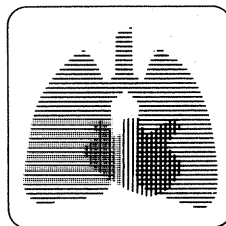


# **Intrathoracic Chemothermotherapy Following Panpleuropneumonectomy for Pleural Dissemination of Invasive Thymoma\***

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## Intrathoracic Chemothermotherapy Following Panpleuropneumonectomy for Pleural Dissemination of Invasive Thymoma\*

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We report a case of pleural dissemination of invasive thymoma, which was successfully treated with intrathoracic chemothermotherapy following panpleuropneumonectomy. Intrathoracic chemothermotherapy in combination with surgery may be a hopeful adjuvant treatment to control pleural disseminated lesions of invasive thymoma. (*Chest* 1994; 105:1884-85)

Although dissemination of thymoma of either invasive or noninvasive type in the pleural cavity is not an uncommon event, the therapeutic approach remains controversial.<sup>1-5</sup> Several treatment modalities, including surgery such as partial resection and panpleuropneumonectomy, intravenous and/or intrathoracic chemotherapy, radiotherapy, and their combination therapy have been proposed, but their effectiveness remains uncertain.<sup>1-5</sup>

In our institute, intrathoracic chemothermotherapy has been applied in order to regulate malignant pleurisy due to lung cancer and metastatic sarcoma, and recent results have been good.<sup>6,7</sup> Recently, we successfully treated a recurrent case of pleural dissemination of invasive thymoma with intrathoracic chemothermotherapy following panpleuropneumonectomy. This is the first report, to our knowledge, of clinical application of the treatment to such lesions.

### CASE REPORT

A 56-year-old woman presented to our institute with a relapse of invasive thymoma in January 1990; there was pleural dissemination in the left thoracic cavity. The patient had previously undergone thymectomy for thymoma with approach via left thoracotomy in May 1986 at another hospital. However, as relapse had occurred in the left thoracic cavity in August 1988, she was treated with intravenous chemotherapy using cisplatin, doxorubicin (Adriamycin), cyclophosphamide, and vincristine, followed by irradiation therapy to the left lung field, but the recurrent lesions showed little change or gradually advanced for 1 year before her admission to our institute.

On admission, although she was asymptomatic, her chest radiograph revealed multiple lesions in the left lung field and slight pleural effusion (Fig 1). No lesion was detected at other sites,

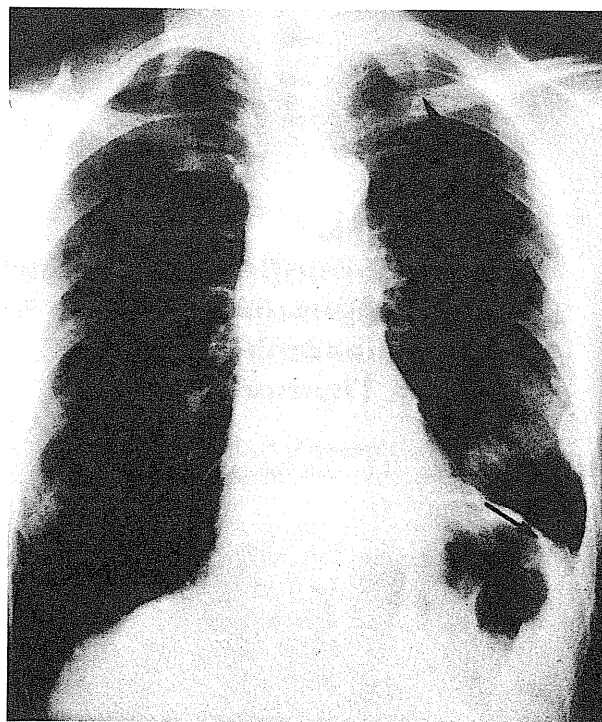


FIGURE 1. Chest radiograph showing multiple lesions (arrowheads) in the left lung field and slight pleural effusion (arrow).

including the right lung field and extrathoracic area. On February 13, 1990, left panpleuropneumonectomy was performed. Multiple nodular lesions, less than 4 cm in diameter, were found to be widely disseminated on the parietal and visceral pleura (Fig 2), and the pleural effusion contained many malignant cells. Histologic examination revealed numerous pleural lesions of invasive thymoma of the lymphocytic type. The hilar lymph nodes and left intrapulmonary parenchyma were not involved.

In March 1990, as soon as she had recovered from surgery, intrathoracic chemothermotherapy, three courses per week, according to a method previously reported,<sup>6,7</sup> was performed. Briefly, it consisted of a bolus intrathoracic injection of 100 mg of cisplatin and local heating using 8-MHz radiofrequency waves (Thermotron RF8) at 42°C for 40 min. After completion of the therapy, as much cisplatin as possible was recovered from the pleural cavity.

