Metastatic Tumors of the Lung*

JEROME L. MARKS, M.D.**
Milwaukee, Wisconsin

From a clinician's viewpoint, carcinomatous pulmonary metastases are still discouraging entities. With the remarkable strides in producing regressive changes of metastatic breast and prostatic carcinoma with hormonal therapy, and the ever widening vista of therapeutic results with artificial radioactive substances, it behooves all of us to re-examine our fundamental knowledge of pulmonary metastases. All too often we become pessimistic about carcinoma and especially about metastases, not realizing that we must be soundly prepared in our diagnostic approach to these conditions for the time when we will sounder therapeutic aids to handle these overwhelming conditions. It is almost heresy to say today that results may be anticipated in pulmonary metastases. Yet, all of us recall that only a short time ago subacute bacterial endocarditis, pneumococcal meningitis, congenital cardiac disorders, pulmonary carcinoma and a horde of other fatal diseases were considered incurable. Now these are being treated with astonishing success in all centers of the world. Can we then dismiss pulmonary metastases with littel foresight? Or shall we examine closely the etiologies, avenues of transmission, clinical and roentgen manifestations of pulmonary metastases and then cautiously approach and await potential strokes of repair?

The question frequently arises, how often do primary lesions of the various organs metastasize to the lung? In an extensive review of over 1300 cases, Turner and Jaffe* list the incidence of lung metastases as in Table 1.

Thus it may be said that the relative frequency of metastases to the lung from malignancies of all organs is approximately 25 per cent. In more simple terms, if a patient has a malignancy there is one chance out of four that he or she will have pulmonary metastases. Further, using rough percentage figures, all neuromuscular, skeletal, glandular, and hemopoietic primary malignancies metastasize 50 per cent of the time. All urinary tract, male and female genital organs, gastrointestinal, and respiratory tract

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**Director, Department of Radiology, Milwaukee County Hospital and Clinical Instructor in Radiology, Marquette University, School of Medicine, Milwaukee, Wisconsin.
lesions metastasize to the lung 25 per cent of the time, and the oral cavity malignant lesions metastasize 10 per cent of the time. (Table 2, Fig. 1).

Next, we must examine the fundamental pathology that occurs in pulmonary metastases. Tumor metastasis, is the translocation of cancerous cells to others parts of the body. The avenues of transmission are principally three: (1) the vascular circulation,

<table>
<thead>
<tr>
<th>No. of Autopsies</th>
<th>Systems</th>
<th>Lung Metastases Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>185</td>
<td>Urinary tract and male genital organs</td>
<td>28.1</td>
</tr>
<tr>
<td>160</td>
<td>Female genital</td>
<td>23.1</td>
</tr>
<tr>
<td>218</td>
<td>Oral cavity</td>
<td>11.9</td>
</tr>
<tr>
<td>391</td>
<td>Gastro-intestinal tract</td>
<td>20.5</td>
</tr>
<tr>
<td>96</td>
<td>Respiratory</td>
<td>28.1</td>
</tr>
<tr>
<td>58</td>
<td>Neuromuscular and skeletal</td>
<td>48.2</td>
</tr>
<tr>
<td>195</td>
<td>Glandular and hemopoletic</td>
<td>49.7</td>
</tr>
<tr>
<td>Total 1303</td>
<td></td>
<td>26.6 Average</td>
</tr>
</tbody>
</table>

TABLE 2 (Summary of Table 1)

<table>
<thead>
<tr>
<th>Site of Origin</th>
<th>Pulmonary Metastases (Approx.) Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuromuscular, skeletal, glandular, hemopoletic</td>
<td>50</td>
</tr>
<tr>
<td>Urinary tract, male and female genitals, G. I. and respiratory</td>
<td>25</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>10</td>
</tr>
</tbody>
</table>

TABLE 3
Avenues of Metastases

The Circulation:
1. General venous system.
   a. Systemic — bones, kidneys, etc.
   b. Portal — stomach, colon, etc.
2. Vertebral vein plexus.
   a. Prostate, etc.

The Lymphatics (Breast, carcinoma of stomach):
1. Thoracic duct and cisterna chyli.
2. Right lymphatic duct.

