Contralateral paradoxical response to chemotherapy in tuberculous pleural effusion

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Introduction

Pleural effusions may occur as a complication of primary tuberculosis or an established pulmonary or extrapulmonary infection. New formation or expansion of a tuberculous lesion during chemotherapy is referred to as paradoxical response. Paradoxical response has been described to occur weeks or months after starting antituberculous chemotherapy for parenchymal lung disease, intracranial tuberculoma, or pleural effusion[1-2].

To our knowledge only one case of contralateral paradoxical effusion that occurred eight weeks after standard antituberculous chemotherapy has been reported in the literature[3]. In this paper, we describe a patient who developed contralateral paradoxical pleural effusion six days after standard antituberculous chemotherapy and prednisolone.

Case Report

A 23-year Asian lady was admitted to our ward (City General Hospital, Stoke-on-Trent) with a three weeks history of shortness of breath on moderate exertion, cough productive of white sputum, night sweats, and one stone weight loss. Clinical examination was normal except for signs of left pleural effusion; this was confirmed on X-ray of the chest (plate 1). The full blood count showed haemoglobin of 8.9 g/dl, white blood cell count 6.2 x 10^9/l, mean corpuscular volume 53.9 fl, mean corpuscular haemoglobin 17.1 pg (patient is known thalassaemia trait). The ESR was 55mm/hr and the C - reactive protein was raised at 171 mg/l. At thoracocentesis straw coloured fluid was aspirated. The fluid was an exudate: protein content was 56 g/l. The Gram stain was negative. A pleural biopsy obtained at the time of thoracocentesis, showed several foci of caseous necrosis surrounded by palisaded histeocytes with scattered langhans cells; Ziehl-Nielsen staining was positive for acid fast bacilli.

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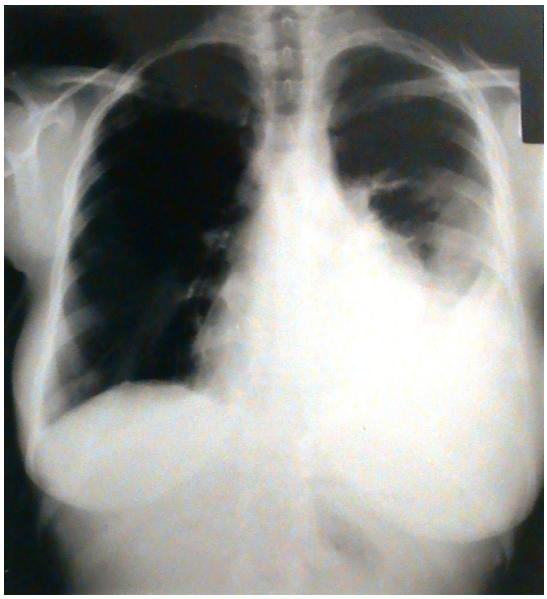
The pleural effusion was drained to dryness and the patient was started on standard antituberculous treatment with rifampicin, isoniazid, and pyrazinamide, in addition to pyridoxine and prednisolone 30 mgs per day. The patient improved clinically and her temperature was normal before she was discharged home to continue on the same medications.

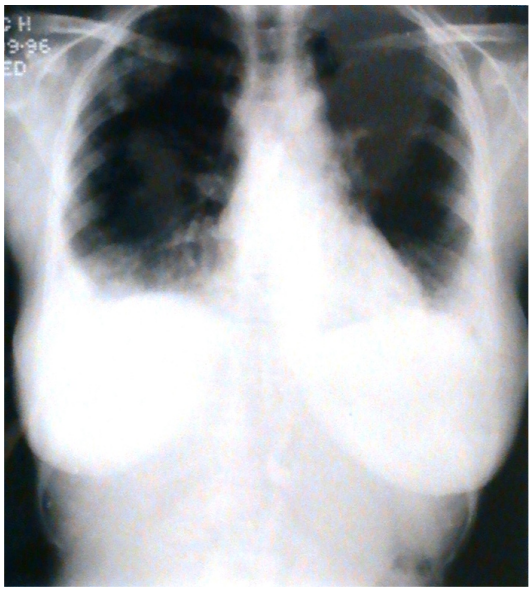
Plate 1:



