÜKLER: Akciğer kanseri, kitle, pulmoner tümör, tüberküloz

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INTRODUCTION

Lung tuberculosis is often seen radiographically in the forms of cavitary, fibroproductive, exudative, acinary, micro and macronodular and miliary types [1]. However, quite variable radiographic appearances may present, mimicking all the other pathological formations of the lung and cause clinic difficulties for diagnosis.

CASE REPORTS

The general characteristics of the patients and the methods of diagnosis were summarized in Table 1 and 2.

Case 1

A 38 year old female patient presented to our clinic with complaints of shortness of breath, fatigue, loss of appetite, weight loss and back pain ongoing from about one month. On her physical examination, bronchial sounds were heard in the left long upper zone and the other system examinations were normal. Biochemical and hematological values were within the normal range. On the tuberculin skin test (PPD test) of the patient who had a Bacillus-Calmette-Guerrin vaccine (BCG) scar, indurations was 20 mm and erythrocyte sedimentation rate (ESR) was 70 mm/hour. A partially smooth contoured homogenous mass lesion was observed in the left apical region on the postero-anterior (PA) chest radiograph. There was a wide pleural based hypodense solid mass lesion in the left lung upper lobe apicoposterior segment, extending to the mediastinum (Figure 1). Density increases related to alveolar type exudation were seen in the lung parenchyma adjacent to the mass. On bronchoscopy, the opening of the left lung upper lobe apicoposterior was blocked with a red colored mass. Acid fast bacilli (AFB) were found positive on the direct microscopic examination of the brushing material from here with Ehrlich-Ziehl-Nielsen stain (EZN). Standard anti-tuberculosis treatment was introduced with isoniazid (INH), rifampicine (RIF), ethambutol (EMB) and morphozinamide (MPZ). The lesion completely regressed on this treatment (Figure 2).

Case 2

A 74 year old male patient referred with complaints of left arm and shoulder pain, coughing, shortness of breath and hoarseness increasing over the previous 5-6 months. The other system examinations were normal on the physical



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Table 1. General characteristics of the patients

No	Age	Sex	Symptom duration (weeks)	Symptoms	TST (mm)	BCG scar pcs	Mass location	Mass Size (cm)	Associated radiological findings
1	38	F	4	Shortness of breath, fatigue, anorexia, weight loss, back pain	20	1	Left upper lobe apico-posterior	5	Alveolar exudation
2	74	M	20	Left arm-shoulder pain, coughing, shortness of breath, hoarseness	5	0	Right upper lobe	4	Mediastinal and hilar LAM
3	41	M	4	Right side pain, shortness of breath, anorexia	15	0	Right upper lobe anterior segment	6	Pleural effusion at right
4	71	M	4	Back pain, coughing, expectorating, weight loss	12	0	Right lower	2	Emphysema
5	38	M	6	Coughing, expectorating, fatigue	5	1	Left upper lobe apico-posterior	2	Consolidation
6	52	M	3	Sore throat, fatigue	18	0	Right upper lobe	6	None

BCG: Bacillus Calmette-Guerin vaccine, LAM: Lmpyadenomegalia, TST: Tuberculin skin test

Table 2. The methods establishing diagnosis

No	Endobronchial component	Diagnosis method	AFB smear	AFB Culture	Cytology
1	Left apicoposterior segment obstructed	Bronchoscopy	Positive	Positive	Acute inflammatory
2	None	Mediastinoscopy	Negative	Positive	Chronic necrotizing granulomatous inflammation
3	None	VATS	Negative	Positive	Chronic necrotizing granulomatous pneumonia
4	None	Right lower lobectomy	Negative	Positive	Chronic granulomatous inflammation
5	None	TTFNA	Negative	Positive	Chronic granulomatous inflammation cells
6	None	TTFNA	Negative	Positive	Chronic granulomatous inflammation

AFB: Acid-fast bacilli, TTFNA: Trans-thoracic fine needle aspiration, VATS: Video-assisted thoracoscopic surgery

examination, except that the liver was 3 cm palpable. Biochemical and hematological values were within the normal range. The patient with 5 mm induration and 104 mm/h ESR on the PPD test had no BCG scar. On the PA chest radiograph, a mass lesion next to the mediastinum was observed in the right upper zone, below the clavicle. Diffuse mediastinal and hilar lymphadenopathy (LAM) were seen on the thorax CT (Figure 3). On his bronchoscopy, the movement of the left vocal cord was restricted and the right lateral wall in the distal trachea was hyperemic, and remaining portion of the bronchial system was

normal and open. Aspiration biopsy was performed with a Wang cytology needle from the subcarinal and paratracheal region. He was reported as having chronic necrotizing granuloma inflammation as the result of the biopsy taken on the mediastinoscopy carried out because no result was obtained with the aspiration biopsy. CD4/CD8 was found as 1.19 activated, T as 3.98% and CD19 was found as 6.29% on the subpopulation analysis of the peripheral blood lymphocytes. The lesions of the patient who received standard anti-tuberculosis treatment with INH, RIF, EMB and MPZ regressed.

