



Radiographic spectrum of adult pulmonary tuberculosis in a developed country

J. T. R. WILCKE, D. S. ASKGAARD, B. NYBO JENSEN AND M. DØSSING

Department of Pulmonary Medicine P, Bispebjerg Hospital, DK-2400 Copenhagen NV, Denmark

Setting. Bispebjerg Hospital, Department of Pulmonary Medicine P. The referral centre of adult tuberculosis in the municipality of Copenhagen, Denmark.

Objective. To evaluate the radiographic spectrum of pulmonary tuberculosis (TB) in adults in a low-prevalence country and to correlate radiographic appearances with bacteriological results, clinical and demographic data.

Design. Retrospective review of medical files on 548 cases with pulmonary TB according to the criteria of WHO.

Results. Usual radiographic pattern of reactivating TB, with upper lobe involvement, was found in 92% ($n=504$). Eight percent ($n=44$) showed unusual X-ray patterns for adults, such as isolated lower lobe infiltrations ($n=19$), hilar adenopathy ($n=10$), miliary TB ($n=7$), tuberculoma ($n=2$), pleural effusion ($n=1$) and normal chest X-ray ($n=3$). Eighty-nine percent of cases with cavitary lesions were positive by microscopy.

Conclusion. The risk of missing a diagnosis of pulmonary TB may be high if patients present with an X-ray unusual for TB, but this is fortunately seen only in 8% of cases of pulmonary tuberculosis. Unusual X-ray is more commonly found in patients with concomitant disease, such as diabetes and cancer.

If chest X-ray shows cavities, but the smear is negative for *Mycobacterium*, TB is unlikely and further diagnostic procedures should be performed without waiting for culture results.

RESPIR. MED. (1998) 92, 493-497

Introduction

The reversal of the tuberculosis (TB) epidemic, with increasing incidences reported from many western countries (1), reminds us of the importance of an effective TB control programme with high quality in diagnosis, treatment, screening of contacts, follow-up of patients and an effective central monitoring system (2). In Denmark, the dramatic decline in the incidence of TB seen in the previous five decades (3,4) has ceased, and during the past 15 years the incidence of TB in Denmark has been stable with a minor increase in 1994 to 7.8/100,000. The increasing incidences in western countries may be explained by increasing problems with TB among minorities, i.e. HIV-positive patients, immigrants and patients who are poorly served by organized medicine, i.e. the homeless, drug and alcohol abusers and poor urban populations with crowded living conditions (1).

With regard to diagnosis, some authors have focused on the problem of increasing delay and frequency of misdiagnosis of not only 'unusual' but also far-advanced pulmonary TB. In low prevalence countries this may be due to decreasing experience with TB (5) and a shift in the care unit of the TB patient from specialized departments to

community hospitals. It has been claimed that an increasing percentage of persons entering adulthood will be uninfected and susceptible to develop primary disease when the incidence is low. Primary TB may be responsible, at least in part, for the so called 'unusual' radiographic presentation of pulmonary TB in adults (6,7).

Our impression, from the daily clinical work with TB patients, is that the problem of unusual chest X-ray in TB is overemphasized. Accordingly, we decided to review hospital records and determine the patterns of presenting roentgenograms in patients over 15 years of age treated for pulmonary TB at our department.

Materials and Methods

Criteria for inclusion were (1) treatment for pulmonary TB in agreement with the WHO definition (2) (sputum/gastric lavage/bronchoalveolar lavage (BAL) positive by culture or lung biopsy with typical histology or radiographic active pulmonary TB, but with ≥ 3 negative sputum cultures for *Mycobacterium tuberculosis* (*M. tuberculosis*)), (2) no history of prior active TB, (3) age ≥ 15 years, (4) no history of human immunodeficiency virus (HIV) infection. HIV testing was not done routinely in the department but was offered to all patients at risk of HIV infection.

Patients with pleural TB, without pulmonary infiltrates and without *M. tuberculosis* cultured in sputum were

Received 14 December 1995 and accepted 19 June 1997.

Correspondence should be addressed to: Dr Jon Torgny R. Wilcke, Department of Pulmonary Medicine P, Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen NV, Denmark.

