Endotracheal/Endobronchial Metastases*

Clinicopathologic Study With Special Reference to Developmental Modes

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Background: Endotracheal/endobronchial metastases (EEMs) from nonpulmonary neoplasms are rare. However, their definition and developmental modes have not yet been fully elucidated.

Methods: EEMs were defined as documented nonpulmonary neoplasms metastatic to the subsegmental or more proximal central bronchus, in a bronchoscopically visible range. The clinical and pathologic features of 16 cases were reviewed, with special emphasis on the developmental modes based on five criteria: location in the tracheobronchial tree, number of lesions, laterality of lesions, depth of lesions, and relationship with the associated bronchus.

Results: The developmental modes were proposed on the basis of the above five criteria as follows: type I, direct metastasis to the bronchus; type II, bronchial invasion by a parenchymal lesion; type III, bronchial invasion by mediastinal or hilar lymph node metastasis; and type IV, peripheral lesions extended along the proximal bronchus. Primary tumors included colorectal in six patients, breast in three patients, uterus in two patients, osteosarcoma of the bone in two patients, and maxillary, larynx, and parotid carcinoma in one patient each, respectively. The mean recurrence interval was 65.3 months. The developmental modes were as follows: type I, five patients; type II, one patient; type III, four patients; and type IV, nine patients. Three patients underwent surgical resection. One patient has remained well for 5 years after operation. Median and mean survival times were 9 months and 15.5 months, respectively.

Conclusion: The mean recurrence interval was long at 65.3 months, but the mean survival time was short at 15.5 months. Type I accounted for only 5 of 16 patients. Type II was found in only one patient. It is thought that this type is a rare form. Type IV affected nine patients. Treatment plans must be individualized, because in some cases, long-term survival can be expected.

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Key words: developmental mode; endotracheal/endobronchial metastasis; flexible bronchoscopy; prognosis; pulmonary metastasis; recurrence interval

Abbreviation: EEM = endotracheal/endobronchial metastases

Endotracheal/endobronchial metastases (EEM) from nonpulmonary tumors are uncommon. Some investigators1–3 have reported comprehensive studies on this topic. However, the frequencies of “endobronchial metastasis” are variable by definition, ranging from 2 to 50% of pulmonary metastases from extrathoracic neoplasms.1–3

A variety of tumors have been associated with EEM. These include breast, colorectal, renal, ovarian, thyroid, uterine, testicular, nasopharynx, prostate, and adrenal carcinomas; sarcomas; melanomas; and plasmacytomas; although breast,4–6 colorectal,7,8 and renal carcinomas9–12 predominate.1,13,14

The developmental modes have not been fully described previously, and the definition of EEM varies according to the author. One definition in-
cludes only direct metastasis to the tracheobronchial wall, and the other secondary involvement as well as direct invasion.

Treatments and management employed in EEM are determined by the histologic identification of the primary tumor, its biological behavior, anatomic location, evidence of other metastatic sites, and the patient’s performance status. It is very important that treatment is individualized. Survival is dependent to a great degree on the biological behavior of the particular tumor and its responsiveness to the palliative measures available.

In this article, we studied developmental modes and proposed the following four developmental conditions according to five criteria: type I, direct metastasis to the bronchus; type II, bronchial invasion by a parenchymal lesion; type III, bronchial invasion by mediastinal or hilar lymph node metastasis; and type IV, a peripheral lesion extended along the proximal bronchus and assessed as having clinical and pathologic features of EEM with special reference to developmental modes.

Materials and Methods

We defined EEM as bronchoscopically visible nonpulmonary tumors metastatic to the subsegmental or more proximal central bronchus and lesions histologically identical to primary tumors previously documented.

Since January 1990, 38 patients with pulmonary metastases from extrathoracic malignant lesions had their conditions diagnosed using fiberoptic bronchoscopy or surgical procedures, and 16 of them (42.1%) had EEM as defined above, the findings for which form the basis of this article.

The patients’ medical records were retrospectively reviewed. Follow-up information was obtained on all patients through medical records. Histologic diagnosis was obtained in all cases by direct biopsy with a flexible bronchoscope and reviewed by one of the authors (K.S.) to confirm the diagnosis. Careful histologic evaluation was made to establish tissue identity between the primary extrapulmonary tumors and EEM.

