Pulmonary Aspergilloma in a Turkish Hospital Population

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Abstract

Aiming to investigate the association between pulmonary aspergilloma and a history of pulmonary tuberculosis, 14 aspergilloma cases (10 males, 4 females) were identified from the patient files of our hospital between 1992-1998. Thirteen of these patients (%93) had a history of tuberculosis with post-tuberculous cavities and 1 patient had a history of diabetes mellitus and adenocarcinoma of the lung. Ten patients had radiographical changes consistent with aspergilloma. Sputum samples had been taken from 12 patients and 7 (%58) were positive for aspergillus on bacteriological smear. Bronchoscopy was performed in 12 patients and 9 were positive for aspergillus in both bronchoalveolar lavage material and tissue biopsy specimens.

Ten patients with recurrent haemoptysis underwent thoracotomy and 1 patient underwent arterial embolization. Despite recurrent haemoptysis, surgical intervention could not be carried out in one patient due to his poor ventilation peformance score. Two patients were followed-up in the outpatient clinic without any intervention.

This study has shown that in our hospital population, aspergilloma cases mostly appear in patients with post-tuberculous cavities rather than patients with other diseases leading to deficiencies in immunocompetence.

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Key words: *Aspergilloma, tuberculosis.*

Introduction

Three different forms of aspergillus associated disease, namely, allergic aspergillosis, colonizing aspergillosis, and invasive aspergillosis, have been described. Pulmonary disease is usually associated with colonizing aspergillosis. Aspergilli usually proliferate and form colonies (mycetoma or fungus balls) in a preexisting pulmonary cavity (secondary aspergilloma). Pulmonary tuberculosis (TB) is the most commonly associated disease in cases of secondary aspergilloma. Less frequently sarcoidosis, cavitary neoplasms, pulmonary fibrosis, lung abscesses can also be associated with secondary aspergilloma (1). In Turkey, TB is a widespread disease and pulmonary cavities associated with TB are also quite frequently encountered (2).

In this present study a history of pulmonary tuberculosis was investigated retrospectively in patients with pulmonary aspergilloma presenting to our hospital.

Materials and Methods

Patients

The diagnosis of pulmonary aspergilloma was based on either identifi-

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cation of aspergilloma in more than two bacteriological smears/cultures from bronchoalveolar washing specimens, or observation of fungus ball images in chest X-rays or thorax computed tomography investigations, or postsurgical pathological findings (1). A diagnosis of aspergilloma was the only criterion for inclusion to our study. The study was carried out retrospectively, by going through our hospital files between 1992 and 1998. The characteristics of the patients are shown in Table 1. Fourteen patients with aspergilloma were included in the study (10 males, mean age 40±10 years [range, 30-69 years]; 4 females, mean age 46±10 years [range, 36-56 years]). Thirteen patients had a history of pulmonary tuberculosis (sputum smear results were positive for *M. tuberculosis* in 12; one patient had a history of pulmonary tuberculosis without any confirmatory document). One patient had a history of diabetes mellitus and adenocarcinoma of the lung.

Investigative procedures and interventions

From patients' files, the following investigations and interventions were compiled:

A diagnosis of Aspergillosis was based on a record of at least 2 sputum samples positive for aspergillus spp. (3-5 colony forming units [CFU]). A diagnosis of TB was based on 3 sputum samples positive for acid-fast bacilli (AFB). Serum IgE levels were also recorded. All patients had had bilateral chest X-rays and thorax computed tomography (CT) (Picture 1) and/or fiberoptic endobronchial biopsy and bronchoalveolar lavage for collection of specimens for bacteriological and histopathological diagnosis of aspergillosis. Interventions such as thoracotomy and surgical resection for aspergilloma and pulmonary arterial embolization were also recorded.

Results

Fourteen aspergilloma cases (10 males, mean age 40±10 years [range, 30-69 years], 4 females, mean age 46±10 years [range, 36-56 years]) were identified from patients' files between 1992 and 1998 (Table 1). Except for one case (case no.13) with no documentation, 13 of the patients (93%) had a past history of bacteriologically confirmed pulmonary tuberculosis. Only one patient (case 2) had a history of pulmonary adenocarcinoma and diabetes mellitus without history of tuberculosis. Mean duration between the diagnosis of tuberculosis and that of aspergilloma was 10 years (range, 1-30 years). The most frequent presenting symptom was haemoptysis (71%, n=10) and cough and dyspnea were the least frequent (29%, n=4 and (8%, n=2 respectively.

All patients had abnormal findings on their postero-anterior chest X-rays. Cases 6 and 14 had dense lesions indicating a mass; cases 1, 5, 6, 7, 8 and 11 had huge cavities; and fungus ball images were identified on the X-rays of cases 1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12 and 13 (Picture 1). Lesions were in the right apical region in 8 patients, in the left apical location in 5 and in the left basal region in one diabetic-lung cancer patient. Twelve thorax CTs were found in the files and most of them had been performed in other medical centers before admission to our hospital. Ten (83%) of these 12 thorax CT depicted lesions highly suggestive of aspergilloma such as the classic crescent-shape patch of air (Monod's sign [1]) and a fungus ball image within a cavity.