TABLE 1. Radiographic findings and result of smear/culture in sputum, gastric lavage or bronchial alveolar lavage

Radiographic category	Usual (n=504)	Unusual (n=44 (8%))					Total (n=548) (5% of all)
		Lower lung field	Hilar adenopathy	Miliary pattern	Tuberculoma	Pleural effusion	
+ Cavities	230	1	—	—	—	—	231
(% of category)	(46)*	(5)					(42)
Bilateral	276	10	3	7	—	—	296
(% of category)	(55)	(53)	(30)	(100)			(54)
Microscopy positive	374	10	3	4	—	—	391
(% of category)	(74)*	(53)	(30)	(57)			(71)
Culture positive	480	18	7	7	2	2	519
(% of category)	(95)	(95)	(70)	(100)	(67)	(100)	(95)
Total	504	19	10	7	3	2	548
(% of all)	(92)	(3)	(2)	(1)	(0.5)	(0.4)	(100)

*Indicates significant difference ($P<0.05$) between the usual and unusual X-ray category.

excluded as having extrapulmonary TB in agreement with the WHO definition (2).

Routinely, three sputum samples were collected and examined by the central mycobacteria laboratory of Denmark (Statens Seruminstitut) for microscopy and culture. Gastric lavage (alternatively BAL/lung biopsy) was performed only if sputum samples were not obtainable. During 11 years, from 1 January 1983 to 31 December 1993, 639 patients were consecutively admitted and treated for pulmonary TB at our department. Of the 639 cases, 548 were included, as six files could not be traced, 74 were excluded due to previous TB and 11 due to age below 15 years.

The presenting chest X-rays were described by one of five specialists in pulmonary medicine employed at the department during the 11-year period. The patients were divided into the following two major categories according to the presenting radiograph. (1) Usual reactivation TB (upper lobe infiltrates defined as infiltrates \pm cavitation, above a line drawn through the hilar region (15)). (2) Unusual TB: (a) lower lung field TB defined as X-ray lesions below a line drawn through the hilar region, (b) isolated hilar adenopathy, (c) miliary TB defined as diffuse micronodular densities in both lungs, (d) tuberculoma, defined as well circumscribed nodular lesions, (e) pleural effusion combined with culture-positive sputum, and (f) normal. Usual reactivation TB associated with lesions in other parts of the lung was classified as usual.

Radiographic data were correlated with results of microscopy/culture and demographic data: age, sex, nationality, predisposing diseases (cancer, diabetes mellitus, peptic ulcer, chronic obstructive pulmonary disease), intravenous drug abuse, alcohol abuse (daily alcohol consumption in excess of 60 g).

Fisher's exact test was used for statistical evaluation and $P<0.05$ was chosen as the level of significance.

Results

Among 548 patients, 504 (92%) had X-rays with usual appearance and 44 (8%) had X-rays with unusual appearance (Table 1).

Of the 504 patients with usual X-ray changes, 82 (12%) had upper lobe infiltrates associated with infiltrates in other localizations, 55% had bilateral lesions and 46% had cavities (Table 1).

Of the 44 patients with unusual X-ray, 19 had isolated infiltrates in the lower lobe, 10 hilar adenopathy, seven miliary pattern, three tuberculoma and three normal X-ray. Isolated pleural effusion associated with culture-positive sputum was observed in two cases.

Among patients with unusual X-ray, 39% were positive by microscopy, compared to 74% in the usual X-ray group ($P<0.05$). No significant differences were found with respect to culture in the two X-ray groups (Table 1).

The three patients with normal X-ray were smear-negative. Two of the three patients were culture-positive in two of three sputa, and one patient only in one of three sputa. Indications for sputum examination were, in two subjects, cough combined with close contact to patients with severe pulmonary TB, and, in one subject, cough combined with positive culture in a lymph node biopsy of the neck.

Out of 231 cases with cavities, 206 (89%) were positive by smear (relative risk 154% of positive smear in patients with cavities compared to patients without cavities ($P<0.05$)). Results of culture did not differ between patients with or without cavity disease. Overall, 391 (71%) patients were positive by direct microscopy and 519 (95%) by culture (Table 1).