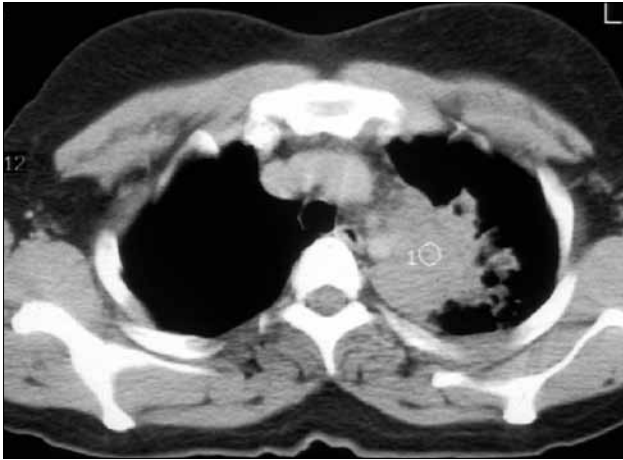


Figure 1. Thorax CT shows a solid mass in Case 1



Figure 2. After two months of tuberculosis treatment the mass is clearly regressing in Case 1

Case 3

A 41 year old male patient was referred with right sided pain, shortness of breath and anorexia of 1 month duration. On his physical examination, the right costophrenic sinus was closed, and respiratory sounds were absent in the right lung lower zones. The other system examinations were unremarkable. Biochemical and hemogram values were in the normal range. The patient had a 15 mm induration and 46 mm/h ESR on the PPD test but had no BCG scar. The right costophrenic sinus was closed on the PA chest radiograph and a nonhomogeneous density increase with partly smooth contours, covering almost all the mediastinal zone was observed in the right lung. On the thorax CT, a paramediastinal located, non-uniform contoured mass lesion extending to the hilum was seen in the right lung upper lobe anterior segment (Figure 4). All the bronchial system was normal and open except for the intermediate carina which was mildly edematous on the right side. Chronic necrotizing granulomatous pneumonia was defined on the right upper lobe biopsy performed through video assisted thoracoscopic surgery (VATS). The lesions of the patient, who received standard anti-tuberculosis treatment with INH, RIF, EMB and MPZ, regressed.

Case 4

A 71 year old male patient had a smoking history of 30 pack/year. The patient, who had complaints of back pain, cough-

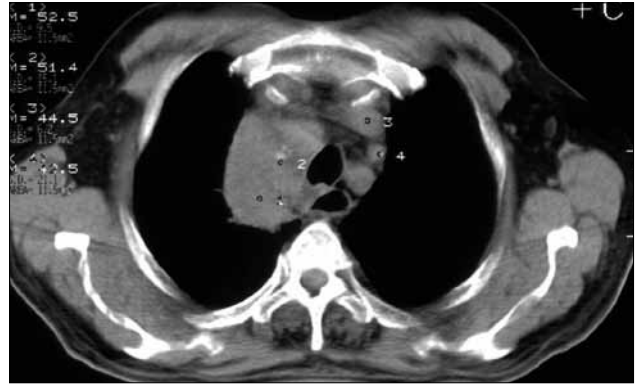


Figure 3. Thorax CT of Case 2



Figure 4. Thorax CT of Case 3

ing, expectorating, xerostomia and weight loss (2 kilos a month) of one month duration was referred to our hospital. There were rhonchi in the bilateral basals and prolonged expiration on his respiratory system examination. Platelet count was 624, haemoglobin 17.1 gram/dL and haematocrit 53.1% on the hemogram and splenomegaly was defined in all abdominal ultrasounds. Diagnosis of polycythemia vera was established with hematologic consultation and a therapy of hydroxyurea 1000 mg/day and allopurinole 150 mg/day was introduced.

In the sections crossing from the subcarinal level on the thorax CT, a paravertebral lesion of 20 mm with central fluid density was seen behind the right bronchus in the posterior mediastinum. There were emphysematous changes in both lungs. There was no endobronchial lesion on the bronchoscopy.

