Lung Cancer and Pleural Effusion*
Clinical Significance and Study of Pleural Metastatic Locations
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We reviewed results of 78 diagnostic thorascopic examinations of patients with lung cancer and homolateral pleural effusion. The study stresses the main locations of pleural metastasis in cases of lung cancer and correlates these data with the pleural spread from extrathoracic primary neoplasms. Also pointed out is the operability of the present series and the different behavior in pleural metastatic spread according to the histologic type with correlation between gross appearance of the effusion and the cytology.

Bronchopulmonary cancer may be accompanied by pleural effusion. LeRoux1 found this association in 7 percent (280/4000) of his series and Storey et al2 found 8 percent (12/145) in their review of bronchoalveolar carcinomas. Frequently, this association of pleural effusion and lung cancer is considered inoperable by many authors. We believe that this association by itself does not provide enough information to place a patient within a poor tumor stage (T3 in most cases), thus excluding him from the potential benefit of curative surgery. In order to rule out etiologies other than pleural metastasis such as secondary pneumonitides, or lymphatic or venous obstruction within the lung itself, we think it is worthwhile to perform routinely an exhaustive pleural study by means of direct thoracoscopy.

Some authors, such as LeRoux1 and Decker et al3 have started to report results enhancing the usefulness of thoracoscopic pleural exploration in lung cancer with pleural effusion. The growing number of publications4-12 including our own14,55 seems to point towards an increasing number of operable cases and the avoidance of many of the so-called “useless thoracotomies.”

MATERIAL AND METHODS
We have performed 535 diagnostic thoracoscopies since 1970. 78 of which correspond to cases of lung cancer with pleural effusion. Local anesthesia was used; when general anesthesia was required, neuroleptanalgesia (I Type), without endotracheal intubation, was used. The thoracoscopy is performed via anterolateral thoracic approach through the 6th or 7th intercostal space.

In 8 percent of our 78 patients, the thoracoscopy and pleural drainage gave location of the primary tumor which was hidden by the massive pleural effusion.

According to some authors, thoracoscopy is indicated only in those cases in which cytoplogic examination of the fluid fails to demonstrate malignant cells. Instead, we use the endoscopic pleural examination as a primary tool right after a patient with pleural effusion and suspected lung cancer is admitted to our service. This approach is based on the importance of the patient and the hospital to shorten the time lapse between admission and treatment. This way, if the patient is found to have grossly identifiable pleural metastases, assessed by means of preoperative frozen section, we are able to perform a pleurodesis (talc in our case) during the same exploratory procedure. Two or three days later, after withdrawal of the drainage tube, the oncologist may begin treatment. Conversely, if no metastatic disease is found after microscopic examination of random samples taken from the more usual sites of metastatic spread, the effusion is drained, and the patient is ready for any additional evaluation needed before thoracotomy.

RESULTS
Sixty of the 78 patients were men and 18 were women. The median age was 61 years with a range between 35 and 80. According to the location, 46 were right sided and 32 left sided, with a 75 percent predominance for the lower lobes. One of the cases, with right upper lobe involvement, had invasion of the thoracic wall, requiring preoperative radiation therapy, after which the pleural effusion appeared.

By means of thoracoscopy, we found pleural metastasis in 62 patients (78 percent). In two patients, results of exploration were negative because of the size of the pulmonary mass and the presence of extensive pleural adhesions, which impaired a complete pleural exploration. The presence of metastatic disease was assessed by means of minimal thoracotomy. The negative cytology results and incompleteness of the exploration in both cases persuaded us to perform the thoracotomy.

In the remaining 14 patients, we did not detect pleural metastasis, after careful microscopic examination. The yield of diagnostic thoracoscopy was (Table 1), thus, 97.4 percent (76 of 78), with no exploratory morbidity nor mortality. Patients with pleural metastasis underwent pleurodesis with talc, with satisfactory

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Table 1—Diagnostic Results and Operability

<table>
<thead>
<tr>
<th></th>
<th>Total Number</th>
<th>Surgical</th>
<th>Nonsurgical</th>
<th>Cytol +</th>
<th>Diag Thoracoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>With metastases</td>
<td>82% (64/78)</td>
<td>. . .</td>
<td>92%</td>
<td>34% (22/64)</td>
<td>96.8% (62/64)</td>
</tr>
<tr>
<td>Without metastases</td>
<td>18% (14/78)</td>
<td>10% (8/78)</td>
<td>8% (6/78)*</td>
<td>0%</td>
<td>100% (14/14)</td>
</tr>
</tbody>
</table>

*Two cases with distant metastases, two cases with respiratory insufficiency, and two cases with mediastinal lymph nodes and small cell Ca histology.

results in all cases. Surprisingly enough, there are a large number of adenocarcinomas in our series (Table 2), despite rigid screening to rule out metastasis of extrapulmonary origin.