Diagnosis was based on examination of sputum in 460 (84%) patients, gastric lavage in 49 (9%), bronchial alveolar lavage in nine (2%), pleural fluid in seven (1%),

TABLE 2. Demographic characteristics of patients with usual and unusual pulmonary tuberculosis ($n=548$)

Parameter	Usual ($n=504$) (92%)	Unusual ($n=44$) (8%)
Age, median (range)	40 (15-90)	42 (15-88)
Sex, male/female	344/160	27/17
Underlying disease (%)		
Alcohol abuse	209 (41)	14 (32)
Cancer	11 (2)*	3 (7)
Diabetes	26 (5)*	8 (18)
Peptic ulcer	3 (0.5)	0
Drug abuse	16 (3)	0
None	266 (53)	24 (55)
Country of origin (%)		
Denmark	328 (65)	26 (59)
Northern Europe	20 (4)	0
Greenland	44 (9)	4 (9)
Southern Europe	20 (4)	2 (5)
Asia	66 (13)	9 (20)
Africa	22 (4)	3 (7)
Others	4 (1)	0

*Indicates significant difference ($P<0.05$) between usual and unusual.

bronchoscopic biopsy with typical histology in seven (1%) and clinical/radiographic picture without bacteriological confirmation in 16 (3%).

The median age for the whole population was 40 years (range 15-90, 67% males). The median age for Danes and Northern Europeans were 45 (range 16-90, $n=374$), for Greenlanders 32 (21-72, $n=48$) and the rest 27 (15-78, $n=126$).

Demographic data according to usual and unusual X-rays are presented in Table 2. No predisposing condition were registered in 290 cases. The number of patients with diabetes mellitus and cancer was significantly higher in the category with unusual X-ray. No significant differences were found with regard to other predisposing conditions, age, sex, nationality, drug- and alcohol-abuse. TB patients from Asia and Africa tended to have a higher incidence of unusual radiographic findings (13%) compared with Danes (8%) and Greenlanders (9%) (Table 2, $P>0.05$).

Discussion

In most cases TB is an airborne infection, resulting in primary TB and, perhaps later, as described by Stead (8), reactivation TB, in which dormant foci of previously disseminated organisms become active. The location of primary TB reflects pulmonary airflow, which favours deposition of inhaled organisms in the mid or lower lung field. From the primary focus, bacteria are spread by the lymph to the pulmonary lymph nodes and, from there disseminated haematogenously. Haematogenous deposition occurs mainly in areas that facilitate bacterial growth, such

as apical regions of the lung. This can be explained by deficient lymph production and drainage, resulting in decreased removal and dormant foci of tubercle bacteria (9).

Stead (6) has characterized radiographic manifestations of primary and reactivation TB. This classification is, however, hampered by uncertainty about the time of tuberculin conversion. Radiographic appearance, such as isolated consolidation in the lower or mid lung field, hilar or mediastinal adenopathy (perhaps with normal chest X-ray) and pleural effusion, are typical manifestations of primary disease. Lower lobe infiltration, miliary TB and tuberculoma may represent primary as well as reactivation disease. What is often described as unusual radiographic presentation of pulmonary TB in adults is, in fact, a typical manifestation of TB as primary disease. What is unusual is primary disease occurring in adults.

Reactivation TB is most often characterized by focal infiltration with or without cavities of the apical and posterior segments of the upper lobes or the superior segment of the lower lobe, leading to infiltration above an arbitrary line drawn through the hilar region (15). Studies in adults suggest a primary TB frequency from 37% (10), 15-17% (5,7,14) to 8% (11), probably reflecting difficulties in recognizing primary TB due to few symptoms, tendency to heal spontaneously, selection bias and the small value of the tuberculin test for demonstrating conversion. Realizing the very limited value of the tuberculin test in a BCG-vaccinated population (12), and classification based only on X-ray changes to be too uncertain, we decided not to classify patients as having primary or reactivation TB.

RADIOGRAPHIC APPEARANCE

Unusual radiographic TB, defined as radiographic manifestations not usual for reactivation TB, has been reported in several studies among more than one-third of adult patients with pulmonary TB (5,12-14). Only Hadlock (11) reports a frequency (12%) as low as the present study (8%). The number of unusual radiographic findings may, in some reports, be too high due to patient selection, as more usual TB cases are diagnosed and treated in the community hospital, while the unusual cases are referred to central urban hospitals for further diagnostic work (12). In 1992, 91% ($n=61$) of adult patients with pulmonary TB in the area of Copenhagen and suburbs, were treated in our department and only 9% (mostly children and HIV-positive patients) were treated in other departments. Due to this and the great number of patients positive by smear (71%) and usual X-ray (92%) findings, we believe that the present material is fairly unselected.

