Endobronchial Tuberculosis in a Patient With Bronchial Asthma Treated With High Doses of Inhaled Corticosteroids

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Abstract

A thirty-seven year-old female patient who was followed with a diagnosis of bronchial asthma admitted to our outpatient clinic with complaints of chest pain and fatigue. She used high doses of inhaled fluticasone propionate (>1000 micrograms) and long acting beta-mimetic inhalers for the last few years. On admission, the patient had a noisy inspiration. Pulmonary function tests were normal except a decreased peak expiratory flow value. A bronchoscopy performed for ruling out laringeal dysfunction revealed diffuse nodular yellowish leisons of 1-3 mm. in diameter in the right bronchial system. Acid fast bacilli (AFB) was negative on a smear of bronchial lavage, while an AFB culture was found to be positive. A second bronchoscopy was performed due to positive culture results and bronchial biopsy of the endobronchial leisons was performed. The pathological examination of bronchial biopsy showed bronchial mucosa with a nonspecific chronic inflammation. The patient was given antituberculous therapy. The complaints of chest pain and fatigue disappeared after treatment.

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Introduction

Endobronchial tuberculosis (EBTB) is often associated with pulmonary tuberculosis. It is most often a complication of primary pulmonary tuberculosis in children, although it may also occur in adults. The peak incidence of EBTB is in the second and third decades and it shows a marked preponderance in female patients (1-3).

The pathogenesis of EBTB is not yet fully established. However, sources of EBTB may include direct implantation of tubercle bacilli into the bronchus from an adjacent pulmonary parenchymal leison, direct airway infiltration from an adjacent tuberculous mediastinal lymph node, erosion and protrusion of an intrathoracic tuberculous lymph node into the bronchus, hematogenous spread, and extension to the peribronchial region by lymphatic drainage (1).

The present case report describes a patient with bronchial asthma who develops EBTB while being treated with high doses of inhaled corticosteroids. There is only one similar case in literature (4).

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Case Report

A thirty-seven year-old female patient admitted to our outpatient clinic with complaints of chest pain and fatigue. She was followed with a diagnosis of bronchial asthma for 12 years. The follow-up of the patient was done by our outpatient clinic for the last six years. During this period, she was hospitalised for four times while receiving systemic corticosteroids on two occasions. The patient was treated with high doses of inhaled fluticasone propionate (>1000 micrograms) and long acting betamimetic inhalers for the last few years. She also had and was treated for atrophic rhinitis causing intermittent nose bleeding.

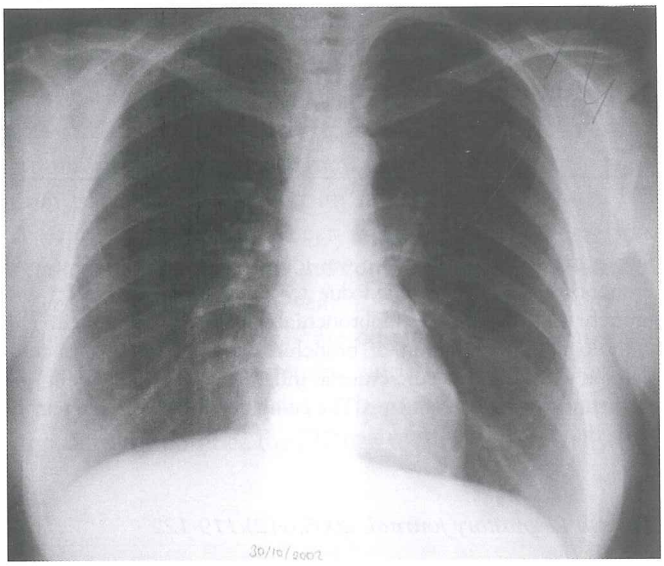

Figure 1. *The chest X-ray of the patient on admission.*

On admission, the patient had a noisy inspiration and prolonged expiration. Chest X-ray was normal (Figure 1). Pulmonary function tests were normal except a decreased PEF value. The chronological results of pulmonary function tests of the patient as well as the administered doses of inhaled and systemic steroids are shown in Table 1. Laboratory examination revealed a normal white blood cell count and erythrocyte sedimentation rate.

