CALIFORNIA TUMOR TISSUE REGISTRY

SEVENTY-TWO SEMI-ANNUAL SLIDE SEMINAR

ON

PULMONARY AND INTRATHORACIC TUMORS

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SUNDAY, DECEMBER 6, 1981
9:00 A.M. - 4:30 P. M.

REGISTRATION: 7:30 A.M.

NEWPORT BEACH MARRIOTT HOTEL
NEWPORT BEACH, CALIFORNIA

Please bring your protocol, but do not bring slides or microscopes to the meeting

CONTRIBUTOR: Patrick W. Riley, M. D.
Los Angeles, California

DECEMBER 6, 1981 - CASE 1

ACCESSION NO. 19855

TISSUE FROM: Left lung

CLINICAL ABSTRACT:

History: This 41-year-old female presented with a 3-day history of cough with pain in the left chest, productive of clear sputum. She had a history of several episodes of pneumonia in the previous year, and had noted a twenty pound weight loss in the last three months. There was also a history of night sweats, and a 25 pack-year history of smoking.

Radiograph: A chest x-ray revealed almost total collapse of the left lung.

SURGERY: (January 6, 1972)

Bronchoscopy revealed a friable mass in the left main stem bronchus, 2 cm. distal to the tracheal bifurcation. On January 13. 1972, a left pneumonectomy was performed.

GROSS PATHOLOGY:

The specimen was a left lung weighing 310 grams in the fixed state, with an attached 3 cm. length of bronchus. Arising 1.5 cm. distal to the surgical margin within the bronchial wall was a yellow tumor measuring 5 x 1.5 x 1.2 cm. It appeared to infiltrate the parabronchial lung parenchyma.

CONTRIBUTOR: W. E. Carroll, M. D.
Santa Barbara, California

DECEMBER 6, 1981 - CASE 2

ACCESSION NO. 22307

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: This 21-year-old female suffered a traumatic pneumothoray in an automobile accident 2 year prior to the current admission. At that time a chest x-ray showed a small right lower mediastinal mass approximately 2.5 cm. thought to be a resolving hematoma. Two months prior to the current admission, a repeat chest x-ray revealed a large mass measuring 8 cm. in a similar location. She was totally asymptomatic.

SURGERY: (April 22, 1977)

A right lower lobectomy was performed. At surgery the tumor was found to be homogenous yellow tumor and was not in the mediastinum as was suspected. It was located in the superior division of the right lower lobe.

GROSS PATHOLOGY:

The specimen was a right lower lobe of lung measuring 15.5 x 8.6 x 5.0 cm. and weighing 145 grams. The external surface was smooth, glistening and pink-tan. Near the hilum, but surrounded by lung parenchyma, was a 5.0 cm. nodule, compressing adjacent lung parenchyma. The cut surface of the nodule was yellow, bosselated, and relatively homogenous. There was no apparent connection to a bronchus.

FOLLOW UP:

As of May 16, 1978, the patient was doing well without recurrence. Since then she has moved and has been lost to follow-up.

CONTRIBUTOR: William E. Cowell, M. D.
Oceanside, California

DECEMBER 6, 1981 - CASE 3

ACCESSION NO. 23010

TISSUE FROM: Right pleura

CLINICAL ABSTRACT:

History: This 59-year-old male presented with a two month history of malaise, anorexia, and fatigue. There was four week history of a dry cough and right pleuritic chest pains.

Physical findings were negative except for diminished breath sounds in the right lower chest and dullness to percussion.

A chest x-ray demonstrated a right pleural effusion that was not apparent in films taken 5 weeks earlier. Also a 1.5 cm. right pleural density was noted.

On November 23, 1977 he underwent bronchoscopy, right scalene lymph node biopsy, and right thoracentesis. The bronchoscopy was negative, the lymph node showed no tumor, and the thoracentesis yielded 1,600 cc of tan, slightly turbid pleural fluid which was negative for tumor.

SURGERY: (December 1, 1977)

A right thoracotomy and biopsy was performed. He had nodules up to 2½ cm. in size studding the parietal pleura and the diapharagmatic pleura.

GROSS PATHOLOGY:

Two portions of fibro-membranous tissue were submitted. Both pieces were studded by 1 to 4.5 cm. yellow-tan nodules, which exhibited a homogenous cut surface.

FOLLOW UP:

Post-operative chemotherapy consisted of cytoxan, 5-fluorouracil, vincristine, and methotrexate. The patient expired on June 25, 1978, without benefit of an autopsy.

CONTRIBUTOR: David Rogers, M. D.
Santa Monica, California

DECEMBER 6, 1981 - CASE 4

ACCESSION NO. 24103

TISSUE FROM: Left lung

CLINICAL ABSTRACT:

History: A 69-year-old Caucasian male was found to have a mass in the left lower lung field on chest x-ray. The mass was benign-appearing and was followed for several years. The mass had recently enlarged, but he was still asymptomatic. He had smoked one pack per day for 35 years but had quit in 1960. There was no history of exposure to carcinogens.

Physical Examination: Lung fields were clear and diaphragmatic excursion was normal.

Radiograph: A mass in the mid to posterior zone of the left lower lobe was present. It was circular and contiguous with the left hemidiaphragm. It appeared to be much enlarged when compared to radiographs from previous years.

SURGERY: (November 14, 1980)

A large mass was attached to the left lower lobe by adhesions to the inferior pulmonary ligament, from which its blood supply originated. The tumor was removed.

GROSS PATHOLOGY:

A bosselated apparently encapsulated 9.5 x 8 x 6 cm. tumor weighing 199 gm. was submitted. The capsular surface was fairly smooth with prominent vascularity. There was a thin 2 x 1.5 cm. attachment to a small portion of visceral pleura and lung. On sectioning half the specimen was comprised of rubbery tan trabeculated tissue with small areas of cystic degeneration, and half was soft friable tan spongy tissue.

FOLLOW UP:

As of July 1981 the patient is currently doing well with no evidence of recurrent tumor.

CONTRIBUTOR: A. L. Dollinger, M. D.
Hanford, California

DECEMBER 6, 1981 - CASE 5

ACCESSION NO. 22681

TISSUE FROM: Lower, lobe, left lung

CLINICAL ABSTRACT:

History: A 63-year-old female had a coin lesion noted on routine chest x-ray. She was entirely asymptomatic. She has been a resident of the San Joaquin Valley during her entire life. Skin tests for Valley Fever and TB were negative.

Radiograph: A 1.8 cm. sharply circumscribed coin lesion was present in the left lower lobe.

SURGERY: (November 29, 1977)

A left thoracotomy with removal by excisional biopsy of a small coin lesion was performed.

GROSS PATHOLOGY:

A 1.8 cm. maximum diameter, nearly spherical, bosselated, firm white nodule with an irregular bulging cut surface exhibiting a little focal hemorrhage centrally was submitted.

FOLLOW UP:

As of November 1980 the patient was alive and well with no significant medical problems.

CONTRIBUTOR: Sorrell N. Glover, M. D.
Thousand Oaks, California

DECEMBER 6, 1981 - CASE 6

ACCESSION NO. 23124

TISSUE FROM: Anterior mediastinum

CLINICAL ABSTRACT:

History: A 50-year-old Caucasian female had a mediastinal mass picked up incidentally on routine chest x-ray while hospitalized for uncontrolled atrial fibrillation. The mass was causing no symptoms.

Radiograph: A mass was present in the right anterior mediastinum. Chest x-rays taken in 1975 and 1976 did not reveal mediastinal mass.

SURGERY: (September 12, 1978)

The mediastinal mass was excised through a mid-sternal incision.

GROSS PATHOLOGY:

Specimen consisted of a 5 x 4.5 x 4 cm. well encapsulated tumor mass weighing 41 gms. The tumor was firm and tan with septated lobulation.

FOLLOW UP:

When last seen in 1980 she was doing well with no evidence of recurrent tumor and was moving to Florida.

CONTRIBUTOR: Doris L. Herman, M. D.
Olive View, California

DECEMBER 6, 1981 - CASE 7

ACCESSION NO. 18640

TISSUE FROM: Right lower lobe bronchus

CLINICAL ABSTRACT:

History: This 20-year-old male was referred to a hospital for a work-up when a routine chest radiograph revealed a homogeneous, well-circumscribed mass which measured 9 x 6 cm. in the postero-medial aspect of the right lower lobe. The questionable presence of an eccentric circumscribed radioluncency and a possible fluid level prompted the radiologist to suggest that the lesion was probably a lung abcess or a sequestration, although a tumor could not be excluded. The patient stated that his appetite was good and he denied any fever, hemoptysis, weight loss, chest pain or production of foul-smelling sputum. His past history included a hospitalization in Mexico for pneumonia when he was five years old.

Two bronchoscopies were performed and revealed possible partial stenosis of the bronchus leading to the right lower lobe. A bronchogram showed non-filling of the right lower lobe.

SURGERY: (June 15, 1970)

A right lower lobectomy was performed. Exploration of the right chest wall revealed a firm atelectatic right lower lobe. There was extensive induration which occupied the entire right lower lobe substance. In addition multiple succulent nodes were present in the entire right hilum.

GROSS PATHOLOGY:

The specimen consisted of a pyramidal-shaped lobe of lung which measured 11 cm. in length and 8.5 cm. in basal diameter. A globoid, rubbery, 7 x 5.5 cm., smooth yellow tumor protruded into and completely obstructed the posterior basilar segmental bronchus at its origin. Finger-like projections of necrotic tumor also extended into the right lower lobe bronchus and almost completely obstructed that airway. Abundant mucus exuded from the cut surface of the tumor.

FOLLOW UP:

The patient was alive as of June, 1973. The last known chest radiograph in December, 1971 revealed no recurrent tumor.

CONTRIBUTOR: E. R. Jennings, M. D.
Long Beach, California

DECEMBER 6, 1981 - CASE 8

ACCESSION NO. 14786

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: This 57-year-old Caucasian male patient was hospitalized in May 1965 because of daily bouts of hemoptysis for five days. The patient had seven episodes of mild hemoptysis beginning at age 18 and recurring during the ensuring years. At no time did he experience chest pain, fever, chill, weight loss or dyspnea. In 1941 the initial chest roentgenograms revealed a 3 x 4 cm. homogeneous, smooth mass in the right paratracheal area. During the next 24 years, radiographs revealed the appearance of multiple isolated masses within both lungs. The patient refused a thoracotomy in 1949.

Physical examination showed a slightly pale, well developed, male with few scattered fine rales in the right posterior lung fields.

Laboratory studies were unremarkable except for a mild anemia.

SURGERY:

The patient was prepared for a right thoracotomy; however, after initiation of anethesia, a massive pulmonary hemorrhage developed which necessitated abandonment of the procedure. One week later a right thoracotomy was performed and the right lower lobe was removed.

GROSS PATHOLOGY:

The right lower lobe contained multiple, well demarcated, soft nodules of friable, white-tan hemorrhagic tissue, the largest measuring 5 cm. in diameter.

FOLLOW UP:

In January 1971 a solitary ulcerated nodule beneath the skin of the left neck was biopsied and interpreted as metastatic adenocarcinoma. The patient died in May of 1971. At autopsy, tumor was found within the left and right lungs, along the peritoneum, mesentery, and serosa of the stomach, small bowel, rectum and within the bone marrow of the vertebral column. Microscopically the tumor consisted of mucous secreting adenocarcinoma.

CONTRIBUTOR: Dennis Kasimian, M. D.
Van Nuys, California

DECEMBER 6, 1981 - CASE 9

ACCESSION NO. 24204

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: A 53-year-old Caucasian male had experienced right lateral chest pain and right upper quadrant abdominal pain related to breathing. The pain had been present for several months. In the past 30+ years he has smoked 2 packs of cigarettes a day. Serial chest x-ray 1963 - January 1980 were within normal limits.

Radiograph: Chest x-ray showed a right upper lobe mass that was peripheral and seemed to involve pleura.

SURGERY: (April 8, 1981)

The patient underwent exploratory right thoracotomy. The right upper lobe was densely adherent to parietal pleura. A bulky nodular pleural mass was removed. Multiple tracts of nodular tissue extended over visceral and parietal pleura near the mass.

GROSS PATHOLOGY:

Several pieces of nodular pink tan to red tissue were submitted. The largest piece was 8 x 6 x 2 cm. The cut surface was white and fibrous-appearing.