Presence of *Aspergillus fumigatus* specific Ig E antibodies (++++) was recorded in only one patient (case 5). The same patient also had *eosinophilia* (1600/mm^3), episodes of bronchial obstruction (FEV_1 1000 mL) and a 7x6 cm cavitary lesion within which a 3x3 cm fungus ball image could be seen (Picture 1).

All patients had had 2-3 sputum examinations for aspergillus identification, but only 8 patients (61%) were found to be sputum smear positive. *Aspergillus fumigatus* organisms were also identified in bacteriological cultures from these 8 patients. All cases were negative for *M. tuberculosis* organisms in sputum cultures repeated on 3 occasions. Fiberoptic bronchoscopy was performed in 12 patients to evaluate the haemoptysis and exclude other pathologies. *Aspergillus fumigatus* was identified in 7 (58%) of these patients in the bacteriological cultures from bronchoalveolar washing and/or from the histopathology of endobronchial biopsy specimens.

In case 6 (Table 1, Picture 1), because of suspicion of malignancy, transthoracal needle aspiration (TTNA) was performed. Pathological and bacteriological findings in this case revealed *Aspergillus fumigatus*.

Out of 14 patients, 10 (71%) underwent thoracotomy for the resection of the aspergilloma. Lobectomy was performed in 8, wedge resection in 1 and pulmonectomy in 1 patient. One other patient had arterial embolization. There were 2 deaths among these 10 patients. Cause of death was cardiac arrest during operation in one and massive haemoptysis in the postoperative period in the second patient.

Three of the patients were followed without any surgical intervention. One of these 3 patients was diagnosed as a case of inoperable lung cancer.

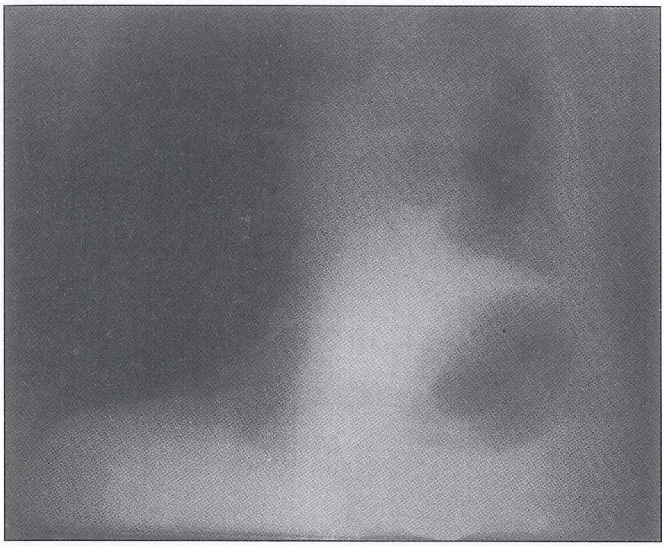
Discussion

In this paper, based on a retrospective study of patient files, we report a group of pulmonary aspergilloma cases (n=14) with posttuberculous cavities (n=13, %93).

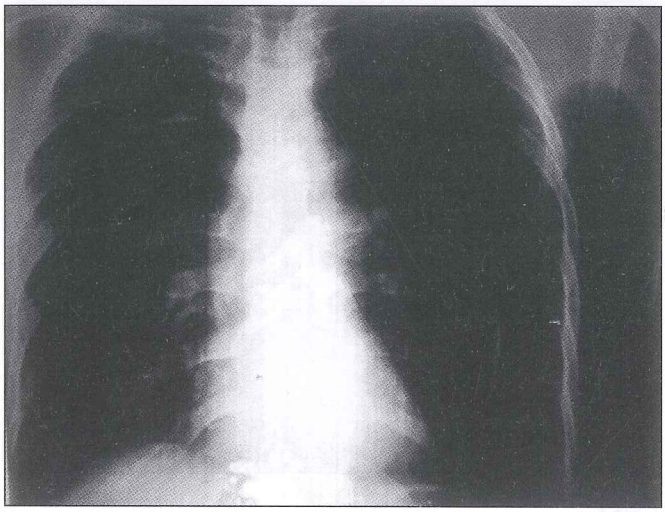
Recently, in a multicenter study (24 centers in the US), it was reported that in patients with aspergillosis, most culture isolates from nonsterile body sites did not reveal the disease. At the same time, the findings showed that for high-risk patients, such as bone marrow transplant recipients, persons with haematologic malignancies, those with neutropenia or malnutrition, a positive culture result was frequently associated with invasive disease. It was emphasized that in the presence of risk factors such as HIV infection or underlying pulmonary disease associated with a positive culture result, clinical judgment and more extensive diagnostic tests were necessary (3).