We evaluated the recurrence interval from the diagnosis of the primary lesions to the diagnosis of EEM, operability, survival time, and the developmental modes. The developmental modes were assessed according to the following five criteria using chest radiography, CT, bronchoscopy, and histology: (1) location in the tracheobronchial tree; (2) number of lesions, solitary or multiple; (3) laterality of lesions, right or left; (4) depth of lesions, mucosal invasion or submucosal invasion; and (5) the relationship with the associated bronchus, EEM without adjacent tumor, EEM with adjacent parenchymal tumor, or EEM with adjacent enlarged lymph node.

The difference in survival between different types was evaluated using the Kaplan-Meier method, and statistical evaluation of the factors was performed using the log-rank test (p = 0.05).

Results

We proposed the developmental modes on the basis of the above five criteria as follows: type I, direct metastasis to the bronchus; type II, bronchial invasion by a parenchymal lesion; type III, bronchial invasion by the mediastinal or hilar lymph node metastasis; and type IV, peripheral lesions extended along the proximal bronchus (Fig 1).

Table 1 shows patient characteristics. In 10 patients free of symptoms, abnormal findings on chest radiographs during follow-up were found and the patients underwent further diagnostic evaluation.

Table 2 shows clinical findings. The time from the diagnosis of the primary nonpulmonary tumors to the diagnosis of EEM was defined as the recurrence interval. The mean recurrence interval for all patients was 65.3 months, and the respective primary sites were as follows: colon and rectum, 59.4 months (range, 1 to 112 months); breast, 86.3 months (range, 78 to 92 months); bone, 63.5 months (range, 31 to 96); uterus, 18.0 months (range, 0 to 36); maxilla, 196 months; larynx, 34 months; and parotid, 31 months. Although the range was large, a patient with maxilla carcinoma, the histology of which was adenoid cystic carcinoma, had the longest recurrence interval (196 months), whereas a patient with uterus carcinoma, whose histology was adenosquamous carcinoma, had the shortest interval (0 months).

The chest radiographic images in patients with EEM were quite variable. All patients revealed abnormal findings. These included multiple pulmonary nodules in six patients (37.5%), hilar masses in five patients (31.3%), atelectasis in four patients (25.0%), and mediastinal lymphadenopathy in three patients (18.8%). Lesions were located in the trachea in five patients (seven lesions), main bronchus in six patients (eight lesions), truncus intermedius in six patients, segmental bronchus in six patients, and subsegmental bronchus in two patients.

Figure 1. Four developmental modes of endobronchial metastases. Type I: direct metastasis to the bronchus. Type II: bronchial invasion by a parenchymal lesion. Type III: bronchial invasion by mediastinal or hilar lymph node metastasis. Type IV: peripheral lesions extended along the proximal bronchus.
Six patients had synchronous, and one metachronous, multiple EEM. Two of six patients with colorectal carcinomas had multiple lesions; one patient had synchronous multiple lesions, truncus intermedius, and segmental bronchus; and the other showed metachronous lesions: one lesion in the left main bronchus (40 months after diagnosis of primary site), three lesions in the trachea, and two lesions in the right main bronchus (46 months after diagnosis of the primary site). All three patients with breast carcinomas had multiple lesions. One patient with osteosarcoma of the bone and another with uterus carcinoma had multiple lesions.

Twenty of 25 lesions (80.0%), except for 7 tracheal lesions, were recognized in the right side and only 5 lesions were in the left side. EEM from colon and rectum cancers, breast cancers, and osteosarcomas of the bone were distributed on both sides, but six lesions from uterus, maxilla, larynx, and parotid cancers were seen only in the right side. Twenty of all lesions (62.5%) involved the submucosal layer, and only 12 lesions developed in the mucosal layer.

Table 3 shows the developmental modes of EEM as defined above: type I, five patients (12 lesions); type II, one patient (one lesion); type III, four patients (8 lesions); and type IV, nine patients (10 lesions). One patient with rectum cancer had one type IV lesion in the left main bronchus and five type I lesions in the trachea and right main bronchus 6 months after surgical resection of the first lesion metachronously (Figs 2, 3). Two of three patients with breast cancer showed type I lesions, and one of them demonstrated a marked lymphangitis carcinomatosa in the submucosal layer. Both patients with uterus carcinomas had type III lesions (Fig 4). One patient with osteosarcoma of the bone showed both type I and type IV lesions in the left lower bronchus synchronously. A patient with maxillary carcinoma had a type II lesion in the right truncus intermedius, in contact with which a metastatic nodule was recognized in the pulmonary parenchyma (Fig 5). One patient with parotid cancer had a type I lesion in the membranous portion of the right main bronchus.