Bronchoscopy performed to rule out laringeal dysfunction revealed diffuse nodular yellowish leisons of 1-3 mm in diameter in the right bronchial system (Figure 2A, 2B). Endobronchial tuberculosis and sarcoidosis were considered in the differential diagnosis. Therefore, a bronchial lavage was performed for bacteriologic and cytologic examination. Acid fast bacilli (AFB) was negative on a smear of bronchial lavage, while an AFB culture was found to be positive after several weaks. Another chest radiograph of the patient was again found to be normal (Figure 3). However, since the symptoms of the patient persisted, a second bronchoscopy was performed for evaluating the appereance of the leisons and for making bronchial biopsy of these endobronchial leisons. The lesions persisted without any more spreading. The pathological examination of the bronchial biopsy showed bronchial mucosa with a nonspecific chronic inflammation. AFB was negative on a smear of bronchial lavage, while polymerase chain reaction was positive for tuberculous DNA.

Nine months before the first bronchoscopy, the patient was hospitalised for an acute asthmatic crisis. Because the patient had decreased FVC values on serial PFTs and FEV1/FVC values were normal on most occasions, a thorax computed tomography (CT) and high resolution CT (HRCT) was performed for ruling out a restrictive pathology. Thorax CT and HRCT had been reported to be completely normal, therefore these roentgenologic investigations were not repeated. The patient was given antituberculous therapy consisting of isoniazid, rifampicin, pyrazinamide and ethambutol in addition to her asthma medication [a combined preparation of salmeterol and fluticasone propionate (250 mg)]. The complaints of chest pain and fatigue disappeared after treatment.

Discussion

EBTB continues to be a health problem because of the following: (1) its diagnosis is frequently delayed because the decreased incidence itself diminishes the suspicion of tuberculosis; (2) bronchostenosis may develop as a serious complication despite efficacious antituberculous chemotherapy; and (3) it is of-

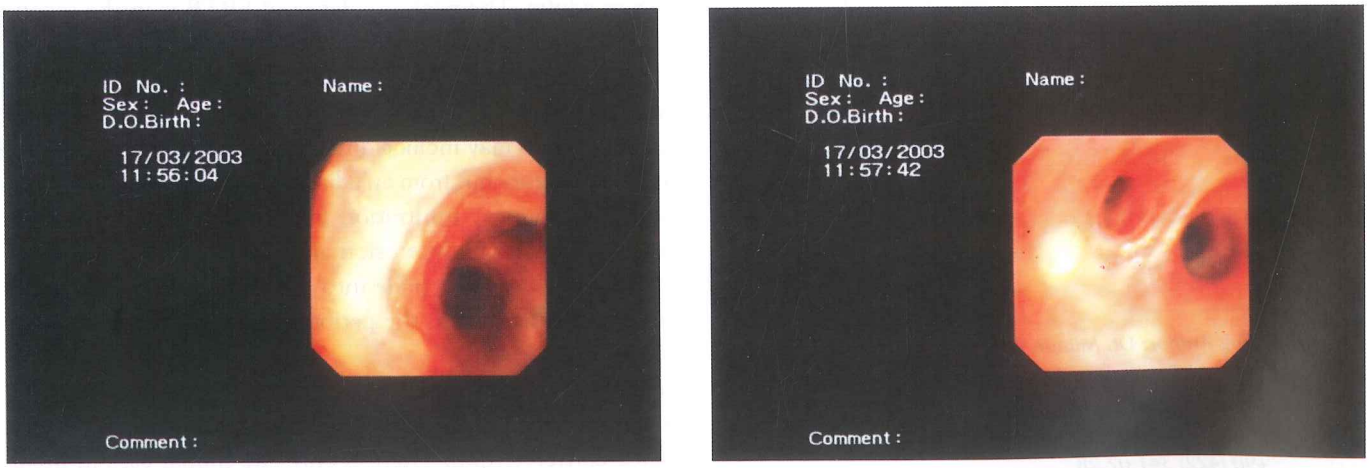

Figure 2A, B. *Fiberoptic bronchoscopic appearance of the nodular leisons in the right bronhial system.*

