PRIMARY APICAL LUNG CARCINOMA

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The usual locations of primary lung cancers and their clinical manifestations have been described in many papers and are today well known. Pancoast (1) recently described an unusual syndrome caused by small cancers at the apex of the lung. It is characterized by pain in the arm and shoulder, Horner's syndrome, atrophy of the hand muscles, and destruction of bone, usually the adjacent vertebrae and ribs posteriorly. There is a striking absence of intrathoracic metastasis, as shown by roentgenologic studies. No post-mortem studies were made in his series of seven cases. In two cases biopsy specimens showed carcinoma. One is recorded as carcinoma spinocellularare and in the other the type is not given. Pancoast calls these cancers "superior pulmonary sulcus tumors," and suggests that they arise from an embryonic remnant of the fifth branchial pouch.

We have studied three cases which seem to belong in this group and from our observations believe that the tumors originated in the lung and that they are a clinically distinct and generally unrecognized type of cancer. Two cases were studied at autopsy; in the other biopsy was done.

Fig. 1. Case I: Dense Apical Shadow Extending from the Apex Down to the Level of the Anterior Portion of the Second Rib (Dec. 11, 1933)

Neither on this film nor on a second one made Jan. 23, 1934, was there evidence of invasion of ribs.
Case I: Clinical History: T. P., an Italian male, machinist, thirty-two years old, was first seen at the University of Chicago Clinics (No. 95380) on Dec. 9, 1933. He had been well until four months before admission, when he first noticed pain in the left scapular region, which became worse and extended to the left axilla, forearm, neck, and shoulder. He had had no dyspnea or cough, but had lost twenty-five pounds in weight. A drooping of the left eyelid had been noticed for approximately four weeks. One month previously the patient had undergone tonsillectomy, had teeth extracted, and had been given vaccine therapy because of the shoulder pain.

Physical examination revealed a Horner's syndrome on the left. There was ptosis of the left eyelid and the left pupil was contracted. The left chest was flushed and warmer than the right. The trachea deviated slightly to the right. The posterior occipital lymph nodes were enlarged and tender. There were dulness, diminished tactile fremitus, and diminished voice and breath sounds over the apex and upper lobe. Fingers and toes were markedly clubbed. The Wassermann and Kahn tests were negative. The red blood cells, hemoglobin, white blood count, differential count, and findings on urine analyses were normal. A biopsy examination of a cervical lymph node showed no tumor tissue.

X-ray examination revealed a dense apical shadow extending down to the second rib anteriorly; no rib involvement was noted (Fig. 1).

The lung tumor was given x-ray irradiation as follows: Anterior left apex, 2822 r measured in air; posterior left apex, 3828 r measured in air; 200 kv., 25 ma., 50 cm. focal skin distance, through 1 mm. copper and 1 mm. aluminum; portals 15 cm. in diameter. This treatment was given over a period of twenty-five days. Erosion of the sixth and seventh cervical vertebral bodies became demonstrable (Fig. 2), and an additional 2550 r units was given to the cervical spine during the following ten days. Nevertheless, the pain increased, and cough, fatigue, and further loss of weight occurred. Intense pain in the buttock and leg later drew attention to a pelvic metastasis, osteolytic in type (Fig. 3). The patient's condition became steadily worse. There was no demonstrable decrease in size of the lung tumor under the x-ray irradiation, and death occurred on Feb. 1, 1934, about six months after the first symptoms appeared.

Post-Mortem Examination: The left pleural cavity was completely obliterated by fibrous adhesions. The apex of the left lung contained a firm tumor mass (Fig. 4) which was adherent to and infiltrated into the first, second, and third ribs posteriorly. It was adherent to the bodies of the seventh cervical and first thoracic vertebrae. The mass extended into the base of the neck to within one centimeter of the thyroid gland. It surrounded the left common carotid and subclavian arteries and accompanying veins but did not invade them. The mass measured 5 by 4.5 by 3.5 cm. It had grown through the
pleura, forming a layer 5 mm. thick in which there was no coal pigment. The mass was firm, pale yellowish gray in color, and showed irregular areas of degeneration. The bronchi coming to this apical tumor were of the usual size and disappeared in the mass. The remainder of the left upper lobe, and the left lower lobe, showed a hyaline bronchopneumonia, hyperemia, and edema.

The right lung showed a fibroplastic tuberculous scar at the apex, a subpleural calcified nodule at the base of the upper lobe, and a hyaline bronchopneumonia, hyperemia, and edema.

