

Concurrent pulmonary tuberculosis and primary carcinoma

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The relationship between chronic pulmonary tuberculosis and primary carcinoma is a purely circumstantial or fortuitous coexistence. Over a period of 14 years, 5,532 new cases of pulmonary tuberculosis and 1,218 new cases of primary malignancy of the lungs were admitted to the Missouri State Sanatorium. This report reviews 54 cases of concurrent disease and discusses the attendant difficulties in their diagnosis and treatment. Eighty-three per cent of the cases reviewed were found to be inoperable or non-resectable, indicating the urgent need for early detection. A close surveillance of patients with chronic pulmonary disease, especially those with tuberculosis and histoplasmosis, could improve the outcome of these concurrent lung diseases.

The interrelationship between coexisting chronic pulmonary tuberculosis and primary carcinoma has been enigmatical since Bayle (1815) reported three cases and classified 'cancerous phthisis' as one of his six types of tuberculosis. Subsequent attempts to relate these two diseases aetiologically varied from marked incompatibility or antagonism (Rokitansky, 1854; Pearl, 1929; Cooper, 1932) to a direct cause and effect relationship (McConkey, 1908; Ewing, 1928; Fried, 1935; Cohen, 1949; Woodruff *et al.*, 1951 and 1952; Hauser and Glazer, 1955; Bender, 1956; Finke, 1956; Weissman, 1956; Jackson, Garber, and Post, 1957; Wofford, Webb, and Stauss, 1962; Gebel, Epstein, Fulkerson, and Sparger, 1962). Several studies reported in the recent past logically speculated on purely circumstantial or fortuitous coexistence, i.e., the increasing association of the two diseases is due to adequate treatment, improved diagnostic methods, changes in the epidemiology, and increasing life expectancy (Bergmann, Shatz, and Flance, 1948; Shefts and Hentel, 1950; Carey and Greer, 1958; White, Beck, and Pecora, 1959; Christoforidis and Browning, 1959; Fontenelle and Campbell, 1970).

In reviewing our cases we could not overlook the fact that there is indeed an alarming increase in the number of patients with coexistent pulmonary diseases.

It is the purpose of this paper to report a series of 54 cases of pulmonary tuberculosis with associated primary carcinoma in the hope that our experience may help to point out the difficulties encountered in the diagnosis and treatment of these concurrent diseases.

MATERIAL

Between January 1954 and December 1968, 54 patients at the Missouri State Sanatorium had simultaneous pulmonary tuberculosis and primary carcinoma. The bacteriological evidence of tuberculosis and the histological diagnosis of primary lung carcinoma obtained in our laboratory were the sole basis for inclusion in this study. Incidentally, there were 54 other patients who had primary pulmonary carcinoma with a positive tuberculin skin test, which is an indication of previous tuberculous infection. Over the same period we admitted 5,344 new cases of typical pulmonary tuberculosis, 188 new cases of pulmonary infection due to atypical acid-fast bacilli, and 1,218 new cases of primary carcinoma of the lung.

There were 8 women in the 54 cases included in this study. Their ages ranged from 45 to 89 years with a median age of 63.5 years. The highest incidence was concentrated in the fifth and sixth decades of life. Forty-five (83.3%) cases had positive sputa for acid-fast organisms at the time the carcinoma was detected. Three of these had had sputum conversion previously—four, six, and nine years respectively. Eight cases had had positive sputa for acid-fast organisms for from one to 14 years and were found to be negative at the time the carcinoma was discovered. In only one patient

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did active tuberculosis develop after a carcinoma (alveolar-cell) had been successfully excised. This series also included three cases of pulmonary infection due to atypical acid-fast bacilli. Two patients had Runyon group III (Runyon, 1959) organism: one of these had an adenocarcinoma and the other had bilateral alveolar-cell cancers. The patient with Runyon group II also had an adenocarcinoma. None of the patients had had previous pulmonary operations for tuberculosis.

DISCUSSION

For 14 years we observed an alarming increase in the incidence of primary lung carcinoma and a gradual decrease in the incidence of tuberculosis (Table I). Noteworthy also is the increase in