In our series, 10 out of 14, cases with positive sputum or BAL culture for aspergillosis were confirmed either by radiological

PA chest X-ray



Case 1



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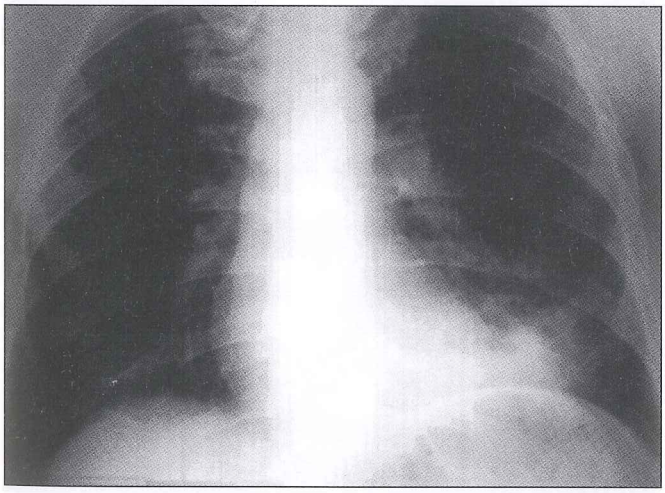
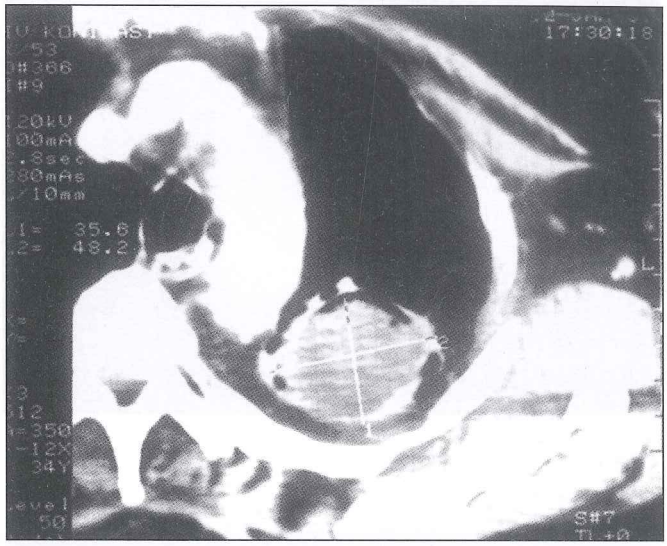


Case 3

Thorax Computed Tomography (CT)



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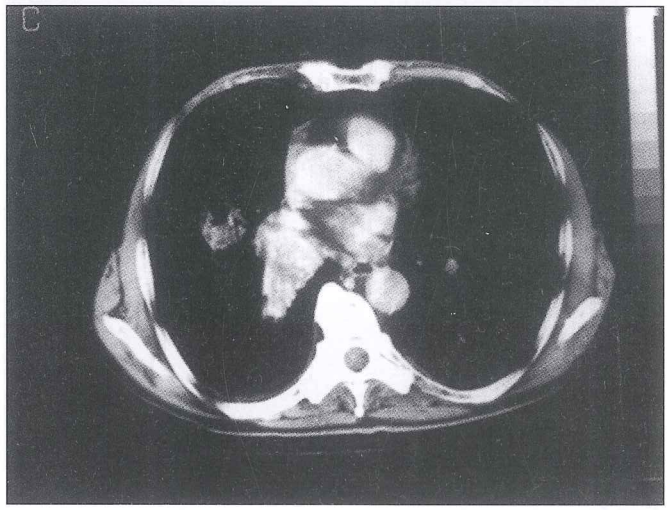

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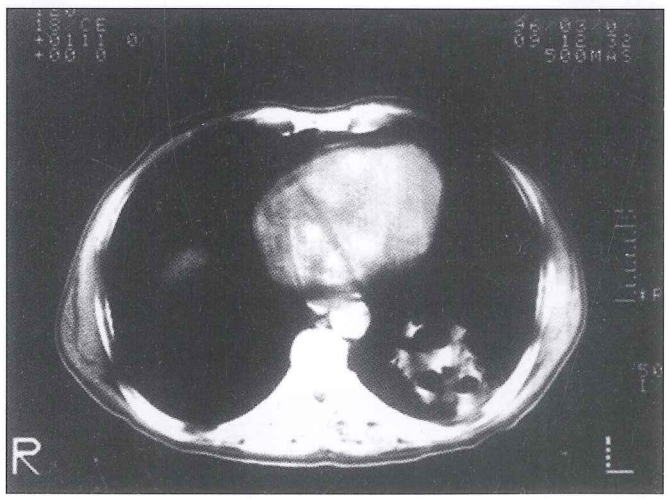

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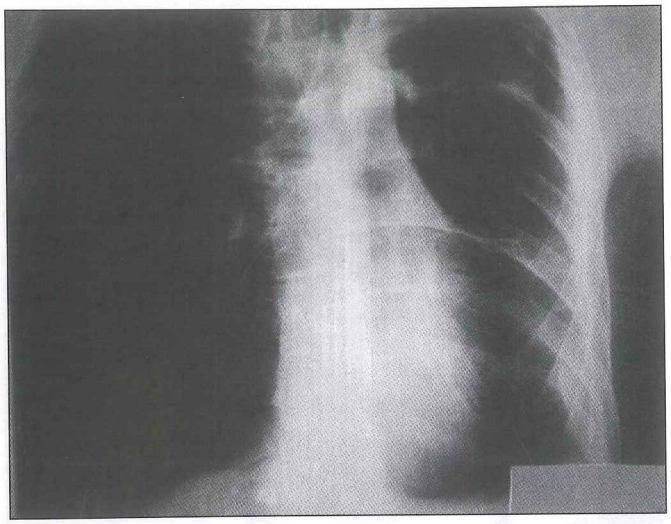