At the time of EEM, 9 of 16 patients (56.3%) had extrabronchial metastatic disease. These extrabronchial metastatic sites included the pulmonary parenchyma (\( n = 6 \)), pleura (\( n = 3 \)), brain (\( n = 3 \)), liver (\( n = 2 \)), and bone (\( n = 1 \)).

Three patients, two with endobronchial metastases from osteosarcoma of the bone and one with metastatic colon cancer, had localized endobronchial metastases, but no metastatic lesions in other sites. These three patients underwent surgery: a right lower lobectomy (bone), a left lower lobectomy (bone), and a left lower lobectomy (colon), respectively. One patient with metastatic osteosarcoma died of brain metastasis 6 months after the operation, and the other patient has remained well for 5 years without any postoperative sign of recurrence. One patient with metastatic colon cancer has survived with recurrence in the tracheobronchial tree 6 months after the operation.

The median and mean survival times from the diagnosis of EEM to death were 9 months (range, 1 to 66 months) and 15.5 months, respectively; the
mean survival times of patients with the respective primary sites were as follows: colon and rectum, 8.7 months (range, 2 to 14 months); breast, 11.0 months (range, 3 to 19 months); bone, 36.5 months (range, 7 to 6 months); uterus, 1 month; maxilla, 31 months; larynx, 9 months; and parotid, 9 months. Although the range was wide, a patient with osteosarcoma of the bone had the longest survival time (66 months), whereas a patient with uterus carcinoma had the shortest (1 month; Table 2).

The mean survival times were as follows: type I, 14 months; type II, 31 months; type III, 2 months; and type IV, 18 months. The survival time of type III was the shortest, and all three operable cases in our series had type IV. There was a significant difference in survival times only between types III and type IV \( (p < 0.05) \), the latter of which had longer survival times, although the number of patients studied was small. In addition, there was no significant difference in survival times between patients with type IV who received operations and those not operated on.

**Discussion**

The frequencies of endobronchial metastasis are variable; the prevalence depends on how they are defined, ranging from approximately 2 to 50%.\(^1\)\(^-\)\(^5\)\(^,\)\(^13\)\(^-\)\(^18\) If one includes invasion of tracheobronchial structures by parenchymal or lymph node masses, the prevalence rate is higher. However, if they are defined as only direct metastases to the tracheobronchial tree from extrapulmonary lesions, the prevalence rate is much lower. We defined EEM as bronchoscopically visible nonpulmonary tumors, metastatic to the sub-segmental or more proximal central bronchus and with lesions histologically identical to primary tumors previously documented. In our series, 16 of 38 patients (42.1%) with pulmonary metastasis from extrathoracic malignant lesions had EEM as defined above.

King and Castleman\(^2\) were the first to emphasize the frequency with which metastatic disease involves the bronchi; they included primary and secondary tracheobronchial tree involvement and did not restrict the order of bronchus. They reported the metastatic involvement of the bronchus, on the basis of pathologic studies in 18.5% of patients (20 of 109 consecutive autopsies) with pulmonary metastatic disease.\(^2\) Braman and Whitecomb\(^1\) limited the definition of endobronchial metastases to involvement of the lobar or main bronchus and reported a 2% prevalence (5 of 244 cases) in an autopsy review series. Baumgartner and Mark\(^13\) defined metastases to the tracheobronchial tree as a primary, not secondary, involvement of these structures, and the prevalence rate was approximately 2%.

