Spontaneous Pneumothorax following Thoracic Irradiation*

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Spontaneous pneumothorax has only very rarely been reported to occur following thoracic irradiation. Four patients who developed this complication following radiation therapy are presented and the literature is reviewed. Spontaneous pneumothorax following thoracic irradiation tends to be recurrent, occasionally bilateral, and in most reported cases, occurs in patients who develop roentgenographic evidence of radiation fibrosis after treatment with mantle-shaped portals for Hodgkin's and non-Hodgkin's lymphomas. Re-expansion often occurs without intervention.

CASE REPORTS

Case 1
A 19-year-old female subject was well until December 1982, when she noticed "bulging" of her left anterior chest wall. Physical examination was remarkable for bilateral cervical and left supraclavicular adenopathy, and protrusion of the chest wall at the left border of her sternum and second intercostal space. Initial chest roentgenogram (Fig 1) revealed a large anterior mediastinal mass, bilateral paratracheal, and left hilar adenopathy. A thoracic CT scan showed extensive mediastinal disease with pericardial and chest wall involvement. Biopsy of a cervical lymph node diagnosed nodular sclerosing Hodgkin's disease. Further staging included bilateral iliac crest bone marrow biopsies and aspirates, an abdominal CT scan, and a pedal lymphangiogram, results of which were normal.

The patient was considered to have clinical stage 2E A nodular sclerosing Hodgkin's disease and was initially treated with three cycles of BCVPP (carmustine [BCNU], cyclophosphamide, vincristine, procarbazine, and prednisone). Because of poor hematologic tolerance, her regimen was changed to C-MOPP (cyclophosphamide, vincristine, procarbazine, and prednisone) which she received for an additional three cycles until September 1983. Chest roentgenogram (Fig 2) in November 1983 was interpreted as normal at which time the patient began radiotherapy. With a 4 MeV linear

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Figure 1. Posteroanterior roentgenogram showing large mediastinal mass in December 1982.
accelerator, 24 treatments were administered over 39 days to a mantle-shaped portal. The mediastinum received 3,720 rads, the medial aspect of the left lung 3,665 rads, the supraclavicular area 4,220 rads, and the axillae 4,086 rads. This was followed by the administration of 2,040 rads to the spleen and para-aortic nodes in January 1984.

Follow-up chest roentgenograms until September 1984 (Fig 3) showed changes suggestive of radiation fibrosis in pulmonary paracapillary areas adjacent to the left hilum and superior mediastinum. The patient was seen in routine follow-up in December 1984. She was completely asymptomatic, and her examination was unremarkable. Chest roentgenogram (Fig 4) showed radiation changes as previously described, but in addition, she had moderate bilateral pneumothoraces estimated to be approximately 20 percent. A chest x-ray film was repeated several weeks later and showed complete re-expansion on the right and almost complete resolution on the left.

A 14-year-old boy presented in May 1982 with right supraclavicular adenopathy, malaise, and weight loss. Chest x-ray film showed superior mediastinal adenopathy, and right supraclavicular lymph node biopsy diagnosed nodular sclerosing Hodgkin's disease. Lymphangiography, bilateral iliac crest bone marrow aspirates and biopsies, and staging laparotomy were all negative for Hodgkin's involvement, and the patient was considered to have stage 2B disease and was treated with radiation therapy. With a 4 MeV linear accelerator, 24 treatments were administered over 35 days to a mantle-shaped portal. The mediastinum received 4,320 rads, the supraclavicular area 4,334 rads, and the axillae 3,843 rads. This was followed by the administration of 3,600 rads to the spleen and para-aortic lymph nodes. Follow-up chest roentgenograms showed fibrotic changes in the paramediastinal and apical pulmonary parenchymal regions.

The patient was well until October 1983 when he suddenly developed left-sided chest pain. Chest x-ray film showed left pneumothorax estimated to be approximately 20 percent. The pneumothorax completely resolved without intervention, and the patient did well until March 1984 when he again experienced sudden left-sided chest pain. Chest roentgenogram showed a new left pneumothorax estimated to be 15 percent which again resolved completely without intervention.

A 15-year-old girl presented complaining of a sore throat in September 1975. Physical examination revealed right supraclavicular adenopathy. Initial diagnostic studies included a chest x-ray film, which showed a superior mediastinal mass and a leukocyte count of 19,000 with 30 percent blasts. Biopsy of the supraclavicular lymph node diagnosed lymphoblastic lymphoma and a bone marrow biopsy revealed lymphomatous involvement.