The tracheobronchial lymph nodes were enlarged and soft, but there was no evidence of tumor metastasis. No metastases were seen in the lymph nodes at the base of the neck or in the superior mediastinum.

In the right ilium, just lateral to the sacro-iliac joint, was an osteolytic tumor mass measuring 10 by 10 by 8 cm. in size. Extending from it was an accessory mass which was invading the muscles of the buttock. It was 9 by 7 by 4 cm. in size. This tumor tissue was pale yellowish gray in color and was softer than the lung tumor. It contained cyst-like areas up to several centimeters in diameter, filled by a thick, tenacious, mucinous material.

There were moderate emaciation, an acute splenic hyperplasia, and parenchymatous degeneration of the liver and kidneys. The brain was not examined.

Microscopic Findings: The lung tumor showed very large, anaplastic cells lying singly and in groups in a dense connective-tissue stroma (Fig. 5). There was great variation in the size, shape, and staining reaction of the cells. Most of them had an abundant, eosinophilic, finely granular cytoplasm. Most of the nuclei were hyperchromatic. On account of the marked anaplasia, mitotic figures could not be definitely identified. Signet-ring cells were occasionally seen. By actual measurement the largest cell seen was 126.5 microns in diameter; the largest nucleus 80 microns. There were large areas of necrosis. In a few places the cells formed small alveoli with a mucin-like material in the lumen. There were other areas in the tumor made up of masses of smaller cuboidal cells with

![Image](image-url)
FIG. 5. CASE I: APICAL LUNG TUMOR, SHOWING MARKED CELL ANAPLASIA AND CELL INJURY APPARENTLY DUE TO X-RAY IRRADIATION. \( \times 240 \)

FIG. 6. CASE I: PELVIC METASTASIS, MUCUS-SECRETING ADENOCARCINOMA. \( \times 85 \)
round to oval nuclei and with a cytoplasm less acidophilic than the larger cells described. In some places they formed tubules. In other portions there was a definite admixture of the two cell types. This tumor had received heavy x-ray irradiation, but some of the cells may have appeared after the treatment was discontinued.

The iliac bone metastasis which had not been irradiated showed a more uniform structure. It was made up mainly of alveoli of varying size with much mucin-like material in the lumina (Fig. 6). The secreting cells were cuboidal to high columnar and were very large. The nuclei tended to be lined up at the base, and the cytoplasm of the free ends was pale and finely vacuolated. The nuclei were hyperchromatic and anaplastic. A few mitotic figures were seen. In a few areas the cells were in sheets and masses, no lumen being present. There were small areas of necrosis. The tumor was actively invading and destroying the gluteal muscles.

Mucicarmine stains of the apical lung tumor and of the iliac metastasis showed some of the material in the lumina to stain like mucin. The distal ends of some of the lining cells took the specific mucin stain. In some isolated cells not related to lumina there were mucin staining globules in the cytoplasm.

There were no microscopic metastases noted other than the pelvic tumor.

Case II: Clinical History: E. R., forty-two years of age, Serbian, unemployed photographer, male, was first admitted to the University of Chicago Clinics (No. 87272) on July 28, 1933. His illness had begun five months before admission, with sharp, shooting pains in the upper right chest and shoulder. Soon after that he had the first of a series of severe chest colds productive of a frothy sputum, and with night sweats. A tonsillectomy had not improved his condition. Three months before admission he first observed a small mass in the right supraclavicular space, and a week later he noticed a chain of small nodules extending up in the neck. Shooting pains now appeared on the ulnar side of the right arm, accompanied by weakness and numbness in the arm. The chest pain became so severe as to cause difficulty in breathing. The left side of the face perspired profusely while the right side was dry. There was a loss of twenty pounds of weight in five months. The patient lost strength rapidly and had been in bed for three weeks before admission. Weakness of the legs was especially marked, and there was numbness of the feet. There had been a brief period of urinary retention and marked constipation.

Physical examination revealed a Horner's syndrome on the right side. The voice was
husky. There was a chain of enlarged posterior cervical lymph nodes. Low in the neck these fused with a mass in the supraclavicular fossa. This in turn appeared continuous with a smaller mass in the infraclavicular fossa. Physical signs pointed to consolidation in the right pulmonary apex. There was atrophy of the muscles of the right hand, with marked loss of strength in the arm. Weakness of the legs and paresthesias below the level of the fourth thoracic segment were present. Spinal puncture revealed a block in the spinal canal. X-ray studies showed a mass in the apex of the right lung (Fig. 7). The vertebrae and ribs were not perceptibly involved.

The blood and urine were normal. The Wassermann and Kahn tests were negative. The histamine test for gastric function was normal. A biopsy specimen from the supraclavicular mass showed an undifferentiated carcinoma.

