Adenocystic Carcinoma and Mucoepidermoid Carcinoma of the Tracheobronchial Tree*  

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Adenocystic carcinoma (cylindroma) and mucoepidermoid carcinoma of the tracheobronchial tree are relatively rare. Three additional cases are described. The malignancy, particularly of the former, is emphasized. One of the patients presented with a "normal" chest x-ray picture. Bronchoscopy is usually required for diagnosis and resection in the treatment of choice.

Bronchogenic carcinoma causes most of the morbidity and mortality associated with neoplasms of the lower respiratory tract. The term "bronchial adenoma" has been used to describe a small subgroup which comprises about 1.5 percent of all neoplasms of the lower respiratory tract. The value of the term "bronchial adenoma" lies in its gross descriptive classification of a group of primary endobronchial tumors with similar clinical features which differ significantly from those of bronchogenic carcinoma. Their relative incidence is rare, their sex distribution is equal if not more common in women. They tend to be located in the proximal portions of the tracheobronchial tree and symptoms are frequently of many years' duration.

Three subgroups of bronchial adenoma are now generally recognized. The carcinoid variety accounts for about 85 percent of all bronchial adenomas. The clinical features, treatment, pathology and malignant potential of the more common carcinoid type of bronchial adenoma, have been the subject of many reports in the literature and will not be considered further in this paper. Adenocystic carcinomas or cylindromas comprise about 10 percent of the so-called bronchial adenomas and the mucoepidermoid carcinomas the remainder. Smetana and co-workers in 1952 are generally credited with the first description of the mucoepidermoid carcinoma although they considered it a form of cylindroma. Two additional cases were added by Liebow in the same year also as variants of cylindroma. As additional cases have accumulated, mucoepidermoid carcinomas have been separated and are now generally felt to be a distinct subgroup of bronchial adenomas. With the increasing recognition of the malignant potential of cylindromas, the term adenocystic carcinoma has been used synonymously in recent years. Recognizing the rarity of these two tumors, it was felt worthwhile to report three additional cases recently seen at the Kansas City Veterans Administration Hospital (KCVAH).

CASE REPORTS

CASE 1

A 22-year-old Negro man was admitted to KCVAH in June 1968 with complaints of cough, fever, chills, and vomiting of approximately one week's duration. He denied hemoptysis. Positive findings on physical examination revealed a temperature of 102°F, diminished breath sounds in the right lower lobe area with dullness to percussion in the lower half of the right chest and occasional rales. Chest x-ray examinations demonstrated a density in the lower one third of the right hemithorax with a rather flat, sharply demarcated upper margin extending downward and anteriorly on the lateral examination (Fig 1). He was treated with ampicillin with good clinical response but little change in the x-ray appearance. He left the hospital before bronchoscopy could be accomplished. He was readmitted in December 1968 with similar symptoms, a 36 pound weight loss and the development of significant anemia (Hgb 9.9 gm). At the time of bronchoscopy the right bronchus intermedius was found to be filled with thick tenacious mucopurulent material which was aspirated with considerable difficulty. In view of the persistence of middle lobe consolidation as shown by x-ray examination bronchoscopy was repeated ten days later and this time a lobulated, grayish mass occluding the right bronchus intermedius and appearing to act as a ball valve was seen. During an attempt to remove secretions distal to the lesion, consider-
able bleeding was encountered and biopsy was not attempted. A clinical diagnosis of bronchial adenoma was made and operation recommended. At the time of thoracotomy there was partial consolidation of the right middle lobe and the basal segments of the right lower lobe. Numerous adhesions were present. Bronchotomy to evaluate the extent of the tumor was performed and it appeared to involve the bronchus intermedius and middle lobe orifice. Right middle and lower lobe lobectomy was accomplished.

Examination of the specimen revealed a 1.6 cm polypoid intraluminal mass arising from the middle lobe bronchus near its orifice. It appeared to grow exophytically and grossly did not infiltrate the wall of the bronchus. Microscopic examination revealed a polypoid neoplasm involving the bronchial mucosa and extending to the level of the bronchial cartilage. In most areas the tumor was covered with respiratory epithelium exhibiting foci of squamous metaplasia. In other areas the covering epithelium was ulcerated and replaced by a fibrinous exudate. There was abundant mucicarmine positive material both extracellular and within tumor cells. Based on the microscopic pattern (Fig 2), a diagnosis of mucoepidermoid carcinoma of the right middle lobe bronchus was made.

The patient's immediate postoperative convalescence was uneventful and he was discharged from the hospital on the ninth postoperative day. He was readmitted six months later following an alcoholic debauch. At that time no evidence of recurrence or symptoms related to his pulmonary disease were noted.

Comment: The clinical features of this case are similar to those of bronchial adenoma and are well documented in the literature. No evidence of invasion or metastases was noted. This is the usual feature of these tumors. The distal location and extent of destruction of the pulmonary parenchyma would have made lesser resection unwise. The occurrence of the lesion in a Negro is particularly unusual. Although follow-up is lacking, the prognosis is good.

