Figure 2 Restriction endonuclease analysis of bacterial DNA from 17 isolates of *Moraxella catarrhalis*. Isolates 1-6: strains from suspected outbreak at the Northern General Hospital, Edinburgh. Isolates 7-17: unrelated clinical isolates (isolates 15-17 were from an unrelated, smaller cluster of infection in a geriatric unit).

with normal human serum and confirmed by restriction endonuclease analysis of bacterial DNA.² The banding patterns of the six isolates from the respiratory unit at the Northern General Hospital were indistinguishable by both methods, whereas the unrelated strains all had different profiles (fig 2). These results provide clear evidence that this cluster of cases was due to cross infection with a single strain of *M. catarrhalis*.

Discussion

Nosocomial infection with *M. catarrhalis* has

been previously reported (McLeod *et al*³), but until recently there have been no reliable typing methods for investigating the epidemiology of this organism. It has not therefore been known whether nosocomial infection is caused by patients' endogenous flora or by cross infection. The first documented outbreak of cross infection with *M. catarrhalis* was described in 1988, at a Veterans' Administration hospital in the United States.⁴ The isolates from this outbreak were successfully typed by restriction endonuclease analysis of bacterial DNA.

The finding that cross infection with *M. catarrhalis* may cause hospital acquired infections has important implications for respiratory units, where large numbers of susceptible patients may be at risk. The reservoir of infection and mode of transmission of *M. catarrhalis* in this setting is still unknown but there is evidence that the organism may survive in the environment for up to 27 days in dried secretions.⁵ Further work is needed to identify appropriate control measures to prevent nosocomial infection with *M. catarrhalis*. Although these infections are not severe, their costs in terms of additional courses of antibiotics and prolongation of hospital stay may be substantial.

- 1 Hager H, Verghese A, Alvarez S, Berk SL. *Branhamella catarrhalis* respiratory infections. *Rev Infect Dis* 1987; 9:1140-9.
- 2 McKenzie H, Morgan MG, Jordens JZ, Enright MC, Bain M. Characterisation of hospital isolates of *Branhamella catarrhalis* by SDS-PAGE of whole cell proteins, immunoblotting and restriction endonuclease analysis. *J Med Microbiol* (In press).
- 3 McLeod DT, Ahmad F, Capewell S, Croughan MJ, Calder MA, Seaton A. Increase in bronchopulmonary infection due to *Branhamella catarrhalis*. *BMJ* 1986; 292:1103-5.
- 4 Patterson TF, Patterson EJ, Masecar BL, Barden GE, Hierholzer Jr WJ, Zervos MJ. A nosocomial outbreak of *Branhamella catarrhalis* confirmed by restriction endonuclease analysis. *J Infect Dis* 1988;157:996-1001.
- 5 Wilson GS, Miles AA. Neisseria. In: Topley WRC, Wilson GS, eds. *Principles of bacteriology and immunity*. London: Edward Arnold, 1964:665-92.

Thorax 1993;48:92-94

Severe bleomycin lung toxicity: reversal with high dose corticosteroids

J Maher, P A Daly

Abstract

A 42 year old man, treated for testicular carcinoma with combination chemotherapy that included bleomycin, developed life threatening interstitial pneumonitis. He recovered successfully after treatment with very high doses of corticosteroids and azathioprine. This report suggests that bleomycin lung toxicity may be reversible if treated aggressively.

(Thorax 1993;48:92-94)

Bleomycin is an effective chemotherapeutic agent in the treatment of many different neoplasms, including testicular carcinoma. Its major toxic effect is pneumonitis with subsequent progression to fibrosis. This case report describes a patient with life threatening bleomycin lung toxicity successfully treated with high dose corticosteroids and azathioprine.

Case report

A 42 year old ex-smoker (15 pack years) presented in November 1989 with stage IIb mixed embryonal cell carcinoma-seminoma of his left testis. His only important previous disorder was an area of localised scleroderma, confirmed by biopsy, on the right chest wall. There was no clinical or serological evidence of systemic sclerosis. After orchidectomy he

Department of
Clinical Haematology/
Oncology, St James's
Hospital, PO Box 580,
Dublin 8, Ireland
J Maher
P A Daly

