Bilateral Primary Invasive Carcinoma of the Lungs

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The multicentric origin of certain neoplasms such as those of the stomach, intestines, skin, female genitalia, and pharynx have been well documented.\textsuperscript{1,4} Until recently, this phenomenon has not been emphasized for carcinoma of the lung except in those examples designated as alveolar cell carcinoma. Excluding the latter, there have been 26 documented cases of multiple primary invasive carcinoma of the lungs with 15 of these appearing in the American literature. McGrath \textit{et al.}\textsuperscript{3} and Auerbach \textit{et al.}\textsuperscript{4} each noted five cases containing two primary invasive bronchogenic carcinomas in the same or different lobe during their independent study of bronchogenic carcinoma, but the histologic types and locations of these carcinomas were not presented. However, the authors were primarily interested in noting all neoplastic change throughout the bronchial mucosa of lungs already known to contain bronchogenic carcinoma. The association of carcinoma \textit{in situ} in one lung with invasive carcinoma in the same or contralateral lung has similarly received recent attention.\textsuperscript{3-7}

The purpose of this report is to present another example of multiple primary invasive carcinomas of the lung and to tabulate the previously reported examples.

This 82 year-old white man was admitted to the Veterans Administration Hospital, Pittsburgh, for repair of a right inguinal hernia. During previous admissions, he had a transurethral resection of the prostate for benign prostatic enlargement and a mid-thigh amputation of the left leg for arteriosclerosis obliterans.

His only complaint on readmission was dry, non-productive cough of several years duration. A routine chest x-ray film revealed an area of increased density about the left hilum extending into the lung and a patchy ill-defined density in the middle of the lower lobe of the right lung.

\textbf{FIGURE 1:} Posterior view of lungs revealing neoplastic mass in superior mediastinum. The tumor evident here histologically was of undifferentiated "oat cell" type.

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Bronchosscopic examination revealed no intraluminal growth and no biopsy was obtained. The bronchial secretions and sputum examinations were negative for neoplastic cells and acid-fast bacilli on smear and culture. A biopsy of a left scalene node revealed chronic lymphadenitis.

Subsequent x-ray examination of the chest revealed enlargement of the two masses as noted previously. Because these radiographic changes were highly suspicious of extensive carcinoma of the lung, x-ray therapy was initiated. He received a total of 5200 r to his left chest and 3200 r to the right, over a two month period. The left hilar mass decreased in size, but the lesion of the right lung appeared larger.

He deteriorated rapidly and died five months after admission.

**Autopsy Examination**

At necropsy, the lungs were partially bound to the thoracic wall by fibrous adhesions and there was bilateral hydrothorax. The superior mediastinum was encased in gray, firm tumor tissue (Fig. 1). The pleural surfaces of the left lung and the pericardium were studded by firm white nodules averaging 0.5 cm. in diameter. The remaining pleural surfaces were bluish gray, smooth and glistening. The cut surfaces of the lungs revealed a gray, firm, demarcated, circumscribed mass of neoplastic tissue averaging 2.0 cm. in diameter located in the middle and lower lobe of the right lung (Fig. 2). The remaining parenchymal surfaces were grayish-pink to black except in the left anterior hilar region where the gray mediastinal tumor infiltrated the adjacent parenchyma. The bronchial mucosa of the left main stem bronchus was red and granular. Metastases were noted in the brain, skin, pancreas, adrenals, bone marrow, and hilar and abdominal lymph nodes.

Additional findings were severe generalized atherosclerosis with arteriosclerosis obliterans of the left iliac artery and a small infarct of the upper lobe of the left lung.

Microscopic examination revealed two distinct histologic types of carcinoma of the lung. The larger tumor present in the left lung was comprised of round, oval, and spindle shaped anaplastic basophilic cells arranged in large sheets and smaller nests. Cell nuclei were oval, hyperchromatic and frequently exhibited mitotic forms (Fig. 3). One section revealed the tumor in continuity with the epithelial surface of an upper lobe bronchus particularly the reserve cell layer. Adjacent mucosal epithelium revealed moderate dysplasia. A considerable amount of desmoplastic tumor stroma was present throughout the neoplasm. This morphologic appearance was apparent in all metastatic sites which included the brain, skin, pancreas, thyroid, adrenals, bone marrow, hilar and abdominal lymph nodes, mediastinum and pleurae.