Case 2

A 59-year-old white man presented at KCVAM with a complaint of hoarseness of 1 1/2 years' duration in April 1969. Past medical history was unremarkable except for thyroidec-tomy in 1952. Hoarseness was not present then. General physical examination and routine laboratory studies were within normal limits. The result of chest x-ray examination was reported as normal. Following the patient's admission endoscopy was performed. A median abductor paralysis of the left vocal cord was noted. Bronchoscopic examination revealed the carina to be thickened with a circumferential firm lesion surrounding the orifice of the left mainstem bronchus. There was mucosal irregularity on the posterior wall of the trachea superior to the carina. Esophagoscopy was also done and the result thought to be essentially normal. The bronchoscopic biopsy specimens consisted of small dark-brown, reddish irregular tissue fragments. Microscopically, multiple small fragments of neoplastic tissue occasionally covered by bronchial mucosa were noted. The biopsy was characteristic of the cylindromatous type of bronchial adenoma or adenoid cystic carcinoma.

Resectional therapy including the potential use of extracorporeal circulation for carinal resection was considered. Careful reexamination of the chest x-ray film suggested a left suprahilar mass. Barium swallow showed anterior compression of the esophagus just below the level of the aortic arch. Bronchography confirmed the presence of the lesion at the left mainstem bronchial orifice and extension along the posterior wall of the trachea.

In view of the presence of tumor above the carina, distortion of the barium filled esophagus, and left vocal cord paralysis, as well as the known propensity for local spread of adenoid cystic carcinomas, it was concluded that this lesion
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had extensively infiltrated the mediastinum and was nonresectable. The patient subsequently received a 3300 rads course of Cobalt irradiation given in a hyperbaric chamber. Follow-up 18 months after completion of therapy indicated that the patient was essentially asymptomatic but with hoarseness persisting. Current x-ray pictures show only fibrosis secondary to irradiation therapy.

Comment: This patient represents a rather typical example of adenocystic carcinoma with local extension. Although initial response to irradiation therapy seems to be satisfactory, future difficulty may be anticipated.

CASE 3

A 60-year-old white man was admitted to KCVAH in July 1969 with a complaint of vague, transient right lower anterior chest pain of two weeks' duration. Significant past history included two renal calculi, a long history of epigastric distress, a known small hiatal hernia and appendectomy for acute appendicitis with perforation previously performed at the same hospital in 1964. Physical examination revealed an elderly white man in mild distress who was rather uncommunicative and appeared depressed. There was moderate dorsal kyphosis and some increase in the anterior posterior diameter of the chest. There was mild epigastric tenderness but the remainder of the physical examination was otherwise within normal limits. A chest x-ray film (Fig 3) demonstrated a rounded discrete mass in the right lower lung field anteriorly. Chest x-ray examinations done in 1964 were reported as normal. A rather complete gastrointestinal and genitourinary work-up failed to reveal any information helpful in establishing a diagnosis and thoracotomy was recommended for diagnosis and therapy.

At the time of thoracotomy a rounded slightly lobulated solid tan-colored mass covered with numerous small vessels was found attached to the inferior posterior surface of a flattened middle lobe and to the anterior surface of the lower lobe. Approximately 50 percent of its surface was covered only by pleura with the medial edge extending superficially into the mediastinum. Resection of the mass in continuity with the middle lobe was performed (Fig 4). Examination of the specimen revealed a tumor measuring $9 \times 8 \times 5$ cm which appeared to arise from the area of the junction between the middle lobe bronchus and its segmental divisions. The tumor was firm, homogeneous, and predominantly yellowish in color (Fig 5). Microscopic examination showed extensive tumor involvement of the middle lobe bronchus with neoplasm invading the bronchial cartilage and surrounding parenchyma. The neoplasm itself was characteristic of adenoid cystic carcinoma. A metastasis to a parabronchial lymph node was noted as well as multiple tumor masses within lymphatics surrounding the bronchus (Fig 6).

Figure 3, Case 3. PA and lateral chest films.

Figure 4, Case 3. Surgical specimen right middle lobe and tumor.

Figure 5, Case 3. Cut section of tumor.

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The immediate postoperative convalescence was uneventful and the patient was discharged from the hospital on the eighth postoperative day. Because of persistent complaints of shoulder, chest and back pain he was readmitted in December 1969. Following evaluation, a diagnosis of reactive depression was made. He was readmitted to the hospital with shock and coma in February 1970. The only history obtainable at that time was that the patient had been anorexic and noted occasional vomiting. In spite of vigorous attempts at resuscitation the patient died a few hours after admission.

Autopsy examination demonstrated widespread metastases of adenocystic carcinoma. There was approximately 75 percent replacement of the liver by metastatic carcinoma with metastatic involvement of the left upper and lower lobes of the lung, both adrenals and the bodies of thoracolumbar vertebra.

