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Short communication

Fatal pneumothorax associated with bleomycin-induced pulmonary fibrosis

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Summary. A patient developed fatal pneumothorax associated with bleomycin-induced interstitial fibrosis. Pneumothorax may be a complication of "bleomycin lung".

Introduction

Pulmonary fibrosis is a well-recognized complication of bleomycin [1, 2]. Spontaneous pneumothorax [3, 5] and pneumomediastinum [3, 5] have occasionally been observed in patients receiving this drug. We report a patient who developed a fatal pneumothorax following treatment with a bleomycin-combination chemotherapy regimen for extragonadal germ cell tumor.

Case report

A 62-year-old retired salesman was admitted to another hospital in September 1984 for investigation of an anterior mediastinal mass, which was found at thoracotomy to be an embryonal cell carcinoma. Except for an alpha fetoprotein level greater than 484, the remainder of his staging evaluation was normal. Renal function showed a creatinine of 0.6 mg/100 ml; creatinine clearance, 72 ml/min. A diagnosis of extragonadal germ cell neoplasm was made, and therapy was commenced with cisplatin, VP-16-213, vinblastine, doxorubicin, and bleomycin. In December 1984, following three courses of chemotherapy, his creatinine had risen to 3.2 mg/100 ml and his creatinine clearance was 12 ml/min. At that time, he had received a total dose of 180 units of bleomycin. Plain radiograph and CT scan of chest revealed a 4×4 cm anterior mediastinal mass and bilateral basilar interstitial markings. Blood gas analysis yielded PCO_2 37 mmHg and PO_2 68 mmHg. The alpha fetoprotein level was normal. Because of renal insufficiency and suspected bleomycin lung, therapy was discontinued. Repeated thoracotomy was advised, but the patient refused.

He complained of mild dyspnea on exertion when referred to our hospital in February 1985 for routine follow-up. Radiography showed bi-basilar infiltrates; tumor markers were normal. In April 1985 he was admitted with increasing dyspnea, malaise, nonproductive cough, fever, anorexia, and weight loss. Examination revealed fever, tachypnea and crepitation at both lung bases. Laboratory testing revealed a creatinine of 3.1 mg/100 ml, and blood gas investigations, PCO_2 34 mmHg and PO_2 52 mmHg. Radiography demonstrated progressive diffuse bi-basilar interstitial infiltrates. An open lung biopsy was performed, and histological examination revealed extensive interstitial fibrosis without any inflammatory component. There was no evidence of malignancy. A diagnosis of bleomycin-induced pulmonary fibrosis was made, and treatment with prednisone, 60 mg/day, started. When seen in the clinic 2 and 4 weeks later the patient stated that his condition had improved; however, his chest X-ray revealed diffuse bilateral lower lobe infiltrate occupying one-third of the lung. In July 1985 he was readmitted with acute dyspnea and chest pain. Radiography demonstrated a large right pneumothorax with greater than 50% collapse of the lung. There were progressive 'honeycomb' infiltrates in both lung fields. Blood gas investigations showed PO_2 25 mmHg and PCO_2 17 mmHg. Despite closed-chest tube drainage a continuous massive air leak persisted, and a bronchopleural fistula was suspected. Ventilating support was begun, but the patient continued to deteriorate and expired in respiratory failure 6 days after this admission. Permission for autopsy was denied.

Comment

Fatal bleomycin-induced pulmonary toxicity has been reported to occur in about 1%–2% of patients, with an additional 2%–3% of patients experiencing nonlethal pulmonary fibrosis [1, 2]. An increased risk of developing pulmonary toxicity is associated with the following: cumulative doses of bleomycin greater than 400 units, age over 70 years, pre-existing lung disease, development of renal insufficiency during treatment, prior or concomitant chest irradiation, exposure to high concentrations of oxygen, and combination chemotherapy. Our patient was treated with combination chemotherapy and he subsequently developed renal insufficiency. Both of these factors may have contributed to the development of lethal pulmonary toxicity. We believe that his pneumothorax was secondary to bleomycin-induced interstitial fibrosis. In support of this suggestion is the fact that pneumothorax is a well-documented complication of interstitital lung diseases, including idiopathic pulmonary fibrosis. Furthermore, histologic studies of bleomycin lung have shown subpleural thickening and fibrosis and subpleural bullae [4]. Spontaneous pneumothorax could therefore be expected to occur in patients with bleomycin-induced pulmonary fibrosis and might be the result of rupture of a subpleural bulla.

We suggest that renal function be carefully monitored in patients receiving bleomycin and cisplatin combination chemotherapy, with downward adjustment of the bleomycin dose if nephrotoxicity occurs. Secondly, pneumothorax should be considered in the differential diagnosis of acute respiratory distress in patients undergoing treatment with this drug; and finally, both pneumothorax and pneu-

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momediastinum should be added to the list of pulmonary complications associated with bleomycin.

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