TUBERCULOUS BRONCHITIS WITH NORMAL CHEST X-RAY AMONG A LARGE BRONCHOSCOPIC POPULATION

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Pulmonary tuberculosis (TB) remains a major health problem in developing countries.[1-2] In the past two decades, many countries in the Middle East region have faced wars, causing poor nutritional and hygienic conditions, and resulting in population migrations to other more peaceful countries in the region. These events can result in increased incidence and prevalence of TB in the countries involved. In this regard, reviewing unusual forms of TB, which can easily confuse clinicians, is useful in increasing their alertness for earlier diagnosis, which is essential for its control and prevention of resulting complications.[3]

Involvement of the tracheobronchial tree by TB is not uncommon.[4-6] Spillage of infected material into the middle and lower lobes causes localized endobronchial infection in some patients with pulmonary TB,[2] which can be suspected in classic cases with suggestive x-rayic findings.[1] In the past two decades, several reports have been published concerning primary endobronchial TB with normal chest x-rays.[4,6] Some of the later cases of TB can cause confusion,[7] which may result in inappropriate treatment. They are best evaluated by fiberoptic bronchoscopy for more definitive diagnosis.[5,8]

The purpose of this study was to introduce nine cases of endobronchial TB with normal chest x-rays collected during a 12-year period in Isfahan, Iran. Macroscopic endobronchial features are also presented.

Materials and Methods

From March 1987 to October 2000 in the Pulmonary Units of Kashani and Al-Zahra Medical Centers in Isfahan, a total of 6147 patients (3766 males and 2381 females) aged 5 to 98 years had undergone fiberoptic bronchoscopy for various indications including hemoptysis, lung infiltrates or masses, chronic unexplained cough, etc. Of the 6147 patients, nine were found to have endobronchial tuberculosis. These patients were subject to fiberoptic bronchoscopy as a result of chronic unexplained cough and a clinical suspicion of proximal airways disease. The diagnosis of endobronchial TB was based on bronchoscopic findings of visible lesions associated with histologic proof and stainable acid-fast bacilli (AFB) on bronchial biopsy, with subsequent growth of *Mycobacterium tuberculosis* on culture of the specimens. Reassessment was designed to detect bronchial stenosis with fiberoptic bronchoscopy.

Only eight out of the nine patients agreed to undergo a second bronchoscopy for reassessment of healing after anti-tuberculosis therapy which, in seven cases, consisted of a combination of isoniazide, rifampicin, pyrazinamide, and streptomycin for two months, to be continued with two drugs for an additional four months. In two cases, ethambutol was used instead of streptomycin. Initial steroid coverage (prednisolone, 30 mg daily for 2-4 weeks) to prevent fibrosis was administered to five patients with more severe infiltrative involvement of the bronchi.

Results

Overall, 117 patients in the series (1.9%) were diagnosed with TB, among whom were nine cases who presented with normal chest x-rays. These nine cases are described in more detail below. Their age range was 26-77, with a mean of 39 years, and the male to female ratio was 2:1. Duration of symptoms, which included cough in all cases, ranged from 2-3 months. The amount of sputum was variable. Sputum was usually mucoid in appearance. Hemoptysis was present in only four patients and was never copious.

Rhonchus was heard over the chest of four patients and wheeze in two. The characteristic localized wheeze suggestive of endobronchial obstruction was heard over the chest of only one patient, while rhonchus, suggesting bronchitis, was audible in four cases. Chest pain, ill-defined in nature, was reported by one patient. Systemic symptoms were not remarkable. Only five patients had low-grade fever while two had weight loss.

Chest x-ray (inspiratory and expiratory films) showed no evidence of air-trapping or any abnormal infiltrate and/or collapse, or hilar enlargement in any of the nine patients.

Only four patients were sputum smear positive for AFB with Ziehl-Neelson stain. The rest were sputum smear negative. Sputum examination was surprisingly not helpful in the diagnosis. Tuberculin skin test was reactive from 10

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FIGURE 1. Bulky grayish white gelatinous tissue blocking right upper lobe bronchus.

to 22 mm in all cases. None of the patients had acquired immune deficiency syndrome.

Bronchoscopic Findings

The typical bronchoscopic finding was the presence of grayish white gelatinous tissue (Figure 1) that was observed in three cases. It was bulky, blocking the lumen of the affected airways and proving difficult to remove by suction. Mucosa were red, nodular and vascular, and sometimes ulcerated with copious exudative discharge. In three patients, the nodules were so prominent with necrotic surface that the appearance was indistinguishable from that of bronchogenic carcinoma. In fact a diagnosis of neoplasm was suggested by the bronchoscopist in 4 of the 9 patients. The lesions were usually unilateral, with the exception of two patients who also had tracheal involvement. The right bronchial tree was affected in six patients and the left bronchus in three patients. Interestingly, five patients had involvement of the upper lobes, whereas four patients had involvement of the middle or lower lobes. Bronchial washing aspirate obtained during bronchoscopy was smear positive for AFB in seven of the patients, but tissue preparations and cultures showed AFB in all. Sensitivity test results were available in six cases which showed no resistance to first-line drugs.

All nine patients were recalled for study 9 to 12 months after completion of anti-tuberculosis chemotherapy. Only three patients were asymptomatic at this time. The remaining six patients had symptoms including scanty cough with mucoid sputum, as well as exertional dyspnea in three. The patients were informed of the potential of acquiring residual bronchial stenosis and offered a second fiberoptic bronchoscopy, to which eight agreed. Six of the eight patients showed various degrees of bronchial stenosis produced by scar tissues. The mucus covering the stenotic areas had a black discoloration (Figure 2) in three cases.