TABLE I
YEARLY DISTRIBUTION OF 6,802 CASES

Year	New Cases of Pulmonary Tuberculosis	New Cases of Lung Cancer	No. with Coexisting Diseases
1954-55	467	63	1
1955-56	523	62	3
1956-57	456	79	2
1957-58	439	79	2
1958-59	516	73	4
1959-60	319	70	7
1960-61	436	68	3
1961-62	392	79	4
1962-63	386	75	4
1963-64	372	91	8
1964-65	317	131	5
1965-66	317	126	3
1966-67	296	125	5
1967-68	296	97	3
Total	5,532	1,218	54

coexistent pulmonary disease. In our institution, the average age of tuberculous patients in 1953 was 49 years; at the present time it is 61 years. This observation seems to substantiate the fact that people with tuberculosis who are adequately treated are now living into the 'cancer age group'. Several reports seem to indicate also that carcinoma of the lung is more frequent in persons who have had pulmonary tuberculosis than in the normal population (Woodruff *et al.*, 1952; Weissman, 1956; Rosenblatt and Yildiz, 1963; Steinitz, 1965). Moreover, there is a very strong suggestion that lung cancer is more likely to follow previous chronic pulmonary disease especially that characterized by the presence of prolonged irritation and a scarring process (Finke, 1956; Ripstein, Spain, and Blunt, 1968). In one case our pathologist was convinced that an alveolar-cell carcinoma had arisen from an old tuberculous scar. Chronic pulmonary histoplasmosis may be implicated as a causative factor.

We have recently reported 14 cases of pulmonary histoplasmosis associated with primary lung carcinoma (Berroya, Polk, and Najafi, 1970).

Carcinoma of the lung may reactivate an old primary tuberculous lesion by breaking into old tuberculous foci (Nuessle, 1953; Greenberg *et al.*, 1964). It could understandably cause tuberculous breakdown or reactivation because of the consequent debility, cachexia, and loss of resistance (Cohen, 1949; Overholt, 1950). These reasons may explain why 83.3% of our cases had active tuberculosis at the time the carcinoma was discovered.

Of the 54 cases, 38 were considered inoperable (Table II). Six of these patients were in the

TABLE II
CONCURRENT LUNG TUBERCULOSIS AND CARCINOMA

Cell Type	Inoperable	Non-resectable	Resectable	Total
Squamous cell	18	3	7	28
Adenocarcinoma	7	-	1	8
Oat cell (Small cell)	3	1	-	4
Anaplastic (Large cell)	6	2	-	8
Alveolar cell	2	-	1	3
Undetermined	2	1	-	3
Total	38	7	9	54

terminal stages of carcinoma and died a few days after admission. All six had positive sputa for acid-fast organisms and one had miliary tuberculosis. The other 32 inoperable cases had clinical evidence of extensive and widespread carcinoma. Seven patients who appeared to be inoperable had exploratory thoracotomies, but the lesions were found to be non-resectable. In only nine cases were the lesions amenable to adequate resection. Four patients were operated upon for residual cavitary tuberculosis, and coincidental primary carcinoma was found in the resected specimen. These four patients survived for more than five years postoperatively. All resectable cases were treated with antituberculosis chemotherapy postoperatively.

Our experience has been that the prognosis in these cases was very poor, generally because they were diagnosed too late and the tumours were large and had spread beyond resectability. Those that were resectable required extensive operation. Residual adhesions and fibrosis of a tuberculous process were usually severe and vascular, which posed great technical difficulty and necessitated prolonged dissection. Many of the patients had had chronic pulmonary insufficiency and this weighed heavily against major operative pro-

cedures. Patients with old chronic tuberculosis have a poor muscle mass and a depleted metabolic reserve so that attendant postoperative complications such as poor healing, fistula formation, superinfection, etc., are fairly common.

A high index of suspicion in high-risk patients will improve the cure rate. We consider as high-risk patients those who are over 50 years and who are chronic cigarette smokers. The earliest sign of pulmonary carcinoma in the presence of tuberculosis is an atypical course of the latter, usually noted in the chest radiograph. All patients treated with antituberculosis drugs, especially with sensitive organisms, should be carefully and closely watched. During the course of such treatment, typical pulmonary lesions which are unresolving or actually worsening demand an aggressive attitude. Such lesions must be explored whenever possible after an early bronchoscopy (Gebel *et al.*, 1962; Woodruff *et al.*, 1952) and adequate tissue biopsy. In cases in which the diagnosis of tuberculosis is not clear-cut, an aggressive diagnostic attitude should also be taken.

Radiologically, the sudden appearance of new lesions, especially in atypical locations, segmental or lobular atelectasis, unilateral hilar enlargement, thick-walled cavities, and a localized pneumonic process are all signs suggestive of carcinoma. Our retrospective review showed that in at least 10 (19%) cases these changes were neglected as evidence of carcinoma by the local practitioners. The review also revealed that 27 (50%) did manifest at one time or another atypical symptoms of pulmonary tuberculosis. It is interesting that physicians tend to consider only one disease process at a time. Clinically, persistent and profuse haemoptysis, localized unilateral wheeze or rhonchi, constant localized pain, persistent cough, paroxysmal dyspnoea, and prolonged low-grade fever are atypical manifestations of pulmonary tuberculosis.

In conclusion, we strongly believe that a close surveillance of patients with pulmonary tuberculosis or chronic pulmonary disease will afford an early opportunity to diagnose and consequently improve the prognosis of this dismal combination of diseases.

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