On the second TTFNA ordered, direct AFB observation was negative, there was rare PMNL in each region and rare malignity suspected squamous cells, keratinous bodies, histiocytes and macrophages defined in the ground with abundant cytology. Although the cytologic findings suggested squamous cell carcinoma in the interpretation, FDG-PET study was ordered since there was not sufficient evidence in the sampling. Hypermetabolic foci of malignant level were observed in the right lung lower lobe superior segment and left lung laterobasal segment on FDG-PET examination. On his latest comparative requested CT, the lesion was the same in size through the right main bronchus in the posterior

mediastinum as described in the previous examination, presenting contrast involvement.

He was staged as T2 NO MO, STAGE 1 and directed to surgery with mediastinoscopy planned.

When the operational platelet was $<400.000/\text{mm}^3$ on the hematological evaluation of polycythemia vera, right thoracotomy right lower lobectomy was performed. Pathological outcome of the preparation was a granulomatous inflammation characterized by a wide necrotic cavitory cystic bronchiectasis and interstitial pneumonic changes in the surrounding parenchyma. There were granulomatous bronchitis, bronchiolitis, squamous metaplasia in the bronchial mucosa. There were no chronic granulomatous inflammations in the 11, 12 and 4R and AFB in EZN. Therefore, the patient was administered tetra anti-tuberculosis therapy, and he completed the 6th month of his treatment.

Case 5

There was a non-homogenous infiltration with non-uniform contours in the PA chest radiograph of the 38 years old male patient who presented to our polyclinic with complaints of coughing, expectorating, anorexia and weight loss. His physical examination was unremarkable and the bilateral respiratory sounds were normal on the pulmonary system examination. There was no symptom on his hemogram and biochemical examination except for the fast sedimentation rate and leukocytosis.

There was a thick walled cavitory lesion of approximately 1.5x2 cm in size in the apicoposterior of the left lung upper zone and a condensation area of 3x3. 5x6 cm in size, presenting partly nodular formation with the borders could not be differentiated from the cavitory lesions adjacent to the right lateral side

On the sputum, AFB was detected as negative twice. AFB outcome of the patient with TTFNA performed from the mass lesion located in the left lung apical was negative. Chronic, granulomatous inflammation cells (granulomas), necrosis leukocytes and macrophages were the blood elements. The case without malignant cell seen in the interpretation was considered as tuberculosis. The patient was administered a full dose of tetra anti-tuberculosis therapy, and his lesion regressed with the treatment.

Case 6

A 52 year old male patient had received nonspecific antibiotic therapy on diagnosis of pneumonia in the hospital that he referred with the complaints of sore throat 3 weeks previously. Although the patient had received this therapy for 2 weeks, his complaints had not regressed. The patient, with a mass detected in the right lung upper zone on the PA chest radiography ordered during his examinations, was admitted to our hospital.

He had no symptom except for a smoking history of 15 pack/year and nephritis he had developed 5 years previously. Respiratory system examination was unremarkable

except for minimal murmurs in the right upper zone. On his abdominal examination, the liver was 1 cm palpable below the rib.

Acid-fast bacilli detection of sputum of the patient ordered twice were negative. There was no endobronchial lesion defined on the bronchoscopy. The outcome of the lavage taken from the upper lobe of the right bronchus system and of the post bronchoscopic sputum was also defined as AFB negative. Although the patient's cranial CT ordered for possible malignant metastasis was within the normal range, on his complete abdominal USG, the liver was in normal shape and size and, there were echogenic mass lesions of 19 mm in diameter adjacent to the gallbladder and 6 mm in the posterior of the right lobe and 28 mm in the left lobe. These findings led to the diagnosis of metastatic lung tumor.

Although there was no malignant cell on the patient's 3rd TTFNA biopsy, since cytologic findings suggested chronic granulomatous inflammation, tetra anti-tuberculosis therapy of full dose (INH 300 mg, RIF 600 mg, MPZ 3 g, ETB1.5 g) was introduced. On the follow-up, the patient's right upper lobe mass lesion had completely regressed.

DISCUSSION

Pulmonary tuberculosis is currently one of the most important infection related morbidity and mortality causes in the world. There were 17781 recorded tuberculosis cases in Turkey in 2007 and 240 of these were resistant to multi drugs [2]. Although the incidence of tuberculosis has declined recently in Turkey, it still remains a public health concern as it is throughout the world. On the other hand, lung cancer is also one of the leading mortality causes worldwide. Lung cancer is often radiographically confused with tuberculosis, especially in the regions in which the tuberculosis is endemic. In the regions with a high incidence of tuberculosis, misdiagnosis of tuberculosis may be established in the patients presenting with a negative sputum smear and mass lesion, and this can lead to delay in diagnosis in the cancer patients. In a study with 70 patients diagnosed with lung cancer in India, 14 of the cases were defined to be misdiagnosed as tuberculosis and accordingly received treatment [3]. The patients with concurrently seen tuberculosis and lung cancer are also another reason for misdiagnosis [4]. On the other hand, the opposite of this situation is also possible. Tuberculosis may be radiographically revealed as mass formation in the cases clinically and radiographically examined, considering lung cancer. In this study, 6 cases studied with pre-diagnosis of cancer upon the mass appearance in the lung were presented.

