The Coexistence of Primary Lung Cancer and Other Primary Malignant Neoplasms*

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A solitary pulmonary lesion in a patient having a proved primary malignant neoplasm in another site presents a crucial problem in differential diagnosis. Many physicians feel that an heroic attempt to remove a pulmonary metastatic lesion by thoracic operation is an unjustifiably radical procedure. The possibility, however, that the presumably metastatic lesion may in fact be a second and potentially curable primary malignant lesion must always weigh heavily in the thoughts of even the most conservative. Cotton,1 as well as others, has presented differential factors in the diagnosis of primary and metastatic pulmonary neoplasms. He pointed out that a history of hemoptysis, the presence of cavitation, and a location in the upper part of the lung are all more characteristic of primary than of metastatic lung cancer. Whereas these features may help characterize a large series of patients, Kelly and Langston2 more recently have demonstrated that for the individual patient, the clinical differentiation between these two situations is difficult if not impossible.

The study by Kelly and Langston2 agreed with another by Cahan3 in demonstrating that the presence of a second primary cancer in the lung is not an uncommon problem. In Cahan’s series of 2502 cases of primary lung cancer seen at the Memorial Cancer Center, a total of 81 patients had proved primary cancers at some extrapulmonary site—a rate of occurrence of 3.2 per cent. During the same period at the same institution, only 18 patients were found to have a solitary pulmonary metastatic neoplasm. From a study of 22 patients undergoing exploratory operation for solitary pulmonary lesions diagnosed preoperatively as metastatic, Kelly and Langston2 reported that four were found at thoracotomy to have unsuspected primary lung cancers. They concluded that in patients in whom there is reasonable evidence that a primary malignancy has been

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controlled, the presence of a discrete pulmonary lesion is an absolute indication for thoracotomy.

Selection of Cases

Cases for the present study were selected from those in which a histologic diagnosis of lung cancer was confirmed at the Mayo Clinic during the 10-year period from January 1, 1944, to December 31, 1953. The clinical and surgical findings were studied in all cases of this group that had been indexed under the diagnosis of a second malignant disease. Cases were accepted for study only if the diagnoses of both neoplasms had been confirmed by laboratory examination of surgical or necropsy specimens; a clinical diagnosis without a pathologist's confirmation was not considered sufficient evidence for inclusion in this study. Also, cases in which the lung cancer was diagnosed by cytologic examination of the sputum alone were excluded. Cases in which a neoplasm had been diagnosed and treated elsewhere prior to diagnosis of another neoplasm at the clinic were accepted for study only if the pathologic material from the former had been submitted to the clinic for examination. In brief, then, all the patients whose cases are included in our study had a lung cancer plus another unequivocally malignant neoplasm verified in the clinic laboratories during the period of this study.

The following criteria established by Warren and Gates in 1932 have been generally accepted in the recent literature dealing with the problem of multiple primary malignant neoplasms, and are the criteria used for the selection of cases in the present study. 1. Each of the tumors must present a definite picture of malignancy. 2. Each must be distinct. 3. The probability that one is a metastatic product of the other must be excluded.

The fact that the lung is a common site for almost all types of metastatic malignant lesions compounds the difficulty of establishing a pul-

FIGURE 1: Bronchogenic carcinoma, small cell type, metastatic to adenocarcinoma, hypernephroma type of the kidney (hematoxylin and eosin; × 75).
monary lesion as a true second primary cancer. Several cases initially diagnosed as presenting second primary cancers in the lung were discarded from present study because after review of the pathologic material doubt existed as to whether the pulmonary lesion was actually a primary lesion. Some of these discarded cases possibly represented true but unconfirmable primary cancers.

**Observations**

During the 10-year period included in this study, a total of 1588 patients at the Mayo Clinic had the diagnosis of primary cancer of the lung, bronchus, or pleura confirmed by laboratory examination of specimens obtained at bronchoscopy, thoracotomy, or necropsy. Of this group a total of 65 patients, or 4.1 per cent, were found to have one or more other primary malignant neoplasms. Of these patients 59 were male and six were female.

In 27 cases the lesions were diagnosed simultaneously; in eight cases diagnosis of the pulmonary lesion preceded the diagnosis of the other neoplasm by periods of one to five years; and in 30 cases the diagnosis of the pulmonary lesion followed the diagnosis of the other neoplasm by periods of one to 29 years (average 9.6 years).

In 24 cases both lesions were diagnosed at operation only; in eight cases both lesions were diagnosed at necropsy only; and in 33 cases one or more lesions were diagnosed both at operation and at necropsy.

The distribution of the specific types of second primary cancers, shown in the table, does not seem significantly different from that to be expected in a random selection of patients of comparable age and sex with single malignant neoplasms. It is of interest that 37 of Cahan's series of 81 patients, or 46 per cent, were found to have their second primary lesions involving the oral cavity or larynx. He postulated that this association could represent the effect of a common etiologic agent in cancers of the oral cavity, larynx, and lung. In our study, only seven of 65 patients, or 11 per cent, had second primary lesions in these locations. Since the vast majority of patients with lung cancer are males in the older age groups,
this does not seem a disproportionate representation of cancers of the
oral cavity and larynx.