FOLLOW UP: (October 14, 1981)

"He had a relatively uneventful postoperative course, and in six weeks after surgery he was back to work and conducting his usual activities. He did well for two months, then began experiencing right chest pain which progressively became worse. He was re-evaluated with chest x-ray and although no enlargement of the tumor was seen he received palliative radiotherapy to the right chest. He received 4000 rads which was completed a week ago."

CONTRIBUTOR: P. L. Morris, M. D.
Santa Barbara, California

DECEMBER 6, 1981 -CASE 10

ACCESSION NO. 24262

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: This 73-year-old white female retired school teacher who was admitted to the hospital for evaluation of a mass in the right mid lung field, detected one month previously and resistant to a course of antibictic therapy. Bronchoscopy and mediastinoscopy revealed no evidence of malignancy.

Past history: The patient had previously undergone evaluation of a suspicious density seen on left chest x-ray 2 years ago and it was concluded that this was a benign lesion on mediastinal biopsy.

SURGERY: (May 21, 1981)

A right middle lobectomy was performed.

GROSS PATHOLOGY:

A right middle lobe of lung, measuring 12.0 x 9.5 x 4.5 cm. and weighing 60 gms., was received. The pleural surface was smooth and glistening. At the anterior edge of the pleural surface was a firm, dull-tan slightly elevated area, measuring 4.5 x 3.5 x 4.0 cm. On cross section, a 3.5 cm. in greatest diameter neoplasm, rubbery, light tan, and homogeneous, was seen immediately beneath the pleural surface. The tumor appeared to be irregularly infiltrating the surrounding spongy pink pulmonary parenchyma.

FOLLOW UP:

Not available.

CONTRIBUTOR: Thomas R. Humphrey, M. D.
Lancaster, California

DECEMBER 6, 1981 - CASE 11

ACCESSION NO. 22066

TISSUE FROM: Left lung

CLINICAL ABSTRACT:

History: This 18-year-old Caucasian female nursing student had a routine chest x-ray in connection with her school physical. A 3.5 x 4.5 cm. sharply circumscribed pulmonary nodule was seen in the left lower lobe. Comparison with films done 2 years previously showed the lesion to have been present at that time. She was asymptomatic.

SURGERY: (June 20, 1976)

A left thoracotomy and excision of the lesion was performed.

GROSS PATHOLOGY:

A sharply circumscribed encapsulated tumor measuring 4 x 4 x 2.5 cm. was removed. The cut surface of the tumor was varigated white-yellow-tan with several foci of hemorrhage.

FOLLOW UP:

As of 6 months ago patient was well and had no evidence of recurrence.

CONTRIBUTOR: Jules Kernen, M. D.
Los Angeles, California

DECEMBER 6, 1981 - CASE 12

ACCESSION NO. 24275

TISSUE FROM: Left lung

CLINICAL ABSTRACT:

History: This 28-year-old Caucasian male, a 4th year medical student, was well until February 1981 when he began developing progressive shortness of breath with decreased exercise tolerance and fatiguability accompanied by a non-productive cough. He had periodic episodes of temperatures as high as 101°F. There was no weight loss, night sweats, or hemoptysis. He did not smoke.

During undergraduate years, he occasionally spent time with his father, a civil engineer in San Diego County, working as a surveyor doing some soil analysis. He had not done this extensively for the past number of months. A few years ago he had also worked in the summers helping to mix cement by hand, but was also involved in chipping out cement mixers. He does not recall wearing any protective respiratory equipment during this very dusty work.

SURGERY: (May 22, 1981)

Open lung biopsies of lingula and upper lobe of left lung were performed.

GROSS PATHOLOGY:

The lingula biopsy was 4.5 x 2 x 1.5 cm. and composed of pink tan crepitant lung tissue. The lingular biopsy was smaller and similar in appearance.

FOLLOW UP:

As of August 1981 patient is virtually asymptomatic.

CONTRIBUTOR: Robert Hufner, M. D.
La Mesa, California

DECEMBER 6, 1981 - CASE 13

ACCESSION NO. 24338

TISSUE FROM: Left lung, upper lobe

CLINICAL ABSTRACT:

History: A 37-year-old Caucasian female had multiple episodes of left lower lobe infection with hemoptysis. She first began to have this problem in 1975 at which time she had evidence of nodular density at the left apex. She continued to have lesions in this area unchanging in 1977 and noted during this time a chronic nonproductive cough which she attributed to the fact that she was smoking about two packs of cigarettes per day. Multiple bronchoscopies were negative.

Radiograph: Bronchograms showed a stenotic lesion in a basilar segmental bronchus of the left lower lobe and a large calcified lymph node overlying the bronchus.

SURGERY: (August 13, 1981)

A left pneumonectomy was performed.

GROSS PATHOLOGY:

In the medial portion of the lower lobe several subpleural 1.5 cm. nodules were present which seemed to be confluent with a hilar mass, 3.5 cm. in maximum dimension. The tumor did not appear to arise from bronchi. Hilar lymph nodes appeared involved with tumor.

CONTRIBUTOR: Roger Terry, M. D.
Los Angeles, California

DECEMBER 6, 1981 - CASE 14

ACCESSION NO. 24235

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: This 29-year-old white male circus clown who presented with a one week history of fever, night sweats, rhinorrhea, diarrhea and weight loss while traveling in Argentina. He was treated with multiple antibiotics by local physicians, but after 3 months of no improvement, he returned to the United States for further medical attention. Further symptoms including sudden hearing loss in the left ear with left facial palsy and numbness developed. The left eye was painful without production of tears. Sense of taste was decreased, and there was loss of sense of balance. He complained of itching in the buttocks and lower back. He also experienced double vision which was most severe upon arising in the morning. On admission to the hospital, his chest x-ray showed irregular nodular densities in both lungs. The hematocrit was 36; WBC's 38,000 with a differential of 68 PMN's, 24 lymphocytes, 10 atypical lymphocytes, 4 monocytes, and 4 eosinophils. A bone marrow biopsy showed mild hypocellularity.

SURGERY: (March 6, 1980)

An open lung biopsy was performed.

GROSS PATHOLOGY:

Multiple greyish-white soft tissue framents measuring up to 3 x 2.5 x 2.5 cm. were received.

FOLLOW UP:

The patient was treated with high dose prednisone and isoniazid. An abdominal cat scan revealed retroperitoneal lymphadenopathy and several renal nodules. His condition remained stable until April 8, 1980 when his mental status abruptly deteriorated. Multiple diagnostic studies revealed a cerebellar mass, and early transtentorial herniation. A posterior fossa exploration revealed a tumor. The tumor was interpreted as proliferating lymphoid tissue with a vasocentric pattern strongly suggesting a malignant lymphoma. Aggressive supportive care and chemotherapy maintained his waxing and waning course. He died on July 13, 1980. Autopsy revealed extensive tumor involvement of lungs, liver, kidneys spleen, cerebrum, meninges, and skin.

CONTRIBUTOR: D. R. Dickson, M. D.
Santa Barbara, California

DECEMBER 6, 1981 - CASE 15

ACCESSION NO. 19610

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: Patient is a 41-year-old female with history of "cigarette cough" and smokes one pack per day. On annual chest films obtained November 1971 there was present bilateral pulmonary densities and she was admitted to the hospital for diagnostic studies. The patient was otherwise asymptomatic.

SURGERY: (November 22, 1971)

Wedge biopsy of the right lung was obtained.

GROSS PATHOLOGY:

The specimen consisted of a wedge-shaped portion of lung weighing 12 gms. and measuring 5.5 x 2.4 x 2.2 cm. The pleura was smooth and transparent. Numerous soft to firm rubbery consolidated nodules and cord-like areas varying 2 - 8 mm. in maximal dimensions were seen.

FOLLOW UP:

Patient was asymptomatic as of February 14, 1972. Chest x-ray, June 15, 1973, revealed infiltrative process in lung had cleared although pleural reaction persisted. Current follow up not available as physician has retired.

CONTRIBUTOR: John P. Blanchard, M. D.
Santa Barbara, California

DECEMBER 6, 1981 - CASE 16

ACCESSION NO. 23711

TISSUE FROM: Left lung

CLINICAL ABSTRACT:

History: A 54-year-old white female complaining of dyspnea on exertion and increasing fatigue sought medical attention. A chest x-ray on March 29, 1978 showed a 3.5 cavitary lesion in the anterior left upper lobe close to the hilum and containing an air-fluid level. There was also an area of density seen in the left lower lobe. The patient had smoked 2 - 3 packs per day for 23 years and had stopped four years previously and had gained 50 pounds over the same period. The patient was placed on tetracycline. Soon thereafter a cough productive of some bloody sputum developed and lasted about three weeks. A concurrent fever was not seen.

Past history: The patient had pulmonary disease 5 years ago in the Canary Islands when she was hospitalized with an infection in her left lung complicated by jaundice.

Radiograph: A repeat chest film April 11, 1978 showed persistence of the cavitary lesion with clearing of the lower lobe. Repeat film April 19, 1978 showed no change.

SURGERY: (May 1, 1978)

A left pneumonectomy was performed.

GROSS PATHOLOGY:

The left lung weighed 440 grms. The pleura was pale pink and smooth with fine anthracosis along the septa. The bronchus was unremarkable. Three soft anthracotic hilar nodes were received. A palpable rubbery mass was located just superior to the base of the bronchus. A secondary branch of the upper lobe bronchus extended into the mass which was cystic and measured 3 x 2.5 cm. The wall was grey and granular and 3 - 5 mm. thick. The mass was rather well demarcated from surrounding pulmonary parenchyma but was not encapsulated. The remaining parenchyma was unremarkable.

FOLLOW UP:

The patient expired in 1979 with widespread metastases. Autopsy was not performed.

CONTRIBUTOR: John P. Blanchard, M. D.
Santa Barbara, California

DECEMBER 6, 1981 - CASE 17

ACCESSION NO. 22369

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: This 37-year-old white male presented to the emergency room complaining of discomfort in the central upper chest area. There were no other complaints or significant medical history. A chest x-ray showed a large mass in the central chest.

SURGERY: (April 19, 1977)

The tumor and pericardium were excised with a wedge biopsy of the lung.

GROSS PATHOLOGY:

The specimen consisted of a mediastinal tumor weighing 335 gms. and measuring 11 cm. in greatest dimensions. A membranous pink peritoneal-like membrane covered an area about 6 cm. in diameter and fatty tissue covered an area 10 cm. in diameter. The remainder showed bulging raw tan nodular tumor. Cut section surfaces showed fleshy tissue with a few foci of hemorrhage and central necrosis, 2.0 cm. in diameter.

FOLLOW UP:

The patient died on April 28, 1977 of a pulmonary embolus.

CONTRIBUTOR: Dorothy Tatter, M. D.
Los Angeles, California

DECEMBER 6, 1981 - CASE 18

ACCESSION NO. 24342

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: This 57-year-old female presented with the acute onset of hypothermia and hypotension. There was a history of an old left-sided cerebrovascular accident, and of rheumatoid arthritis for 4 years, treated with steroids. She was admitted to the hospital, where blood cultures subsequently grew Staph. aureus. She was treated with multiple antibiotics, but developed decubitus ulcers and candida sepsis. Her clinical course was one of progressive deterioration, and she expired on February 9, 1981.

AUTOPSY: (February 10, 1981)

The cut surface of the right lung revealed four nodular lesions measuring up to 2 x 2.5 cm. The nodules exhibited a 1 mm. fibrous capsule with a soft, yellow-white core. The nodules were located near the periphery of the lung.

The remainder of the autopsy revealed an old healed antero-septal myocardial infarction, deforming rheumatoid arthritis, chronic pyelonephritis, a remote infarct of the right internal capsule, a left renal calculus, adrenal atrophy, and multiple decutitis ulcers. Post mortum cultures grew Staph., Proteus and Pseudomonas species.

CONTRIBUTOR: Kenneth A. Frankel, M. D.
Covina, California

DECEMBER 6, 1981 - CASE 19

ACCESSION NO. 23682

TISSUE FROM: Left upper lobe of lung

CLINICAL ABSTRACT:

History: This 57-year-old Caucasian female presented to her private physician complaining of shortness of breath. A chest x-ray revealed evidence of pneumonia of the left upper lobe. She related a long history of smoking 1 - 2 packs per day, but no hemoptysis, weight loss, or cough. A course of antibiotic therapy was without demonstrable benefit.

