Adenocarcinoma Arising in a Ghon Complex and Presenting with Massive Pericardial Effusion*

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A patient with carcinoma arising in the peripheral scar of a Ghon complex is reported. The tumor had an unusual presentation, suggestive of pericardial mesothelioma. The smallness of the primary lesion, its rapidly fatal course,

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superimposed consumption coagulopathy and histologic difficulties in diagnosis of the original biopsy add to the interest and complexity of the case.

Scar cancers of the lung are now recognized as a distinct entity. Much has been written about the various etiologies of scarring and the theories concerning the induction of tumor in the scar. However, the presentation and clinical course of these are seldom discussed. Because of the peripheral origin of these lesions the initial signs and symptoms are often those of metastatic (or superficial infiltrative) spread rather than the primary hilar space occupying lesion found in most bronchogenic carcinomas. This report describes such a patient in whom the presenting symptoms were due to pericardial metastasis.

**CASE REPORT**

The patient was a 33-year-old white woman who had smoked two to three packs of cigarettes per day for an unspecified length of time. Five years before her present illness she had carcinoma-in-situ of the cervix treated by hysterectomy. In February, 1970, two months before her first hospital admission, she developed a flu-like illness from which she never fully recovered. In April, she noticed a feeling of pressure in her chest accompanied by dyspnea. She was admitted to another hospital where a pericardial effusion was tapped, yielding 900 ml of bloody fluid. Cytologic examination of the fluid did not reveal malignant cells and no organisms were recovered on culture. An intermediate strength tuberculin test was negative. A diagnosis of viral pericarditis was made and the patient begun on steroid therapy. In May, her effusion recurred and was aspirated again. Cytologic examination and culture of the fluid were again negative. Six weeks later, the patient developed phlebitis in the left leg followed by multiple pulmonary emboli. She was admitted to our hospital for placement of a Mobin-Uddin "umbrella" filter in the inferior vena cava. A few hours later the patient suffered a short hypotensive episode. Subsequently, her right leg became cold and swollen. She recovered from this only to have her pleural effusion recur and a pericardectomy was performed. Histologic examination showed extensive involvement of the pericardium by...
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a poorly differentiated malignant tumor. Following operation she developed left 7th cranial nerve palsy with a positive Babinski response and a cold swollen left leg. Coagulation tests revealed a platelet count of 65,400 per mm³, a prothrombin proconvertin level of 25 percent, and a positive plasma protamine test. These results were consistent with diffuse intravascular coagulation. Treatment was begun with vincristine, methotrexate and anticoagulants. For a brief while she rallied, only to die in early July after a total illness of less than six months.

Pathologic Findings

Pericardectomy specimen. The specimen consisted of gray membranous tissue measuring 11 × 6 × 1 cm, weighing 28 gm. Microscopically, a fibrinous exudate covered and replaced most of the mesothelial surface of a thickened pericardium. Malignant tumor cells were present both singly and in small clusters in the fibrous tissue of the pericardium as well as within numerous lymphatics. In a few areas tumor cells could be seen beneath an intact, but hyperplastic mesothelial surface (Fig 1). They measured from 20 to 60 μ in diameter and possessed an irregularly outlined cytoplasm containing occasional coarse aggregates of periodic acid Schiff (PAS) and mucicarmine-positive material. Their nuclei were large, irregular and vesicular with prominent nucleoli and occasional mitotic figures. Tumor giant cells with single and multiple nuclei were frequent.

Autopsy. The heart measured 12 cm in maximum transverse diameter and weighed 400 gm. The entire epicardial surface was roughened and measured up to 0.5 cm in thickness. Most of the pericardium had been removed surgically and the pericardial space obliterated by fibrous adhesions.

The right lung weighed 900 gm and the left 950 gm. The latter was completely adherent to the parietal pleura. Situated at the apex of the right lung was a 1 cm firm nodule with a gray homogeneous cut surface. There were no other scars and no other tumor nodules within the lung parenchyma. Both lungs were congested and showed multiple small infarcts. The pulmonary arteries to both lower lobes were occluded by organizing thrombi.

Lymph nodes at the hilum of both lungs were enlarged up to 2 cm in maximum diameter and their cut surfaces were variegated black and gray. A single enlarged lymph node 2 cm in diameter was present near the head of the pancreas, which when cut into was gray and firm.