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Patients, No.</th>
<th>Recurrence Interval (Mean), mo</th>
<th>Operability, No.</th>
<th>Survival, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon/rectum</td>
<td>6</td>
<td>1–112 (59.4)</td>
<td>Yes: 1 No: 6</td>
<td>Mean: 8.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Range: 2–14</td>
</tr>
<tr>
<td>Breast</td>
<td>3</td>
<td>78–92 (86.3)</td>
<td>Yes: 2 No: 3</td>
<td>Mean: 11.0</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Range: 3–19</td>
</tr>
<tr>
<td>Bone</td>
<td>2</td>
<td>31–96 (63.5)</td>
<td>Yes: 2 No: 4</td>
<td>Mean: 36.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Range: 7–66</td>
</tr>
<tr>
<td>Uterus</td>
<td>2</td>
<td>0–36 (18.0)</td>
<td>Yes: 3 No: 1</td>
<td>Mean: 3.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Range: 1–9</td>
</tr>
<tr>
<td>Maxilla</td>
<td>1</td>
<td>196</td>
<td>Yes: 3 No: 1</td>
<td>Mean: 9</td>
</tr>
<tr>
<td>Larynx</td>
<td>1</td>
<td>34</td>
<td>Yes: 1 No: 3</td>
<td>Mean: 9</td>
</tr>
<tr>
<td>Parotid</td>
<td>1</td>
<td>31</td>
<td>Yes: 1 No: 3</td>
<td>Mean: 9</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>0–196 (65.3)</td>
<td>Yes: 12 No: 14</td>
<td>Mean: 15.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Range: 1–66</td>
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</tbody>
</table>

Table 3—Developmental Modes of EEM

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Patients, No. (No. of Lesions)</th>
<th>Type I, No. (No. of Lesions)</th>
<th>Type II, No. (No. of Lesions)</th>
<th>Type III, No. (No. of Lesions)</th>
<th>Type IV, No. (No. of Lesions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon/rectum</td>
<td>6 (13)</td>
<td>1 (5)</td>
<td>1 (1)</td>
<td>6 (7)</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>3 (8)</td>
<td>2 (5)</td>
<td>1 (3)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>2 (3)</td>
<td>1 (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td>2 (4)</td>
<td></td>
<td>2 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxilla</td>
<td>1 (1)</td>
<td></td>
<td>1 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>1 (1)</td>
<td></td>
<td></td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Parotid</td>
<td>1 (1)</td>
<td></td>
<td>1 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>16 (31)</td>
<td>5 (12)</td>
<td>1 (1)</td>
<td>4 (8)</td>
<td>9 (10)</td>
</tr>
</tbody>
</table>
A variety of primary tumors have been associated with EEM, although breast, colon, and renal carcinomas predominate. In our series, 6 of 16 patients had colorectal carcinomas, and 3 of them had breast carcinomas. Sarcomas are also capable of causing EEM, and we described two patients with endobronchial metastases because of osteogenic sarcomas in this article.

The symptoms and roentgenographic manifestations of patients with EEM were identical to those associated with primary bronchogenic carcinomas. As a result, it was difficult to differentiate between the two diagnoses on the basis of the symptoms and radiographic signs alone. The most common symptoms are coughing and hemoptysis, with dyspnea and wheezing occurring less often. However, the lesions are asymptomatic in some patients. reported that 52% of their patients were asymptomatic. In our series, 10 of 16 patients (62.5%) were asymptomatic and abnormal shadows were detected with follow-up chest radiography. The radiographic findings are quite variable. Patients may present with evidence of atelectasis, multiple pulmonary nodules, hilar masses, mediastinal lymphadenopathy, or a normal chest radiographic finding. Colletti et al reported that CT was sensitive in detecting and localizing endobronchial neoplasms, including metastatic lesions, and correlated well with bronchoscopic findings.
Diagnosis of EEM with fiberoptic bronchoscopy is usually precise. Bronchoscopic results revealed EEM and were diagnostic in all our patients. The histologic identification of the tissue can be correlated with previously documented primary tumors or can serve as a guideline for subsequent investigation in those patients in whom the underlying tumor has not been identified. Bronchoscopy should be performed early in patients with breast, colon, and renal cancer who have pulmonary symptoms such as coughing and a normal chest radiograph. Extra pulmonary EEM are likely to be found.

As has been stated, EEM tend to occur at a significant interval from the diagnosis of the primary tumor, indicating a relatively slow disease progression. Baumgartner and Mark, Katsimbri et al, and Heitmiller et al reported that the mean intervals from the diagnosis of the primary carcinoma to the diagnosis of tracheobronchial tree involvement were 5.4 years (n = 8), 41 months (n = 8), and 59.9 months (n = 23), respectively. Baumgartner and Mark and Salud et al found that the median interval was 5.0 years and 50.4 months (n = 32), respectively. In our series, the mean recurrence interval for all cases was 65.3 months. The longest recurrence interval was 196 months in a patient with maxilla carcinoma, whereas the shortest was zero months in a patient with uterus carcinoma.