Membranous Surfaces:
1. Peritoneum, etc. — carcinoma of ovary.
2. Organs — carcinoma of bladder.
(2) the lymphatics, and (3) the membranous surfaces (Table 3).

The Circulation: Emboli of malignant cells carried by the bloodstream are common, especially in highly vascular tumors and those which tend to invade blood vessels. The tumors associated with the systemic circulation (bones, kidneys, etc.) tend principally to invade the lungs, while those in the portal circulation (stomach, colon) tend to metastasize to the liver.

The Lymphatics: Carcinoma cells tend to grow into the connective tissue spaces and to invade the lymphatics. This may occur by permeation of lymphatics (a method of spread seen in cancer of the breast) or by lymphatic emboli, as in secondary growth in regional lymph nodes (e.g. cancer of the stomach may metastasize to the supraclavicular lymph nodes).

The Membranous Surfaces: Secondary carcinomatous growths may scatter over a serous or a mucous surface and gain a strong foothold in the area surrounding the primary growth. An example is the implantation of the surrounding peritoneum in a carcinoma of the ovary.

If we understand these three fundamental principles of metastasis, we can immediately anticipate the roentgen manifestations

**METASTASES TO LUNGS**

(From All Organs)
of pulmonary metastases. Characteristic patterns can therefore be anticipated in blood-borne, lymphatic disseminated, and membranous surface extension types of metastases.

**The Roentgen Patterns of Pulmonary Metastases**

A. *The Circulatory Pattern (Hematogenous Metastases):* The route of hematogenous metastases is through the veins. Certain lesions (e.g. sarcomas and carcinomas of the kidney) spread principally by this method. Tumor cells may grow into a vein, form a thrombus, and then disperse tumor emboli. These tumor emboli reach the right heart and then enter the lung via the pulmonary arteries. Here the characteristic circulatory pattern of a metastasis will be produced. From the lung, tumor cells may invade the pulmonary veins, destroy them and thus reach the left side of the heart and systemic circulation.

Of extreme interest is the phenomenon of systemic metastasis without lung metastases. For example, a carcinoma of the prostate will frequently metastasize to the bones, yet repeated careful examinations will reveal no evidence of metastases to the chest. This phenomenon is now adequately explained by Batson's studies of the vertebral vein plexus. This plexus has no valves and communicates with the other main systems (Fig. 2). When pressure changes occur within the abdominal or pleural cavity, retrograde
flow of carcinoma cells takes place through these veins without valves producing metastases to unexpected organs. It has been shown by this method that when opaque material is injected into the dorsal vein of the penis, it can reach the vertebral system without first entering the pulmonary circulation. Thus carcinoma of the prostate may reach the vertebrae, pelvis and upper ends of the femur without evidence of disease in the lungs. Also with cough, a carcinoma of the lung located in the area of the posterior bronchial vein, may metastasize through this vein into the vertebral vein plexus and thence to the brain, without evidence of pulmonary metastases.

In the hematogenous pulmonary metastases the rich capillary network in the lungs filters out the tumor cells reaching this organ. This filtering mechanism gives rise to two main types of metastatic lesions: (1) the solitary nodular shadow and (2) the multiple nodular shadows. These in turn may vary all the way from "miliary" deposits to the huge, so-called, "cannon-ball" metastases. We may then classify hematogenous metastases as follows:

**Solitary Nodular Shadow:**
1. Small type (Figure 3).
2. Large type (Figure 4).

**Multiple Nodular Shadows:**
1. Miliary type (Figure 5).
2. Small nodular type (Figure 6).
3. Large nodular type.
4. Huge nodular or "cannon-ball" type (Figure 7).

**FIGURE 3**
*Fig. 3: Solitary Nodular Shadow—Small Type.*

**FIGURE 4**
*Fig. 4: Solitary Nodular Shadow—Large Type.*
The solitary nodular metastasis is perhaps the most difficult pulmonary lesion to differentiate and the list in Table 4 is an indication of the multiple lesions which can stimulate this particular finding.