Other positive findings included extensive thrombi in the inferior vena cava and leg veins. The liver weighed 2400 gm and showed chronic passive congestion. There were old infarcts in the spleen and both kidneys. The brain contained microscopic infarcts with Candida albicans infection.

Sections of the scar at the apex of the right lung (Fig 2) revealed an area of caseous necrosis with fibrosis and focal collections of pigment containing macrophages, with a massive accumulation of elastic tissue. Situated within and surrounding the scar was a malignant tumor. This consisted of trabeculae of large polygonal cells which in places formed glands (Fig 3). The tumor cells had eosinophilic and faintly granular cytoplasm which contained coarse droplets of mucin confirmed by special stains. Tumor giant cells up to 50 μ in diameter were present.

Microscopically the hilar, mediastinal and pancreatic lymph nodes were extensively replaced by tumor. In one right hilar node an inactive and calcified granuloma was present, surrounded by metastatic tumor. (Fig 4).

The pericardial space was largely obliterated by fibrous tissue, although in places a layer of mesothelial cells was

Figure 2. Tumor (lower right) in relationship to scar. Note dense elastic fibers (Orcein Van Gieson, x 23).

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Figure 3. A high power view of part of the lower right hand portion of Fig 2 showing detail of tumor. Note pigment in scar in upper right hand corner (H and E, x 200).

Figure 4. Tumor lying adjacent to a partially calcified caseous granuloma in hilar lymph node (H and E, x 200).
discernible. There was extensive infiltration of the fibrous tissue and pericardial lymphatics by tumor identical to that seen in the pericardial biopsy and similar to that seen in the lung and lymph nodes.

**DISCUSSION**

Although lung cancer arising in a scar was first described by Friedrich in 1939 and later by Rossle, it remained for Raeburn and Spencer to establish its importance and frequency, which has been estimated to be as high as 25 percent of all lung carcinomas.

It has been generally considered that the diagnosis of scar cancer requires the demonstration of a hyalinized fibrous scar, with abundant elastic fibers and the accumulation of anthracotic pigment. A wide diversity of etiologic agents has been held responsible for the scar. These have included tuberculosis and other granulomatous infections, as well as old infarcts, gunshot and stab wounds, and metallic foreign bodies. This multiplicity of etiologic agents has led investigators to suggest that it was the scar itself rather than its etiology which was important in the genesis of these tumors. Experimentally, Montgomery has demonstrated in cats striking proliferative activity of the bronchi in relationship to wounds of the lungs; Raeburn and Spencer have seen all grades of change in the bronchial epithelium, from simple hyperplasia to frank carcinoma.

The stimulus for these changes in the bronchial epithelium has yet to be determined. It has been suggested that the scar causes lymphatic obstruction with possible localization and concentration of potential carcinogens in the scar. However, the widespread lymphatic metastasis that is one characteristic of scar cancer does not support the concept of lymphatic obstruction. In our case the tumor cells appeared to have travelled down the same lymphatic pathway as the original infectious agent. Scar cancers are often small; 34 of 50 such tumors reported by Yokoo and Suckow measured 3 cm or less in diameter. Frequently the presenting symptoms and signs have been related to metastases rather than the primary tumor itself. The presentation of our case was most unusual and we can find no report in the literature of a scar cancer presenting with pericardial effusion.

Histologically the tumors have been typically mucin secreting adenocarcinomas, although squamous and large cell undifferentiated carcinomas also have occurred. Kitagawa commented on the occurrence of psammoma bodies in 8 of his 21 cases. Clearly the diagnosis of malignant pericardial effusion can only be established by cytologic and histologic methods. At the time of pericardectomy we were uncertain whether the tumor was primary or secondary and were impressed with the morphologic similarities between the tumor cells and the hyperplastic pericardial mesothelial cells (Fig 1). In retrospect there were a number of histologic features that should have led us away from the diagnosis of primary mesothelioma. These include the persistence of a normal mesothelial surface overlying the tumor, the very extensive lymphatic permeation, and the absence of malignant cells in the pericardial fluid. Both the mesothelial and adenocarcinoma cells contained diastase-resistant, PAS-positive material, although the distribution was different. In the tumor cells it was present as coarse droplets, while in the mesothelial cells it consisted of a few fine granules. In addition, mucin was present as large coarse droplets in a few scattered tumor cells. The mesothelial cells were mucin negative.