Lower lobe infiltration was found in 3.4% of our patients, which is at the lower end of the previously reported incidences, ranging from 4 to 7% (7,11,15). Based on X-ray findings, this manifestation is not easily differentiated from other infectious diseases, and *M. tuberculosis* may be difficult to demonstrate (only 53% positive by smear). TB must be considered if lower lobe infiltrates do not regress in spite of conventional treatment of bacterial pneumonia and especially in patients with diabetes (16) (Table 2), immunodeficiency or recent exposure to *M. tuberculosis*.

Hilar adenopathy was found in 10 patients (2.5%), seven unilaterally and three bilaterally. Hilar adenopathy is a hallmark of primary TB, but, in adults from western countries, it is commonly related to bronchogenic carcinoma, metastatic neoplasm, sarcoidosis, lymphoma and, rarely, fungal disease. *M. tuberculosis* is often difficult to demonstrate in these patients (30% positive by smear, 70% by culture) and in 30% of the patients a tissue biopsy was necessary to verify the diagnosis.

Miliary TB was found in seven patients (1%), two of which had predisposing disease (one diabetes, one myloid leukaemia).

Normal X-ray was observed in three patients (0.5%), in agreement with some studies (7,11), but few compared to other studies with up to 3–5% (5,12). One patient had lymph node TB with sputum positive by culture on several occasions, two patients had a history of recent *M. tuberculosis* exposure, and sputa were culture-positive on two and one occasion, respectively. It should be remembered that, in patients with little clinical evidence of TB (including normal chest X-ray) and only one positive sputum sample out of several, false-positive cultures may be very common in some settings (17). Even in good laboratories, about 1% of the specimens may be false-positive due to contamination (18,19). Restriction fragment length polymorphism (RFLP) analysis may be an effective tool for identifying false-positive cultures of *M. tuberculosis* and for minimizing this problem in laboratories (17,20).

TB patients with normal chest X-ray are thought to have endobronchial TB, and a CT scan in these patients may show endobronchial lesions, peribronchial lymphadenopathy and small atelectasis (21). Realizing that less than 0.2% of patients with pulmonary symptoms and normal X-ray are positive for *M. tuberculosis* (22), we find that CT scan due to suspicion of TB is reasonable only in highly selected patients, i.e. HIV-positive patients.

CULTURE AND SMEAR

Cavities appeared in 231 (42%) patients, in agreement with previous studies (11,12) and almost exclusively associated with apical involvement (usual X-ray Table 1). If X-ray showed cavities, 89% were positive by smear, in contrast to only 58% of patients without cavities ($P < 0.05$), indicating that further diagnostic procedures, such as bronchoscopy, should be performed to rule out alternative diagnosis, i.e. malignancy (23) in patients with cavities, but negative for *M. tuberculosis* by smear.

PREDISPOSING DISEASE, ALCOHOL AND DRUG ABUSE, AGE, SEX AND ETHNICITY

In accordance with other studies, the group with unusual X-ray included significantly higher frequencies of diabetes (especially lower lobe involvement (15,16) and cancer patients (24 (Table 2). In these and other immunosuppressed patients (i.e. HIV-positive patients, steroid and cytostatic treated patients) suspicion of TB must be strong if X-ray is unusual or even normal.

Alcoholics and drug addicts were more prominent among patients with usual X-ray, probably reflecting social deprivation and homelessness associated with abuse, rather than an increased susceptibility to TB (none of the patients was known to be HIV-positive). In agreement with the study of van den Brande *et al.* (25), ages were similar among cases with usual and unusual X-ray.

We found a non-significant tendency towards a higher frequency of unusual chest X-ray findings in Asian and African TB patients. This is not a surprise, because these patients originate from areas of the world with very different TB epidemiology and incidence of TB. The different origin of the TB patients is also reflected in the distribution of extrapulmonary TB in Denmark, where 37% of foreign compared to 17% of Danish TB patients present with extrapulmonary TB (3). However, the present study seems to have too little statistical power to demonstrate a similar relationship among the subgroup with pulmonary TB.