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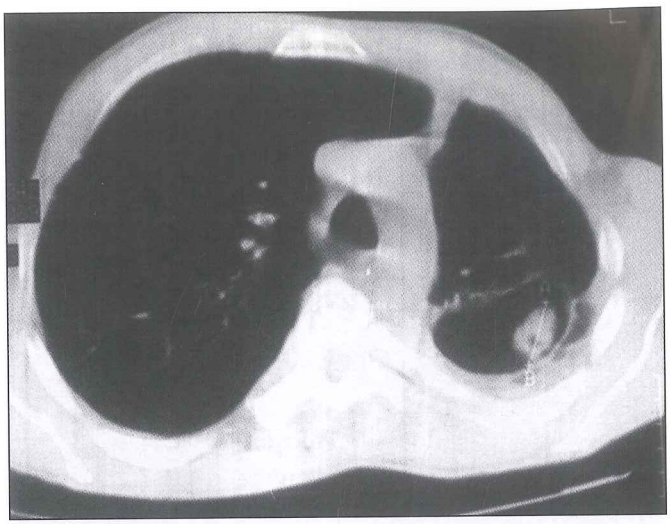

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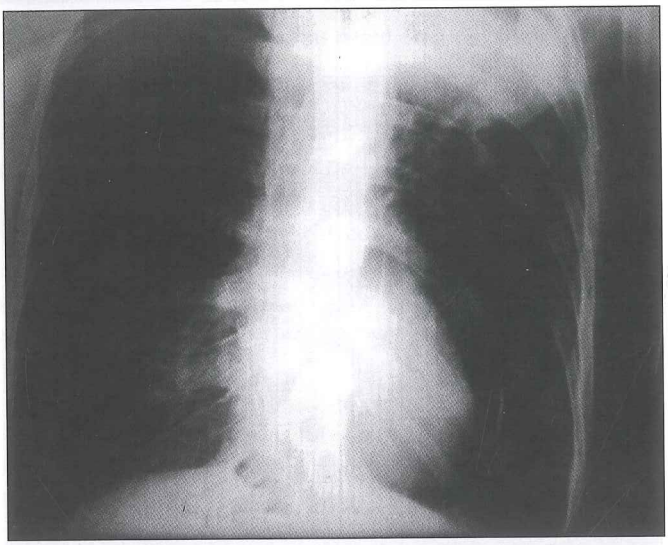

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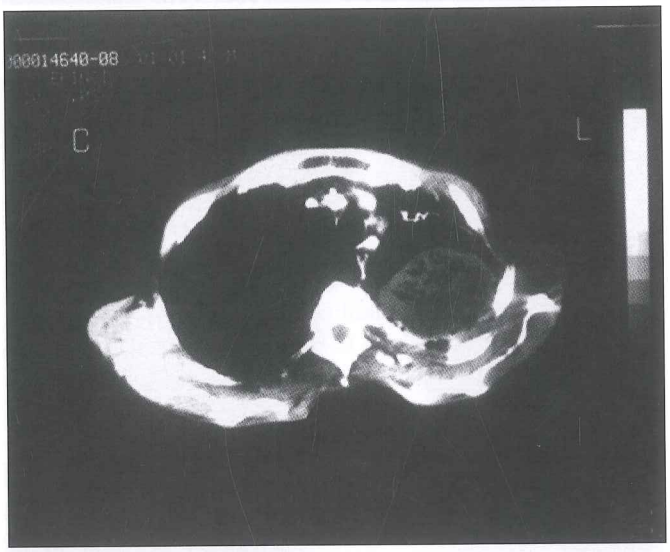

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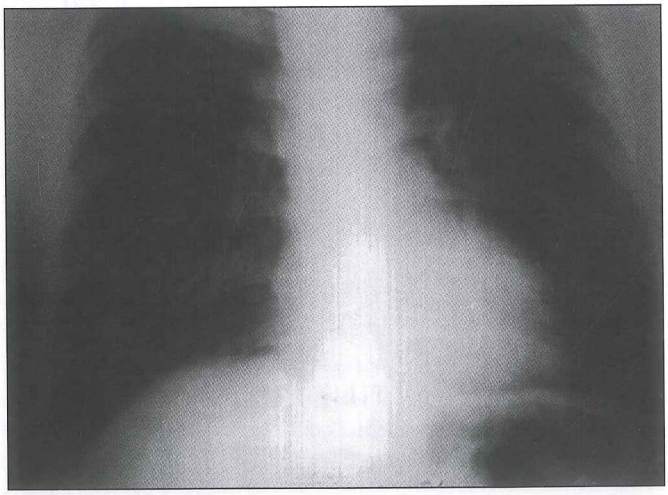