With such an imposing array of lesions, it is no wonder that the roentgenologists and chest men throw up their hands in despair when a solitary nodular lesion appears on a film. Yet, if we will follow a certain routine procedure in the presence of a solitary nodular shadow, rather than “guess” at the possibility, we may arrive at the correct diagnosis more frequently than anticipated. Table 5 is an all inclusive procedure to follow for the differential diagnosis of the solitary pulmonary nodule.

Multiple nodular metastases may vary, as described, from the minute almost pin-point lesions to the huge “cannon-ball” type. Miliary hematogenous metastases is usually referred to as “miliary carcinosis” and presents sometimes an extremely difficult differential diagnosis from miliary tuberculosis and pneumoconiosis. Miliary tuberculosis, however, changes fairly rapidly and serial films will distinguish it from the carcinomatous lesion. Pneumoconiosis, on the other hand, will show no change over a long period of time as compared to miliary carcinosis, and further, the history of exposure will aid in the differential diagnosis.

In turn, a wide host of conditions will simulate the multiple

| TABLE 4 |

Differential Diagnosis of a Solitary Pulmonary Nodule

I. Chest Wall:
   - Nevii, nipple shadow, rib neoplasm and nerve root neoplasm.

II. Mediastinum:
   - Dermoids, teratomas, thymic neoplasms, esophageal diverticula, diaphragmatic hernia, neurofibroma, ganglioneuroma, dumbbell lipoma of pericardium.

III. Pleura:
   - Benign tumors (fibroma, lipoma).
   - Malignant tumors (fibrosarcoma).
   - Loculated effusions.

IV. Lungs:
   - Primary malignancy — Carcinoma, Sarcoma, Chorionepithelioma.
   - Benign — Chondroma, Adenoma of bronchus.
   - Inflammatory — Nodular Tuberculosis, Abscess, Segmental pneumonia, Mycotic, Gumma.
   - Cysts — Congenital fluid, Echinococcus.
   - Foreign bodies — Interbronchial Lymph Nodes — Tuberculosis, Hodgkin's disease, Lymphosarcoma.
TABLE 5
Routine Procedure for Differential Diagnosis of the Solitary Nodular Shadow

1. Examine patient:
   Clinical survey (rectal, prostate, temperature, blood count, etc.)
   (exclude naevi, nipple shadows, etc.)

2. Stereoscopic roentgenograms:
   Exclude the chest wall and pleural lesions.

3. Lateral and oblique roentgenograms:
   Determine position of lesions — anterior (dermoids, thymus, etc.)
   posterior (ganglioneuromas, neurofibroma, etc.)

4. Antero-posterior Bucky chest films and tomographs:
   Calcification — dermoids, nodular tuberculosis.
   Cyst wall — Echinococcus disease, congenital cysts.

5. Routine bone films:
   Lateral skull, ribs, dorso-lumbar spine, pelvis, humeri, femurs.
   Exclude osseous metastasis.

6. Esophagram and complete gastrointestinal and gall bladder studies:
   Diverticula, diaphragmatic hernia, primary carcinoma.

7. Sputums and gastric specimens:
   Tuberculosis, mycoses, bacterial pathogens, tumor cells.

8. Bronchoscopic examination (with aspiration for smear and culture):
   Foreign bodies, primary neoplasms, inflammatory lesions.

9. Systemic tests:
   Pyelograms and others.

10. Exploratory thoracotomy.

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TABLE 6
Differential Diagnosis of Multiple Nodular Shadows

**Millary Shadows:**
1. Millary tuberculosis.
2. Boeck's sarcoid.
3. Millary carcinoma.
4. Hyphomycetosis.
5. Bronchiolitis.
6. Pneumoconiosis.
7. Congestion.

**Large Nodular Shadows:**
1. Metastatic neoplasms of lung.
2. Metastatic neoplasms of pleura and ribs.
3. Multiple echinococcus cysts.
5. Infarcts.
7. Metastatic lung abscesses.
8. Coccidioidomycosis.
nodular metastases. Table 6 will aid in considering some of the lesions producing similar roentgen shadows.