The patient was discharged from our hospital uneventfully in April 1990, but was readmitted in December 1990 because of nonbronchofistulous empyema in the left thoracic cavity, possibly associated with contamination due to thoracocentesis. Thoracoplasty with rib resection and stuffing of flaps of the omentum, pectoralis major, and latissimus dorsi muscles was performed in February 1991. Then, tumor-free status in the pleural cavity was confirmed intraoperatively. As of August, 1993, the patient is free from tumor in the local space as well as in distant areas.

### DISCUSSION

Our institute has been engaged in ongoing treatment of patients with lung cancer with carcinomatous pleuritis using pulmonary resection and postoperative intrathoracic chemotherapy.<sup>6</sup> We previously reported a case of malignant pleurisy due to Ewing's sarcoma treated with intrathoracic chemothermotherapy.<sup>7</sup> Although excellent response in the local lesions has been obtained, the distant metastases frequently shown by such malignancies as lung cancer and some sarcomas, which metastasize via the lymphogenous

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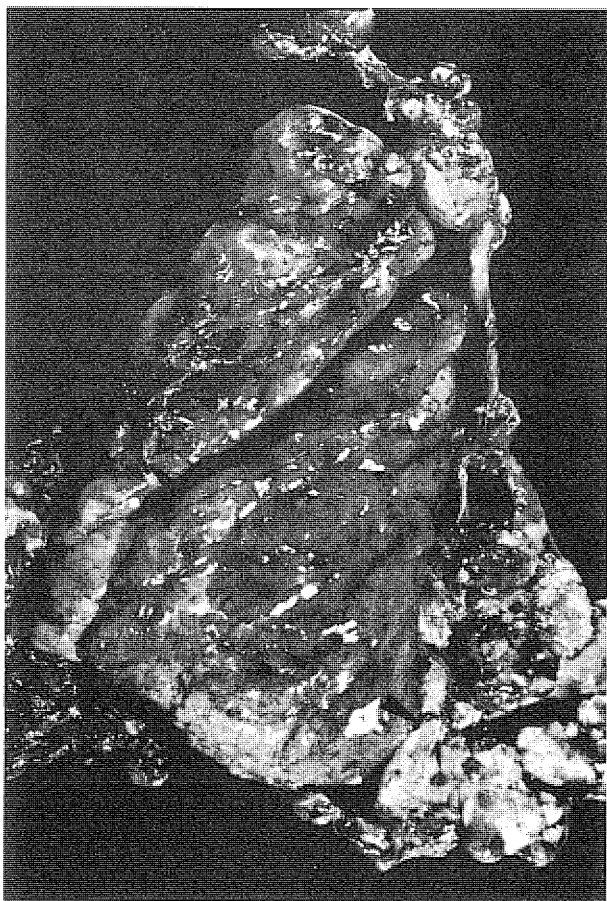


FIGURE 2. The specimen by panpleuropneumectomy showing multiple disseminated lesions on parietal and visceral pleura (arrowheads).

or venous route, gravely affect clinical outcomes. In this respect, distant metastasis of invasive thymoma via such routes is considered rare, amounting to a few percent in primary cases and to a maximum 26 percent in recurrent cases,<sup>2,4,5</sup> indicating that treatment of the local lesions related to thymoma may be the most pressing problem.

Treatment of disseminated lesions of invasive thymoma in the pleural and/or pericardial cavity has included chemotherapy (including immunotherapy), radiotherapy, surgery, and their various combinations.<sup>1-5</sup> Chemotherapy agents, including cisplatin, cyclophosphamide, doxorubicin, vincristine, and corticosteroids are commonly applied, and partial to unilateral irradiation of the total thoracic field at varying doses has been performed. Surgical approaches have included partial resection of the lung and/or pleura to the greatest extent, and, when possible, panpleuropneumectomy.<sup>1,3-5</sup> However, as disseminated lesions often show varying degrees of resistance to such therapies, repeated relapse during the clinical course may lead to death. Intrathoracic chemothermotherapy combined with surgical therapy may represent a new treatment modality for residual disseminated lesions of invasive thymoma which addresses this problem.

This patient showed little response to chemotherapy and radiotherapy at another hospital, and even panpleuropneumectomy might have been insufficiently radical, because of the large number of widely disseminated lesions

in the pleural cavity. Cytologic examination following panpleuropneumectomy, in fact, demonstrated that the pleural effusion contained malignant cells. However, after the third course of intrathoracic chemothermotherapy, the cytologic results for the pleural effusion became negative; this finding was confirmed at the subsequent exploratory operation performed because of empyema, and the patient is now free from tumor. Considering these observations together, the intrathoracic chemothermotherapy in the present patient might be an apparently extremely effective postoperative adjuvant therapy.

At present, as the effect of intrathoracic chemothermotherapy on thymoma cells has not been sufficiently analyzed, for example, using *in vitro* assay to study chemothermal sensitivity of thymoma cells, it is unknown whether this therapy may be routinely applied to malignant pleurisy of invasive thymoma; this issue requires further study. Nevertheless, on the basis of our clinical experience in the present case, we are hopeful that intrathoracic chemothermotherapy may become a useful adjuvant treatment to control disseminated lesions in the pleural cavity, especially when other therapies are unsuccessful or insufficient.

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