FIGURE 2. Anthracotic fibrous tissue developed in the involved bronchus after treatment.

Forced inspiratory and expiratory flow-volume loops were obtained in all patients, but did not show any evidence of upper airway obstruction. Pre- and post-treatment results of pulmonary function tests are summarized in Table 1. The data are expressed as percentages of prediction.

Discussion

Involvement of the trachea and major bronchi by TB is not rare,[3,5] however, such involvement in those with normal chest x-rays is less frequently observed.[4] In our series, 9 out of 117 patients (10.5%) with TB showed endobronchial involvement. This relatively high rate may reflect the referral situation of our institutions, which are naturally faced with many unusual cases. Patients with parenchymal pulmonary TB and endobronchial involvement usually present with atelectasis.[9] Atelectasis is usually lobar and right sided, and can be as frequent as 10%-30% in children,[10] however, it can also be observed in adults.[1] These findings may develop during active tuberculous pulmonary infection or many years after its treatment.[11]

Endobronchial TB is thought to arise by direct implantation of tuberculosis bacilli in the bronchi. This is supported by the frequency of tuberculosis in the stem bronchus opposite the opening of the airway draining the tuberculous cavity or focus.[12] Another cause of endobronchial TB is the direct infiltration by adjacent mediastinal lymph nodes,[1,13] which is more common in children. Lymphatic and hematogenous spread is much less common.[1] It is not known why some patients are more likely to develop endobronchial involvement.[12] As cited by Ip, Salkin et al. found endobronchitis was more common in those with advanced cavitating forms of TB.[12] However, a tuberculous cavity was not found in any of our patients, and the exact mechanism by which patients without detectable parenchymal disease catch the infection is not clear. More recent high-resolution CT scan findings suggesting TB as an initially endobronchial process [1,6] need further investigations.

Classically, endobronchial TB was considered a disease of young females.[14] However, in our study, male patients were affected twice as often as females, which is in agreement with some recent reports,[12] which suggest that it is no longer a disease of the young.

The diagnosis of endobronchial TB is established most readily by fiberoptic bronchoscopy.[5,8] The typical bronchoscopic findings are the same as observed in our patients, and the diagnosis of bronchogenic neoplasm is often suggested [15] until pathologic examination of biopsy material has been carried out.[11] Usually after healing of the endobronchial lesions, fiberotic tissue with resultant bronchial stenosis will ensue,[16] which may have a black-colored surface mimicking bronchial anthracosis, as was observed in three of the Isfahan patients (Figure 2).

Interest in parenchymal pulmonary TB has eclipsed the study of endobronchial TB after the introduction of modern anti-tuberculosis chemotherapy.[12] In the Isfahan series, systemic symptoms of infection were minimal; for example, fever was low grade and present in only five patients. This would make it difficult to differentiate endobronchial TB from bronchogenic carcinoma, especially when other respiratory symptoms of tuberculous endobronchitis were also nonspecific. The characteristic localized wheeze was found in only one patient and its absence, therefore, does not exclude endobronchial involvement.

On the other hand, the diagnosis of pulmonary TB is generally suggested on the basis of epidemiological data, clinical picture, tuberculin skin test result and chest x-ray,[3] and should be confirmed by identification of

Mycobacterium tuberculosis in tissue or sputum smears and/or culture.[3] If chest x-rays were normal, as in our nine patients, one of the main bases of diagnosis would be missing. In such a situation, early diagnosis would be possible only if TB had been included in the initial list of differential diagnosis.[3]

With endobronchial involvement, one can expect to find sputum smear positive for AFB.[12] Unexpectedly, the majority of our patients had either no sputum or were smear negative, the reason for which was not clear. It is possible that expectoration of sputum is difficult because of entrapment of mucus by proximal endobronchial tissue, or that ulceration of involved mucosa is necessary for a positive AFB smear result. Nevertheless, the message is clear: a negative smear for AFB does not exclude endobronchial tuberculosis.

Bronchoscopic findings usually provide the clue for the correct diagnosis of TB.[8] Irrespective of how many times the wrong bronchoscopic diagnosis of bronchogenic carcinoma is made,[11] as happened in four cases in the Isfahan series, this misinterpretation is more common when the lesions are nodular. The similarity between the two disorders has prompted us to exclude TB in all cases of suspected bronchogenic carcinoma.

Residual bronchostenosis was found in six patients, including three of five patients receiving oral steroids. This is somewhat in agreement with the report of Ip et al. who found a prevalence of more than 90% bronchial stenosis.[12] Chest x-ray and pulmonary function tests are insensitive in the assessment of endobronchial TB and the resultant stenosis, however, they are usually necessary to rule out other disorders, and bronchoscopy is the method of choice for early detection.[12] For ill patients, CT scan of the thorax may help.[4,6]

Whether steroid therapy can help prevent bronchostenosis is not clear. Only five patients received steroid therapy in the Isfahan series, but they did not show any difference from those not using steroids. However, the two groups were not similar with regards to the severity of their involvement. It should be mentioned that other investigators have also found that steroid therapy does not reduce the incidence of residual fibrosis,[12,15] and that it has some effects only if started very early in the course of the illness.[17] Unfortunately, surgical correction of the stenosis and placement of stents have not been encouraging.[16,18]

In conclusion, endobronchial tuberculosis is not rare. Clinically, it presents with chronic non-responding cough, which may resemble bronchogenic carcinoma. Bronchoscopy should be done whenever suspicion arises, even when chest x-ray is clear and sputum examination is negative. Close follow-up is advisable as stenosis may develop later despite modern anti-tuberculosis chemotherapy with or without steroid prophylaxis.

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