Table 1. The chronological list of PFT results and dosage of inhaler and systemic corticosteroids

Date	FVC %, L	FEV_1 %, L	FEV_1/FVC %	$FEF_{25-75\%}$ %, L/s	FIVC %, L	$FEF_{50\%}$/ $FIF_{50\%}$	Comment
Mar 1997							Admission to clinic, discharged on beclomethasone dipropionate 2x500 µg
Jul 1998	51 1.92	43 1.41	73	33 1.31	42 1.61	1.14	Treated with budesonide 2x400 mg, admission to clinic, IV prednisolone (40 mg – 5 days), bronchoscopy
Oct 1998	63	62	85	52			Budesonide 2x600 µg was prescribed
Apr 1999	75 2.68	68 2.10	78	55 2.13	63 2.24	1.21	Admission to clinic with pneumonia, discharged on budesonide 2x400 µg
Jul 1999	56 1.98	59 1.82	92	49 1.88	60 2.12	0.89	Fluticasone propionate discus 2x250 µg was prescribed
Sep 1999	79 2.82	67 2.07	73	46 1.79	78 2.78	1.29	
Jan 2000	82 2.91	89 2.76	95	83 3.19	71 2.53	1.16	
Nov 2000	61 2.14	69 2.11	98	67 2.57	58 2.06	0.85	
Dec 2001	63 2.23	69 2.13	95	68 2.57	61 2.18	1.45	
Feb 2002	64 2.27	68 2.11	93	56 2.13	35 1.27	2.53	Treated with fluticasone propionate 4x500 µg, admission to clinic, IV prednisolone 40 mg – 5 days
Feb 2002	84 3.02	89 2.75	91	77 2.90	80 2.85	1.35	Thorax CT + HRCT was normal
Mar 2002	71 2.52	76 2.36	94	69 2.61	74 2.63	1.09	Fluticasone propionate 2x500 µg was prescribed
Mar 2002	87 3.13	96 3.01	96	87 3.34	74 2.67	1.33	
Apr 2002	58 2.06	66 2.03	99	62	51 1.83	1.59	Fluticasone propionate 3x500 µg was prescribed
Nov 2002	84 3.0	89 2.76	92	79 2.99	76 2.70	1.16	First bronchoscopy was done, fluticasone propionate 2x250 µg was prescribed
May 2003	118 3.92	117 3.36	86	89 3.29	111 3.70	0.94	At the end of the second month of anti-TB treatment

FVC, forced vital capacity; FEV_1, forced expiratory volume in one second; $FEF_{25-75\%}$, maximal midexpiratory flow rate; FIVC, forced inspiratory vital capacity; $FEF_{50\%}$, forced expiratory flow at 50% of FVC; $FIF_{50\%}$, forced inspiratory flow at 50% of FIVC.

ten misdiagnosed as bronchial asthma or lung cancer (1,5,6). The clinical course of EBTB is variable. Symptoms are non-specific and they represent mainly the co-existing pulmonary tuberculosis (7). The chief complaint in most patients is intractable cough (3,8). Sputum expectoration, wheezing and discomfort under sternal area are other symptoms (3). Although rare, expectoration of bronchial cartilage can also be one of the clinical features of EBTB (9).

In EBTB the radiological appereance may be entirely normal as it was in the presented case. But, atelectasis, consolidation, obstructive hyperinflation and hilar enlargement may also be seen. Hilar enlargement (22 cases, 44%), was the most common finding in chest roentgenography in a series of 50 patients from Turkey (10).