It was thought that the spinal canal was invaded by tumor tissue causing a partial block at the fourth dorsal segment and that the disturbances in the right arm and hand were due to direct involvement of the cervical roots on that side by tumor tissue.

X-ray irradiation was given as follows: 200 kv., 25 ma., 50 cm. focal skin distance, with 1 mm. copper filter and 1 mm. aluminum filter, four portals each 15 cm. in diameter—(a) anterior right apex, 3467 r measured in air; (b) posterior right apex, 365 r; (c) right cervical, 3726 r; (d) cervical spine, 3770 r. This treatment was given between Aug. 3 and Sept. 21, 1933. At first the neurological symptoms progressed, resulting in a complete paraplegia. As the treatment was continued, however, sensation, motion, and visceral control returned, and spinal puncture showed the block to be relieved.

The lung mass under treatment showed no change in size and density. The patient was discharged symptomatically improved. He died, however, at another hospital two months later, and nine months after the onset of symptoms. There was no autopsy, and it is not known if there was finally invasion of bone.

Biopsy Specimen: The specimen consisted of a group of lymph nodes, the largest of which was about 1.5 by 0.75 cm. The cut surface was soft and bulging, with no visible areas of necrosis except in one of the smaller nodes.

Microscopic study of the largest node showed it to be replaced by an undifferentiated type of carcinoma except for a narrow zone of cortical tissue at the periphery (Fig. 8). The tumor cells were densely packed, with no stroma, and with a tendency to radial ar-
rangement around blood vessels. This seemed to compress the cells into spindle shapes in some places. The cells were of medium size with moderately abundant cytoplasm and pale nuclei. Cell anaplasia was very marked, and among the numerous mitotic figures a fair number were multipolar. The original trabeculae were much widened and bore an increased blood supply. Groups of tumor cells occupied the lymphatics of the capsule. In relation to an area of thickened capsule in one lymph node, marginally infiltrated by tumor, the connective tissue showed myxomatous changes. In different lymph nodes there was a varying degree of tissue necrosis, one being almost entirely necrotic.

Case III: Clinical History: Mrs. C., white, sixty-two years old, had had a dull pain in the left shoulder, left side, and back for six months. This was continuous and grew worse. Six weeks before death she had a general bronchitis and at that time dullness

was first noticed over the upper part of the left lung. X-ray studies were not made. No other history was available. The patient died in 1907.

Post-Mortem Findings: The examination was made by Dr. H. Gideon Wells. The left pleural cavity was obliterated by dense fibrous adhesions except for a few small spaces in the lower portion, which were filled with fluid. The upper lobe of the left lung and the posterior parietal pleura from the summit of the apex to the fourth rib were occupied by a large tumor mass which bound them together (Fig. 9). Over an area 7 cm. in diameter which included the second and third ribs from the vertebra out, the tissue was completely eroded and infiltrated with the tumor mass, and the ribs in this area were destroyed. The tumor involved the back muscles as far as their attachment to the vertebrae but did not affect the scapula. The tumor itself measured 8 cm. in diameter. The overlying visceral pleura was thickened to one centimeter. The tissue was of uniform yellowish white color and of cartilaginous consistence at the site of the pleura, but grew softer and softer as it invaded the muscles and lung. It did not extend beyond the upper border of the lower lobe.

The peribronchial, mediastinal, infraclavicular and supraclavicular lymph nodes contained metastatic tumor growth. The right lung showed no evidence of tumor tissue. In
the right kidney a tumor mass measuring 3 cm. in diameter was found. It resembled the lung tumor and was free of degenerative changes.

The left common carotid artery was completely occluded by a red fibrous thrombus which extended to and protruded into the aorta. A similar clot filled the beginning of the left subclavian artery. This artery was surrounded by a mass of enlarged lymph nodes, densely adherent to each other. There were no other essential findings.

**Histopathology** (Fig. 10): The tumor consisted of cords and islands of large, irregular, polygonal, deeply-staining cells. They had considerable cytoplasm and large vesicular nuclei with a fair number of intermixed multinucleated cells. Nucleoli were of moderate size and sometimes multiple. Giant cells were seen, especially in the lung, where the tumor was older. Mitotic figures were numerous. There was much fibrous tissue re-

**Discussion**

Cases I and II unquestionably belong in the group described by Pancoast. These patients had small apical lung tumors which showed no ante-mortem evidence of intrathoracic metastasis, and Case I showed erosion of cervical vertebrae. Both patients had Horner’s syndromes, pain in the arm and shoulder, and in Case II there was atrophy of the hand muscles. Neither patient showed any roentgenological evidence of involvement of any of the upper three ribs, but it is known from the autopsy findings that this was present in Case I. The absence of roentgenologically manifest invasion in Case II, therefore, does not indicate that it did not occur.