The other neoplasm which was in the right lung arose from a bronchial epithelium which had undergone squamous metaplasia. It was composed of irregular sheets and whorls of differentiated squamous epithelial cells with acidophilic cytoplasm and varying sized hyperchromatic nuclei some of which contained mitotic forms (Fig. 4).

**FIGURE 2:** Anterior view of right lung revealing squamous cell carcinoma.
Discussion

The identification of multiple primary invasive carcinomas of the lung may be attendant with difficulty. It is apparent that pulmonary metastases from an ipilateral or contralateral primary pulmonary neoplasm may at times provoke such a diagnostic problem. Analysis of previously reported cases, as well as that presented herein allow for certain criteria which permits such a diagnosis.

The microscopic demonstration of an invasive carcinoma arising from an area of carcinoma in situ or adjacent dysplastic epithelium at two distinct bronchial sites would appear to represent absolute diagnostic features for multiple primary bronchogenic carcinomas. Since the local tumor growth may destroy the area of in situ change, the presence of two or more distinct cellular types of bronchogenic carcinoma may be considered acceptable. Examples in which one neoplasm represents an undifferentiated polymorphous large cell type and the other a squamous cell carcinoma do not appear acceptable unless their mucosal origins can be clearly visualized histologically since the former may actually represent anaplastic change of the squamous variant. It is obvious that extrapulmonary carcinomas may give rise to pulmonary metastases simulating primary bronchogenic carcinomas. Examples of pulmonary neoplasms morphologically resembling other extrapulmonary tumors should not be included as examples of multiple bronchogenic carcinomas. Extreme caution in this regard is necessary since an occasional pulmonary metastasis may erode into bronchi and thus simulate a primary mucosal tumor.

The case presented fulfills the criteria noted above. It is of interest that despite the anaplastic small cell nature of one of the growths dysplastic mucosal change was evident. It is noteworthy that this type of bronchogenic carcinoma rarely allows for the clear demonstration of its derivation from the surface epithelium of the bronchial mucosa as indicated by Williams. Further, the metastatic deposits were all of the anaplastic variety being morphologically identical to the tumor of the left lung. It would be highly unlikely that the more differentiated squamous cell carcinoma metastasized to the opposite lung and other visceral sites as an extremely anaplastic form. Conversely, it is unlikely that the latter metastasized to the other lung as a well differentiated squamous cell carcinoma. Although Simpson in 1929 indicated that squamous cell carcinoma may metastasize as an oat cell variety, more recent experience with pulmonary carcinoma contradicts such a statement. McGrath, et al. have indicated from their meticulous study that mixed histologic patterns were produced by independent growth which subsequently coalesced. It is highly conceivable that the primary tumor described by Simpson may have been a mixed histologic pattern with only the oat cell exhibiting metastases, since it has been shown that the mixed morphologic tumors become more frequent with increased sampling of the lesions. The paucity of reported cases of multiple primary invasive pulmonary carcinoma suggests that such an event is rare. However, attention to the association of invasive bronchogenic carcinoma with multiple areas of carcinoma in situ within the bronchial mucosa would indicate the multicentric potential of pulmonary tissue for neoplastic growth.

### Figures

**FIGURE 3:** Photomicrograph of classical undifferentiated, "oat cell" carcinoma in left lung. (X 250)

**FIGURE 4:** Photomicrograph of apparent site of origin of squamous cell carcinoma of right lung. Severe squamous metaplasia and dysplasia is subverted by invasive squamous cell carcinoma. (X 120)
REFERENCES


8 Rostoski and Saude: "Die Bergkrankheit der Erzbergleute in Schneeberg in Cachsen (Schneeberger Lungenkrebs)," Z. Krebsforsch, 23:360, 1926.


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