Six of the 14 patients in whom surgery seemed to be advisable, because of the absence of pleural metastasis, were found to be inoperable for other reasons that are detailed in Table 1. The remaining eight cases underwent operation including four lower lobectomies, one upper lobectomy with resection of thoracic wall (above mentioned), and three pneumonectomies, two of them with intrapericardial hilar dissection. The histologic findings of these cases were as follows: five epidermoid carcinomas, two adenocarcinomas, and one small cell carcinoma (in which no preoperative histologic diagnosis was obtained because of the peripheral location of the tumor).

The survival of surgically-treated patients correlates, so far, with tumor grade. Two of the patients who underwent curative resection are alive and well 2.5 and four years after surgery. The average survival period of the remaining patients was 18 months, with a range between five and 36 months. The average survival period of patients with pleural metastasis who received therapy was six months with a maximum of two years in one patient with epidermoid carcinoma who received radiation therapy.

Table 2 shows the histologic findings of cases with pleural metastasis. Cytology of pleural fluid was negative in all patients who underwent surgery and positive in 34 percent (22 of 64) of those with pleural metastasis (Table 1). Therefore, the remaining 66 percent represent false negatives which indicate that negative cytology should not be relied upon as a criterion of operability. The histology of these cases were as follows: epidermoid carcinoma, 4.5 percent; small cell carcinoma, 36 percent; adenocarcinoma, 55 percent; and carcinoma not otherwise specified (NOS), 4.5 percent.

The following data enhanced the chance of positive cytology: (a) widespread pleural metastasis involving all pleural surfaces; (b) bloody fluid (Table 3); (c) adenocarcinoma; and (d) diffuse involvement of visceral pleura. Figure 1 represents the various locations of metastatic disease in different pleural surfaces of the 64 patients with pleural involvement. We have expressed in percentages the index of metastases obtained by dividing the number of dots at each location by the total number of cases examined. This is compared with pleural metastasis of extrapulmonary origin as was described in a previous paper, after exclusion of pulmonary neoplasms from this second drawing. The results show a higher percentage of metastatic disease in visceral pleura in lung cancer as opposed to a higher number of inferior mediastinal and diaphragmatic pleural involvement in cases of extrapulmonary origin of the tumor. These figures, as checked by means of the chi square statistical analysis, are significant. Represented in Figure 2 are the different histologic types, excluding the three cases with nontypified carcinomas; the different pattern of metastasis in the different subtypes and the frequency of spread in the contact zone between tumor and neighbor pleura is also shown.

**Conclusions**

Study of the results obtained in the present work points towards a first conclusion: the presence of pleural effusion in a patient with lung cancer is not always a sign of inoperability. An exhaustive evaluation has to be done in all cases of pleural effusion in patients with lung cancer, in order to rule out metastatic spread. In our hands, thoracoscopy seems to be the method of choice to perform this study.

The gross appearance of the effusion is not by itself an indicator of malignancy, although the serohemorrhagic nature of the fluid is usually suggestive, not diagnostic,

Table 2—Relationship Between Histological Type and Operability

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>With Metastases</th>
<th>Without Metastases</th>
<th>Operated on</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermoid Ca</td>
<td>22</td>
<td>14</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>24</td>
<td>21</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Small cell Ca</td>
<td>29</td>
<td>26</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Carcinoma not otherwise specified</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>64</td>
<td>14</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 3—Relationship Between Pleural Liquid Appearance, Cytology and Metastases Present

<table>
<thead>
<tr>
<th></th>
<th>With Metastases</th>
<th>Without Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cytol+</td>
<td>Cytol−</td>
</tr>
<tr>
<td>Serous</td>
<td>47</td>
<td>10</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>31</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>22</td>
</tr>
</tbody>
</table>

Lung Cancer and Pleural Effusion (Cantó et al)
of malignancy, which is in agreement with LeRoux. Of course, a negative result of cytology does not indicate a benign process. Conversely, positive cytology indicates pleural metastasis or pleural invasion by the lung tumor itself. According to Miguieres et al., the yield of pleural fluid cytology increases in case of adenocarcinoma, or in any type of tumor when there is invasion of visceral pleura. The etiology of pleural effusion when no metastatic spread is detected, has to be attributed to the presence of atelectasis, secondary pneumonitis, tumor necrosis, radiation therapy, lymphatic or venous obstruction, or hypoproteinemia.

When the lower lobes are the seeding of lung cancer, there is a higher risk of pleural effusion, a fact that may be explained by its larger lymphatic network. When the primary tumor is an epidermoid carcinoma, pleural effusion is likely to be benign, which is explained by the more frequent endobronchial location of these tumors which may produce atelectasis or distal pneumonitides. There is a clear difference in the location of pleural metastasis from lung cancer as compared with those from extrapolmonary origin.

The oat-cell carcinoma metastasizes more frequently into the visceral and costal pleura than the epidermoid, and also involves the costal pleura more frequently than the adenocarcinoma.
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17 Miqueres and others. Place de la Ponction-biopsie à l'aiguille et du cytodiagnostic dans le diagnostic des pleurésies malignes. Le Poumon et le Coeur 1981; 37:29-34

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