Radiograph: Planograms showed an irregular marginated lesion in the posterior aspect of the left upper lobe.

SURGERY: (March 20, 1979)

A left thoracotomy and wedge biopsy of lung was performed.

GROSS PATHOLOGY:

Received was a wedge-shaped piece of pulmonary parenchyma measuring 7 x 3.5 x 2.5 cm. The specimen was partially covered by a glistening, smooth pleural surface. The cut surface of the lung exhibited focal areas of firmness within which were small accumulations of yellow-white purulent material.

FOLLOW UP:

Four months postoperatively she was doing well with no other lesions in the lung. She is presently lost to follow up.

CONTRIBUTOR: Richard N. Lucas, M. D.
Fairfield, California

DECEMBER 6, 1981 - CASE 20

ACCESSION NO. 23319

TISSUE FROM: Right lung

CLINICAL ABSTRACT:

History: A 72-year-old white male, a smoker of 1+ pack per day for 55 years, had a low grade chronic cough for many years. In June 1978 he developed a severe persistent chronic cough; there was little sputum production. In December, however, sputum was blood-tinged on several occasions.

Radiograph: Chest x-ray showed emphysematous change, but no definite mass. A lesion at the junction of the right main stem and lower lobe bronchi with intra-bronchial growth into the middle lobe bronchus was seen on endoscopic examination and biopsied.

SURGERY: (February 27, 1979)

A right radical pneumonectomy was performed.

GROSS PATHOLOGY:

The specimen consisted of the right lung weighing 740 gms. The upper and middle lobes were well inflated. The lower lobe was atelectatic. The pleural surfaces showed a few fine fibrous adhesions in the apex and antracotic laden lymphatics. A grey-tan somewhat necrotic tumor bulged into the right main stem bronchus and measured 1.5 cm. across and comes to 1 cm. of the surgical margin. The tumor grew down the middle lobe bronchus and completely involved the lower lobe bronchus where it had penetrated into the surrounding lung parenchyma as an 8 x 4 x 3.5 cm. lobulated pink white unencapsulated mass with areas of hemorrhage and necrosis. Cut surface of the tumor was soft, bulging and fleshy.

FOLLOW UP:

Following surgery he developed increasing respiratory insufficiency, then pneumonia which led to his death on June 29, 1979. At autopsy the remaining lung showed bronchopneumonia with fibrosis and emphysema. The only remaining tumor was a small 1 cm. nodule in the left lung.

California Tumor Tissue Registry

72nd Semi-Annual Slide Seminar

Tumors and Tumor-Like Lesions of the Lung

Michael N. Koss, M.D. John G. Pearce, M.D.

December 6, 1981

Newport Beach, California

THE AUTHORS WOULD LIKE TO THANK DR. L. HOCHHOLZER, CHIEF DEPARTMENT OF PULMONARY AND MEDIASTINAL PATHOLOGY, AFIP, WITHOUT WHOSE SUPPORT THIS CONFERENCE COULD NOT HAVE TAKEN PLACE.

PULMONARY AND INTRATHORACIC TUMORS

MICHAEL KOSS, M. D.
JOHN G. PEARCE, M. D.

DECEMBER 6, 1981

DIAGNOSTIC INDEX

DECEMBER 6, 1981 - CASE NO. 1

ACCESSION NO. 19855

MODERATORS' DIAGNOSIS: ADENOID CYSTIC CARCINOMA, BRONCHUS

CLINICAL HISTORY:

The patient was a 41 year-old woman with a history of recurrent episodes of pneumonia and recent 20 lb. weight loss. Chest x-rays showed atelectasis of the left lung. When the left lung was resected, a 5 x 1.5 x 1.2 cm. yellow tumor was found obstructing the left main stem bronchus and infiltrating into the peribronchial lung parenchyma.

RADIOGRAPHS:

Not available.

MICROSCOPIC DESCRIPTION:

The section available for review shows a bronchus with circumferentially spreading tumor extensively involving its wall. The histology of the tumor is distinctive for adenoid cystic carcinoma, in that it shows cords of small dark cells arranged about cores of mucinous and/or hyalinized matrix. In one area, tumor cells invade perineural spaces.

DISCUSSION:

Adenoid cystic carcinoma is the second most common of the so-called bronchial adenomas, constituting 12-15% of these tumors. Unlike the other adenomas, it is more common in the trachea and less frequent as one proceeds down the respiratory tract. Affected patients show a wide age range (18 - 70 years). The average age at presentation is 40 years, a figure which does not differ significantly from that of bronchial carcinoids, but is lower than that of bronchogenic carcinoma. Symptoms are related to bronchial irritation and obstruction.

Adenoid cystic carcinoma is typically central in location, and protrudes into the bronchus as a white, sessile mass with "heaped up" margins. The tumor usually spreads beyond the bronchial cartilage into the surrounding tissue.

The microscopic appearance of adenoid cystic carcinoma is well demonstrated by our case. The tumor consists of small, darkly staining cells arranged in cylinders, solid or cystic cords, or glands. A double layer of cells can be appreciated about the "glands", which contain mucinous or hyaline-like material. The tumor typically invades both circumferentially about the airway and proximally and distally from the main tumor mass. Local submucosal spread produces the heaped-up margins seen in the gross specimen. In addition, perineural invasion is common. It is not unusual for mediastinal tissue and adjacent lymph nodes to be involved by tumor at the time of thoracotomy. The tendency of adenoid cystic carcinoma to spread submucosally has several important clinical sequelae. Large operations are generally required for removal of the

tumor (pneumonectomy as opposed to lobectomy), there is an increased frequency of inoperability, and there is a tendency of the tumor to recur locally as long as 30 years after resection. Five year survival is therefore a poor measure of prognosis in these lesions; only 25% of patients are alive and well after 15 years of follow-up.

In the differential diagnosis of adenoid cystic carcinoma, one might consider pleomorphic adenoma of the bronchus, a rare benign tumor which is histologically identical to the pleomorphic adenoma of the salivary glands. The typical cartilagincus stroma and variety of patterns, commonly including sheets of neoplastic cells, should allow ready separation of the two lesions. Mucoepidermoid tumors of the bronchus may also show glandular spaces, but sheet-like areas of cell growth and the presence of intracytoplasmic mucin within tumor cells distinguish it from adenoid cystic carcinoma. In addition, mucoepidermoid tumors are more frequent in bronchi than in the trachea and lack heaped-up margins in the gross specimen.

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DECEMBER 6, 1981 - CASE NO. 2

ACCESSION NO. 22307

MODERATORS' DIAGNOSIS: INFLAMMATORY PSEUDOTUMOR, FIBROXANTHOMA TYPE, LUNG

CLINICAL HISTORY:

This asymptomatic 21 year-old woman had a two year history of a slowly enlarging mass in the right lower lobe following an automobile accident. At the time of thoracotomy, the mass measured 8 cm. in diameter. The right lower lobectomy specimen showed a 5 cm. well-demarcated but nonencapsulated yellow, bosselated mass near the hilum. There was no apparent connection to a bronchus. After one year of follow-up, the patient was alive and well without recurrence.

RADIOGRAPHS:

Admission PA and lateral film clearly demonstrate approximately 8 cm. mass lesion that is well circumscribed but nonhomogeneous and without calcification. The patient's previous films from 7-3-74, 10-2-75 and 4-21-77, show the evolution of this mass lesion situated in the right cardiophrenic region at a level at the posterior border of the heart. It should be noted that the margins of the lesion is well delineated indicating intrapulmonary location. The nonhomogeneous nature of this lesion, its size, location, and slow growth are suggestive of an inflammatory process or a very slow growing benign tumor. There is no associated pleural effusion and the remainder of the chest is essentially normal.

While nonspecific, the above features of this lesion are consistent with the diagnosis of inflammatory pseudotumor.

The radiological differential diagnosis is that of a mass greater than 4 cm. in diameter. This is a small differential list and while pulmonary metastases should be considered, other diagnoses are hyadatid cyst, liposarcoma, and on occasion and coccidiomyocosis can create a pulmonary nodular lesion of this size. Noncavitating abscess should also be clinically considered.

MICROSCOPIC DESCRIPTION:

The normal lung architecture has been completely effaced by a proliferation of spindle cells (in areas showing a distinctly storiform pattern of growth), mononuclear cells resembling histiocytes, and multinucleated giant cells, some of which are of the Touton type. Islands of xanthoma cells with clear cytoplasm are also present. Finally, a sprinkling of lymphocytes and plasma cells is seen. A number of pertinent negatives should be noted: There are few mitoses, vascularity is not prominent, and abundant iron deposition is not seen.

DISCUSSION:

In 1954 Umiker and Iverson suggested the name inflammatory pseudotumor

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for sharply circumscribed, usually single, tumor-like lesions of lung. A variety of terms have subsequently been used to describe similar lesions, including xanthoma, xanthofibroma, xanthogranuloma, sclerosing hemangioma, histiocytoma, mast cell granuloma, fibrous histiocytoma, and plasma cell granuloma of lung. This confusing welter of names reflects the polymorphous microscopic appearance of inflammatory pseudotumors, as well as the conflicting theories of pathogenesis of these lesions. Currently, at the Armed Forces Institute of Pathology, three major subclasses of inflammatory pseudotumor are recognized: Fibroma, fibroxanthoma (fibrous histiocytoma), and plasma cell granuloma. Sclerosing hemangioma is considered to be a separate entity.

Clinically, inflammatory pseudotumors demonstrate a wide range of presentation, but Bahadori and Liebow have remarked on the predilection of this lesion for involvement of the pediatric age population. In particular, more than two-thirds of their patients were less than 30 years of age, they also suggested that "plasma cell granulomas" were prominent amoung the causes of large solitary intrapulmonary lesions in children. The sex ratio of inflammatory pseudotumors is equal. Sixty percent of the patients are asymptomatic, their lesions being discovered by routine chest x-ray. There is an antecedent upper respiratory tract infection in 25% of cases, a finding which has been used by some to suggest that inflammatory pseudotumors may evolve from an infectious process. Inflammatory pseudotumors may occasionally arise as sessile or polypoid intrabronchial masses, or may impinge on a bronchus during their growth. In such cases, cough or hemoptysis may be the initial presenting symptom (5% of patients).

The chest x-ray finding is usually that of a solitary, well demarcated mass which may be as large as 13 cm. or as small as 1 cm. in diameter. Any lobe may be affected, although there is a predilection for the lower lobes. Focal calcification, cavitation, or multiplicity of lesions have been reported occasionally, but most inflammatory pseudotumors do not demonstrate these features. When inflammatory pseudotumors have been followed by serial roentgenograms (as in the present case), the usual course is one of slow growth over a period of years or even no growth at all. The usual clinical diagnosis in an older individual is granuloma or carcinoma, an impression which may be further strengthened by the finding of enlarged hilar or mediastinal lymph nodes.

Grossly, inflammatory pseudotumors are well circumscribed, nonencapsulated masses. Their color depends on the relative proportions of the major histologic components. Thus, those lesions rich in xanthoma cells are distinctly yellow, while those consisting largely of fibrous connective tissue are white and firm. Cystic degeneration may occur.

Microscopically, inflammatory pseudotumors consist of varying proportions of mononuclear histiocytes, xanthoma cells, multinucleated giant cells, and spindled fibroblasts with associated collagen. A sprinkling of lymphocytes and plasma cells is usually present. If fibroblasts predominate, the lesion is

classified as fibroma. If spindle cells, mononuclear histiocytes, and Touton giant cells predominate, then it is termed fibrous histiocytoma; and if these are admixed with foamy macrophages it is called fibroxanthoma. Lesions consisting principally of collagen, fibroblasts and plasma cells are designated plasma cell granuloma. The lipid in xanthomatous lesions is believed to be endogenous in orgin, and biochemical analysis has shown it to consist of ethanolamine and an N-acetyl neuraminic acid.

Only two ultrastructural studies of inflammatory pseudotumors have been reported. These have shown the presence of fibroblasts, myofibroblasts, hyperplastic pericytes around small vessels, plasma cells and relatively primitive mesenchymal cells.

