ORIGINAL ARTICLE

Chest Radiographic Findings in Neurotuberculosis without Pulmonary Signs and Symptoms

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ABSTRACT

Objective: To determine the chest radiographic findings in patients of adult neurotuberculosis, with no pulmonary signs and symptoms.

Study Design: Descriptive study.

Place and Duration of Study: Department of Neurology, Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from January 2004 to January 2006.

Patients and Methods: A total of 100 patients fulfilling pre-defined criteria of neurotuberculosis were included. Chest radiographic (CXR) evidence of pulmonary TB was looked for in those patients and its frequency, pattern and association with the clinical grades at presentation was determined by using Chi-square test.

Results: Out of the 100 patients of neurotuberculosis, with no clinical evidence of pulmonary TB, radiographic evidence of pulmonary TB was seen in only 30% patients. The predominant patterns on CXR were apical infiltration (26.6%), miliary mottling (20%) and hilar enlargement (16.6%). Positive CXR was found in 16.7% patients in clinical grade I and 40% and 43.3% in patients in grade II and III respectively. There was a strong association of grade II and grade III with positive chest radiographic findings (p= 0.03).

Conclusion: Patients of neurotuberculosis may have chest radiographic evidence of pulmonary TB even in the absence of pulmonary signs and symptoms at presentation. There is a strong association of clinical grade II and grade III with positive chest radiographic findings.

Key words: *Neurotuberculosis. Chest radiography. Pulmonary tuberculosis.*

INTRODUCTION

Tuberculosis remains a major global problem and a public health issue of considerable magnitude. Involvement of the Central Nervous System (CNS) is an important and serious type of extra-pulmonary involvement. It has been estimated that approximately 10% of all patients with tuberculosis have CNS involvement.[1] The incidence of CNS tuberculosis is directly proportional to the prevalence of tuberculous infection in general. In developing countries, CNS tuberculosis is a disease of younger age group, usually childhood.

Neurotuberculosis has a wide range of presentations, including tuberculous meningitis (TBM), tuberculoma, tuberculous abscess, spinal TB and tuberculous encephalopathy.[2] TBM is the commonest form and makes up 70-80% of the cases of neurotuberculosis. The development of neurotuberculosis is a 2-step process. *Mycobacterium tuberculosis* bacilli enter the host by droplet inhalation, the initial point of infection being the alveolar macrophage. Localized infection escalates within the lung, with dissemination to the regional lymph nodes to produce the primary complex. During this stage, a short but significant bacteremia is present, which can seed tubercle bacilli to other organs in the body.[3] In those who develop tuberculous meningitis (TBM), bacilli seed to the meninges or brain parenchyma, resulting in the formation of Rich foci.

Chest radiography finds active or previous TB infection in about 50% of those with TBM and these findings lack specificity in settings with high prevalence of pulmonary TB. Miliary TB strongly suggests multiorgan involvement; therefore, it is very helpful when it is shown by chest radiograph.[3]

The objective of this study was to determine the frequency and pattern of chest radiographic evidence in patients of neurotuberculosis who had no pulmonary signs and symptoms.

PATIENTS AND METHODS

This descriptive study was carried out on 111 indoor and outdoor adult patients of the Department of Neurology, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, from January 2004 to January 2006.

A standardized case report form was used to document demographic data, clinical symptoms and signs, laboratory findings and radiographic findings of each patient at the time of presentation. All patients underwent detailed history taking and physical

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examination with special emphasis on CNS and chest. Clinical grading at the time of presentation was done according to the modified British Medical Research Council clinical criteria for TBM severity[4] as grade I was alert and oriented without focal neurological deficit (FND), grade II: Glassgow Coma Scale (GCS) 14-10 with or without FND or GCS 15 with FND and grade III: GCS less than 10 with or without FND.

