Coexisting Bronchogenic Carcinoma and Tuberculosis*

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ANY TUBERCULOSIS SANITARIUM DEALING actively with diagnostic problems in chest diseases is faced with the differentiation of pulmonary tuberculosis and bronchogenic and metastatic pulmonary carcinomas. The advancing average age of patients being treated for tuberculosis in sanatoria coupled with the well known increasing incidence of bronchogenic carcinoma brings to the fore a common problem related to the identification of these two conditions and their treatment.

There are many case reports of coexisting tuberculosis and carcinomas in the literature. There have been many attempts to relate these two conditions etiologically. As early as 1855 Rokitansky expressed his view upon the apparent incompatibility of these two diseases, based on pathologic findings. Fried in 1935 expressed a more acceptable theory that they might in fact be etiologically related by an unknown mechanism. Early theories pointed out that the changes produced in lung parenchyma and bronchi by tuberculosis, as metaplasia, smouldering infection and chronic irritation by calcified lymph nodes could easily be carcinogenic.14 However, as often as not the two conditions were found in many case reports to be in entirely separate portions of the lung.

We should like to present some of the relationships that were found to exist in patients who had both diseases during a nine year study at Suburban Cook County Tuberculosis Sanitarium in Hinsdale, Illinois. During this period, there were 105 cases of pulmonary carcinoma. Ten of these were eliminated from the present study because they were considered to be metastatic tumors or because the follow-up was incomplete. We have had 100 per cent follow-up on the remaining 95 cases.

MATERIAL AND METHODS

All 95 patients were admitted to the sanitorium with a positive tuberculin skin test. Most, in addition, had positive sputums or suggestive x-ray changes. The patients came from three sources: Some of them were referred directly by private physicians, others were referred from our own out-patient clinics where they had been followed-up for some time, and others were referred through mobile unit follow-up sequences, started in our out-patient clinics. The management of this group of cases conforms to the management of other patients with obvious active tuberculosis in which instance bed rest and immediate routine antituberculosis chemotherapy would be started. An undiagnosed lesion would be given close scrutiny. Patients admitted with positive smears for tuberculosis were often found to have atypical scotochromogens on culture. This finding delays diagnosis and definite treatment. Once a group of three to six sputum cultures has been obtained by routine direct methods and by heated aerosol procedures, these patients were started on a tentative chemotherapy program.

When the diagnosis of tuberculosis was not clear cut, an aggressive diagnostic attitude was found well worth while. Early bronchoscopy, deep cervical node biopsy, pleural needle biopsy and exploratory thoracotomy were used. When, in the course

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of treatment, typical pulmonary tuberculous lesions were seen on x-ray film to resolve slowly or actually enlarge, clinical suspicion was heightened and such lesions explored where possible. While many times the accurate differential diagnosis of these two conditions was extremely difficult, it was true that the single most important point in the differentiation was the managing physician's index of clinical suspicion.

Clinical evaluation of these patients with actual or suspected bronchial carcinoma was done according to standard routine procedure. Extensive disease with pleural involvement or obvious mediastinal metastasis proved by biopsy, main bronchial fixation and extension to mediastinum and involvement of recurrent and phrenic nerves, malignant effusion, definite evidence of distant metastasis, were the established criteria for inoperability. An aggressive attitude was maintained for cases lacking these stigmata.

RESULTS

The 95 patients in this report were found to divide themselves into two groups: 54 with primary bronchogenic carcinoma had at the time of their diagnosis active or chronic inactive tuberculosis. A comparable group of 41 cases was seen during this same period of time with only a positive tuberculin skin test as indication of previous tuberculosis.