There was no predilection for the airway location in our series, although Heitmiller et al reported the lobar bronchus was the site in 19 of 23 patients. The primary sites of endotracheal metastases included the breast (two patients), colon (one patient), and uterus (two patients) in our series. Seven of 16 patients had multiple lesions. The primary sites were as follows: breast (three patients), colon (two patients), bone (one patient), and uterus (one patient). All three patients with breast carcinomas had multiple lesions. Six patients had synchronous multiple lesions and another patient with colon cancer had metachronous multiple lesions. Of particular interest is the fact that 20 of 25 lesions, except 7 tracheal lesions (80.0%), were recognized in the right side, but only 5 were in the left side. The cause of this predilection is uncertain.

We also found that 20 of 32 lesions (62.5%) involved the submucosal layer, and 12 lesions developed...mucosal layer (hematoxylin-eosin, original × 200).
oped in the mucosal layer. Schoenbaum and Vi-amonte\textsuperscript{22} stated that tumor cells carried to the lung by the pulmonary arteries or lymphatic channels may enter the peribronchial lymphatics and, after antegrade or retrograde propagation, give rise to a discrete subepithelial deposit of tumor growth in the bronchial wall. Heitmiller et al\textsuperscript{16} reported that deep endobronchial biopsy specimens in 13 patients revealed metastases in the bronchial submucosa, and in 9 patients, biopsy specimens from exophytic endobronchial tumors revealed metastatic tumors only. They stated that histochemical studies of biopsy specimens from patients with known submucosal involvement failed to show tumors within the submucosal lymphatics or blood vessels, and that the most likely explanation was that the metastatic tumor migrated along the lymphatics with subsequent egress into the submucosal space.

We proposed four types of developmental modes of EEM: type I, direct metastases to the bronchus; type II, bronchial invasion by a parenchymal lesion; type III, bronchial invasion by mediastinal or hilar lymph node metastasis; and type IV, peripheral lesions extended along the proximal bronchus. As stated by Baumgartner and Mark,\textsuperscript{13} we should estimate EEM by separating primary lesions, direct bronchial wall metastases, and secondary lesions because of invasion of tracheobronchial structures by parenchymal or lymph node masses because of the difference in pathogenesis and clinical significance between each of the lesions. In the four types proposed by us, primary lesions correspond to type I, and secondary lesions to type II, type III, and type IV. In our series, type I accounted for only 5 of 16 patients (31.3%), 2 patients with breast cancer, 1 with colon cancer, 1 with osteogenic sarcoma, and 1 with parotid cancer. As for secondary lesions, type II accounted for only one patient with maxillary carcinoma. It is thought that this type is a rare condition. However, type IV affected 9 of 16 patients (56.3%). It is thought this type is the most common condition.

Although it is difficult to differentiate type II from type IV lesions using clinical findings and chest imaging alone, it is possible to differentiate these two types by the depth of lesions, such as whether there is mucosal or submucosal invasion. In this study, almost all type IV lesions (six of seven lesions) showed mucosal invasion, whereas type II lesions showed submucosal invasion. The developmental modes of these two types of lesions are useful for understanding these mechanisms and findings.

Also, of all patients in our series, only one patient with breast carcinoma who revealed type I had lymphangitis carcinomatosa. We think that lymphangitis carcinomatosa is one of accompanying manifestations of type I.