Of incidental interest is the fact that at necropsy a primary carcinoma
of the lung was found that had metastasized to a primary cancer of the
kidney (figure). It appears that instances in which one malignant neo-
plasm is found to have metastasized to a second independent malignant
neoplasm are exceedingly rare; when Ortega and associates\(^3\) reviewed the
literature in 1961 they could find only eight reported cases.

Comment

The evidence presented here as well as in the other works cited seems
to establish definitely that the occurrence of an independent primary
lung cancer in a patient with known malignant neoplastic disease at
another site is not uncommon. Therefore no solitary pulmonary lesion
in a patient with a previously diagnosed cancer may be simply assumed
to be metastatic without positive laboratory confirmation. The present-
day risk of thoracotomy in an otherwise doomed patient should be incon-
sequential when weighed against the possible tragedy of ignoring a poten-
tially curable lung cancer on the grounds that it may be a solitary meta-
static lesion. Indeed, even if the lesion should prove to be metastatic, hope
may be found in Cahan's\(^3\) records of many patients with surprisingly long
survival and no evidence of metastasis to other sites following excision of
a solitary metastatic pulmonary lesion.

SUMMARY

A total of 1,588 cases of pathologically confirmed primary lung cancer were
seen at the Mayo Clinic from January 1, 1944, to December 31, 1953. Of this
group, 65 patients, or 4.1 per cent, were found to have an independent primary malignant
neoplasm at some other site.

The distribution of the specific types of associated primary malignant neoplasms did
not differ significantly from that expected in a comparable group of patients with
single malignant neoplasms.

The coexistence of primary cancer of the lung and other primary malignant neo-
plasms occurs with sufficient frequency that no single pulmonary lesion may be
assumed to be metastatic without positive pathologic confirmation. This series serves
as further evidence supporting the conclusion of Kelly and Langstron\(^2\) that in cases
affording reasonable evidence that a primary malignancy elsewhere has been con-
trolled, the presence of a discrete pulmonary lesion is an absolute indication for
thoracotomy.

RESUMEN

Se han visto un total de 1,588 casos de cáncer primitivo del pulmón confirmados
anatomopatológicamente en la Clínica Mayo, desde Enero 1, de 1944 hasta Diciembre
31 de 1953. De este grupo 65 enfermos o sea el 4.1 por ciento se encontró que tenían
una neoplasia primaria maligna independiente en alguna otra parte del organismo.

La distribución de las formas específicas de la asociación primaria maligna no se
difirió significativamente de lo que se esperaba en un grupo comparable de enfermos
con neoplasias malignas únicas.

La coexistencia de cáncer primitivo del pulmón y de otras neoplasias malignas
primitivas ocurre con suficiente frecuencia de tal modo que no se puede asegurar
que haya una metástasis verdadera sin la confirmación histopatológica. Esta serie
sirve para afirmar más la conclusión de Kelly y Langstron de que en casos que
ofrezcan razonable evidencia de que un neoplasma primario en otra parte, ha sido
dominado, la presencia de una lesión pulmonar discreta es una indicación absoluta
para la toracotomía.

RESUME

Un total de 1,588 cas de cancer primitif du poumon confirmé anatomo-pathologique-
ment, ont examiné à la Clinique Mayo, de janvier 1944 au 31 décembre 1953. Sur cet
ensemble 65 malades, c'est-à-dire 4,1% furent trouvés porteurs d'un cancer d'un cancer
primitif indépendant siégeant à un autre endroit.
Les types spécifiques de cancers primitifs associés ne diffèrent pas d'une façon importante de ce qu'on a constaté communément chez un groupe comparable de malades atteints de néoplasie maligne à localisation unique.

La coexistence de cancer primitif du poumon et d'autres néoformations malignes primitives se rencontre avec une fréquence suffisante pour qu'on ne puisse jamais assurer sans confirmation anatomo-pathologique, qu'une lésion pulmonaire est métastatique. Cet ensemble d'observations apporte une démonstration ultérieure à l'affirmation de Kelly et Langstrom que, lorsqu'on a la preuve incontestable qu'un cancer primitif a été traité efficacement quelque part, la présence d'une lésion pulmonaire discrète est une indication absolue de thoracotomie.

ZUSAMMENFASSUNG


Die Aufteilung der spezifischen Typen von gleichzeitig vorkommenden primären bösartigen Tumoren differierte nicht wesentlich von einer solchen, die zu erwarten war in einer vergleichbaren Gruppe von Kranken mit nur einem einzigen bösartigen Neoplasma.

Die Koeexistenz von primärem Lungenkrebs und anderen primären bösartigen Neoplasmen ereignet sich mit genügender Häufigkeit, sodass man von einem einzelnen Lungenherd nicht mit Sicherheit sagen kann, er sei metastatisch ohne positive pathologisch-anatomische Bestätigung. Diese Serie dient als weiterer Beweis zur Stütze der Schlussfolgerung von Kelly und Langstrom, wonach in Fällen, die genügend Anhaltspunkte dafür bieten, dass ein primärer bösartiger Tumor mit anderem Sitz beherrscht ist, das Vorliegen eines diskreten Lungenherdes eine absolute Indikation zur Thorakotomie bedeutet.

REFERENCES