Although chemotherapy was not interrupted at any time, the patient was readmitted three days after discharge (six days after initiation of anti tuberculous therapy) with feeling cold and shivery and had right

side pleuritic chest pain and headache. Physical examination revealed: temperature raised at 38^0C and there were signs of right side pleural effusion which was confirmed on X-ray of the chest (plate 2). Full blood count had not changed. Liver function test showed a slightly raised Gamma Glutamyl transferase at 38 U/L (normal 0 - 35), and the CRP was 178 mg/l.

Plate 2



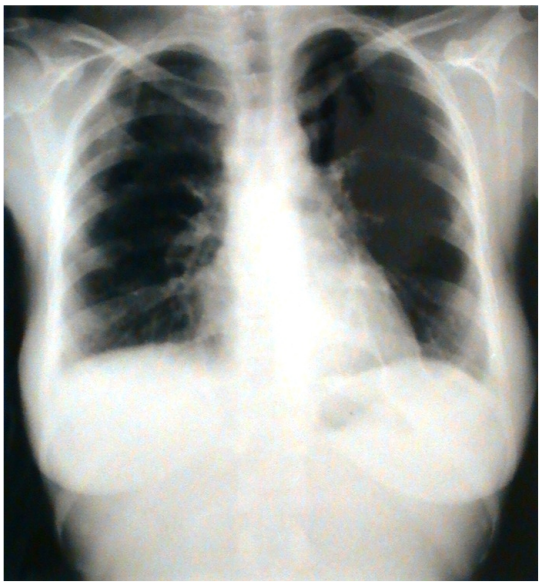
Atituberculous chemotherapy and prednisolone were continued. Thoracocentesis was not performed on this admission. The patient continued to have high temperature for six days; this eventually settled and she was discharged home after seven days of hospitalization on rifampicin, isoniazid, pyrazinamide, pyridoxine and 30 mg prednisolone. The prednisolone was continued for further four weeks and stopped after gradual reduction over 20 days. The patient was followed-up in clinic and after two months of treatment the chest X-ray was normal (plate 3).

Discussion:

Modern chemotherapy regimens for the treatment of tuberculosis are associated with high level of effectiveness and minimal side effects[4]. Paradoxical worsening of pleural effusions has, however, been described[1-3, 5]. A survey reported an incidence of 16% among 61 patients with tuberculous pleural effusions[5].

The mechanisms by which paradoxical response occur are speculative.

Plate 3



In the past such response was thought to result from rupture into the pleural space of subpleural caseous foci, mediastinal lymph nodes, or haematogenous dissemination, and mycobacterium was cultured from pleural fluid several weeks after initiation of therapy. In recent years, however, this response is thought to represent local manifestations of heightened delayed hypersensitivity mounted against immunogenic cell wall substances resealed from dying tuberculous bacilli in patients whose level of cellular immunity is enhanced as a result of chemotherapy[6].

Two points, however, deserve special discussion in this case. Firstly, contralateral effusion developed only six days after initiation of treatment whereas a previous case report has shown this to occur many weeks after starting therapy[3]. It would, therefore, be important to consider such a reaction in the differential diagnosis of patients who develop new symptoms soon after initiation of antituberculous chemotherapy. Secondly, our patient was taking prednisolone when she developed the paradoxical pleural effusion. Although steroids are known to modify the severity of clinical manifestations of tuberculosis, it has clearly failed to prevent the paradoxical response in this patient.

Interestingly, the only case of paradoxical

response reported in the literature was also taking prednisolone[3]. What we can not be certain of is whether the prednisolone has reduced the severity of reaction in these two patients. Indeed, the pleural effusion that developed in the patient we report was not large and required no drainage. In the series reported by Al-Majed[5] six of ten patients who developed paradoxical worsening of their effusion had respiratory distress with massive effusions requiring pleural aspirations; none of these patients were taking steroids at the time of presentation. Clearly a prospective placebo-controlled study to address this issue is warranted.

References

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