The extent and activity status of pulmonary tuberculosis are shown in Table 1, at the time carcinoma was diagnosed. While active tuberculosis was not in itself a contraindication to resection for carcinoma, extensive lung destruction by active pulmonary tuberculosis did form a deterrent to an aggressive surgical attitude toward the patient's carcinoma. However, in no instance was active or inactive tuberculosis by itself the primary contraindication to surgical treatment for carcinoma; there were four patients with sputum-positive pulmonary tuberculosis having pulmonary resections for carcinoma. The stage or extent of tuberculosis did not appear to change the ultimate prognosis of the patient with operable or inoperable carcinoma.

The localization of the bronchogenic carcinoma by cell type (Table 2) shows a predilection for the two upper lobes in a manner seen in a general tumor group. However, more often than not, the localization of carcinoma and tuberculosis even within...
Squamous

Right upper lobe 4 5 1 1 11
Left upper lobe 3 2 3
Right lower lobe 2
Left lower lobe 3
Right main bronchus 1
Middle and upper lobes 1
Right intermediate bronchus 1
Unspecified 2 6 4 2 1 15
Total 13 16 8 3 1 41

Table 4 demonstrates the distribution of the five major carcinoma cell types among the 54 patients with tuberculosis arranged by extent of disease and activity at the time of diagnosis. The overall incidence of the various bronchogenic carcinoma cell types corresponds well with the incidence among general necropsy surveys, surgical specimens and statistical groups reported in the recent past. The pathologic differentiation between squamous cell and undifferentiated large cell carcinoma was obviously one of degree. In general, the pathologist labeled the tumor cell type according to the most undifferentiated portion seen in the specimen. An unusually low number of squamous cell carcinomas was found among the cases of active tuberculosis. Undifferentiated carcinomas and adenocarcinomas were found more often among cases of active tuberculosis.

Table 5 summarizes the general management of each group of patients. The chests of 49 per cent of those with tuberculosis were explored. Of this group, 20 were treated by lung resection, ten by pneumonectomy, and ten by lobectomy with a resection rate of 77 per cent. In the 41 non-tuberculous cases, exploratory operation was done in 61 per cent and the resectability rate for this group was 60 per cent, or
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15 cases. Those clinically inoperable in either group had an average survival time of six months. Those who had exploratory surgery and were found to have unresectable carcinoma similarly were all dead within one year.

Table 6 records surgical procedures, localization and tumor type by survival in the group having active or inactive tuberculosis. Eighty per cent of those having lobectomies survived as compared to 30 per cent survival among the pneumonectomies. Among similar resections in the 41 nontuberculous patients seen in Table 7, there were roughly 50 per cent survivals in each group.

**TABLE 6—OPERATIVE RESULT BY TUMOR TYPE AND EXTENT OF RESECTION IN 20 PATIENTS WITH BRONCHOGENIC CARCINOMA AND TUBERCULOSIS**

<table>
<thead>
<tr>
<th>No.</th>
<th>Cell Type</th>
<th>Living</th>
<th>Expired</th>
<th>No.</th>
<th>Cell Type</th>
<th>Living</th>
<th>Expired</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LUL Adenocarcinoma</td>
<td>6 Yrs.</td>
<td>1</td>
<td>1</td>
<td>Squamous</td>
<td>16 Mos.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>LUL Adenocarcinoma</td>
<td>4½ Yrs.</td>
<td>2</td>
<td>2</td>
<td>Large cell</td>
<td>6½ Yrs.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>RLL Squamous</td>
<td>6½ Yrs.</td>
<td>3</td>
<td>3</td>
<td>Large cell</td>
<td>7 Yrs.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>RLL Adenocarcinoma</td>
<td>4 Yrs.</td>
<td>4</td>
<td>4</td>
<td>Squamous</td>
<td>3 Yrs.</td>
<td>3 Mos.</td>
</tr>
<tr>
<td>5</td>
<td>RUL Squamous</td>
<td>2 Yrs.</td>
<td>5</td>
<td>5</td>
<td>Large cell</td>
<td>4 Mos.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>RUL Squamous</td>
<td>3 Mos.</td>
<td>6</td>
<td>6</td>
<td>Large cell</td>
<td>1 Wk.</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>RM and LL Large cell</td>
<td>1 Yr.</td>
<td>7</td>
<td>7</td>
<td>Bronchiolar</td>
<td>1 Yr.</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>RUL Adenocarcinoma</td>
<td>1 Yr.</td>
<td>8</td>
<td>8</td>
<td>Squamous</td>
<td>15 Mos.</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>RUL Squamous</td>
<td>2 Yrs.</td>
<td>9</td>
<td>9</td>
<td>Squamous</td>
<td>9 Mos.</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>LUL Squamous</td>
<td>1 Yr.</td>
<td>10</td>
<td>10</td>
<td>Squamous</td>
<td>2 Yrs.</td>
<td></td>
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advanced carcinoma, whether or not accompanied by tuberculosis, deteriorated rapidly and died frequently within one year of diagnosis. Those with localized and early carcinoma and coexisting tuberculosis, with present day antituberculosis chemotherapy and management, responded well to surgical treatment.