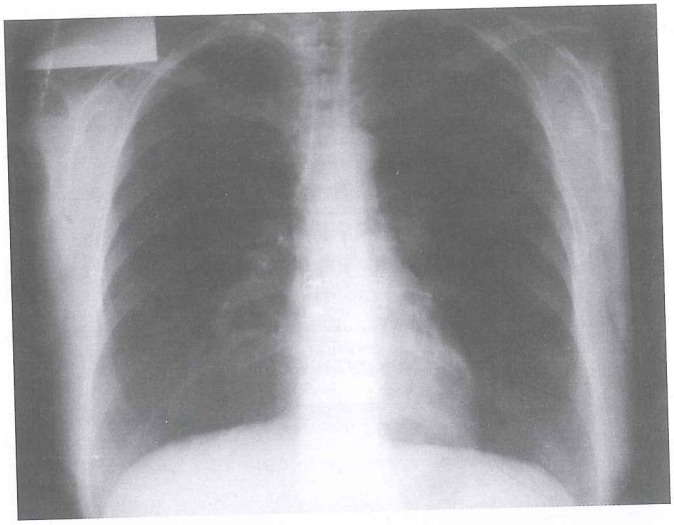

Figure 3. *The chest X-ray of the patient on the day before the second bronchoscopy.*

In three large series, 10.71% (6/56), 8.3% (10/121) and 13% (8/61) of the patients had plain radiographs revealing no abnormalities (2,3,8). Tracheobronchial tuberculosis without parencymal involvement on chest X-ray is a rare clinical entity. Pathogenesis is unclear but it is thought that it is the result of direct inhalation of *Mycobacterium tuberculosis* into the bronchial wall (5). Due to normal chest X-rays, the diagnosis may be difficult and delayed. Fiberoptic bronchoscopy is the most suitable tool for visualizing such leisons.

EBTB is classified into seven subtypes according to bronchoscopic features by Chung's Classification: actively caseating, fibrostenotic, edematous-hyperemic, tumorous, ulcerative, granular and non-specific bronchitic type (1). The course of disease differs according to the type; the prognosis is good for granular and non-specific bronchitic type (11). In our case, the form of EBTB was probably the granular type. According to Chung's classification, granular EBTB appears like scattered grains of boiled rice, and the underlying bronchial mucosa shows severe inflammatory change (1).

Four of the subtypes –actively caseating, edematous-hyperemic, fibrostenotic, and tumorous EBTB– show varying degrees of luminal narrowing of the bronchus, while the other three subtypes –granular, ulcerative, and nonspecific bronchitic EBTB– do not (1). Luminal narrowing was not observed in the present case.

Prompt diagnosis and efficacious treatment are of paramount importance in EBTB in order to minimize the resultant bronchial stenosis (12). Bronchoscopic approach is mandatory, not only for the prompt diagnosis of EBTB, but also for the prevention of further bronchostenosis (1).

In a series of 38 EBTB patients, indications for bronchoscopy were radiographic features (87%), microscopy smear negatives (8%), wheezing (3%) and blood stained sputum (3%) (7). In our case, bronchoscopy was performed to rule out a diagnosis of laryngeal dysfunction due to the patient's noisy inspiration.

EBTB was diagnosed in our case with positive AFB culture of bronchial washings. However, bronchoscopic biopsy and brush cytology are also useful for diagnosing EBTB (10,13).

EBTB is treated with standard antituberculous therapy. However, there are few studies using inhaled antituberculous drugs in addition to standard chemotherapy of pulmonary tuberculosis (8,14). Hypersensitivity reactions associated with initiation of antituberculous treatment may constitute a special group where corticosteroids are indicated in the treatment of EBTB (15,16). In other situations, the usefulness of corticosteroids for treatment of EBTB is not well documented (12).

In this case and a similar case in literature, it was speculated that high doses of inhaled corticosteroids may have the potential to cause EBTB (4). The previous patient, however, was also given systemic corticosteroids for five months for treatment of eosinophilic pneumonia before she was diagnosed to have EBTB. Since our patient used prednisolone for a short period of time (five days) and nine months before admission, the development of EBTB was considered to be unrelated with the usage of systemic steroids in this case.

Conclusion

Some airway leisons like EBTB may present with a normal chest X-ray and delay the diagnosis. Careful history taking and observation of clinical symptoms and signs are important in the final diagnosis of these patients.

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