References

1. American Thoracic Society. Medical section of the American lung association. Control of tuberculosis in the United States. *Am Rev Resp Dis* 1992; **146**: 1623–1633.
2. WHO. Framework for effective tuberculosis control. *TB* 1994; **94**: 179.
3. Statens Seruminstitut, Copenhagen, Department of epidemiology. Annual report, 1994.
4. Kok-Jensen A. When can tuberculosis be eradicated in Denmark? *Danish Med Bul* 1995; **157**: 273–279.
5. Miller WT, MacGregor RR. Tuberculosis: frequency of unusual radiographic findings. *AJR* 1978; **130**: 867–875.
6. Stead WW, Kerby GR, Schueleter DP, Jordahl CW. The clinical spectrum of primary tuberculosis in adults. Confusion with reinfection in the pathogenesis of chronic tuberculosis. *Ann Intern Med* 1968; **68**: 731–741.
7. Khan MA, Kovnat DM, Bachus B, Whitcomb ME, Brody JS, Snider GL. Clinical and roentgenographic spectrum of pulmonary tuberculosis in the adult. *Am J Med* 1977; **62**: 31–38.
8. Stead WW. Pathogenesis of a first episode of chronic pulmonary tuberculosis in man: recrudescence of residuals of the primary infection or the exogenous reinfection? *Am Rev Resp Dis* 1967; **95**: 729–745.
9. Dock W. Apical location of pthisis: its significance in treatment by prolonged rest in bed. *Am Rev TB* 1946; **53**: 297–307.
10. Woodring JH, Vandiviere HM, Fried AM, Dillon ML, Williams TD, Melvin IG. Update: the radiographic features of pulmonary tuberculosis. *AJR* 1986; **146**: 497–506.
11. Hadlock FP, Park SK, Awe RJ, Rivera M. Unusual radiological findings in adult pulmonary tuberculosis. *AJR* 1980; **134**: 1015–1018.
12. Kadjito T, Grange JM. A clinical evaluation of the diagnostic usefulness of an early dermal reaction to

- tuberculin: a failure to distinguish between tuberculosis and other respiratory disease. *Tubercle* 1985; **66**: 129–132.
13. Korzeniewska-Kosela M, Krysl J, Muller N, Black W, Allen E, FitzGerald JM. Tuberculosis in young adults and the elderly. *Chest* 1994; **106**: 28–32.
 14. Krysl J, Korzeniewska-Kosela M, Muller NL, FitzGerald JM. Radiologic features of pulmonary tuberculosis: an assessment of 188 cases. *Can Ass Radiol J* 1994; **45**: 101–107.
 15. Berger HW, Margarito GG. Lower lung tuberculosis. *Chest* 1974; **65**: 522–526.
 16. Weaver R. Unusual radiographic presentation of pulmonary tuberculosis in diabetic patients. *Am Rev Resp Dis* 1974; **109**: 162–163.
 17. Small PM, McLenny NB, Singh SP, Schoolnik GK, Tompkins LS, Mickelsen PA. Molecular strain typing of *Mycobacterium tuberculosis* to confirm cross-contamination in mycobacteriology laboratory and modification of procedures to minimize occurrence of false positive cultures. *J Clin Microbiol* 1993; **31**: 1677–1688.
 18. Aber VR, Allen BW, Mitchison DA. Quality control in tuberculosis bacteriology: laboratory studies on isolated positive cultures and the efficiency of direct smear examination. *Tubercle* 1980; **61**: 123–133.
 19. MacGregor RR, Clark L, Bass F. The significance of isolating low numbers of *Mycobacterium tuberculosis* in culture of sputum specimens. *Chest* 1975; **68**: 518–523.
 20. Hayward AC. Restriction fragment length polymorphism typing of *Mycobacterium tuberculosis*. *Thorax* 1995; **50**: 1211–1218.
 21. Lee KS, Song KS, Lim TH, Kim PN, Kim IY, Lee BH. Adult-onset pulmonary tuberculosis: Findings on chest radiographs and CT scans. *AJR* 1993; **160**: 753–758.
 22. Hansen M, Kok-Jensen A. Culture of sputum for *Mycobacterium tuberculosis*. *Ugeskr Læger* 1981; **143**: 1010–1014.
 23. Kwale PA, Johnson MC, Wroblewski DA. Diagnosis of tuberculosis: routine cultures of bronchial washings are not indicated. *Chest* 1979; **76**: 140–142.
 24. Kaplan MH, Armstrong D, Rosen P. Tuberculosis in cancer patients. *Cancer* 1974; **3**: 550–858.
 25. van den Brande P, Vijgen J, Demedts M. Clinical spectrum of pulmonary tuberculosis in older patients: comparison with younger patients. *J Gerontol* 1991; **46**: 204–209.