Routine investigations of complete blood counts, ESR, liver function tests, renal function tests, blood sugar random, serum electrolytes, Chest X-ray (CXR) and Mantoux test were carried out on every patient. Eighty-three patients underwent cranial CT scan and the presence of hydrocephalus, infarction and meningeal enhancement was recorded. Lumbar puncture (LP) was performed in 95 patients and CSF was sent for analysis for total leucocyte count (TLC), glucose, proteins, staining and culture. Polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* was also done in majority of the patients.

All chest radiographs and CT scans were read by at least two consultant neurologists and one senior radiologist, independent of one another.

Criteria for inclusion were: (1) definite neurotuberculosis: when acid fast bacilli (AFB) was stained or cultured from CSF and/or PCR was positive and (2) highly probable neurotuberculosis: when two or more of the clinical, CSF findings, imaging or evidence of TB elsewhere were fulfilled. Patients who complained of respiratory symptoms like productive cough, breathlessness or chest pain and/or had abnormal findings on chest examination or who were already diagnosed as pulmonary TB were excluded from the study.

Radiographic features were classified as: normal, apical infiltration and/or cavitation, miliary mottling, lower/middle zone infiltration, hilar enlargement (hilar or paratracheal lymphadenopathy), acute on chronic TB (active tuberculosis like cavitation or soft infiltrates on the background of old fibrosis/ calcification) and findings other than the above mentioned.

The data was entered and analyzed using SPSS version 12.0. Descriptive analysis was done and reported as mean, median and standard deviation for continuous variables and frequencies and percentages for categorical variables. For comparison, univariate analysis was done by using Chi-square test and p-value was reported. P-value <0.05 was considered statistically significant.

RESULTS

A total of 111 patients of neurotuberculosis were enrolled during the study period. Clinical evidence of pulmonary TB was found in 11(9%) patients, who were excluded from the study. Of these patients, 6 (5.4%) had history of productive cough and abnormal chest examination, 3 (2.7%) were diagnosed but non-compliant cases of pulmonary TB, while 2 (1.8%) had completed full course of ATT before developing meningitic features. CXR was suggestive of pulmonary TB in all these patients except two.

Hundred patients fulfilled our predetermined criteria of inclusion. Radiographic evidence of pulmonary TB could be seen in 30 (30%) patients. These were labelled as CXR-positive. The predominant patterns on CXR were apical infiltration (26.6%), miliary mottling (20%) and hilar enlargement (16.6%). Middle/lower zone infiltration and combination of above mentioned CXR signs was found in 10% each. Evidence of acute on chronic TB was seen in 6.6% patients while pleural effusion, old fibrotic scars and Gibbus at T6/7 was seen in one patient each. Only 10 (33.3%) CXR positive patients showed a positive mantoux test in contrast to 45 (64.2%) patients with negative CXR.

Most of the patients (75%) presented in advanced clinical grades (II and III). CXR suggestive of concomitant pulmonary TB was found in16.7% patients in clinical grade I and 40% and 43.3% in patients in grade II and III respectively. There was a strong association of clinical grade at presentation and positive chest radiography when grade I was compared with grade II and III, (p- value 0.03).

DISCUSSION

The relationship between pulmonary and cranial miliary lesions is controversial and there is a paucity of work done on adults in this regard. In this study a strong association was found between clinical grade at the time of presentation and positive chest radiography. The magnitude of bacillary population in the lungs can be inferred from the extent and morphology of the disease, as determined by chest radiograph.[5] It was hypothesized that the overwhelming bacteremia that accompanies advanced grades of neurotuberculosis, may explain the higher incidence of positive chest radiography in these patients.