The patient was initially treated with an induction regimen consisting of vincristine and prednisone. Radiotherapy with a 60Co source was begun in October 1975, the patient receiving 3,000 rads to the mediastinum over 24 days to a mantle-shaped portal. In November 1975, the patient was considered to be in a complete remission, and she received prophylactic cranial irradiation consisting of 2,400 rads and was subsequently treated with a maintenance
regimen consisting of vincristine, prednisone, 6-mercaptopurine, cyclophosphamide, systemic and intrathecal methotrexate until December 1978.

Follow-up chest roentgenograms showed changes suggestive of radiation fibrosis in the paramediastinal and biapical pulmonary parenchyma. In February 1977, routine chest roentgenogram revealed right pneumothorax estimated to be approximately 20 percent. A follow-up roentgenogram showed complete re-expansion, but, in December 1978, the patient presented complaining of acute left-sided chest pain. Chest roentgenogram showed a left apical pneumothorax which again completely resolved without intervention. She remains well in March 1985.

**CASE 4**

A 14-year-old girl presented with right cervical and supraclavicular adenopathy in February 1975. A biopsy of a supraclavicular lymph node diagnosed nodular sclerosing Hodgkin’s disease. Further staging included a chest roentgenogram, bilateral iliac crest aspirates and biopsies, a liver-spleen scan, lymphangiography, and a staging laparotomy, results of which were normal.

The patient was considered to have stage 2A nodular sclerosing Hodgkin’s disease and was treated with radiotherapy. Utilizing a 60Co source and a mantle-shaped portal, she received 3,600 rads to her mediastinum.

Follow-up chest x-ray films revealed evidence of bilateral fibrosis, and the patient did well until October 1975 when she experienced the sudden onset of right-sided chest pain. Chest x-ray film showed a pneumothorax estimated to be approximately 40 percent and chest tube was inserted which resulted in prompt re-expansion of the lung. The patient subsequently was admitted on two occasions, in November 1975 and February 1976 for left-sided pneumothoraces estimated to be 15 percent; they re-expanded without intervention.

**DISCUSSION**

Spontaneous pneumothorax is a recognized complication of primary and metastatic pulmonary malignancies and is occasionally the presenting event. The most common group of neoplasms associated with spontaneous pneumothorax are the sarcomas, including osteogenic sarcomas, fibrosarcomas, sarcomas of the synovial cell and synovial sheath, Ewing’s sarcoma, and hemangiendothelial sarcomas. This complication is also associated with nonsarcomatous tumors including Hodgkin’s disease, non-Hodgkin’s lymphomas, teratomas, Wilm’s tumor, renal cell carcinoma, and primary pulmonary malignancies including adenocarcinoma, small cell, and squamous cell carcinomas. Autopsy studies show that the majority of spontaneous pneumothoraces secondary to malignancy are caused by direct rupture of necrotic neoplastic tissue into the pleural cavity. Others are thought to occur when tumor nodules act as ball valves producing partial bronchial obstruction and hyperinflation of alveoli; this results in the formation of interstitial air and subpleural blebs which eventually rupture.

Spontaneous pneumothorax following thoracic irradiation has rarely been reported. The first case is the only known report of simultaneous bilateral spontaneous pneumothoraces in the literature. Libshitz and Banner reviewed approximately 250 patients who received radiation therapy with conventional mantle ports for lymphomas and over 1,000 patients treated postoperatively with thoracic irradiation for carcinoma of the breast and found two patients who subsequently developed spontaneous pneumothorax after receiving mantle therapy for Hodgkin’s disease. Including the present cases, there are 11 reported instances, in the English medical literature, in which the development of spontaneous pneumothorax can be reasonably associated with the effects of thoracic irradiation (Table 1).

Ten episodes followed mantle irradiation for Hodgkin’s and non-Hodgkin’s lymphomas. Pneumothorax occurred in one patient following radiation therapy to the chest wall after mastectomy for breast carcinoma. Nine of the 11 episodes involved patients without concurrent malignant pulmonary involvement. In case 6, pulmonary Hodgkin’s disease was documented by postmortem examination, and in case 7, the patient’s clinical course was consistent with pulmonary Hodgkin’s disease although never proven pathologically.

