Table 2—The Differential Cytology of Bronchoalveolar Lavage Fluid Showed a Predominance of Neutrophils*

<table>
<thead>
<tr>
<th>Bronchoalveolar Lavage Fluid</th>
<th>3/29/90 (Day 4)</th>
<th>4/2/90 (Day 8)</th>
<th>Normal Range, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrophages, %</td>
<td>8</td>
<td>23</td>
<td>90-96</td>
</tr>
<tr>
<td>Lymphocytes, %</td>
<td>8</td>
<td>9</td>
<td>6-8</td>
</tr>
<tr>
<td>Neutrophils, %</td>
<td>65</td>
<td>64</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Eosinophils, %</td>
<td>20</td>
<td>4</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Urokinase (free activity)</td>
<td>nd</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Plasmin</td>
<td>nd</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Plasminogen</td>
<td>nd</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>PAI-1</td>
<td>nd</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Antiplasmins</td>
<td>nd</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

*Cell-free bronchoalveolar lavage fluid revealed no detectable, free fibrinolytic activity. nd = not detectable; PAI-1 = plasminogen-activator inhibitor 1.

stable for the following days, the respiratory function eventually declined and the patient died 15 days after paraquat ingestion. The postmortem examination of the lung (Fig 1) confirmed severe intra-alveolar hemorrhage; in addition, multiple fibrin deposits were found in the airways. Most alveolar air spaces were denuded of their cellular lining. A considerable proliferation of interstitial fibroblasts was seen; definite fibrosis, however, was absent.

DISCUSSION

The contact herbicide paraquat, available as dichloro, dibromide, or dimethanosulfate salt, has caused hundreds of accidental or intentional deaths. Following survival of the acute stage of paraquat poisoning, toxic involvement of the kidney and later on of the lung, due to active concentration in excess of that in any other organ, ensues. After oral ingestion, paraquat is rapidly absorbed by the gut. The peak serum concentration declines within a few hours due to filtration and active secretion by the kidney and to a lesser extent to organ uptake. With the onset of renal failure, organ uptake increases. Due to the complex pharmacokinetics of paraquat, the most effective treatment is thus limited to a very short period in the initial phase. Although treatment had been started very early in our patient and the paraquat serum level had been rapidly removed by continuous hemoperfusion and hemodialysis, the initial high serum concentration accounted for the progressive pulmonary damage. The finding of reduced or absent intra-alveolar fibrinolytic activities in the course of pulmonary fibrosis (adult respiratory distress syndrome) has not been sufficiently elucidated for their prognostic relevance. According to a report by Webb and associates, we employed radiotherapy of both lungs to stop fibroblast proliferation and interstitial fibrosis; however, the fatal course of respiratory failure (due to toxic alveolitis) remained unchanged. Thus, caution toward the expected therapeutic value of radiotherapy in paraquat-induced pulmonary damage seems warranted.

ACKNOWLEDGMENT: We are indebted to H. Keuper of Behring Diagnostics, Marburg/FRC, for performing the assays for measurement of the fibrinolytic activities in the bronchial lavage fluid.

REFERENCES


Recurrent Massive Pleural Effusion as a Late Complication of Radiotherapy in Hodgkin's Disease*

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We report a very unusual case of a patient with recurrent massive PE's eight years after mediastinal radiotherapy for HD, in which evidence of lymphomatous recurrence could not be demonstrated. The diagnosis of PE as a complication of radiation is presumptive, and other disorders causing PE must be excluded. This condition requires symptomatic treatment and a close follow-up of the patient.

(Chest 1991; 100:1165-66)

CT = computed tomography; HD = Hodgkin’s disease; MOPP = mechloretamine - vincristine - procarbazine - prednisone; ABVD = doxorubicin - bleomycin - vinblastine - dacarbazine; PE = pleural effusion; PPD = purified protein derivative

Radiation therapy of the thorax is common in patients with lymphoma. These patients occasionally show some evidence of pneumonitis, pleuritis or pericarditis after treatment. Thus, complications of radiotherapy must be included in the differential diagnosis of a PE that develops in the setting of malignancy previously treated with radiation.

We report a patient suffering recurrent bilateral massive PE's who had received mediastinal radiation (4,000 rads) for HD eight years before. We ruled out recurrence of lymphoma and other disorders causing PE. It led us to consider

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the massive PE as a very unusual complication of radiation therapy that, to our knowledge, has not been reported previously.