Our clinicians were interested in this apparent marked difference between the prognosis of those having tuberculosis and those without tuberculosis. While a study of all facets involved becomes exceedingly complicated, it may be said that those with tuberculosis were in general slightly younger and had been followed-up more closely by clinicians interested in chest diseases. The lesions found were in general smaller, making lesser resections possible. It should be added that although extensive lymph node dissections were done, even in lobectomies, study failed to reveal metastatic carcinoma among hilar nodes. Patients with tuberculosis requiring pneumonectomy had larger tumors and led precarious lives due to pulmonary insufficiency. The 41 nontuberculous patients in general were older and had been referred to the hospital with much more extensive disease with larger tumors and evidence of hilar metastasis. As might be expected, no one bronchial carcinoma cell type had a better prognosis than the other, except that the patients with undifferentiated carcinomas did poorly.

We recognize that the association of tuberculosis and carcinoma comes at a time when there is an increasing incidence of bronchogenic carcinoma being reported generally, along with an aging and increasingly older population hospitalized for tuberculosis. If we generalized about the occurrence of each disease, we would have to say that squamous carcinoma is seen more frequently with inactive tuberculosis while undifferentiated carcinoma and adenocarcinoma are seen more often with active disease. One might say cautiously that there would be a relationship between squamous carcinoma and old healed tuberculosis, though the occurrence of these tumors among people with tuberculosis does not show the accurate localization that would be necessary to make such a statement a truism. Early carcinoma with coexisting tuberculosis presents a more favorable situation in the light of better chemotherapy and aggressive management. Again, early diagnosis and early resection appear to offer the best chances for cures. We have considered the localization of carcinoma and the length of time that the disease may be kept localized because lymphatic pathways have been disrupted and obliterated by previous tuberculous infection.

**SUMMARY AND CONCLUSION**

1. The x-ray films and pathologic findings in 54 patients with coexisting bronchogenic carcinoma and tuberculosis were com-

<table>
<thead>
<tr>
<th>Table 7—Operative Result by Type of Tumor in 17 Non-Tuberculous Patients (Positive Tuberculin Skin Test Only)</th>
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<tbody>
<tr>
<td><strong>Lobectomy</strong></td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
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</tr>
<tr>
<td>1</td>
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pared to those of 41 nontuberculous cases seen in the same institution.

2. Type of carcinoma seen in tuberculous patients appears to have the same distribution as compared to that of reported bronchogenic carcinoma not affected by tuberculosis.

3. Chronic inactive pulmonary tuberculosis was seen more frequently in patients with squamous cell carcinoma while active tuberculosis was more often associated with adenocarcinoma and undifferentiated carcinoma.

4. Errors in diagnosis due to cavitary carcinoma and negative sputum cultures showing scotochromogen organisms were responsible for delays in treatment.