At the time of diagnosis, the patients’ age with Hodgkin’s and non-Hodgkin’s lymphomas ranged from 13 to 30 years. The interval between completion of the radiation courses and the development of spontaneous pneumothorax ranged from three to 65 months in the lymphoma patients as a group, but ranged from four to 16 months in those patients who were known not to have malignant pulmonary involvement. In case 5, spontaneous pneumothorax occurred in a 55-year-old woman two months after postmastectomy chest wall irradiation.

Additional cases of spontaneous pneumothorax associated with thoracic irradiation can be found in the literature. Stolzenberg and Clements described a patient with osteogenic sarcoma metastatic to lung who developed a pneumothorax during radiation therapy administered to both lung fields. There have also been several case reports describing patients with bronchogenic carcinoma, all developing spontaneous pneumothorax during or only very shortly after the completion of radiation therapy—before significant histologic, physiologic, or roentgenographic changes are known to occur, and therefore, pneumothorax in these cases, is most likely a result of direct neoplastic involvement, not radiation-induced.

Histologic changes in virtually all pulmonary structures have been reported in pathologic material obtained four to 12 weeks after completion of pulmonary irradiation. It is uncommon for clinical radiation pneumonitis characterized by dyspnea, cough, and fever to occur less than six to 12 weeks after radiation therapy. Roentgenographic changes consistent with pneumonitis can be expected, as a rule, to occur eight weeks after 4,000 rads to a significant volume of lung, and one
<table>
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<tr>
<th>Case</th>
<th>Authors</th>
<th>Age/Sex</th>
<th>Malignancy and Stage at Diagnosis</th>
<th>Lung Involvement</th>
<th>Prepneumothorax Treatment</th>
<th>Postradiotherapy X-Ray Appearance</th>
<th>Postradiotherapy Pneumothorax Interval</th>
<th>Side of Pneumothorax</th>
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<tbody>
<tr>
<td>1</td>
<td>Twiford et al</td>
<td>13/M</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 3A; mediastinal mass present</td>
<td>None</td>
<td>MOPP X2, RadioRx with °Co: -3,000 rads to pelvis upper abdomen; -3,500 rads in mantle distribution to mediastinum.</td>
<td>Not stated</td>
<td>9 Months</td>
<td>Recurrent right followed by left apical</td>
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<tr>
<td>2</td>
<td>Twiford et al</td>
<td>30/M</td>
<td>Unclassified Hodgkin’s disease, Stage 2A</td>
<td>None</td>
<td>RadioRx with °Co: -5,975 rads in mantle distribution to mediastinum.</td>
<td>Not stated</td>
<td>6 Months</td>
<td>Recurrent left apical</td>
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<td>3</td>
<td>Libshitz and Banner</td>
<td>14/F</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 2A; mediastinal mass present</td>
<td>None</td>
<td>RadioRx with °Co: -3,900 rads in mantle distribution to mediastinum.</td>
<td>Radiation fibrosis</td>
<td>8 Months</td>
<td>Left apical</td>
</tr>
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<td>4</td>
<td>Libshitz and Banner</td>
<td>22/M</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 3B; mediastinal mass present</td>
<td>None</td>
<td>RadioRx with °Co: -3,250 in mantle distribution to mediastinum.</td>
<td>Radiation fibrosis</td>
<td>4 Months</td>
<td>Left apical</td>
</tr>
<tr>
<td>5</td>
<td>Gross</td>
<td>55/F</td>
<td>Right breast carcinoma. Postmastectomy</td>
<td>None</td>
<td>Chest wall irradiation, details not stated.</td>
<td>Radiation pneumonitis</td>
<td>2 Months</td>
<td>Right apical</td>
</tr>
<tr>
<td>6</td>
<td>Plowman et al</td>
<td>20/F</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 3A; mediastinal mass present</td>
<td>Biopsy proven</td>
<td>MOPP-like regimen X3 RadioRx: -4,000 rads in distribution to mediastinum.</td>
<td>Radiation fibrosis and Hodgkin’s disease</td>
<td>3 Months</td>
<td>Right apical</td>
</tr>
<tr>
<td>7</td>
<td>Plowman et al</td>
<td>26/F</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 2A; mediastinal involvement not stated</td>
<td>Highly probable</td>
<td>Unspecified combination chemoRx including Bleomycin. RadioRx: -3,500 rads in mantle distribution to mediastinum.</td>
<td>Radiation fibrosis, probable Hodgkin’s disease</td>
<td>5 Months</td>
<td>Left apical</td>
</tr>
<tr>
<td>8</td>
<td>Present report (Case 1)</td>
<td>19/F</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 2E A; mediastinal mass present</td>
<td>None</td>
<td>BGVFP x3, C-MOPP X3; RadioRx with 4 MeV: -3,720 rads in mantle distribution to mediastinum; -2,040 rads to spleen and para-aortic nodes.</td>
<td>Radiation fibrosis</td>
<td>11 Months</td>
<td>Biapical</td>
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Table 1 (Continued)—Spontaneous Pneumothorax after Thoracic Irradiation: Summary of Clinical Data on Reported Cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Authors</th>
<th>Age/Sex</th>
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<th>Side of Pneumothorax</th>
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<tr>
<td>9</td>
<td>Present report (Case 2)</td>
<td>14/F</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 2B; mediastinal mass present</td>
<td>None</td>
<td>RadioRx with 4 MeV: -4,320 rads in mantle distribution to mediastinum. -3,600 rads to spleen and paraaortic nodes.</td>
<td>Radiation fibrosis</td>
<td>16 Months</td>
<td>Recurrent left apical</td>
</tr>
<tr>
<td>10</td>
<td>Present report (Case 3)</td>
<td>15/F</td>
<td>Lymphoblastic lymphoma; mediastinal mass present</td>
<td>None</td>
<td>Prednisone, vincristine induction followed by: RadioRx with (^{137}) Co: -3,000 rads in mantle distribution to mediastinum. ChemoRx with prednisone, vincristine, 6-MP, MTX, cyclophosphamide.</td>
<td>Radiation fibrosis</td>
<td>16 Months</td>
<td>Right followed by left apical</td>
</tr>
<tr>
<td>11</td>
<td>Present report (Case 4)</td>
<td>14/F</td>
<td>Nodular sclerosing Hodgkin’s disease, Stage 2A; mediastinal mass</td>
<td>None</td>
<td>RadioRx with (^{137}) Co: -3,600 rads in mantle distribution to mediastinum.</td>
<td>Radiation fibrosis</td>
<td>7 Months</td>
<td>Right followed by recurrent left apical</td>
</tr>
</tbody>
</table>