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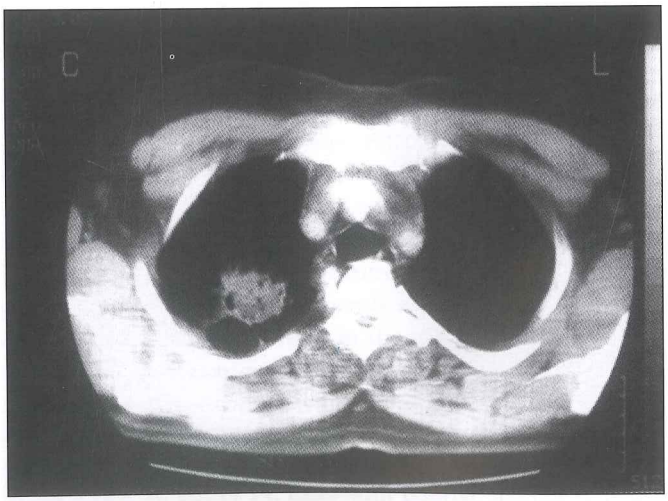

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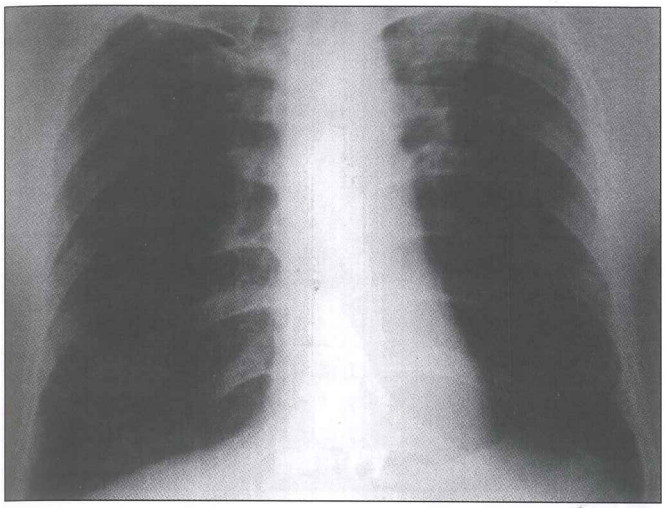

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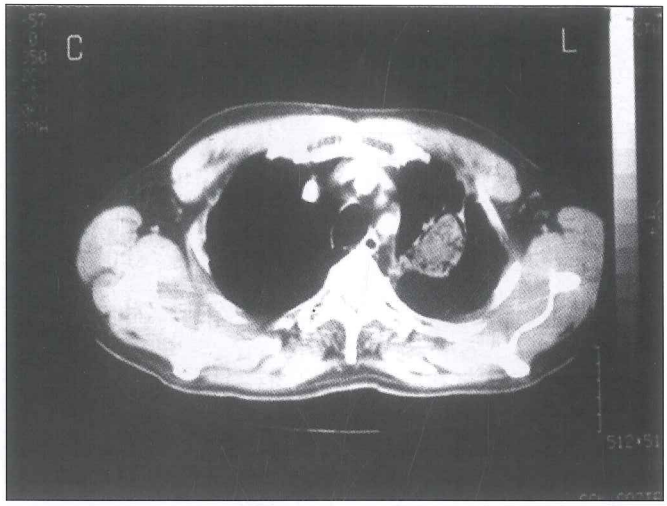

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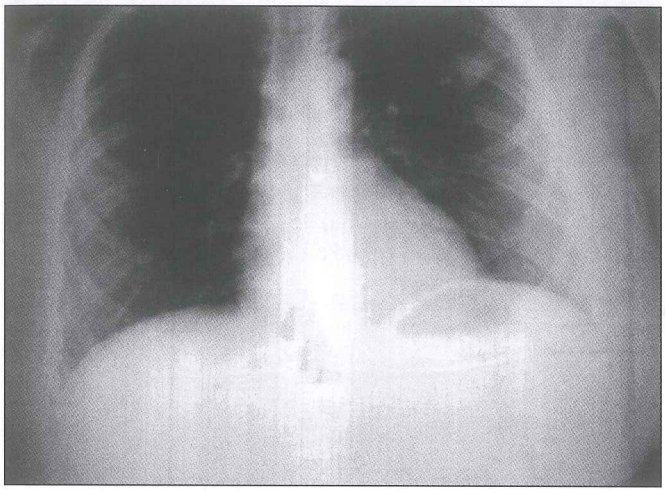

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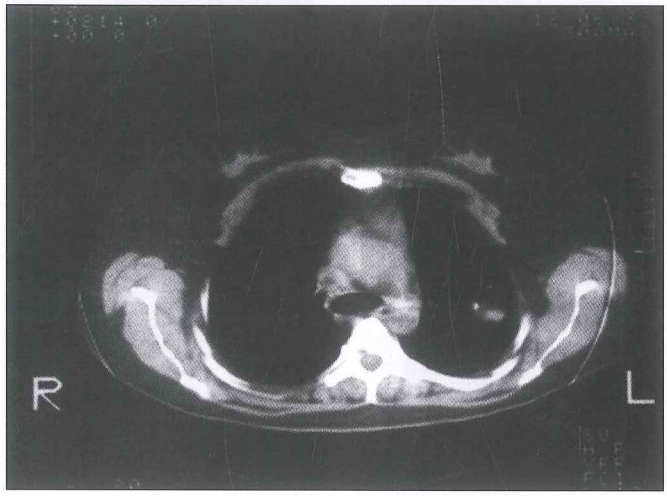