CASE REPORT

A 35-year-old woman was admitted to the hospital in April 1989 because of pain on the right side of the chest and exertion dyspnea. The patient had a history of Hodgkin's lymphoma (stage IV B, sclerosis nodular type) diagnosed in our institution in November 1981 that was treated with eight courses of alternate MOPP/ABVD chemotherapy at full doses, and mediastinal radiation of 4,000 rads. On admission, physical examination showed dullness of the right hemithorax as the only positive data. She was afebrile and in a good performance status. A wide serologic and biochemical study was normal. A PPD test was negative. A chest x-ray film evidenced a large right PE. Computed tomography of the thorax disclosed massive right PE's as well as pericardial thickening. There was absence of mediastinal or hilar lymph node involvement and the lungs were not infiltrated. Abdominal CT scans were normal. An echocardiographic study revealed a small pericardial effusion without constriction or tamponade signs. Bronchoscopic examination and radiologic study of the breast were normal. Bone marrow examination also was normal. The pleural fluid was a serohemorrhagic exudate without malignant cells. Histologic study of four specimens of the pleura obtained by percutaneous biopsy showed multiple reactive mesothelial cells without neoplastic cells.

The patient received 150 mg of indomethacin daily, following which symptoms and pleurisy improved dramatically, and the patient was discharged three weeks after entry. A repeated chest x-ray film taken two months later was normal.

She was well until April 1990 when chest pain developed. She had experienced no evidence of weight loss or fever. On examination, there were signs of left PE. The remainder of the physical examination disclosed no abnormalities. A chest x-ray film revealed a large left PE. Computed tomography of the thorax disclosed diffuse thickening of both pericardium leaves and both left pleural leaves with homogeneous enhancement after intravenous administration of contrast material, associated with left PE (Fig 1). A residual right PE also was seen, but there was no evidence of mediastinal lymph node involvement. The PPD test was still negative. A left-sided thoracotomy showed diffuse thickening of the pleura, yielding a straw-colored fluid without tumor cells. Microscopic study of a pleural biopsy specimen revealed chronic inflammation with absence of granulomas or neoplastic cells. On the 21st hospital day, a chest x-ray film demonstrated a small residual PE in both of the costophrenic sulci and the patient was released from the hospital. Six months after discharge, the patient is well and free of symptoms and no other change is seen on the chest film.

DISCUSSION

In the reviewed literature, two cases of recurrent benign PEs as the only clinical manifestation of HD have been reported. In one case, bilateral PE resulted from neoplastic involvement of hilar lymph nodes that became evident later and finally was proven by autopsy. In the other patient, unilateral recurrent PEs were due to nodular thickening of the parietal pleura that were evident when CT scans were performed. In both of the cases, B symptoms and progressive deterioration of their clinical condition were seen. It is remarkable that our patient was in good condition since completion of the HD treatment and during recurrent PEs. Moreover, a second malignancy could not be demonstrated, although it is well known that the incidence is high of second tumors in patients treated for HD.

The diagnosis of PE as a complication of radiation therapy is presumptive. Radiation therapy can cause PE by two mechanisms: radiation pleuritis and systemic venous hypertension or lymphatic obstruction from mediastinal fibrosis. As a general rule, PE is a small unilateral serohemorrhagic exudate, and resolution may occur either with steroids or spontaneously. Pleural effusion secondary to radiation pleuritis is observed within six months following completion of radiotherapy. The PEs not associated with radiation pleuritis tend to occur one to two years following intensive (4,000 to 6,000 rads) mediastinal radiation. Mechanisms for development of PE as a late complication of radiation therapy include constrictive pericarditis (with or without tamponade), superior vena cava obstruction and lymphatic obstruction, all complications of mediastinal fibrosis.

Clinical and radiologic data ruled out a superior vena cava syndrome. While pericarditis was discovered at the first large PE, no evidence of ventricular function impairment through its evolution was found. This feature is in agreement with a non-neoplastic origin of the pericarditis. Signs and symptoms of pericardial effusion and cardiac tamponade associated with extensive nodular tumor infiltration of the pericardium are typical in patients with HD. In addition, in patients with HD, radiation-induced pericarditis may occur as late as eight years after therapy.

We believe that recurrent massive PEs in patients cured of their HD may result from impaired lymphatic drainage due to mediastinal and pleural fibrosis induced by radiation therapy. This benign condition requires only symptomatic measures and not chemotherapy.

REFERENCES