week earlier for each 1,000 rads increment above 4,000 rads. The majority of patients with clinical radiation pneumonitis become asymptomatic although nearly all will develop roentgenographic evidence of radiation fibrosis which is generally established by the ninth to 12th month following completion of therapy.\(^{20}\)

In nine of the 11 cases of postradiation spontaneous pneumothorax in Table 1, roentgenographic changes consistent with radiation effect were noted prior to pneumothorax; prepneumothorax roentgenographic descriptions are not given for the other two cases. The descriptions are consistent with radiation pneumonitis in the woman with breast carcinoma in case 5 and consistent with radiation fibrosis in the remaining eight patients who were all treated with mantle fields. It is interesting to note that four patients had recurrent unilateral pneumothoraces, and four patients had pneumothoraces involving both lungs at some time in their course.

Radiation-induced pulmonary changes, apical pleural injury, parenchymal injury, and focal emphysema most likely increase the chance of forming and rupturing subpleural blebs, with the subsequent development of pneumothorax. Almost all reported cases of pneumothorax following thoracic irradiation occur in patients treated with mantle fields, fields that encompass and expose a relatively large amount of pleural surface area to radiation injury as compared to other radiotherapy fields. Because the size of pneumothorax and associated symptomatology was mild to moderate, since re-expansion was often spontaneous, and because patients without malignant pulmonary involvement might not have had frequent follow-up postradiotherapy chest x-ray examinations, postradiation subclinical pneumothorax might be relatively more common than previously appreciated.

In summary, most cases of spontaneous pneumothorax following thoracic irradiation occur in patients with Hodgkin’s disease who develop roentgenographic fibrosis after treatment with mantle fields. The pneumothorax is usually mild to moderate in size, and because re-expansion is typical, immediate intervention is often not necessary.

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2 Johnson RF, Green RA. Pneumothorax. In: Fishman AP, ed.

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