Although the clinical record in Case III is incomplete, from the avail-

**Fig. 10. Case III: Apical Tumor, Medullary Carcinoma with Areas of Degeneration and Secondary Infection. × 140**

action. Large areas of necrosis were present. In the lung the tumor formed anastomosing irregular cords and plugs of the cells. Here there were much necrosis and leukocytic infiltration around the tumor.

The tumor metastases in the lymph nodes and kidney showed a microscopic structure similar to that in the lung.
able history, and from the post-mortem findings of apical lung tumor with destruction of ribs and relative absence of intrathoracic metastasis, this case probably also belongs in this group.

In the clinical findings and gross pathological characteristics these cases are unlike the picture expected in carcinoma of the lung. However, microscopically they represent three types of growth commonly found in primary lung carcinomas. Case I is an adenocarcinoma secreting much mucin. It reproduces the histopathological structure seen occasionally in cancers arising from the large and medium-sized bronchi. Case II is a very anaplastic, undifferentiated carcinoma. In some places its structure strongly suggests the "oat-cell" type formerly considered to be sarcomatous. It is one of the commonest histopathological types of carcinoma of the lung. Case III is an undifferentiated, medullary carcinoma, a common type of lung cancer.

While these tumors from their histopathological appearance might well have originated in the lung, there is nothing to suggest from either their gross or microscopic characteristics that they arose in remnants of branchial pouches. Ewing states (2) that the structure of branchiogenic carcinomas is commonly that of adult acanthomas and that they are commonly cystic.

It is interesting that neither of the lung tumors changed in size while under observation, a period of about seven weeks in Case I and two months in Case II. If the tumor originated in a branchial pouch situated low in the cervical region, one would expect early involvement of the brachial plexus by the tumor on its way of invasion into the thorax and lung. In the first case, where symptoms of peripheral nerve involvement appeared only four months before admission and of sympathetic involvement only one month before admission, we should expect most of the pulmonary growth to occur subsequent to this, if the tumor originated in the neck. In this event we would expect some change in size of the intrathoracic portion of the tumor during the period of observation, if it were as rapidly growing as the above reasoning would indicate. However, since no change in size occurred, it is more logical to assume that the tumor originated in the upper portion of the lung, grew slowly, probably over a period of months, and finally produced symptoms and precipitated the rapid decline after it began to invade the surrounding structures. As a result of its position in the apex and probable origin in a very small bronchus, it did not produce symptoms as early as the usual carcinoma of the lung, which begins in a relatively large bronchus and early causes obstruction with consequent severe symptomatology. We have seen carcinomas of the lung which were so small as to produce no pulmonary symptoms but with widespread metastasis. In one case, beginning in a small bronchus in an apex, the tumor early in the course of its growth invaded a blood vessel and the patient died of widespread bony metastasis, before any pulmonary symptoms or x-ray findings were present. Without this accidental direction of growth the tumor might have grown to produce one of these so-called superior pulmonary sulcus tumors. In another case a carcinoma sol-
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idly involved an apex but did not produce any neurological changes, death occurring in this case also from widespread metastasis.

It is also of interest that in both Cases I and II tonsillectomies were performed, presumably because it was thought that the shoulder pain was rheumatoid in origin. In Case I the clubbing of the fingers was marked and out of all proportion to the extent of the pulmonary involvement.

It is logical to assume that the discrepancy in the histological appearance of the pulmonary tumor from that of the pelvic metastasis in Case I was due to irradiation of the former. This difference is described and illustrated because these changes due to irradiation together with the dosage employed are altogether too uncommonly recorded in cancer literature.

Jacox (3) has recently reported two cases studied in detail that seem to belong in this group of intrathoracic tumors. He also considers them an atypical form of primary bronchogenic carcinoma. Fried (4) is of the same opinion concerning these tumors.

SUMMARY

Three cases of primary apical lung carcinoma resembling those described by Pancoast and considered by him to originate in remnants of branchial pouches are described. The clinical studies, biopsy examination in one case, autopsy findings in two cases, and the effects of x-ray irradiation in one case are described and illustrated. The evidence from these cases points to an intrapulmonic origin.

Note: The irradiation therapy in Cases I and II was given under the direction of Dr. Alexander Brunschwig of the Tumor Clinic.

References