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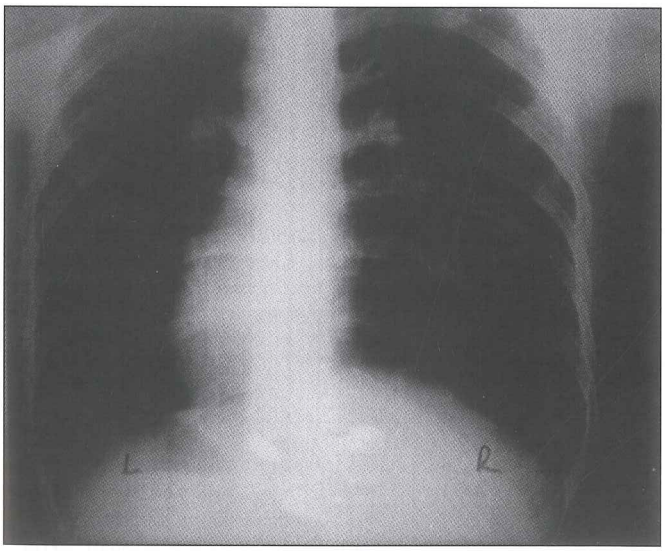

Case 10

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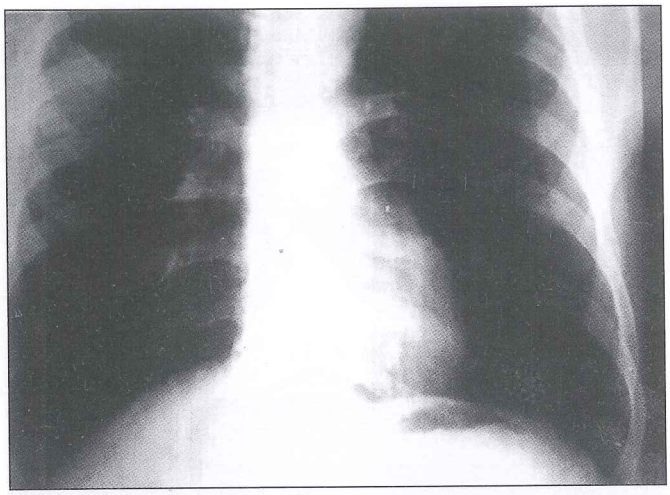

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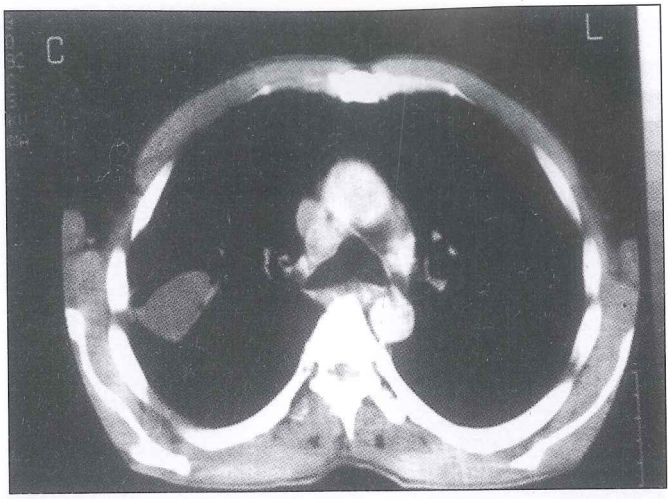

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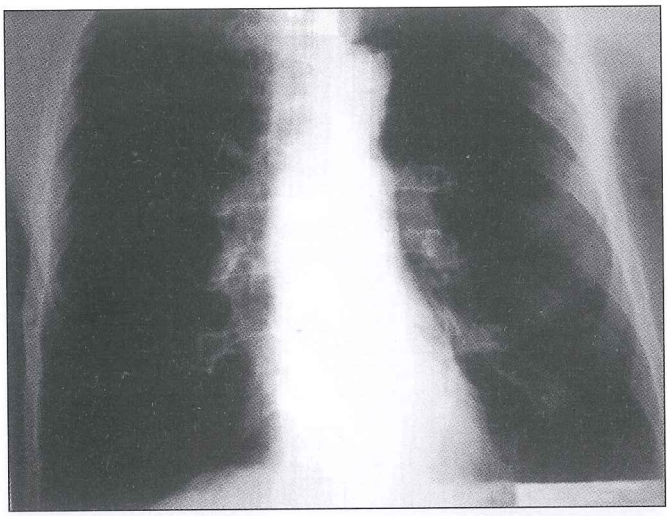