The histogenesis of inflammatory pseudotumors is unknown, although hypotheses abound. The histologic resemblance to fibrous histiocytoma arising in the soft tissues, the tendency of the lesions to enlarge slowly over a period of years, and the report of at least two patients with invasion of mediastinum raise the possibility of a neoplastic origin. At the same time, the polymorphous and cytologically benign histology of inflammatory pseudotumors, the report of cases following infection or (as in the present patient) traumatic injury, and the microscopic finding in a few instances of lesions histologically intermediate between organized pneumonias and inflammatory pseudotumors suggest a reactive histogenesis.

The differential diagnosis of inflammatory pseudotumors is equally complex. Lung is the most frequent site of metastasis from malignant fibrous histiocytomas (MFH) but usually clinical investigation serves to exclude an extrapulmonary MFH. The very existence of malignant fibrous histiocytoma primary in lung has been controversial, but at least one example is presented in the Fascicle of Carter and Egleston and more than 50 cases of lesions diagnosed as pulmonary malignant fibrous histiocytoma have been collected at AFIP. These lesions typically present as large masses, show a storiform pattern and consist of spindled cells and multinucleated giant cells. The marked cellular anaplasia, the frequent mitoses, and the presence of atypical mitoses usually readily distinguish malignant fibrous histiocytomas from inflammatory pseudotumors. Occasionally, however, distinct cellular atypia may be found in lesions otherwise acceptable as inflammatory pseudotumors. Such cases demonstrate that the dividing line between malignant fibrous histiocytoma and fibrous histiocytoma (inflammatory pseudotumor) in lung is not always clear-cut.

Pleomorphic carcinomas of lung show numerous giant cells with or without spindled tumor cells. They usually present as peripheral mass lesions, and pursue a fulminant course with widespread metastasis. The numerous mitoses, including atypical mitoses, and the suggestion of an epithelial pattern (nesting) in areas or the demonstration of intracellular mucin allow one to separate these lesions from inflammatory pseudotumors.

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Sclerosing hemangiomas of lung are distinguished from inflammatory pseudotumors on the basis of light microscopic and ultrastructural appearance as well as clinical presentation. Sclerosing hemangiomas show a heavy female predominance, are much more likely to be hemorrhagic in the gross specimen, and are microscopically composed of bland, uniform, round to polygonal cells. The latter bear no ultrastructural relationship to myofibroblasts or fibroblasts, typical constituents of inflammatory pseudotumors. Indeed, it is now considered that sclerosing hemangiomas of the lung are neoplasms of undetermined histogenesis.

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DECEMBER 6, 1981 - CASE NO. 3

ACCESSION NO. 23010

MODERATORS' DIAGNOSIS: DIFFUSE MALIGNANT EPITHELIAL MESOTHELIOMA, PLEURA

CLINICAL HISTORY:

This 59 year-old man had a brief history of malaise, dry cough, and right pleuritic chest pains. Chest x-ray showed a right pleural effusion. At thoracotomy, yellow-tan nodules measuring up to 2 1/2 cms. in size studded the parietal and diaphragmatic pleura. The patient died 8 months after biopsy despite intensive multidrug chemotherapy.

RADIOGRAPHS:

This 59 year-old man had nonspecific historical features described above but does have a dry cough and right pleuritic chest pain. The radiographs at the time of presentation clearly demonstrate a peripheral lobulated mass density in the right side strongly suspicious for pleural based lesion. This was associated with a large effusion and has classical radiographic features consistent with pleural mesothelioma. The radiological differential diagnosis would include noncalcified pleural plaque formation, perhaps associated with asbestosis, or subpleural deposits such as often seen in lymphoma and malignant melanoma metastases.

MICROSCOPIC DESCRIPTION:

This epithelial tumor shows a variety of histologic patterns, including glands, papillae, and sheets of neoplastic cells. The tumor invades the fat of the parietal pleura. Neoplastic cells show relative uniformity, with one or two prominent nucleoli and ample pale cytoplasm. Despite this uniformity, the abundant mitoses and presence of necrosis, as well as the aforementioned invasion of subpleural fat, indicate the malignant character of the tumor.

DISCUSSION:

Diffuse malignant mesothelioma of pleura is a tumor of diverse histology, which presumably originates from the mesothelium and superficially grows along the serosal planes. The age range of 65 patients with diffuse pleural mesothelioma collected from the literature is shown in Table 1. In our experience, there are few patients under the age of 30 years, a feature which probably relates to the known long (20-40 years) latent period between exposure to asbestos and development of this tumor. Most patients are men (Table 2), a feature which again undoubtedly reflects the occupation-associated pathogenesis of diffuse mesothelioma. Indeed, about 80% of patients with this type of tumor have documented direct or indirect exposure to asbestos. The character of this exposure differs from that accompanying pulmonary asbestosis, in that it is often brief or of low intensity. The fact that 20% of patients do not have an elicitable history of asbestos exposure may reflect vagaries of

patients' long-term memories, the ubiquity of asbestos in the urban environment, or the presence of an as yet unknown etiologic agent.

About 80% of patients with mesotheliomas have pleural tumors, while the remainder have peritoneal neoplasms (Table 2). Peritoneal mesotheliomas are usually associated with pulmonary asbestosis (fibrosis), while pleural mesotheliomas are not.

The clinical features of 193 patients with malignant pleural mesotheliomas collected from published reports are shown in Table 3. The most frequent signs and symptoms relate to local spread of the tumor, including pleural effusion (with or without resulting dyspnea), chest pain and cough.

The prognosis of patients with diffuse mesothelioma is abysmal. All patients eventually die of the tumor, with average survival of 1 year (Table 4). It is unusual for patients to live over 2 years.

The diagnosis of diffuse mesothelioma is dependent upon a compatible gross appearance, histology, and histochemistry. Mesotheliomas typically cover the pleura with multiple nodules, plaques, or a continuous rind of tumor. In later stages of disease, metastasis to hilar lymph nodes, to contralateral lung in the form of multiple nodules, or to extrathoracic sites such as bone and liver, may occur.

Diffuse malignant mesotheliomas are characterized by cytologic uniformity and histologic diversity. The neoplastic mesothelial cells of epithelial mesotheliomas are often bland in appearance, with ample cytoplasm, uniform nuclei, and a single prominent nucleolus. Similarly, the spindled tumor cells of diffuse malignant fibrous mesotheliomas may show only mild to moderate nuclear hyperchromasia.

The histology of diffuse mesothelioma is characteristically complex. Epithelial tumors may show tubules, papillae, sheets of tumor cells, or a combination of these patterns. Diffuse malignant fibrous mesothelioma typically shows a storiform, herringbone or palisade pattern. Diffuse malignant biphasic mesothelioma shows tubules or nests of epithelial cells together with spindled "sarcomatous" cells. The incidence of these histologic subtypes is shown in Table 5.

The epithelial component of mesotheliomas shows a distinctive histochemistry (Table 6). Typically, an acid mucin which is hyaluronidase-sensitive and periodic acid - Schiff (PAS) negative is present within the cytoplasm of the tumor cells, or within glandular lumens. Hyaluronic acid may also be found within the stroma of the tumor, but in this location is not specific for mesothelioma. Since the hyaluronic acid of mesotheliomas is soluble in aqueous fixatives, small biopsies may not show the characteristic mucinous material.

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The differential diagnosis of diffuse malignant epithelial mesothelioma primarily revolves around metastatic adenocarcinoma. The latter may occasionally metastasize to pleura diffusely in a manner simulating mesothelioma. Most frequently, the primary tumor is a small peripheral adenocarcinoma of lung. Tomographic chest x-rays or CAT scans are important in excluding such a possibility. The histology of the two tumors may be similar, although adenocarcinomas tend to show more simplified glands and greater nuclear pleomorphism than mesotheliomas. A battery of histochemical stains may be crucial in distinguishing these neoplasms (Table 6). The mucin of adenocarcinomas is diastase-predigested PAS (d-PAS) positive, while that of mesotheliomas is an acid mucin which is hyaluronidase sensitive. We have found that the single best stain for distinguishing metastatic adenocarcinoma from mesothelioma is the d-PAS, for a positive finding excludes the diagnosis of mesothelioma. The mucicarmine stain is not a useful stain, since it may be positive in both tumors.

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DECEMBER 6, 1981 - CASE NO. 3

ACCESSION NO. 23010

TABLE 1: AGE MEAN AND RANGE IN THREE SERIES OF DIFFUSE PLEURAL MESOTHELIOMAS

AUTHOR(S)	NO. OF PATIENTS	AGE MEAN (YRS.)	AGE RANGE (YRS.)
OELS	37	55	20 - 79
HOURIHANE	17	53	23 - 77
TARYLE ET AL	11	54	21 - 75

TABLE 2: INCIDENCE OF MESOTHELIOMA BY SEX *

TOTAL NO. PATIENTS	SEX		SITE	
	MALE	FEMALE	PLEURA	PERITONEUM
559	415	144	458	101
	(74%)	(26%)	(82%)	(18%)

* 4 COMBINED SERIES FROM USA, ENGLAND, CANADA

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TABLE 3: CLINICAL FEATURES OF MALIGNANT PLEURAL MESOTHELIOMA IN 193 PATIENTS

FEATURE	NO. PATIENTS	% TOTAL PATIENTS
CHEST PAIN	134	69
DYSPNEA	131	68
COUGH	62	62
WEIGHT LOSS	40	20
FEVER	26	13
EFFUSION	150	78

TABLE 4: PROGNOSIS OF PATIENTS WITH DIFFUSE MALIGNANT MESOTHELIOMA

TOTAL NUMBER OF PATIENTS	AVERAGE SURVIVAL (MONTHS)	RANGE OF SURVIVAL (MONTHS)
267	12.5	10 - 20

TABLE 5: DIFFUSE MALIGNANT MESOTHELIOMA: HISTOLOGIC SUBTYPES

SITE	PATIENTS	HISTOLOGIC TYPE		
		EPITHELIAL	FIBROSARCOMATOUS	BIPHASIC
	NO.	%	%	%
PLEURA	382	54	21.5	24
PERITONEUM	82	75	3	22

TABLE 6: HISTOCHEMICAL STAINING OF EPITHELIAL MESOTHELIOMAS AND METASTATIC ADENOCARCINOMA

STAIN	MESOTHELIOMA	ADENOCARCINOMA
PAS	+ (GLYCOGEN)	+
DIASTASE - PAS	-	+ (MUCIN)
AMP	+ (MUCIN)	+
HYALUR - AMP	0	+

DECEMBER 6, 1981 - CASE NO. 4

ACCESSION NO. 24103

MODERATORS' DIAGNOSIS: LOCALIZED FIBROUS MESOTHELIOMA, PLEURA, PROBABLY MALIGNANT

CLINICAL HISTORY:

This 69 year-old man had a mass contiguous to the left lower lobe and left hemidiaphragm seen on chest x-ray for several years. The mass had recently enlarged, but the patient was still asymptomatic. At thoracotomy, a 9.5 x 8 x 6 cm. tumor with a smooth capsular surface was resected. The mass was attached to visceral pleural by a 2 x 1.5 cm. peduncle. The cut surface of the mass was rubbery, tan, and trabeculated with areas of cystic degeneration. Follow-up 8 months after resection showed that the patient was alive and well.

RADIOGRAPHS:

This patient had a rounded apparent intrapulmonary lesion in the right lower lobe medially probably related to the medial basal segment. The history given includes the fact that this mass on chest x-ray had a benign appearance and had been followed for some years in this asymptomatic patient. Although the patient smoked for 35 years he did quit in 1960. Recent growth of this mass prompted further tissue investigation and at that time the radiographs clearly demonstrate a large approximately 9 cm. mass lesion in the right lower zone associated with the medial basal segment. This was a little lobulated, homogeneous in nature, and appeared to have its epicenter more intrapulmonary in nature. No distinct pedicle was identified. Again, this is a noncalcified lesion and is nonspecific. In view of the nature of the history this would be compatible with a slow growing tumor, and having undergone a recent malignant change and would fit the diagnosis of malignant fibrous mesothelioma. There is no specific radiologic feature for this other than the fact that these lesions usually do project into the lung.

MICROSCOPIC DESCRIPTION:

This tumor shows a fibrous capsule and is composed of round to fusiform cells in a fibrous stroma. The neoplasm demonstrates prominent and uniform cellularity, 3-5 mitoses per 10 high power microscopic fields and occasional pleomorphic, hyperchromatic tumor cell nuclei. Scattered large vascular spaces are present and fibrous septae penetrate from the capsule into the mass.