The histologic recognition of mesotheliomas has always been difficult because of the way in which they can be mimicked by metastatic carcinomas. Indeed, Willis went so far as to doubt the existence of these tumors. This difficulty has led to several attempts to define a specific histochemical test. It would appear that these tumors are either PAS negative or contain only fine droplets of PAS positive material best seen under oil immersion. On the other hand, adenocarcinomas of the lung characteristically contain large droplets of PAS positive material that also stain with mucicarmine. It has been claimed that mesotheliomas also contain a large amount of hyaluronidase stainable by Hale's method and removable by testicular hyaluronidase.

The cause of the scar in our case was unknown. Histologically, the caseating granuloma resembled those found in tuberculosis, although neither mycobacteria nor fungi could be demonstrated. A negative tuberculin reaction cast serious doubts on this diagnosis; unfortunately, skin tests for histoplasmosis and coccidioidomyositis were not performed.

Terminally, the patient's illness was dominated by extensive venous thromboses, necessitating the insertion of a Mobin-Uddin umbrella filter. The syndrome of diffuse intravascular clotting has been characterized by a low platelet count, positive plasma protamine test, a prolonged thrombin time and low levels of fibrinogen, all of which this patient exhibited. Widespread malignancy is one of the common causes of this syndrome.

The management of these cases has been particularly difficult, as the disease is usually inoperable at the time it presents. According to Walter and Pryce it has been the high incidence of peripheral carcinoma of the lung (including scar cancer) that is responsible for the low surgical cure rate in carcinoma of the lung. While pathologists habitually meticulously dissect the major bronchi in autopsies on patients with widespread metastatic malignancy and occult primary tumors, the importance of similar attention to minute peripheral lung nodules has been less well appreciated.

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Bronchobiliary Fistula Secondary to Amebic Liver Abscess*

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A case of bronchobiliary fistula with bilious complication amebic liver abscess, is described. The patient recovered on conservative treatment.

Bronchobiliary fistula is a rare complication of amebic liver abscess. There are only a few reports of this complication. Ten such cases are on record up to 1942. In 1942, Cooray described one case and in 1958 Cleve and Correa described three cases of bronchobiliary fistula. Most of the other reports are concerned with bronchohepatic fistula which is a more common complication. In the former there is biliousness, whereas in the latter there is only chocolate-colored sputum. We report a case of bronchobiliary fistula with biliousness.

CASE REPORT

A 45-year-old farmer was admitted to our ward with fever, cough with expectoration and pain in the right hypochondrium for two months. The sputum was mucoid; there was no history of hemoptysis. Three months prior to admission, he had an attack of dysentery and since had had loose stools periodically.

Examination at the time of admission revealed an ill-looking, emaciated individual with pyrexia of 38°C, pulse rate 100 and respirations 28 per minute, pallor and minimal pitting edema of ankles. The liver was enlarged 5 cm below the right costal margin and was highly tender. The lower right intercostal spaces were bulging and the skin was edematous with marked intercostal tenderness. The cecum was palpable and tender. The percussion sound on the right infrascapular region was dull, the air entry here was diminished and marked crepitations were present. Other systems were within normal limits.

Laboratory investigations revealed a total leukocyte count of 7,500/cu mm with 51 polymorphs and 49 lymphocytes. The hemoglobin was 7.5 g and ESR 44 mm in the first hour. The sputum was negative for acid-fast bacilli. The stool showed trophozoites of Entamoeba histolytica. Blood urea was 20 mg percent. The liver function tests showed thymol turbidity 5 units, serum bilirubin 1 mg percent and alkaline phosphatase 14 KA units. Chest x-ray film (Fig 1), revealed a homogeneous opacity of the right lower zone. A diagnosis of amebic liver abscess with pleuropulmonary complication was made.

Antiamoebic treatment with dehydroemetine, chloroquine and diiodohydroxyquin (Diodoquin) were instituted along with supportive therapy. Liver aspiration was performed and 900 ml of chocolate-colored pus was removed. No ameba could be demonstrated in the aspirated pus. However, the next day the patient started expectorating chocolate colored sputum. This also did not reveal any ameba. Pleural aspiration did not yield any pus. His general condition was improv-