Reprint requests to:
Dr P A Daly

Received 21 January 1992
Returned to authors
13 March 1992
Revised version received
2 April 1992
Accepted 14 April 1992

completed four cycles of chemotherapy with bleomycin, etoposide, and cisplatin. The bleomycin was administered as a 30 mg bolus intravenous injection given weekly, the total dose being 360 mg. Six weeks later he developed a dry cough and progressive breathlessness and had bilateral fine inspiratory crackles on auscultation. There was no evidence of activity of his carcinoma. Chest radiography showed bilateral interstitial infiltration and lung function tests confirmed a restrictive defect with total lung capacity (TLC) 3.74 (expected 6.68) l and carbon monoxide transfer factor (TLCO) 6.9 (expected 19.6) ml/min/mm Hg. Blood gas analysis showed arterial oxygen tension (P_{aO_2}) to be 11.8 kPa, carbon dioxide tension (P_{aCO_2}) 4.6 kPa, and oxygen saturation (S_{aO_2}) 96% while he was breathing air. Bronchoalveolar lavage fluid contained no microorganisms. Trans-bronchial biopsy specimens showed interstitial fibrosis. We thought that bleomycin lung toxicity was the most likely diagnosis and he was given 80 mg prednisolone daily for 10 days, with good symptomatic improvement. The dose was tapered to 20 mg/day over the following week, but within four days his symptoms had recurred and his P_{aO_2} in room

air was 6.5 kPa. He was again given prednisolone 80 mg/day, with 35% oxygen; but he again deteriorated when the dose was reduced to 40 mg a day.

Bronchoscopy was repeated. No evidence of infection was found and biopsy specimens again showed interstitial fibrosis. Chest radiographs now showed extensive intra-alveolar shadowing throughout both lung fields (figure, A). After five days he was given methylprednisolone 1 g/m² a day for five days, after which the dose was halved each day. During the first 10 days of this treatment he also received ceftazidime 2 g eight hourly. When the dose of methylprednisolone had been reduced to the equivalent of 80 mg prednisolone a day prednisolone was substituted and no further reduction in dose was made. Azathioprine 50 mg thrice daily was added once the dose of methylprednisolone had been reduced to 500 mg/day. After 12 days of this treatment the inspired oxygen fraction was reduced to 40% with continuous positive airway pressure (7.5 cm H₂O) administered by face mask.

Over the following month he gradually improved and oxygen therapy was discontinued on day 48. From day 56 the prednisolone dose was reduced by 5 mg a week to 15 mg daily. Subsequently the dose was reduced by 1 mg a week, and steroids were discontinued 49 weeks and azathioprine 60 weeks after being introduced. He is back at work, leading a normal life, and remains in remission from testicular carcinoma. Chest radiographic appearances have returned to normal (figure, B), but his TLC has changed from the normal pretreatment value of 6.83 to 6.0 (predicted 6.68) litres and TLCO from 24.9 to 12.3 (predicted 19.6) ml/min/mm Hg.

Discussion

The bleomycins are a mixture of glycoprotein antibiotics isolated from *Streptomyces verticillus* by Umezawa and coworkers.¹ The drug acts by forming an unstable ternary complex with iron and oxygen, resulting in the generation of superoxide radicals capable of scission of DNA strands.² Generation of superoxides is also believed to be responsible for bleomycin's major forms of toxicity, which seem to affect the tissues with the highest concentrations—namely, the lung and skin.³ Though bleomycin lung toxicity is occasionally manifested as an acute hypersensitivity pneumonitis⁴ it usually presents in the sub-acute fashion typified by this case. Though its exact incidence is disputed (estimates range from 2% to 40%), overall mortality is 1–2%. Histologically it is characterised in its early stages by interstitial oedema with an associated mononuclear cell infiltrate and subsequent formation of hyaline membranes. The risk of developing bleomycin lung toxicity is enhanced by high concentrations of oxygen, advancing age, a cumulative bleomycin dose in excess of 400 mg, previous radiotherapy to the chest, and impaired renal function.⁵

Chest radiographs (A) at the peak of the interstitial pneumonitis and (B) after recovery.

Management of bleomycin lung toxicity is frequently difficult, though steroids are widely recommended and evidence supporting their role comes from both animal studies⁶ and clinical reports on a few patients.⁵

Less settled, however, is the value of these agents in advanced bleomycin lung toxicity. Samuels and coworkers⁷ described a series of five such patients, all of whom received prednisolone in doses of 60–100 mg daily. All five died of acute respiratory failure despite this treatment. Gilson and Sahn⁸ reported a patient with bleomycin lung toxicity who developed the adult respiratory distress syndrome after surgery and ultimately responded to a combination of antibiotics and methylprednisolone 500 mg a day. Recently Hartmann and colleagues⁹ also described a patient with life threatening bleomycin lung toxicity successfully treated with methylprednisolone 1 g daily. Our case, taken in conjunction with these, suggests that severe bleomycin lung toxicity may be largely reversible provided that the treatment regimen incorporates corticosteroids in very high doses that are tapered gradually. We elected to use azathioprine in addition because of its

immunosuppressive and known steroid sparing effects.