DISCUSSION:

Localized fibrous mesotheliomas may be either benign or malignant. A summary of significant clinical features of patients with solitary fibrous mesotheliomas (both benign and malignant) is presented in Table 1. Localized mesotheliomas differ in a number of ways from diffuse mesotheliomas. In particular,

the proportion of affected women is relatively higher and pleural effusion is less frequent in localized than diffuse tumors, and asbestos exposure is typically absent in localized neoplasms. Eighty percent of patients with localized tumors are between 40 and 70 years old (as in the case of our patient), but fully 10% are less than 30 years old. By contrast, diffuse mesotheliomas are exceedingly rare in patients in the third decade of life or younger. Solitary fibrous mesotheliomas have been associated with the unusual clinical finding of digital clubbing, but the latter is rarely encountered in practice (see Table 1). In fact, patients with solitary fibrous mesotheliomas are typically asymptomatic, as in the present case. Three-quarters of localized fibrous pleural tumors are attached to the visceral pleura, as in this patient. They are often pedunculated, and vary in size between 1 and 20 cms. The cut surface of our case is quite typical: a white-tan trabeculated mass which, if large, may show zones of cystic softening. The light microscopic appearance of benign localized fibrous mesotheliomas typically shows variable cellularity and a variety of histologic patterns (the so-called patternless pattern). Localized epithelial mesotheliomas have not been reported, while localized biphasic tumors are exceedingly rare.

About 5% of localized fibrous mesotheliomas show microscopic and/or gross criteria of "malignancy". Microscopically, the finding of a spindle cell tumor exhibiting marked cellularity, increased mitoses and cellular anaplasia, i.e., resembling a sarcoma, suggests malignancy. The histologic pattern may resemble fibrosarcoma, malignant fibrous histiocytoma, or even hemangiopericytoma.

Prognosis in localized fibrous mesotheliomas is less dependent on the histology of the lesion than on the presence and degree of invasion of surrounding tissue (Table 2). Surgical resection is the sine qua non for curability. An important corollary is that the prognosis of pedunculated tumors is excellent, no matter what the histologic appearance. A good prognosis can therefore be expected in the present case. The converse is also true, namely that microscopically bland tumors may on occasion be locally invasive, particularly if very large, and may demonstrate a poor prognosis.

Typically, localized malignant fibrous mesotheliomas show a tendency toward local recurrence, rather than distant metastasis (Table 3).

The differential diagnosis of localized fibrous mesothelioma includes diffuse mesothelioma and fibrosarcoma originating in the lung. Both localized and diffuse mesotheliomas share a pleural location, but localized tumors are for all practical purposes always fibrous, while diffuse mesotheliomas show a high proportion of biphasic or epithelial forms. The distribution of tumor at thoracotomy is crucial for distinction. Localized tumors may on occasion show satellite lesions, but multiple nodules or a rind-like covering of the pleura suggests diffuse mesothelioma. Diffuse mesotheliomas may on occasion show a predominant mass, but this always occurs in the setting of numerous nodules covering the pleura, a feature which was not present in this case. Clinical

differences between these two types of mesothelioma have already been mentioned, but to these one must add the important feature that diffuse mesotheliomas are inevitably fatal tumors, while the mortality of localized malignant fibrous mesothelioma is significantly lower (Table 3).

Fibrosarcoma of the lung may be microscopically indistinguishable from localized malignant fibrous mesothelioma (which is essentially fibrosarcoma of the pleura). Distinction between the two neoplasms is based largely on the predominant location of the tumor. Occasionally, subpleural pulmonary fibrosarcomas may extend to the pleura, and localized mesotheliomas may invade into lung, but if the location of the neoplasm is predominantly pleural, it should be classified as a mesothelioma. This distinction is not necessarily trivial, because fibrosarcomas of lung, even those originating in a subpleural location, show a significantly worse prognosis with a higher rate of distant metastasis than do localized malignant fibrous mesotheliomas (See Table 3).

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TABLE 1: CLINICAL FEATURES IN 360 SOLITARY FIBROUS MESOTHELIOMAS

FINDING	% PATIENTS
MEN	46
ASYMPTOMATIC	36
COUGH	46
CHEST PAIN	44
OSTEOARTHROPATHY	35
HYPOGLYCEMIA	4

TABLE 2: PROGNOSIS IN LOCALIZED MALIGNANT MESOTHELIOMA

FACTOR	PROGNOSIS	TUMOR MORTALITY
INVASIVE NON-RESECTABLE	POOR	66%
NON-INVASIVE ENCAPSULATED	GOOD	20%
PEDUNCULATED	EXCELLENT	0%

TABLE 3: MORTALITY DATA IN LOCALIZED MALIGNANT FIBROUS MESOTHELIOMA AND INTRAPULMONARY FIBROSARCOMA

	INTRAPULMONARY FIBROSARCOMA	LOCALIZED MALIGNANT FIBROUS MESOTHELIOMA
MORTALITY	HIGH (75%)	LOW TO MEDIUM (20-66%)
SURVIVAL	SHORT (< 2.5 yrs)	VARIABLE
DISTANT METS.	FREQUENT (90%)	INFREQUENT (< 33%)

DECEMBER 6, 1981 - CASE NO. 5

ACCESSION NO. 22681

MODERATORS' DIAGNOSIS: HAMARTOMA, LUNG

CLINICAL HISTORY:

The patient was a 63 year-old asymptomatic woman who had a 1.8 cm. sharply circumscribed coin lesion noted in the left lobe of the lung by chest x-ray. Excisional biopsy of the lesion revealed a 1.8 cm. spherical, bosselated, white nodule with an irregular, bulging cut surface. The patient was alive and well 3 years after surgery with no significant medical problems.

RADIOGRAPHS:

This patient had a somewhat typical radiological presentation. He presented for a routine chest x-ray and had no symptoms. The patient was found to have a coin lesion. This was situated behind the heart and is a typical area of the chest x-ray that lesions are sometimes missed. When viewing a chest film, the retrocardiac area is one of the five review areas (namely, apex, below the first rib and medial clavicle; hilar structures; retrocardiac area; diaphragmatic reflection; and lateral chest wall). That should be reassessed after a general screening process. After generally viewing a chest film it is these review areas that should be revisited because they are notoriously associated with missed lesion.

This small coin lesion on tomography clearly demonstrated some intralesional calcification and clarified its well demarcated margins. While calcific density did not have any specific ectodermal form, it tends to signify a benign process and is often associated with hamartomas such as in this case.

MICROSCOPIC DESCRIPTION:

This well-demarcated lesion consists of lobules of cartilage surrounded by fibromyxoid connective tissue and fat. Between the lobules are in-branching clefts lined by respiratory epithelium.

DISCUSSION:

The so-called hamartoma (hamartochondroma, chondromatous hamartoma) is the most common benign tumor of lung (.25% of autopsies). Despite its name, this lesion is most frequently encountered in the sixth decade of life and is rarely seen in children. It is more common in men than in women, and typically presents as an asymptomatic coin lesion or as an unexpected finding at autopsy.

Endobronchial or central lesions constitute about 15% of hamartomas; the remainder are usually peripheral in location and without apparent connection to a bronchus. The central or endobronchial hamartoma usually projects as a polypoid mass within the lumen of a large bronchus. Obstruction and bronchial irritation are common sequelae. Peripheral hamartomas

are well-circumscribed lesions that are infrequently symptomatic. The white color, firm consistency and bulging cut surface typically exhibited by these lesions are due to the presence of fibrocartilaginous tissue. The surgeon often reports that the lesion readily "shells out". The average size is 4 to 5 cms. Calcification is an important roentgenographic sign and may be noted in the gross specimen.

By definition, hamartoma is an abnormal mixture of normal elements of an organ. The hamartoma of lung consists of a mixture of cartilage, fibromyxoid tissue, fat, and less frequently bone or smooth muscle. In addition, in-branching clefts lined by respiratory epithelium are found at the periphery of these lesions. Central hamartomas are always associated with a bronchus, and the cartilaginous element is predominant. Peripheral hamartomas usually show no obvious bronchus, cartilage may be rarely absent, and in-branching epithelium is prominent.

Bateson has suggested that hamartomas, rather than being developmental abnormalities, are mesenchymal neoplasms arising in all cases from pluripotential peribronchial mesenchyme. The epithelial elements are considered to be entrapped by the tumor as it grows. The presentation of hamartomas in middle-aged individuals, the absence of associated congenital defects, and the occasional large size of hamartomas in the face of previously negative chest x-rays would seem to support this hypothesis. The apparent absence of a bronchial origin in peripheral hamartomas is presumably due to destruction of the original airway by the tumor. Further, Stone and Churg, using electron microscopy and histochemistry, found the epithelial component of hamartomas to be comprised of elements similar to those lining the distal bronchioles and alveoli of normal lung.

The differential diagnosis of pulmonary hamartoma consists of mesenchymal neoplasms, either benign or malignant, which may entrap alveolar or bronchial epithelium as they grow. For example, benign metastasizing leiomyomas (BML), that is, multiple circumscribed deposits of smooth muscle in the lung of a patient with a past history of leiomyomata uteri, may entrap respiratory epithelium. However, the absence of true cartilage or fat and the multiplicity of lesions in BML set it apart from hamartomas.

The chondrocytes of chondromatous hamartomas may on occasion be markedly atypical in appearance, that is, more cellular and hyperchromatic than is typically seen in chondromas in other sites. This atypia may suggest chondrosarcoma of lung, but these lesions demonstrate a benign prognosis. The admixture of benign fat or smooth muscle further supports the diagnosis of hamartoma in these instances.

DECEMBER 6, 1981 - CASE NO. 5

ACCESSION NO. 22681

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DECEMBER 6, 1981 - CASE NO. 6

ACCESSION NO. 23124

MODERATORS' DIAGNOSIS: THYMOMA, PREDOMINANTLY LYMPHOCYTIC TYPE, ANTERIOR MEDIASTINUM

CLINICAL HISTORY:

A 50 year-old white woman had an asymptomatic anterior mediastinal mass found on routine chest x-ray. The resected specimen consisted of a well-encapsulated and lobulated tumor measuring about 5 cm. in greatest dimension. Two years after surgery, the patient was doing well, with no evidence of recurrence.

RADIOGRAPHS:

This 50 year-old white female presented for a routine chest film and was found to have an indistinct mediastinal mass that projected in the PA film over the root of the aorta simulating possible aneurysmal dilatation of the ascending aorta. However, on the lateral view the retrosternal area was abnormal and clearly indicated that this somewhat lobulated mass was visible anteriorly in the anterior mediastinum apparently separate from the aorta. Subsequent nuclear angiography clarified that the mass effect was not related to the aorta. The conventional tomography confirmed a homogeneous mass without evidence of calcification and there were no major cystic components. Computerized tomography again confirmed the presence of the mass lesion and the absence of any major fat densities consistent with mediastinal fat deposits. The patient's age and presentation plus the radiographic features are strongly suspicious for a thymic tumor, but again are nonspecific in nature.

MICROSCOPIC DESCRIPTION:

Some histologic sections of this tumor show it to have a thick fibrous capsule, while others demonstrate fibrous septae coursing through the tumor and dividing it into lobules. A dense infiltrate of small lymphocytes is present throughout the neoplasm. In areas, however, large cells with pale nuclei and indistinct cytoplasm are present. Mitoses are abundant. No Hassall's bodies or perivascular spaces are seen.

DISCUSSION:

Thymoma is a neoplasm composed of thymic epithelial cells with or without an associated benign lymphoid infiltrate. About 50% of patients with thymoma present clinically with an asymptomatic mediastinal mass found on routine chest x-ray, as in this case. Patients complain of local chest symptoms (pain, cough, dyspnea) in about 25% of cases, while another 25% manifest one of a number of systemic disorders such as myasthenia gravis, red cell hypoplasia, or hypogammaglobulinemia. Thymomas are usually located in the anterior mediastinum but may also be found in other compartments of the mediastinum, including (in decreasing order of frequency) superior, middle, and even posterior mediastinum. The gross appearance of our patient's lesion is typical. Thymomas are

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usual solitary, encapsulated and lobulated masses which may or may not be cystic. The prognosis of thymoma is critically dependent on the finding of gross or microscopic invasion of the capsule and surrounding thoracic structures. Encapsulated and surgically resectable lesions have a 10 year survival of 100% while invasive/metastatic thymomas have a dramatic reduction of survival to 20% at 10 years. Myasthenia gravis is an additional adverse prognostic finding - no patient with invasive thymoma and myasthenia gravis survives 10 years. About 60% of thymomas are encapsulated (benign), while about 40% are invasive or metastatic. These figures probably overstate the relative frequency of invasive thymomas, since they largely derive from larger referral centers specializing in "complicated" lesions.