B. The Lymphatic Pattern (Lymphangitic Metastases): To fully understand lymphangitic metastases a fundamental knowledge of the lymphatic drainage of the body is essential. Two principal routes of lymphatic drainage are present: (1) through the thoracic duct, and (2) through the right lymphatic duct (Fig. 8a).

The Thoracic Duct and cisterna chyli drain the left side of the head, neck and thorax, the left upper extremity, left lung, left heart, and the lower and front part of liver. It also drains the lower limbs, walls and viscera of pelvis, kidneys, suprarenal glands, stomach, intestine, pancreas, and spleen (Fig. 8b).

The Right Thoracic Duct drains the right side of the head, neck and thorax, right upper extremity, right lung, right side of heart, and the convex surface of the liver (Fig. 8b).

With these anatomical facts in mind, it is easy to understand the presence of the Virchow node in a carcinoma of the stomach or pancreas, or the presence of metastatic supraclavicular or axillary lymph nodes on the right side in a primary carcinoma of the right lung.

The anatomical lymphatic drainage of the lung is essential to the understanding of the roentgen picture of lymphangitic metastases.

In each lung there are three areas of lymphatic drainage: superior, middle and inferior:

**LYMPHATIC DRAINAGE IN MAN**
Right Lung:
1. Superior area — right laterotracheal nodes.
2. Middle area — right laterotracheal nodes.
   intertracheobronchial nodes.
3. Inferior area — bifurcation nodes.

Left Lung:
1. Superior area — left laterotracheal nodes.
   anterior mediastinal nodes.
   subaortic nodes.
2. Middle area — anterior mediastinal nodes.
   laterotracheal nodes.
   bifurcation nodes.
3. Inferior area — bifurcation nodes.

The lymphatics of the parietal pleura are divided into those of the diaphragm and the thoracic wall. The lymphatics of the diaphragm empty into the lateral precardiac and anterior mediastinal nodes on the left, and the posterior mediastinal on the right. The posterior portion of the diaphragm connects with the subperitoneal infra-diaphragmatic lymphatics which terminate into the abdominal para-aortic nodes. They are also in communication with the lymphatics of the liver, adipose capsule of the kidney and the suprarenal gland. The thoracic pleural lymphatics are in three regions: (1) from 1st rib to pleural dome, (2) 2nd to 4th rib, and (3) 4th to 6th rib.

Roentgenologically, lymphangitic carcinoma shows a diffuse, string-like formation of increased density, which radiates from the hilum to the periphery. The design is more marked in the central and basal portions of the lung but may extend into the

**FIGURE 9**
**FIGURE 10**
*Fig. 9:* Lymphangitic Pulmonary Metastases—Diffuse “String-like” Formation.
*Fig. 10:* Lymphangitic Pulmonary Metastases—Matted Irregular Type.
periphery and also the upper portions. If it arises from an intra-pulmonary tumor, the lymphatic spread may be unilateral. The fine string-like formations may give rise in certain areas to a "matted irregular appearance" or to numerous adjacent miliary nodules (Figs. 9 and 10).

The differential diagnosis of intra-pulmonary lymphangitic carcinoma is as follows:³

1. Miliary tuberculosis—hilar shadows less dense, upper portions involved.
2. Pulmonary congestion and edema.
4. Sarcoid—sharply defined hilar masses.
5. Fibrosis with emphysema.
7. Atypical pneumonia—history.

SUMMARY

The various forms of pulmonary metastases are presented, (1) the circulatory, (2) lymphatic, and (3) membranous surface extensions. The differential diagnosis of pulmonary metastases on the roentgenograms are described and methods utilized to differentiate the lesions are explained. The incidence of pulmonary metastases from all organs is discussed. The present-day concept of osseous and systemic metastases without pulmonary metastases is presented.

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RESUMEN

Se han presentado las diversas formas de tumores pulmonares metastásicos, (1) circulatorios, (2) linfáticos y (3) extensiones de las superficies membranosas. El diagnóstico diferencial de las metástasis pulmonares en las radiografías se describe y se explican los métodos empleados para diferenciar las lesiones. Se discute la frecuencia de las metástasis pulmonares a partir de todos los órganos. El concepto actual de las metástasis óseas y de sistemas sin metástasis pulmonares se presenta.

REFERENCES