It was observed that 70% of neurotuberculosis patients had normal CXR. Chest radiographs are normal in most patients with primary TB, perhaps because films are obtained after the pulmonary process has resolved.[6] Often the peripheral lesions are small in size and hilar or paratracheal lymphadenopathy may remain invisible on CXR initially and may later become evident as small calcified or fibrotic nodules. CXR may even be normal in early miliary TB, as these tubercles are not visible until these get 1-2 mm in diameter.[7,8]

In this study only 30% adults with neurotuberculosis without pulmonary signs and symptoms had positive chest radiographic findings. In an Indian study of 20 TBM patients with miliary tuberculosis, where 19 were

adults, all belonged to a tubercular endemic area and 3 had a history of tuberculosis. None of those patients presented with pulmonary symptomatology.[9] In another study on TBM, Kilpatrick *et al.* showed that 61% of the chest X-rays were consistent with pulmonary tuberculosis and 39% were normal.[10] Associated lung pathology on CXR was found in 37%, 80% and 37% in three local studies carried out in Faisalabad and Karachi respectively[11-13] but the presence or absence of pulmonary symptoms was not taken into account in those studies. Secondly, all these studies aimed at TBM only and not at the whole spectrum of neurotuberculosis.

In contrast, TBM has been studied in more detail in pediatric population. While abnormal chest radiograph are found in about 30% of adults, most of the studies on TBM on pediatric population give a much higher incidence of positive CXR finding, of upto approximately 80%.[14,15] However, in a study based on pediatric neurotuberculosis (TBM and tuberculomas), abnormalities of chest X-ray were found in 40%[16], which is consistent with the present study.

The predominant radiographic patterns of pulmonary TB in this study were apical infiltrates (26.6%), miliary mottling (20%) and hilar enlargement (16.6%). The predominant patterns in a Turkish study on adults turned out to be miliary pattern (28%) and active infiltration and cavitation in 26%.[17] In a study carried out in prisons in Pakistan, 58% showed the typical pattern (infiltration and/or nodules with or without cavitations, involving upper zone), while 42% showed atypical patterns.[18] Malik *et al.* also reported pulmonary infiltrates on chest x-ray in 33.3% and miliary pattern in 13.3% only.[19] However, in pediatric population Yarami *et al.* noted abnormal chest radiography in 87% patients, with a variety of abnormalities including hilar adenopathy (34%), miliary pattern (20%), pneumonic infiltrate (18%) and bronchopneumonic infiltrate (15%).[14]

Kondo *et al.* revealed that chest radiological examinations of infants and young children of TBM showed swelling of the mediastinal lymph nodes and/or parenchymal infiltration in all patients (100%). So they concluded chest and cranial CT scans to be useful adjuncts for diagnosis of TBM in infants and young children, in addition to conventional methods such as the tuberculin skin test, plain chest radiography, and staining for mycobacteria in body fluids.[15] Since neurotuberculosis is a fatal illness and early diagnosis and prompt treatment is essential to better prognosis, this claim needs to be substantiated with further studies.

It was also noticed that 55% patients had positive Mantoux test. However, only 33.3% CXR positive patients had positive Mantoux test in contrast to 64.2% patients with negative CXR. Kalita *et al.* also demonstrated that 45% patients of TBM with pulmonary miliary tuberculosis had negative Mantoux test.[9] Although, the diagnostic practice in our country gives much value to Mantoux test for the diagnosis of tuberculosis, current reviews suggest that skin testing is probably of limited value, except in infants.[3,20]

Approximately 75% of the patients in this study were diagnosed at stage II or III of neurotuberculosis. The advanced clinical grade at presentation is probably attributable to the low socioeconomic and educational levels of most of our patients, leading to the general practice not to seek medical assistance until the terminal stages of the disease.

As for limitations, the diagnosis of TBM was based mainly on clinical criteria and few patients had microbiological confirmation. The diagnosis of TBM cannot be made or excluded on clinical grounds alone and definitive diagnosis depends on the detection of the tubercle bacilli in the CSF, either by staining, culture or PCR.

CONCLUSION

Patients of neurotuberculosis may have chest radiographic evidence of pulmonary TB even in the absence of pulmonary signs and symptoms at presentation. There is a strong association of clinical grade II and grade III with positive chest radiographic findings.