Comment: This patient represents an unusual example of adenocystic carcinoma from several respects. First the lesion arose in a segmental branch of the middle lobe bronchus—a location far more peripheral than usually noted. Second because of its distal location, the patient did not present the usual symptoms of cough, hemoptysis, and pulmonary infection and atelectasis. Third, the clinical course of this particular tumor was far more aggressive and rapid than most adenocystic carcinomas even those eventually culminating in death by metastasis. Representative tissue slides were submitted to the Armed Forces Institute of Pathology for review where the diagnosis of adenoid cystic carcinoma was confirmed.

Discussion

Clinically, the adenoid cystic and mucoepidermoid carcinomas closely resemble the carcinoid form of bronchial adenoma. The nature of the symptom complex depends primarily on the location and structure of the tumor. The more proximal lesions generally produce cough from endobronchial irritation, hemoptysis, and if they reach the size sufficient to produce mechanical obstruction, then secondary infection, atelectasis and their accompanying symptoms develop. The more peripheral lesions may be associated with vague symptoms, pain or may be entirely asymptomatic. Symptoms, when present, may be of long standing duration. Diagnosis is usually made by x-ray examination of the chest followed by bronchoscopy. The presence of a normal chest x-ray picture does not eliminate the diagnosis as in case 2. Normal chest x-ray pictures may be seen in up to 15 percent of patients harboring bronchial adenomas and only further emphasizes the need of bronchoscopy. Whether biopsy should be performed remains somewhat controversial. The mucoepidermoid tumors may usually be recognized by their polypoid exophytic appearance but the adenoid cystic variety frequently are grossly indistinguishable from bronchogenic carcinoma. Fatal hemorrhage from bronchial biopsy of a bronchial adenoma has been reported but biopsy is generally recommended unless obvious vessels are seen on the lesion or hemoptysis has been massive.

Surgical resection is a treatment of choice. Although some authors have advocated local resection for cylindroma, others feel that the infiltrative nature of the adenoid cystic carcinoma requires more radical resection. Unfortunately, significant numbers of patients harbor adenoid cystic carcinomas unresectable by the usual clinical criteria. Radiation therapy with repeated local endoscopic removal of obstructive tumor has been found to provide reasonable palliation in unresectable cases of adenoid cystic carcinoma.

Although the malignancy of adenoid cystic carcinomas is now well recognized, bronchial adenomas of all three types continue to be described under headings or titles of benign tumor and unfortunately are so listed even in a recent standard textbook of thoracic surgery. At least one author specifically excluded them from a review of benign tumors of the lung. Widespread metastasis to liver, adrenals and bones, as illustrated in case 3, has been noted previously. The rapidity of death in our patient is greater than those reported in the literature.

It appears justified to separate the mucoepidermoid carcinomas as another subgroup of bronchial adenomas and not as a variant of adenoid cystic carcinoma or cylindroma. The malignant potential of mucoepidermoid carcinoma of the tracheobronchial tree is not as clearly demonstrated as those of adenoid cystic carcinoma. Absence of invasion and distal metastases have been noted in several reports. In fact, Payne and associates raise the question that patients thought to have mucoepidermoid carcinomas with metastases possibly should be considered as having bronchogenic carcinomas with mucous elements. On the other hand Ozlu and co-workers in reporting on four patients found lymph node metastases in one and multiple pleural implants in another, with a third patient...
having mediastinal extension with partial superior vena caval obstruction prohibiting resection. Their other patient, an elderly man, died without having had an operation but had no evidence of metastatic spread at autopsy. Dowling and colleagues in collecting 11 cases of mucoepidermoid carcinomas from the literature, presented one patient with widespread metastases in which areas of the tumor showed evidence of frankly epidermoid carcinoma.

It would appear that adenoid cystic carcinomas of the tracheobronchial tree should be managed as malignant tumors. It should be recognized that they may be associated with prolonged clinical courses but also that they may cause extremely rapid deterioration and death. Until the clinical features of the mucoepidermoid carcinomas are better defined and additional experience with documented cases developed we would be inclined to agree with those who advocate pulmonary resection as the treatment of choice for all bronchial adenomas and the restriction of local resection to those patients who cannot tolerate loss of functioning parenchyma, and have proved evidence of the carcinoid form without metastases.

REFERENCES
8 Liebow AA: Tumors of the lower respiratory tract, in Atlas of Tumor Pathology, Sect. V., Fasc., 17:26, Armed Forces Institute of Pathology, Washington, DC, 1952
14 Tiata JO, Maier HC: The treatment of adenoid cystic carcinoma (cylindroma) of the respiratory tract by surgery and irradiation therapy. Dis Chest 31:493, 1957
22 Boyd AD, Spencer FC, Lind AL: Why has bronchial resection and anastomosis been reported infrequently for treatment of bronchial adenoma? J Thorac Cardiovasc Surg 59:359, 1970