We believe that all patients with bleomycin lung toxicity should receive a trial of corticosteroids. The dose used should depend on the severity of the pneumonitis.

- 1 Umezawa H, Maeda K, Takeuchi T, Okami Y. New antibiotics, bleomycin A and B. *Journal of Antibiotics (Tokyo)* 1966;19:200–9.
- 2 Kuo MT, Haidle CW. Characterization of chain breakage in DNA induced by bleomycin. *Biochem Biophys Acta* 1974;335:109–14.
- 3 Chandler DB. Possible mechanisms of bleomycin-induced fibrosis. In: Cooper J Allen D, ed. *Clinics in chest medicine*. Philadelphia: Saunders, 1990:21–30.
- 4 Holoye PY, Luna MA, Mackay B, Bedrossian CWM. Bleomycin hypersensitivity pneumonitis. *Ann Intern Med* 1978; 88:47–9.
- 5 Jules-Elysee K, White DA. Bleomycin-induced pulmonary toxicity. In: Cooper J Allen D, ed. *Clinics in chest medicine*. Philadelphia: Saunders, 1990:1–20.
- 6 Sterling KM, Di Petrillo T, Cutroneo KR, Perstayko A. Inhibition of collagen accumulation by glucocorticoids in rat lung after intratracheal bleomycin instillation. *Cancer Res* 1982;42:405–8.
- 7 Samuels ML, Johnson DE, Holoye PY, Lanzotti VJ. Large dose bleomycin therapy and pulmonary toxicity: a possible role of prior radiotherapy. *JAMA* 1976;235: 1117–20.
- 8 Gilson AJ, Sahn SA. Reactivation of bleomycin lung toxicity following oxygen administration. *Chest* 1985;88: 304–6.
- 9 Hartmann LC, Frytak S, Richardson RL, Coles DT, Cupps RE. Life-threatening bleomycin pulmonary toxicity with ultimate reversibility. *Chest* 1990;98:497–9.

Pseudomyxoma of the pleural and peritoneal cavities

G Radosavljević, B Nedeljković, V Kačar

Abstract

Pseudomyxoma peritonei is a rare clinical manifestation of mucin producing adenocarcinomas. An extensively metastasised adenocarcinoma developed a pseudomyxoma that affected not only the peritoneal cavity but also the pleura.

(*Thorax* 1993;48:94–95)

Pseudomyxoma peritonei is a rare clinical entity characterised by mucinous tumour masses in the peritoneum and omentum with gelatinous ascites. It usually originates from adenocarcinoma of the appendix or ovary and less frequently from adenocarcinoma of other organs.^{1–4}

We present a patient with pseudomyxoma that affected not only the peritoneum but also the pleura.

Case report

A 41 year old farmer, a non-smoker, was admitted to hospital in December 1988 because of mild chest pain and breathlessness, clinical signs of ascites, and homogeneous shadowing in the left hemithorax on the chest radiograph (fig 1). His general condition was good. All the results of routine laboratory investigations were within normal limits.

Two and a half years earlier he had had an

acute perforation of the appendix, and he had an appendectomy at a regional hospital. The wound discharged for two months. Six months later he noticed abdominal swelling.

Abdominal ultrasound during his first admission showed massive, loculated ascites without enlargement or metastatic involvement of abdominal organs. Thoracic computed tomography showed thickened pleura and a homogeneous mass in the left hemithorax, described as “a dense pleural effusion” (fig 2). Abdominal computed tomography suggested “mucinous ascites,” partly localised around the liver, following the intestinal curve and concentrated in the pelvis.

Pleural aspiration on several occasions disclosed no malignant cells but a few were found in one sample of pleural gelatinous material. A diagnosis of adenocarcinoma was confirmed by percutaneous biopsy of the main thoracic mass.

Figure 1 Posteroanterior chest radiograph: homogeneous shadowing in the left hemithorax.

Institute for Lung Diseases and Tuberculosis, University Clinical Centre, 11000 Belgrade, Višegradska 26, 11000 Belgrade, Serbia

G Radosavljević
B Nedeljković
V Kačar

Reprint requests to:
Dr G Radosavljević

Received 21 October 1991
Returned to authors
19 December 1991
Revised version received
23 January 1992
Accepted 28 January 1992