5. The absence of early hilar lymph node metastasis suggests that tuberculosis may impede the spread of carcinoma.

6. We have not been able to relate the origin of carcinoma to the exact area of pulmonary tuberculosis.

7. The combination of these two diseases is not hopeless by any means. An aggressive attitude is warranted. We submit that a closer surveillance of patients in tuberculosiis out-patient services seems to afford an opportunity to treat carcinoma earlier.

**RESUMEN**

1. Las radiografías y los hallazgos anatómico-radiológicos en 59 pacientes con carcinoma broncógeno y tuberculosis pulmonar coexistentes fueron comparados con los de 41 pacientes con cáncer broncógeno, pero no afecto de tuberculosis. Todos fueron observados en la misma institución.

2. La tipología del carcinoma parece ser la misma en ambos grupos.

3. La tuberculosis crónica inactiva coincidía más frecuentemente con el carcinoma a células escamosas y la tuberculosis activa con el adenocarcinoma o el cáncer a células indiferenciadas.

4. Algunos errores de diagnóstico ocasionados por el carcinoma cavitado o por espugno-cultivos que rindieron bacilos escotochromogénesi resultaron en tratamientos tardíos.

5. La ausencia de metástasis a los ganglios linfáticos parece indicar que la tuberculosis retarda la invasión carcinomatosa.

6. No han sido posible correlacionar en este estudio el origen del carcinoma con el área afectada por la tuberculosis.

7. La coincidencia de ambas enfermedades no excluye la actuación terapéutica enérgica. Opinamos que la vigilancia atenta de los pacientes tuberculosos en los dispensarios y servicios externos de los hospitales puede propiciar el tratamiento precoz del cáncer pulmonar en un cierto número de casos.

**Zusammenfassung**

1. Die Filme, sonstigen röntgenologische und pathologisch-anatomischen Befunde von 54 Patienten, bei denen gleichzeitig ein bronchogenes Karzinom und Tuberkulose bestanden, wurden einem Vergleich unterzogen mit solchen Befunden von 41 nichttuberkulösen Patienten, die in der gleichen Anstalt zur Untersuchung kamen.

2. Der Typ des bei tuberkulösen Patienten aufgetretenen Karzinoms scheint dieselbe Verteilung zu haben im Vergleich zu den in der Literatur mitgeteilten bronchogenen Karzinomen, bei denen keine Tuberkulose bestand.


5. Das Fehlen von frühzeitigen Hiluslymphknoten-Metastasen läßt vermuten, daß die Tuberkulose die Aussaat des Karzinoms verhindern könnte.


REFERENCES

RUPERTY OF THE BRONCHUS

Traumatic tears of the major bronchial tree may be associated with a trivial, serious, and at times, fatal injury. These injuries are usually the result of crushing trauma to the chest, most commonly due to road accidents, but occasionally they arise from direct blows to the chest. At the time of the accident, the fixed, more rigid bronchus with its more resistant wall ruptures, whereas the soft mobile structures of the hilum and mediastinum usually escape injury.

Two cases of ruptured bronchus are discussed with a brief review of the literature and with essential points in diagnosis and treatment emphasized.


DETERMINATION OF TOTAL LUNG CAPACITY

The total lung capacities of 50 subjects, including both normal and pathologic states, were determined by radiographic and plethysmographic methods. The radiographic method as originally described by Barnhard, et al. was reviewed and modified. A nomogram was devised relating data to height and weight. The method of calculation was simplified. The resulting modification was tested against the original method and found to produce data of equal validity when compared to plethysmographic results.

A statistical analysis showed that the radiographic method was a reliable predictor of the plethysmographically determined total lung capacity ($r=0.966$), $p<0.001$. The overall mean difference radiographic total lung capacity-plethysmographic total lung capacity was $-62$ ml. S. D. 322 ml. The mean per cent difference $((\text{mean difference}/\text{mean plethysmographic TLC}) \times 100)$ was 1.5 per cent, S. D. 9.7 per cent.

The radiographic method produced reliable measurements of the total lung capacity with an acceptably small error in both diseased and normal chests.