The principle microscopic features of thymomas are shown in Table 1. Our case illustrates a number of these, including the presence of a fibrous capsule, fibrous septae dividing the tumor into lobules, and a biphasic cell population. Especially in unusual sites such as the middle mediastinum, a study of tissue adjacent to the neoplasm may demonstrate residual thymic epithelium and relieve the pathologist of his reluctance to make a diagnosis of thymoma.

The variable lymphocytic infiltrate in most thymomas creates three major patterns, listed in Table 2. An alternate classification system for thymomas is shown in Table 3. From this, it can be seen that the spectrum of lymphocytic infiltration in thymomas may be interpreted as continuous. Note that only 4% of thymomas fail to show a lymphoid component. Interestingly, most mitoses in thymomas derive from the benign lymphoctic element rather than the neoplastic epithelial cells, and are therefore <u>not</u> an indicator of malignancy.

In sum, the presence in this case of a mediastinal tumor with a fibrous capsule, fibrous septae and biphasic cell population should suggest thymoma. The differential diagnosis of such a lesion may include non-Hodgkin's lymphoma, either of the mixed lymphocytic and histiocytic or well-differentiated lymphocytic types. Just under 40% of cases of mediastinal non-Hodgkin's lymphomas were of these histiologic subtypes (Table 4). In these instances, the tumor involves mediastinal lymph nodes, normal remnants of which may still be present. Further, lymphomas will usually not show a thick fibrous capsule or fibrous septae. Additional features which suggest the diagnosis of thymoma over lymphoma are the presence of neoformation of Hassall's bodies and perivascular "edematous" spaces. Systemic nodal disease or leukemia of course favors lymphoma. In difficult cases, electron microscopy may be of aid by demonstrating the characteristic ultrastructural features of thymic epithelial cells (Table 5).

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TABLE 1: HISTOLOGICAL FEATURES OF THYMOMAS *

FEATURE	% CASES
FIBROUS CAPSULE	100
ADJACENT THYMIC TISSUE	50
FIBROUS TRABECULAE	> 95
BIPHASIC CELL POPULATION	96

* ROSAI AND LEVINE

TABLE 2: 272 THYMOMAS: FREQUENCY BY HISTOLOGIC TYPE *

TYPE	NO. PATIENTS	% SERIES
BIPHASIC	52	19
EPITHELIAL	148	54
LYMPHOCYTIC	72	27

* BERNATZ ET AL; BATATA ET AL; SALYER AND EGGLESTON

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TABLE 3: LYMPHOID COMPONENT IN 164 THYMOMAS *

LYMPHOCYTES	% SERIES
PREDOMINANT	37
MODERATE	39
SCANT	20
ABSENT	4

* AFTER ROSAI AND LEVINE

TABLE 4: DISTRIBUTION OF HISTOPATHOLOGIC TYPES IN 40 CASES OF MEDIASTINAL NON-HODGKIN'S LYMPHOMA *

TYPE	NO. CASES
W D LYMPHOCYTIC	5
LYMPHOBLASTIC	19
MIXED L & H	10
HISTIOCYTIC	6

* VAN HEERDEN ET AL.

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TABLE 5: ELECTRON MICROSCOPIC DISTINCTION
BETWEEN THYMOMA AND MEDIASTINAL LYMPHOMA

	THYMOMA	P D L *	W D L **	HISTIOCYTIC
TONOFIBRILS	+	-	-	-
DESMOSOMES	+	-	-	-
NUCLEARBLEBS	-	+	-	-
CONVOLUTED NUCLEI	-	+	-	+

* P D L = POORLY DIFFERENTIATED LYMPHOCYTIC LYMPHOMA

** W D L = WELL DIFFERENTIATED LYMPHOCYTIC LYMPHOMA

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DECEMBER 6, 1981 - CASE NO. 7

ACCESSION NO. 18640

MODERATORS' DIAGNOSIS: MUCOEPIDERMOID TUMOR, BRONCHUS

CLINICAL HISTORY:

This 20 year-old man had an asymptomatic 9 x 6 cm. mass in the right lower lobe, discovered by routine chest x-ray. Bronchogram showed obstruction of the right lower lobar bronchus. At thoracotomy, the right lower lobe was atelectatic, and a globoid, rubbery, 7 x 5.5 cm. smooth, yellow tumor was found protruding into and completely obstructing the posterior basal segmental and right lower lobar bronchi. Abundant mucus exuded from the cut surface of the tumor. The patient was alive and well three years after surgery.

RADIOGRAPHS:

Twenty year-old male presented with an large mass in the right lower zone that was nonhomogeneous in nature and was suspect for cavitation. The patient was asymptomatic and there was no associated effusion. The chest x-rays at admission demonstrate approximately 5 cm. mass in the right lower lobe posterior segment. This was found to be nonhomogeneous and contained no calcifications on tomography. The mass was well demarcated and intrapulmonary in nature. There was no calcification identified.

The bronchogram that was also available clearly indicated amputation of the bronchus and the meniscus of the bronchographic contrast media at the site of amputation was suggestive of a large intraluminal mass effect. These radiographic features are not specific for mucoepidermoid cyst but do strongly suggests large tumoral mass lesion with possible associated obstructive pneumonitis or abscess formation.

MICROSCOPIC DESCRIPTION:

The tumor is well-circumscribed and lies adjacent to a large muscular pulmonary artery. This finding suggests, in the absence of a demonstrable bronchus adjacent to the artery, that the neoplasm may have originated in and destroyed the bronchial wall. The tumor consists of enlarged cells exhibiting little nuclear atypia and forming numerous mucin-containing glands of various size and shape. Occasional small nests of tumor cells with eosinophilic cytoplasm are noted, as well as individual mucous-producing cells. Mitoses are absent, but a focus of hemorrhage with extensive fibrinous exudate is noted.

DISCUSSION:

Mucoepidermoid tumors constitute 2-3% of so-called bronchial "adenomas", and are therefore uncommon. The average age of affected patients is 40 years, and there is a preponderance of men. Mucoepidermoid tumors are typically

located in the lobar or main bronchi. Symptoms reflect the endobronchial location of the tumor.

The bronchoscopic and gross appearance are those of an endobronchial, exophytic polypoid mass which often exudes mucus on its cut surface. The tumor may extend through the bronchial wall into the surrounding tissues or may be confined to the bronchus itself.

Histologically, mucoepidermoid tumors consist of mixtures of mucous-producing cells forming glands or large mucous-filled cysts. Sheets of uniform cells with a vaguely epidermoid appearance but lacking definitive keratinization or intercellular bridges are often seen. Mitoses and nuclear atypia are rare. Occasionally, a granulomatous reaction to mucous and lipid liberated from distended tumor glands may be present.

The overwhelming majority of mucoepidermoid tumors, including the neoplasm in this case, fall into the category of "low grade" lesions. These tumors are locally invasive, but are not reported to metastasize to the regional nodes or elsewhere. The prognosis of these low grade neoplasms is excellent. Some debate exists over the presence of "high grade" tumors, analogous to those occurring in the salivary gland. These lesions have been defined as showing sheets of squamous epithelium, and significantly more nuclear atypia, mitoses and necrosis than is seen in low grade tumors. High grade mucoepidermoid tumors often demonstrate regional node metastasis at thoracotomy, and their prognosis is uniformly bad, nearly all patients dying within four years of diagnosis. The distinction between these tumors and adenoepidermoid carcinomas of the bronchus may be difficult. Adenoepidermoid carcinomas, or bronchogenic carcinomas with mixed mucinous and squamous differentiation, constitute about 2% of lung cancers. They are often found in the periphery of the lung, show ample zones of necrosis, and are cytologically more pleomorphic than high grade mucoepidermoid tumors. It is possible that some of the mucoepidermoid tumors with very poor prognosis reported by Turnbull et al, are actually adenoepidermoid carcinomas.

Of the bronchial "adenomas", only the rare mucous gland adenoma is truly benign. This lesion, consisting of glands and cysts of variable size which replicate the normal mucous glands of the bronchus, may simulate mucoepidermoid tumor. However, these glands are usually more organized and regular in appearance than those seen in the mucoepidermoid tumor, and "epidermoid" foci are absent.

The cellular atypia and mitoses of bronchogenic adenocarcinoma are absent in the low grade mucoepidermoid tumor.

Bronchial carcinoids may show a glandular pattern, with extracellular mucin. However, intracytoplasmic mucin or glycogen, which are typically seen in mucoepidermoid tumors, are not found in carcinoid tumors, while the argyrophilia of carcinoid tumors has not been reported in the mucoepidermoid tumor.

DECEMBER 6, 1981 - CASE NO. 7

ACCESSION NO. 18640

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DECEMBER 6, 1981 - CASE NO. 8

ACCESSION NO. 14786

MODERATORS' DIAGNOSIS: CARCINOSARCOMA, LUNG

CLINICAL HISTORY:

This 57 year-old white man had a 24 year history of roentgenographically demonstrable pulmonary lesions, beginning with a right paratracheal mass which evolved into multiple isolated masses within both lungs. A right lower lobectomy was performed, and the resected lobe demonstrated multiple well-demarcated, soft white-tan and hemorrhagic nodules, the largest of which measured 5 cm. in diameter. The patient died six years after thoracotomy, and was found to have widespread metastatic mucous-secreting adenocarcinoma.

RADIOGRAPHS:

This old case dating back to 1941 presented initially with a chest radiograph revealing a 3 x 4 cm. homogeneous smooth mass in the right paratracheal area. This was homogeneous in nature, and did not cavitate. It appeared to have its epicenter more intrapulmonary and was apparently left untouched for 24 years due to the patient's refusal for thoracotomy. Subsequently multiple pulmonary mass lesions were identified in the periphery of the lung, particularly in the right lower zone. These two were round, smooth mass lesions that did not cavitate and had a slightly lobulated edge. The overall appearance is nonspecific but would be consistent with fungus ball formation. Naturally this radiographic appearance would raise strong suspicions of malignancy but the somewhat benign course of this patient would tend to negate malignant tumor.

MICROSCOPIC DESCRIPTION:

The histologic section available for review shows a relatively well-demarcated nodular lesion consisting of irregular, branching glands of variable size lined by a single layer of columnar, mucin-secreting epithelium. These glands are set within a primitive mesenchyme consisting of oval and spindled cells. In areas, mesenchymal cells contain a brown pigment which does not stain for either melanin or iron. The mesenchyme does not demonstrate recognizable cartilaginous, bone or muscle differentiation.

DISCUSSION:

The presence of a biphasic tumor containing intimately admixed epithelium and mesenchyme suggests carcinosarcoma. Two main types of pulmonary carcinosarcomas exist. Carcinosarcomas of embryonal type were initially described by Barnard in 1952, at which time they were termed pulmonary embryomas. In 1961, Spencer reported three cases and first used the term pulmonary blastoma, in the belief that the tumor was the pulmonary analogue of nephroblastoma. Pulmonary blastomas are characterized by epithelial-lined tubules and glands and a primitive stroma, both of which histologically resemble structures found in fetal lung. Specifically, the glandular component is lined by stratified columnar epithelium rich in glycogen but lacking mucin. Recently, neurosecretory

granules have been demonstrated in one case of pulmonary blastoma by electron microscopy. The stroma of blastomas is variable in extent and in many cases may be quite scant. It consists typically of primitive oval and spindled cells, similar to those seen in the present case. Cartilage and smooth muscle may be found in some instances. Pulmonary blastomas usually present as large (average size 8 cm.), solitary lesions in lung. The clinical presentation of the present case would therefore be unusual for pulmonary blastoma. Furthermore, overall mortality is fairly high (approximately 70% of cases) and about two-thirds of deaths occur within two years. Once again, the long history in our case would seem unusual for blastoma. The course of these tumors is not readily predicted from histology, but the presence of metastasis at thoracotomy, and tumor size greater than 5 cm. do seem to adversely affect survival (Table 1).