The treatments and management employed in EEM are determined by the histologic identification of the primary tumor—its biological behavior, the anatomic location of lesions, evidence of other metastatic sites, and the patient’s performance status—and must be individualized.\textsuperscript{13,14} Treatments and management include surgical excision, local radiotherapy, especially endobronchial irradiation,\textsuperscript{23} chemotherapy,\textsuperscript{13} and transbronchial endoscopic procedures, such as photodynamic therapy, electrocoagulation, forceps, intratumoral ethanol injections, diathermic snare, prosthetic stents, and Nd-YAG laser-debulking therapy.\textsuperscript{14} Surgical resection should be confined to patients with localized disease, because most patients have extrabronchial metastatic disease at the time of EEM,\textsuperscript{14} and mediastinal lymph node metastases are frequently present at the time of postmortem examination.\textsuperscript{1} Salud et al\textsuperscript{14} reported that at the time of endobronchial metastases, 20 of 23 patients (87%) had extrabronchial metastatic disease; in our series, 9 of 16 patients (56.3%) had extrabronchial metastatic disease. Braman and Whitecomb\textsuperscript{4} also emphasized that mediastinoscopy must be performed to evaluate the possibility of mediastinal involvement before consideration is given to surgical excision of the lesion. However, long-term survival is expected after surgical resection in some patients with localized disease. In our series, a patient with metastatic osteosarcoma in the left lower bronchus has been alive and well without evidence of recurrence 5 years after a left lower lobectomy.

Survival is dependent to a great degree on the biological behavior of the particular tumor and its responsiveness to the treatments and management available.\textsuperscript{13} Although the recurrence-free interval from diagnosis of primary tumor to the discovery of EEM is almost 5 years, survival after the diagnosis of EEM is poor because it is generally a manifestation of a far-advanced disease stage. Heitmiller et al\textsuperscript{16} reported that the mean survival time from the diagnosis of EEM to death was only 12.5 months (range, 1 to 26 months); in our series, it was 15.5 months (range, 1 to 66 months). However, some studies have reported long-term survival: Ettensohn et al\textsuperscript{10} reported a 21-month mean survival in patients with endobronchial metastases of the breast, and Baumgartner and Mark\textsuperscript{13} reported an overall 32-month mean survival in their patients and concluded that aggressive treatment should be considered in these patients, because survival after treatment in this type of metastatic tumor is not necessarily short. Therefore, it should be emphasized that treatment plans must be individualized, because some patients can achieve long-term survival.\textsuperscript{14–16}

The mean survival times, evaluated according to the developmental mode as proposed above, were as follows: type I, 14 months; type II, 31 months; type
III, 2 months; and type IV, 18 months. The survival time of type III was the shortest, and all three operable patients in our series had type IV. There was a significant difference in survival times only between type III and type IV (p < 0.05), although there was no significant difference in survival times between patients with type IV who were operated on and those who were not operated on. Although only a small number of patients were evaluated in our series, our findings suggest that the developmental mode of EEM may be one of the survival determinant factors.

We also should pay careful attention to a few clinical problems with EEM. First, the symptoms and radiographic manifestations of patients with EEM are indistinguishable from those associated with a centrally located primary bronchogenic carcinoma, especially when there has been a long recurrence interval between the occurrence of the primary tumor and EEM, or when the discovery of EEM antedates diagnosis of the primary tumor. Gerle and Felson, in a review of endobronchial metastases from renal cell carcinomas, reported that in 7 of 17 such patients, the metastasis was diagnosed before the primary tumor was identified. Second, there are several situations in which bronchial biopsy specimens may not prove diagnostic. Stated that no absolute histopathologic criteria differentiate primary and secondary tumors, although the clinical setting and immunohistochemical techniques can be useful indicators. Rosenblatt et al reported that, on occasion, metastatic adenocarcinomas may occur with areas of undifferentiated cellularity interspersed with areas of greater differentiation. This may be a source of confusion and result in an inaccurate diagnosis of undifferentiated bronchogenic adenocarcinoma. Braman and Whitecomb also reported that in some instances, it may be impossible to differentiate metastatic involvement of the bronchus by an asymptomatic extrathoracic adenocarcinoma from a primary central adenocarcinoma of the lung. Another source of misdiagnosis may arise when a squamous cell carcinoma presents as polypoid endobronchial growth. The histologic appearance of the endobronchial biopsy specimen may be so pleomorphic that a mistaken impression of metastatic disease is made. However, the demonstration of carcinoma in situ in the adjacent bronchial epithelium strongly suggests the diagnosis of a primary lung tumor.

In conclusion, if atypical clinical features are present or an atypical cell type is discovered after biopsy of the lesion, appropriate diagnostic studies should be undertaken to exclude the possibility of EEM from an asymptomatic extrathoracic tumor before definitive therapy is undertaken. Unless careful attention is paid to the clinical, laboratory, and pathologic features of each case, a misdiagnosis of primary bronchogenic carcinoma may be made and inappropriate therapy instituted.

REFERENCES