

Clinical Note

Paradoxical response to chemotherapy in tuberculous pleural effusion.

A 31-year-old patient presented to Vallabhbhai Patel Chest Institute, Delhi, India, with a 6 week history of cough, weight loss, anorexia, low grade fever with evening rise of temperature, night sweats and breathlessness. Physical examination revealed signs of left sided pleural effusion. On investigation hemoglobin is 10.1 gm %, total leukocyte count is 6,800/- cumm, differential leukocyte count is - P 80, L 20 and erythrocyte sedimentation rate (ESR) is 50mm for the first hour by Wintrobe method. His tuberculin test was positive. His sputum sample for AFB (Acid Fast Bacilli) was positive (all the 3 samples). Chest x-ray confirmed the presence of left sided pleural effusion along with the dense non-homogenous opacity in the right upper zone of the lung parenchyma (Figure 1a). A diagnosis of tuberculous pleural effusion (Sputum for acid fast bacilli, 3 samples were positive) was made and he was started on anti-tuberculous chemotherapy (Isoniazid 300mg, rifampicin 600mg, ethambutol 750mg, pyrizinamide 1500mg daily). His symptoms were not improved and another x-ray of the chest was taken one month later (Figure 1b) which, showed increase in the size of left sided pleural effusion. We continued the same anti-tuberculous regimen as culture/sensitivity of the sputum sample did not show resistant AFB. Later, the effusion responded to the same anti-tuberculous regimen.

Although short course chemotherapy in tuberculous patients has a good outcome and minimal toxicity, paradoxical increase of the disease

manifestations has been documented to occur weeks or months after the administration of anti-tuberculous therapy. This paradoxical response has been frequently reported in tuberculous lymphadenitis and tuberculoma. Intracranial tuberculomas start to enlarge up to 7 months after starting chemotherapy before the full resolution is obtained. Up to 30% of patients with tuberculous lymphadenitis have paradoxical response to chemotherapy. In contrast such a reaction is rarely reported in tuberculous pleural effusion. Few workers have reported development of contralateral pleural effusion during chemotherapy for tuberculous pleurisy in one patient occurring 4 weeks after initiation of anti-tuberculous chemotherapy.⁴ Development of the pleural effusion after starting chemotherapy for pulmonary tuberculosis has also been reported. The paradoxical response in tuberculous pleural effusion has been reported to occur in 16% of the cases³ which is less than 30% documented in cases of tuberculous lymphadenitis. The appearance of new lesions or expansion of pre-existing lesions in patients treated for tuberculosis should raise questions regarding diagnosis, compliance and drug resistance. In our patient there was no reason to believe that he was non compliant, and full recovery on the same medications exclude the possibility of drug resistance. The other explanation is the paradoxical response to chemotherapy which, is the case in our patient. The exact cause of this response is not clear but probably has an immunological basis. Workers have speculated on the mechanism of the paradoxical response in cases of tuberculoma and lymphadenitis, and attributed it to the 'immunological rebound' by

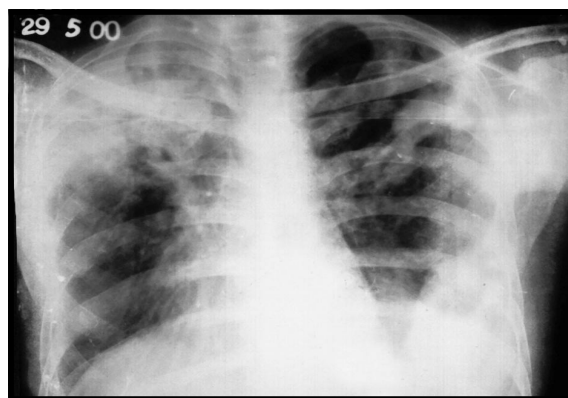
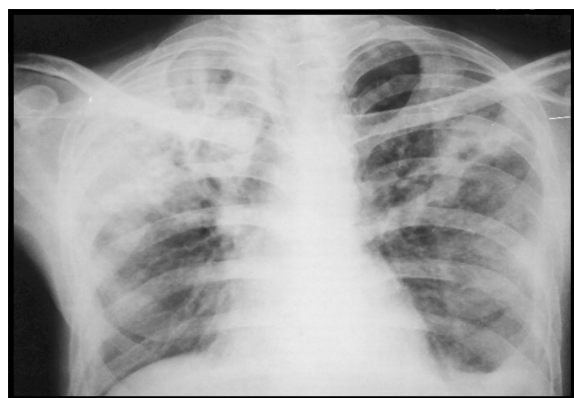


Figure 1 - (a) Chest x-ray (PA view) shows the presence of left sided pleural effusion with non homogenous opacity in the right upper zone of the lung parenchyma. (b) Chest x-ray (PA view) shows increase in the size of the left sided pleural effusion compared with Figure 1 (a) along with the non homogenous opacity in the right upper zone.

which the improved cell mediated immunity after treatment coincided with excessive antigen load (bacterial cell wall residues) resulting from rapid bacterial lysis. The same workers also suspected that rapid bactericidal drugs like Isoniazid and rifampicin could be the worse offenders than bacteriostatic drugs. The same mechanism could be operational in the case of pleural effusion. Corticosteroids are known to modify the severity of the clinical manifestations of tuberculosis.⁵ However there is no data that corticosteroids prevent the paradoxical worsening seen in various organs.

Raj Kumar
Tajenders S. Vasu
Department of Respiratory Medicine
Vallabhbai Patel Chest Institute
University of Dehli
Dehli - 110007, India

References

1. Benoosh A, Lieberman J. Paradoxical enlargement or development of Intracranial Tuberculomas during therapy: case report and review. *Clin Infect Dis* 1994; 19: 1092-1099.
2. Onwubalili JK, Scott GM, Smith H. Acute respiratory distress related to chemotherapy of advanced pulmonary tuberculosis: a study of two cases and review of the literature. *Q J Med* 1986; 59: 599-610.
3. Majed S. Study of paradoxical response to chemotherapy in tuberculous pleural effusion. *Respir Med* 1996; 90: 211-214.
4. Al-Ali M, Al-Masri N. Development of contralateral pleural effusion during chemotherapy for tuberculous pleurisy. *Saudi Med J* 2000; 21: 574-576.
5. Senderovitz T, Viskum K. Corticosteroids and tuberculosis. *Respir Med* 1994; 88: 561-565.