Carcinosarcoma of lung consists of intimately admixed epithelium and mesenchyme of a type ordinary seen in malignancies of adults. Interestingly, glandular epithelium is distinctly unusual in pulmonary carcinosarcomas, most cases (85%) showing epidermoid differentiation. Carcinosarcomas typically present in older patients (average age 60 years) as hilar (bronchogenic) masses. The prognosis is very poor. Again, the leisurely course of this patient's disease would seem unusual for pulmonary carcinosarcoma.

To summarize, the presence of (adult) epithelium consisting of mucin-secreting cells in our case militates against the diagnosis of pulmonary blastoma. At the same time, the primitive mesenchyme of the case would be unusual for carcinosarcoma, and more in keeping with blastoma. A review of patients with pulmonary carcinosarcomas and pulmonary blastomas suggest that biphasic tumors with an histology intermediate between blastoma and carcinosarcoma may exist. If this is so, our case properly fits into this category.

Two other possibilities need to be considered briefly. Hamartoma of lung is rarely multiple. Of greater significance, the presence of a mucin secreting epithelium and the absence of mature stromal derivatives (cartilage, fat, smooth muscle) militates against a diagnosis of harmatoma. The biphasic character of the tumor with a primitive stroma would also militate against primary or metastatic adenocarcinoma.

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TABLE 1: PROGNOSIS OF PULMONARY BLASTOMAS *

FEATURE	NO. PATIENTS	2 YR. SURVIVAL
METASTASIS		
YES	16	12.5%
NO	8	62.5%
TUMOR SIZE		
$<$ 5 CM.	7	14.0%
$>$ 5 CM.	32	53.0%

* FUNG, C. H. ET AL.

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DECEMBER 6, 1981 - CASE NO. 9

ACCESSION NO.24204

MODERATORS' DIAGNOSIS: DIFFUSE MALIGNANT FIBROUS MESOTHELIOMA, PLEURA

CLINICAL HISTORY:

This 53 year-old man had right chest pain of several months duration. Chest x-ray showed a peripheral right upper lobe mass which seemed to involve the pleura. At thoracotomy, multiple tracts of nodular tissue extended over the visceral and parietal pleurae and a bulky pleural mass was found adherent to the parietal and visceral pleurae in the region of the right upper lobe. The patient suffered a clinical relapse two months after operation.

RADIOGRAPHS:

This 53 year-old Caucasian male had normal chest films until January of 1980. At that time it was discovered he had a lobulated pleural based mass lesion that was a noncalcified and approximately 3-4 cm. in greatest diameter situated in the right side. This lobulated mass had classical extrapulmonary signs indicating pleural base and again while nonspecific raises the question of a pleural based tumor such as fibrous mesothelioma. Because of the somewhat rapid growth of the lesion over less than one year, malignant nature of this pleural tumor should immediately be considered. Thus this rapid pleural based lobulated lesion and these radiographic features are consistent with a malignant fibrous mesothelioma.

MICROSCOPIC DESCRIPTION:

A collagenized, relatively acellular, hyaline pleural plaque is present. The plaque is contiguous to and surrounded by a spindle cell neoplasm demonstrating the following characteristics: bland and relatively uniform nuclei, a distinct tendency towards a storiform pattern of growth in areas, a paucity of mitoses, and unequivocal invasion of the muscle of the chest wall. A patchy, chronic inflammatory infiltrate is present within the tumor. No ferruginous bodies are seen and no lung parenchyma is present.

DISCUSSION: See Case 3 for primary discussion

Diffuse malignant fibrous mesothelioma must be distinguished from reactive pleuritis. The bland cytologic appearance of diffuse malignant fibrous mesothelioma, well-illustrated in this case, might suggest a reactive process, especially in a small biopsy. The surgeon's description of masses or nodules, and the microscopic findings of high cellularity and a prominent storiform pattern should suggest a malignant rather than reactive pleural process. Most importantly, invasion of the subpleural tissues (either fat or muscle or lung) strongly supports a neoplastic diagnosis.

Asbestos-associated hyaline pleural plaques, one of which was present in this case, are typically found on parietal pleura, especially diaphragmatic

pleura. They are characteristically paucicellular, and therefore readily distinguished from mesothelioma. No report of malignant transformation of hyaline plaques has as yet been recorded.

One further point of interest in this case should be mentioned. No ferruginous bodies were seen within the tumor, and a similar experience was noted in Case 3. It is, in fact, unusual to find ferruginous bodies within mesotheliomas themselves. The subjacent lung parenchyma is the area to investigate for detection of ferruginous bodies.

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DECEMBER 6, 1981 - CASE NO. 10

ACCESSION NO. 24262

MODERATORS' DIAGNOSIS: PROBABLY PLASMACYTOID LYMPHOCYTIC LYMPHOMA, LUNG

CLINICAL HISTORY:

This 73 year-old white woman had a mass in the right middle lobe followed with repeated chest x-rays for two years. A mediastinal biopsy two years prior to the current surgery had been interpreted as showing no neoplasm. Resection of the right middle lobe of lung showed a 3.5 cm. rubbery, tan homogeneous lesion beneath the pleural surface which irregularly infiltrated the surrounding lung parenchyma. No follow-up clinical information is available.

RADIOGRAPHS:

This 73 year-old white female has a history of a mass in the chest x-ray with a previous suspicious density in the left lung two years ago. Although bronchoscopy was negative and previous needle biopsy negative, the current CT that was available clearly demonstrated an anterior nonhomogeneous somewhat irregular lesion with its epicenter more entrapped pulmonary but adjacent to the mediastinal reflections. Nonhomogeneous nodular densities, usually somewhat spiculated or lobulated and less discretely marginated, associated with air bronchograms, are strongly suspicious of entrapped pulmonary lymphoma or pseudolymphoma from the radiologic point of view. At times alveolar cell carcinoma can present with this radiological pattern and is usually not associated with any effusion. That is, from the radiological point of view, nodular pulmonary lesions that are somewhat lobulated or have spiculated edges associated with air bronchograms within the lesion should suggest the possibility of pulmonary lymphoma.

MICROSCOPIC DESCRIPTION:

The histologic sections demonstrate a lymphoid infiltrate obliterating much of the normal architecture of the lung. The lesion shows a number of significant characteristics. First, it invades through the perichondrium of at least one cartilage-bearing bronchus. In some sections, the tumor penetrates through the visceral pleura in the form of polypoid protrusions. The neoplasm consists of sheets of small lymphocytes and, especially about airways, clusters of plasma cells and plasmacytoid lymphocytes, some of which contain eosinophilic intranuclear inclusions. A PAS stain demonstrates scattered Dutcher bodies(PAS-positive intranuclear inclusions). A number of reactive lymphoid follicles are seen within the infiltrate. They are most prominent adjacent to residual airways.

DISCUSSION:

Lymphoid lesions arising in lung pose extraordinary problems of differential diagnosis. In this particular case, we should consider plasmacytoid lymphocytic lymphoma, small lymphocytic lymphoma (well-differentiated lymphocytic lymphoma in the Rappaport classification) and pseudolymphoma in our differential diagnosis.

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Plasmacytoid lymphocytic lymphoma is the second most frequent primary pulmonary lymphoma. In a series of 161 primary pulmonary lymphoid lesions, we found that approximately 20% of cases were lymphomas of this type. They are characteristically cytologically diverse, with admixed plasma cells, plasmacytoid lymphocytes and small lymphocytes (as in our patient). PAS-positive intranuclear inclusions (Dutcher bodies) are found in about one-half of these lymphomas and are suggestive of, but not pathognomonic for, the tumor. The invasion of bronchial cartilage and pleura in this case are additional histologic features suggestive of a neoplastic rather than reactive lymphoid process.

Immunoperoxidase studies for cytoplasmic light chain immunoglobulin typically show a monoclonal pattern in plasmacytoid lymphocytic lymphomas. In this case, immunoperoxidase studies showed a few polyclonal areas, but demonstrated no staining in most areas. This inconclusive result may have arisen from inadequate fixation or other technical difficulties.

Small lymphocytic lymphoma is readily excluded on cytologic grounds, since it consists of sheets of small lymphocytes, without plasmacytoid cells containing Dutcher bodies.

Pseudolymphoma is excluded with more difficulty. Pseudolymphoma is a reactive lymphoid proliferation which manifests itself in lung as one or several masses or localized infiltrates. Histologically, it consists of "mature" polymorphous lymphoid cells (lymphocytes, plasma cells) and admixed reactive germinal centers. The present of reactive germinal centers in our case raises the diagnosis of pseudolymphoma. However, in a study of malignant lymphomas of lung, we found 15 to 61% of tumors (depending on histologic type) showed scattered reactive germinal centers, so that this criterion cannot be used to exclude lymphoma. Further, none of the cases of pseudolymphoma that we studied contained Dutcher bodies. Finally, as previously mentioned, we found that plaque-like invasion of visceral pleura or penetration of perichondrium of bronchial cartilage (both of which were seen in our case) occurred significantly more frequently in malignant lymphomas than in pseudolymphomas, and we therefore believe that these architectural abnormalities are suggestive (although not pathognomonic) of malignancy. The best criterion for distinguishing malignant lymphoma and pseudolymphoma is involvement of hilar or mediastinal lymph nodes, but it is unfortunately infrequently found in primary pulmonary lymphomas, and was absent in our case.

Primary pulmonary non-Hodgkin's lymphomas are themselves infrequent lesions. As of 1982, fewer than 200 cases had been reported. In an as yet unpublished review of 161 primary pulmonary lymphoid lesions (excluding LIP), we have found that about 80% can be classified as lymphoma. The age distribution of patients ranges from the third to ninth decades, with a unimodal peak in the sixth decade. The sex ratio of patients with pulmonary lymphoma is approximately equal. More than one-half of the cases are asymptomatic, the pulmonary lesions being found on routine chest x-ray. Some patients are followed with a slowly growing mass up to 3 1/2 years before being subjected to

thoracotomy (as in the present case). When symptoms are present, they are usually nonspecific and related to the chest (cough, dyspnea, chest pain, hemoptysis). Typically, most patients with lymphoma show no abnormalities on physical examination. The distribution of primary pulmonary lymphomas by histologic class is shown in Table 1. Ninety-two percent of lymphomas are small cell lymphoid tumors, i.e. small lymphocytic (well-differentiated lymphocytic), plasmacytoid lymphocytic, or small cleaved follicular center cell (FCC) lymphomas. These tumors typically grow as solid lesions, obliterating normal lung architecture, as in the present case. In some instances, an interstitial and perivascular pattern simulating lymphoid interstitial pneumonia is present. Residual alveoli often contain eosinophilic and PAS-positive fluid resembling edema. Giant cells and noncaseating granulomas occur in 25 to 53% of cases, and tumor necrosis is rare.

About one-half of patients with primary pulmonary lymphomas develop recurrence, usually within three years of initial diagnosis. The most common site of recurrence is lung, pleura or mediastinum. Contralateral spread may occur without dissemination beyond the thorax. Metastasis to unusual extrathoracic sites (gastrointestinal tract, salivary glands, orbit) may occur. In our experience with follow-up of 101 patients, only 12 tumor-related deaths were recorded by 5 years, and 18 deaths by 15 or more years after diagnosis. Further, distant spread of tumor is compatible with long survival.

The normal treatment for localized pulmonary lymphoma is excision, with post-surgical radiation therapy or chemotherapy employed if effusion, hilar node involvement, or other factors suggest the need. Extensive non-resectable pulmonary disease, after biopsy, is usually treated with radiation or chemotherapy, but prognosis in such instances is poor, 40% of patients dying of tumor.

DECEMBER 6, 1981 - CASE NO. 10

ACCESSION NO. 24262

TABLE 1: HISTOPATHOLOGIC CLASSIFICATION OF 161 PRIMARY PULMONARY LYMPHOID LESIONS*

DIAGNOSIS	NUMBER OF PATIENTS	O/O SERIES
LYMPHOMA		
SMALL LYMPHOCYTIC	51	31.6
PLASMACYTOID LYMPHOCYTIC	36	22.4
FCC		
SMALL CLEAVED	19	11.8
SMALL NON-CLEAVED	1	0.6
LARGE CLEAVED	3	1.9
LARGE NON-CLEAVED	3	1.9
B-IMMUNOBLASTIC SARCOMA	2	1.2
SMALL LYMPHOID, NOS	15	9.3
PSEUDOLYMPHOMA, FOLLICULAR	18	11.2
PSEUDOLYMPHOMA, DIFFUSE	5	3.1
QUESTIONABLY REACTIVE	8	5.0
TOTAL	161	100.0

* LUKES-COLLINS CLASSIFICATION

DECEMBER 6, 1981 - CASE NO. 10

ACCESSION NO. 24262

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DECEMBER 6, 1981 - CASE NO. 11

ACCESSION NO. 22066

MODERATORS' DIAGNOSIS: SCLEROSING HEMANGIOMA, LUNG

CLINICAL HISTORY:

The patient was an 18 year-old asymptomatic white woman in whom a 3.5 x 4.5 cm. sharply circumscribed pulmonary nodule was seen in the left lower lobe by chest x-ray. Six months after excision of the lesion, the patient was well without evidence of recurrence.