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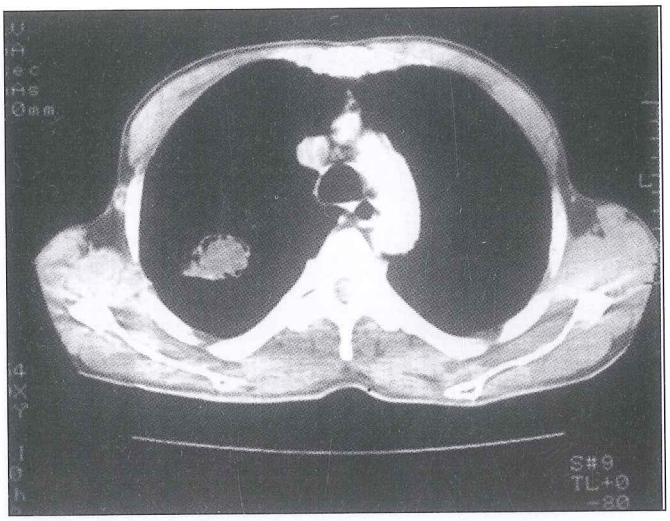
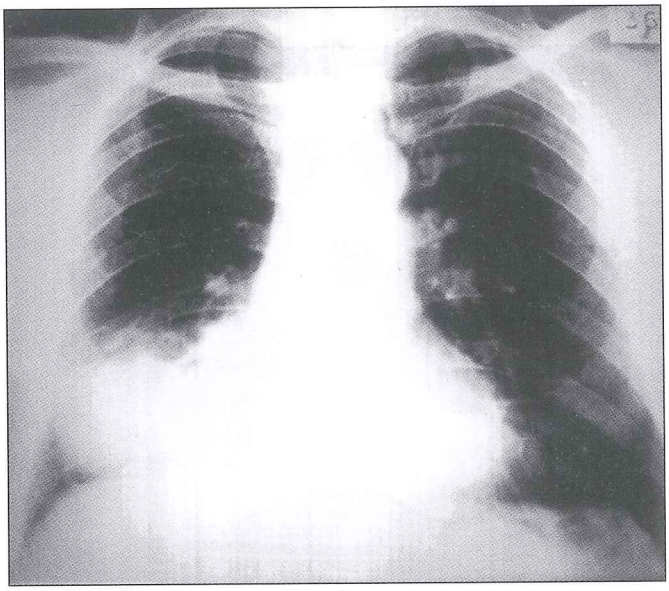


Case 12



Case 14

Picture 1. *Radiographical appearence of pulmonary aspergilloma. Except for case 2, all patients with a history of tuberculosis show the classic cresent-shaped patch of air (Monod's sign) and fungus ball moving when patients change position (upright position for postero-anterior chest X-ray and supine position for thorax CT).*

Table 1. Patient characteristics

Case no	Age	Symptom	Post TB	İmm.♦ Com.	Chest X-ray Thorax CT	Sputum Smear	FOB*	Surgery	Outcome
1	56 F	Haemopt 70 cc 3/day	AFB♣ + 16 years ago	-------	Left upper lobe 4x3 cm cavity fungus ball	+ bact. aspergl.	+ path. aspergl	Left upper lobect.	Follow-up
2	69 M	Cough Dyspnea	------	DM, lung cancer	Right upper lobe 2x1 cm fungus ball	+ bact candida	+ path. aspergl	Inop.	Chemotr and exitus
3	50 M	Sputum	AFB + 1 years ago	-------	Left lower lobe 3x2 cm cavity	+ bact aspergl	(-)	No surgery	Follow-up
4	36 F	Cough Haemoptysis 30-50 cc per/day	two times AFB + 10,1 years ago	-------	Right upper lob. fungus ball (2x3 cm)	(-)	+ path and + bact aspergl	Right upper lobe wedge resect.	Follow-up
5	30 M	Dyspnea Haemoptysis 30 cc/day	AFB + 2 years ago	-------	Left upper lobe cavity (7x6 cm) 2x2 fungus b.	(-)	+ path aspergl	Inop FEV_1 <800 ml	Arterial embol. alive
6	55 M	Sputum, Stridor	AFB + 10 years ago	-------	Left upper lobe 10 cm cavity in 7x5 cm fungus ball	+ bact fungus	+ path candida TTNA +path asperl	Left lobect.	Follow-up
7	39 M	Haemoptysis 200 cc per/day	AFB + 5 years ago	-------	Right upper lobe 5x4 cm cavity fungus ball	+ bact aspergl	+ path aspergl	Right upper lobect	Follow-up
8	46 M	Haemoptysis 150 cc per/day	AFB + 24 years ago	-------	Left upper lobe 4x3 cm fungus ball	+ bact aspergl	+ path aspergl	Left upper lobect.	Died after surgery
9	43 F	Haemoptysis 200 cc per/day	AFB + 12 years ago	-------	Left upper lobe 2x1 cm fungus ball	(-)	(-)	Left upper lobect aspergl	Follow-up
10	31 M	Cough Haemoptysis 30 cc/day	AFB + 9 years ago	-------	Right upper lobe 1x2 cm fungus ball	(-)	(-)	Right upper lobect aspergl	Follow-up
11	49 M	Cough Sputum	AFB + 2 years ago	-------	Right upper lobe 3x3 cm fungus ball	(-)	(-)	Right upper lobect aspergl	Follow-up
12	44 M	Haemoptysis 1000 cc 2 -week	AFB + 4 years ago	-------	Right upper lobe 3x3 cm fungus ball	(-)	(-)	Right upper lobect aspergl	Follow-up
13	51 M	Haemopt 10-30 cc 3-day	TB? 30 years ago	-------	Right upper lobe 1x1.5 cm fungus ball	+ bact aspergl	+ path aspergl	No surgery right lw	Just follow up
14	51 F	Haemopt 50-70 cc per day	AFB + Two times 10,1 years ago	-------	X-ray Right lower lob 5x6 cm mass	+ bact aspergl	Not done	Lobect mid l. wed res	Died during surgery