REFERENCES

1. Chronic meningitis. In: Wood M, Anderson M, (edi). Neurological infections; major problems in neurology. Vol 16. Philadelphia: *WB Saunders;* 1998:p.169-248.
2. Garg RK. Tuberculosis of the central nervous system. *Postgrad Med J* 1999; **75**:133-40.
3. Thwaites GE, Tran TH. Tuberculous meningitis: many questions, too few answers. *Lancet Neurol* 2005; **4**:160-70.
4. British Medical Research Council. Streptomycin treatment of tuberculous meningitis. *BMJ* 1948;**I**: 582-97.
5. Infectious diseases of the lungs. In: Murray JF, Nadel JA, (edi). Text book of respiratory medicine. 2nd ed. Philadelphia: *WB Saunders;* 1994: p.1098-120.
6. Toosi Z, Ellner JJ. Tuberculosis. In: Gorbach SL, Bartlett JG, Blacklow NR,(edi). Infectious diseases. 2nd ed. Philadelphia: *WB Saunders*; 1998. p.1505-13.
7. Raviglione MC, O'Brien RJ. Tuberculosis. In: Kasper DL, Braunwald E, Hauser S, Longo P, Jameson JL, Fauci AS, (edi). Harrisons principles of internal medicine. 16th ed. New York: *McGraw Hill*; 2005:p.953-65.
8. Holgate ST, Frew A. Respiratory diseases. In: Kumar P, Clark M, (edi). Clinical medicine. 5th ed. Edinburg: *WB Saunders*; 2002: p.892-7.
9. Kalita J, Misra UK, Rawjan P. Tuberculous meningitis with pulmonary miliary tuberculosis: a clinicoradiological study. *Neurol India* 2004; **52**:194-6.
10. Kilpatrick ME, Girgis NI, Yassin MW, Abu el Ella AA.Tuberculous meningitis-clinical and laboratory review of 100 patients. *J Hyg* (*Lond*) 1986; **96**: 231-8.

11. Qureshi HU, Merwat SN, Nawaz SA, Rana AAK, Malik A, Mahmud MK, *et al.* Predictor of mortality in 190 adult patients with tuberculous meningitis. *J Pak Med Assoc* 2002; **52**:159-63.
12. Ayesha H, Javed F. Tuberculous meningitis (TBM): an experience of 100 pediatric patients. *Professional Med J* 2002; **9**: 65-70.
13. Qureshi HU, Merwat SN, Nawaz SA, Rana AAK, Malik A, Mahmud MK, *et al*. Predictor of mortality in 190 adult patients with tuberculous meningitis. *Infect Dis J* 2000; **9**:15-8.
14. Yaramis A, Gurkan F, Elevli M, Söker M, Haspolat K, Kirba G, *et al*. Central nervous system tuberculosis in children: a review of 214 cases. *Pediatrics* 1998;**102** (5): p.E49.
15. Kondo S, Ito M. Usefulness of cranial and chest imaging in the diagnosis of tuberculous meningitis among infants and young children. *Kekkaku* 2003; **78**:89-93.
16. Farinha NJ, Razali KA, Holzel H, Morgan G, Novelli VM. Tuberculosis of the central nervous system in children: a 20-year survey. *J Infect* 2000; **41**: 61-8.
17. Sengoz G. Evaluating 82 cases of tuberculous meningitis. *Tuberk Toraks* 2005; **53**:51-6.
18. Rao NA, Sadiq MA. Recent trend in the radiological presentation of pulmonary tuberculosis in Pakistani adults. *J Pak Med Assoc* 2002; **52**: 501-3.
19. Malik ZI, Ishtiaq O, Shah NH, Anwer F, Baqai ZH. Analysis and outcome of 30 patients with tuberculous meningitis. *Pak J Med Res* 2002; **41**:137-41.
20. Thwaites G, Chau TT, Mai NT, Drobniewski F, McAdam K, Farrar J. Tuberculous meningitis. *J Neurol Neurosurg Psychiatry* 2000; **68**: 289-99.