Lung tuberculosis is often radiographically observed with the cavitory involving the upper lobes and exudative appearances, although it may be radiographically revealed also with a mass appearance suggesting cancer. In a review of a study published in 1984, of 26 patients with presumed cancer, but finally diagnosed with tuberculosis the case with tuberculosis mimicking carcinoma were

studied, and the diagnosis was shown to be achieved through the clinical courses and sophisticated methods similar to our cases [5]. The mean symptom duration was found as 2.8 months for that study and the classical symptoms of tuberculosis were underlined as infrequent. In our study, the mean symptom duration was 7 weeks (3-20 weeks), while constitutional factors such as fatigue and weight loss were frequent. However, the pain symptom, which was not frequently encountered in tuberculosis out of the pleurisy and complications, was in the forefront. While there were no laboratory anomalies defined for the same series except for the elevation of the platelet count, only one case had an elevated platelet count and was diagnosed as polycythemia vera as the result of the hematological evaluation. In a series of 597 patients diagnosed as tuberculosis studied by Cherian et al. [6], 11 cases who presented with a mass lesion were encountered. There was lower lobe involvement in the majority of these cases, but concomitance of a cavitation, calcification or satellite lesions was not defined. In contrast, in another study including 58 patients and conducted in Argentina in some patients with the previous diagnosis of cancer also, tuberculosis has been emphasized to be considered as well as the local recurrent in endemic regions [7]. The lesion was most common in the lung parenchyma and second common in the mediastinal lymph nodes in each of the three studies.

Although the tuberculosis forms leading to mass appearance have been underlined as mostly endobronchial tuberculosis in a few case reports in our country, six cases we presented forming mass appearance in different pathological processes such as endobronchial tuberculosis, tuberculous pneumonia and mediastinal lymphadenitis tuberculosis, required a wider look at the clinical situations in which the tuberculosis mimics carcinoma [8]. However, when the reasons of mass appearance are examined as a whole, we are faced with endobronchial tuberculosis as the most common cause, unlike our series [9,10]. In this series that we presented, endobronchial involvement was observed in only one case. In addition, it should be remembered that tuberculosis, related either to conglomerated lymph nodes or parenchymal granulomatous formations, may be the cause of the mass [11].

The mass due to tuberculosis mainly consists of the inflammatory cells and presents the absence of mitosis with the mature fibroblastic process. In an article evaluating high resolution computed tomography (HRCT) findings of 10 patients with mass lesion who were diagnosed as tuberculosis, the mean diameter of 13 masses was found as 2.3 cm. Calcification was found in only 2 of the lesions, while the most common localization was the right lower lobe (38.5%). Contrast-enhanced imaging was performed in only 7 patients, and involvement was detected in 2 of them. Mediastinal lymphadenomegalia (LAM) was found in 8 (80%) of the cases [12]. In this series mediastinal LAM was observed in

only one of the cases and the mean mass diameter was 3.16 cm (2-6 cm). Unlike other series, lesion location was frequently in the upper lobes. Only in one case was the lesion right lower lobe located.

In the above mentioned series by Pitlik et al. [5], the lesion was parenchyma located in 14 of 26 patients and mediastinal in the other 12 cases.

Since positron emission tomography (PET-CT), used to aid in the differential diagnosis of the lung cancers and in the definition of their extensity and staging, gives a false positive response, this method has limited use in tuberculosis patients. Therefore, although the maximum value of glucose uptake that is requested for the patients who presented with mass tuberculosis, especially in the regions where tuberculosis is endemic, it does not contribute to the diagnosis because of the values higher than normal as in our one case [13]. Tuberculosis having a high metabolic activity like carcinoma obviously restricted the value of PET to be used in the differential diagnosis.

In this study, we would like to emphasize that difficulties may be encountered in the differential diagnosis due to the similar constitutional symptoms such as fatigue and anorexia both in tuberculosis and carcinoma, and the radiologic appearance is also confusing. In conclusion, post-primary tuberculosis emerging as a large nodular or mass-like radiographic appearance is uncommon and this can be easily mixed with the tumoral formations.

Conflict of Interest

No conflict of interest was declared by the authors.

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