♦All cases HIV (-) and AFB (-)
♣AFB: acid fast bacilli
*FOB: fiberoptic bronchoscopy
TTNA: transthoracic needle aspiration

(chest X-ray, thorax CT) and pathological examinations (examination of postoperative tissue, TTNB, or FOB biopsy specimens) and clinical judgement (n=1). Despite a high suspicion of aspergilloma, TTNA biopsy was performed in Case 6, to exclude malignancy. Bandoh et al. also reported one case with clinical and radiological findings suggestive of aspergilloma but who got worse after 6 months of antifungal treatment, at which time a CT guided TTNA biopsy from the wall of cavity was performed. The pathology of this fungus ball like lesion revealed epidermoid lung cancer (4).

The ratio of aspergilloma associated with posttuberculous cavities was 93% in our series. This ratio was 66% in the experience of Al Kattan et al. (5) and 25% as reported by the British Thoracic and Tuberculosis Association (6). In Turkey TB is still a frequently encountered infectious disease (2) and for this reason the association of aspergilloma with TB may be higher than other countries. A few cases of aspergilloma within cavitating pulmonary carcinomas have been reported in the literature. Tomika et al. reported that an epidermoid lung cancer was thought to arise from preformed lung scars surrounding a posttuberculous cavity that contained an aspergilloma (8). In one case in our series, a patient who had no history of tuberculosis (case 2), the pulmonary aspergilloma was associated with pulmonary adenocarcinoma and diabetes mellitus.

In our series, haemoptysis was the most frequently observed presenting symptom (71%). Many studies also reported that this symptom was seen in 50% to 95% of aspergilloma cases (1,8,9). In a recent study on the aetiology and evaluation of haemoptysis in third world countries, it was reported that the percentage of aspergilloma among other causes was 1.9%; tuberculosis being responsible for 17% of the haemoptysis episodes, and bronchiectasis for 21% (10). Other aspergilloma associated symptoms include wheezing, chest pain, cough and fatigue (1).

In our series, we believe thorax CT as a diagnostic test was overused, since in many of the patients the clinical findings, postero-anterior chest X-ray and serology were diagnostic for aspergilloma. However, thorax CT can at times be highly contributory to the diagnosis of pulmonary aspergillosis, particularly in cases with small cavities that may be missed on standard films. Recognition of mobility of the fungal ball enables differentiation from lesions associated with tumors or infections (9). In our study, the standard films were not diagnostic in a number of the patients (cases 2, 3, 13 and 14), but in these patients, CT showed a rounded mass of soft tissue density filling a portion of a preexisting cavity, a finding consistent with an air crescent sign. Unfortunately we could not demonstrate the mobility of the fungus ball by comparison of the prone and supine CT images.

Surgical resection for pulmonary aspergilloma in selected patients provides the best chance of cure (1). In our series, 10 cases (71%) underwent thoracotomy and recurrent haemoptysis constituted the indication for surgery in all patients. Two patients died; one from a heart attack during surgery and the other because of massive bleeding after surgery. Recently it was reported that pulmonary resection for posttuberculous complex aspergilloma was associated with higher morbidity (25%) than resection for immuno-compromised patients (5%) (4).

In our series lobectomy was the most frequent surgical intervention, performed in 7 patients (70%). Pneumonectomy, wedge resection, lobectomy plus wedge resection, constituted other types of surgical interventions resorted to. In other series, again mostly lobectomy was performed (17 lobectomies in 20 cases and 29 lobectomies in 44 cases) (4, 11). One case in our series underwent bronchial embolization instead of an operation because he he had limited pulmonary capacity (FEV_1 less than 800 mL). Generally bronchial embolization is valid for the immediate control of life threatening haemoptysis and has a low rate of severe complications; recurrence is relatively common (24%) (12). The patient in our series had no recurrent bleeding in the follow-up period.

Therapeutic approach in pulmonary aspergilloma will vary, depending on the extent of the disease and the clinical state of the patient, but when possible, surgical resection in combination with pharmacological therapy (itraconazole or amphotericin B, flukanozole) is the treatment of choice (7). No patient in our series had received any antifungal drug.

In conclusion, we hope that this attempt to evaluate retros-pectively 14 pulmonary aspergilloma cases identified in our hospital files and comparing the data of our patients with previous reports in relation to incidence, symptoms, methods of diagnosis, treatment modalities, success rates, complications and prognosis has contributed to accumulation of experience in this area. Our results show that the frequency of tuberculosis as an underlying disease for pulmonary aspergilloma may vary among countries and is higher in Turkey as compared to some western countries.

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