RADIOGRAPHS:

PA and lateral radiographs of this 18 year-old female clearly demonstrate a left lower lobe nodule, approximately 3 cm. in greatest diameter and nonhomogeneous in nature. This asymptomatic nodule was found on routine physical. There was no history of acute illness. Careful examination indicates that there is no radiological calcification demonstrated within the lesion. The hilar structures were normal and there were no evidence of effusion.

The well circumscribed lesion appears benign in nature and in a patient of this age with very low statistics for malignancy, the differential diagnosis would include pulmonary sequestration, organizing pneumonia, pulmonary hamartoma (although no internal ectodermal elements were visualized). Neuroenteric cyst, possibly a bronchogenic cyst although the situation is a little inferior and vascular malformation. Thus there are no specific radiological features demonstrated for the diagnosis of sclerosing hemangioma. It is of interest to note that there are no large vessels clearly demonstrated coming to or from this lesion.

MICROSCOPIC DESCRIPTION:

The lesion was said to be sharply circumscribed and encapsulated in the gross specimen, but the margins are fragmented in the microscopic section. This tumor lies adjacent to a bronchus and has a varied microscopic appearance. Papillary areas alternate with sheets of tumor cells and fibrotic zones. Clusters of foamy macrophages are seen within some of the alveolar spaces. The lesion shows a characteristic double cell population. Within the core of the papillary fronds and within the sheet-like zones, the dominant cell is a uniform, round to polygonal cell with ample pale cytoplasm. The outer surfaces of the papillary fronds are lined by a layer of cuboidal epithelial cells.

DISCUSSION:

The so-called sclerosing hemangioma of the lung is a benign tumor of undetermined histogenesis, characterized by an interstitial proliferation of cells of unknown type with associated sclerosis and blood-filled spaces. The age

range of patients with this lesion is wide, varying between 15 years and 69 years, with a mean of 42 years. The female to male ratio is 4 to 1. Ninety percent of the patients are asymptomatic, while the rest have either cough, chest pain, or hemoptysis. Surgical excision of these lesion is curative.

Katzenstein has reported four major histologic patterns in pulmonary sclerosing hemangiomas. Usually, a combination of these patterns is found in any given case. A solid pattern of tumor growth consists of nests and sheets of the characteristic bland, uniform cells. Hemorrhagic areas, consisting of dilated, blood-filled spaces may be seen. In some cases, as in our own, a papillary component is dominant. Sclerotic foci are found in nearly all cases. In addition, intra-alveolar collections of foamy macrophages may be seen. No matter what the predominant histologic pattern, one always sees within these lesions interstitial collections of round to oval uniform and bland cells with fine chromatin and inconspicuous nucleoli. The interstitial location of these cells has been confirmed by electron microscopic studies. Ultrastructurally, they are rectangular or polygonal with clear cytoplasm, scant organelles and occasional microvilli and tight junctions, and they occasionally have basement membranes around them. Haas and Yunis, and Kay et al. have interpreted the cells as endothelial in origin, while Spencer, Hill and Eggleston, Kennedy, and Heilman and Feiner believe them to be of epithelial origin. Katzenstein, Weise, et al. have recently suggested a mesothelial histogenesis. Our own immunopathologic studies using Factor VIII-associated antigen, as well as those of Katz et al., failed to show an endothelial origin. The cuboidal cells lining the alveolar lumens have been shown by electron microscopy to be Type 2 pneumocytes.

Sclerosing hemangiomas must be distinguished from other types of inflammatory and vascular lesions in lung. Inflammatory pseudotumor is a term used to designate a non-neoplastic mass consisting of inflammatory mesenchymal cells, including plasma cells, histiocytes (often xanthomatous), mast cells, lymphocytes and spindle-shaped mesenchymal cells. By custom, they are designated by their predominant component, namely, fibroma, fibrohistiocytoma or fibroxanthoma, and plasma cell granuloma. Sclerosing hemangiomas share with these lesions the presence of sclerosis, collections of xanthoma cells, and a heavy infiltration of cells which were once considered to be histiocytes. However, it is now clear that a histiocytic interpretation for the characteristic cells of sclerosing hemangioma is incorrect, that the foamy macrophages seen in sclerosing hemangiomas are due to obstruction of adjacent airways, and that sclerosing hemangiomas bear no histogenetic relationship to inflammatory pseudotumors, even though both share a benign course.

The presence of blood-filled spaces in sclerosing hemangioma may suggest a vascular tumor. Carcinoid adenomas are typically richly vascular, consist of uniform round to oval cells, and may show pseudopapillary structures in zones of degeneration, thereby mimicking sclerosing hemangioma. However, the characteristic cells of sclerosing hemangioma are typically interstitial in location, a

feature not seen in carcinoid tumors. Ultrastructurally, the neurosecretory granules of carcinoid tumors have not been reported in sclerosing hemangiomas.

The papillary foci of sclerosing hemangiomas call to mind papillary adenocarcinomas, either primary or metastatic to lung. However, atypical cells are usually not seen in sclerosing hemangiomas, and the interstitial location of the cellular proliferation should suggest the correct diagnosis.

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DECEMBER 6, 1981 - CASE NO. 12

ACCESSION NO. 24275

MODERATORS' DIAGNOSIS: GRANULOMATOUS INTERSTITIAL PNEUMONITIS (HYPERSENSITIVITY PNEUMONITIS, EXTRINSIC ALLERGIC ALVEOLITIS), LUNG

CLINICAL HISTORY:

This 28 year-old man had a 4 month history of progressive shortness of breath and intermittent temperature spikes. Chest x-ray showed bilateral reticulonodular infiltrates. The patient was subjected to open lung biopsy. Three months later, after a regimen of corticosteroids, he was virtually asymptomatic.

RADIOGRAPHS:

A diffuse interstitial lung disease consisting of a very fine reticular nodular radiographic pattern in a young male with progressive shortness of breath is more suggestive of an active inflammatory process. It is not uncommon for such radiographic appearances not to be associated with any productive cough. In this case there was normal previous chest film 9-27-77. There was no effusion associated with any of the available films and the process appeared to be entirely interstitial in nature.

Diffuse fine reticular nodular interstitial disease has a long radiological differential which is somewhat narrowed by the presence of hilar adenopathy which this case presented on 5-11-82. Because there is improvement in the radiographic pattern following therapy, the pattern is not consistent with any major fibrotic process at this time. The overall appearance is compatible with the diagnosis of hypersensitivity pneumonitis. In such cases close clinical correlation and detailed history information is critical to narrow down the large differential diagnosis into most probable categories. Close correlation between clinician, radiologist and pathologist is very important during the diagnostic work-up of such a patient.

MICROSCOPIC DESCRIPTION:

The biopsy shows three diagnostic findings: a patchy, interstitial lymphoplasmacytic infiltrate; small, poorly-formed interstitial and peribronchial granulomas consisting of aggregates of histiocytes with occasional admixed giant cells; and tufts of fibrous connective tissue in alveoli and bronchioles (bronchiolitis obliterans). Intra-alveolar collections of foamy macrophages, presumably secondary to the bronchiolitis obliterans, are also seen. There is no necrosis, and special stains for bacteria and fungi are negative.

DISCUSSION:

Granulomatous interstitial pneumonitis, or hypersensitivity pneumonitis, is the term used to describe diffuse interstitial microgranulomatous disease

in lung following exposure to organic and inorganic antigens. The offending organic antigens can be divided into three broad groups: thermophilic organisms (such as thermophilic actinomycetes or Micropolyspora faeni), molds (such as Cryptostoma corticale or Aspergillus clavatus) and animal proteins (such as avian droppings). These organisms or antigens are encountered in a variety of occupations (most of them quite unusual), as shown in Table 1. However, thermophilic organisms can also cause disease in urban or suburban settings, where they may be present in home or office air conditioners or humidifiers (this patient had a window air conditioner).

The histologic findings in lung vary with the chronicity of exposure to antigen. Four to eight hours after a single exposure to large amounts of offending antigen, the patient develops severe dyspnea, cough and fever. The few biopsies performed in such circumstances show an acute inflammatory process, with polymorphonuclear leucocytes in bronchioles and interstitium. Usually, symptoms resolve spontaneously 12-18 hours after a single exposure.

Chronic exposure (months) to small amounts of antigen is usually manifested by progressive dyspnea, fatigue, malaise and bilateral interstitial pulmonary infiltrates (as seen in our patient). Interstitial, ill-formed granulomas, interstitial lymphoplasmacytic infiltrates, and bronchiolitis obliterans are typical and distinctive morphologic findings which suggest the diagnosis, even without benefit of history. Prolonged disease results in honeycombing fibrosis.

The immunopathogenesis of hypersensitivity pneumonitis is complex and uncertain. Currently, delayed hypersensitivity and possibly local immune complex formation are believed to produce this disease. Pulmonary eosinophilia is not a typical finding in microgranulomatous interstitial pneumonitis.

The differential diagnosis of hypersensitivity pneumonitis consists of other interstitial and/or granulomatous diseases in lung. In usual interstitial pneumonia, the interstitial lymphoplasmacytic infiltrate is not accompanied by interstitial granulomas.

Sarcoidosis may show a mild interstitial lymphoid infiltrate, but the granulomas of sarcoid are usually larger, more cohesive, and better delimited than those of hypersensitivity pneumonitis.

Lymphoid interstitial pneumonia (LIP) may show poorly-formed interstitial granulomas, but they occur in a lymphoid infiltrate so extensive and marked that it resembles pseudolymphoma. Germinal centers are found in 30 percent of cases of LIP but are not seen in hypersensitivity pneumonitis.

Interstitial, perivascular granulomas are seen in the lungs of intravenous

drug abusers. The presence of birefringent talc and cotton fibers are pathognomonic of this disease, and readily distinguish it from our patient's lesion.

Finally, necrotizing sarcoid granulomatosis shows interstitial and perivascular granulomas, but also exhibits distinct granulomatous vasculitis and parenchymal necrosis, findings which have never been reported in hypersensitivity pneumonitis.

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DECEMBER 6, 1981 - CASE NO. 12

ACCESSION NO. 24275

TABLE 1: FORMS OF HYPERSENSITIVITY PNEUMONITIS AS KNOWN CAUSES OF POSSIBLE EXTRINSIC ALLERGIC ALVEOLITIS *

FORM OF HYPERSENSITIVITY	AGENT
FARMER'S LUNG	MICROPOLYSPORA FAENI
MOLDY-HAY DISEASE	M. FAENI; A. FUMIGATUS
BAGASSOSIS	THERMOACTINOMYCES VULGARIS
MUSHROOM WORKER'S DISEASE	M. FAENI and T. VULGARIS
SUBEROSIS (OAK-BARK)	M. FAENI and T. VULGARIS
MALT-WORKER'S LUNG	A. FUMIGATUS and A. CLAVATUS
MAPLE-BARK STRIPPER'S LUNG	CRYPTOSTROMA CORTICALE
SEQUAIOSIS	GRAPHIUM and AUEROBASIDIUM
CHEESE-WORKER'S LUNGS	PENICILLIUM
INSECT-ANTIGEN'S LUNG (WHEAT WEEVIL)	SITOPHILUS GHONVIRUS
PITUITARY-SNUFF-TAKER'S LUNG	PITUITARY SNUFF
BIRD-FANCIER'S LUNG	PIGEONS and BUDGERIGARS (AVIAN ANTIGEN)
ENZYME LUNG	BACILLUS SUBTILIS
SISAL-WORKER'S DISEASE	?
COFFEE-WORKER'S DISEASE	?
BYSSINOSIS	COTTON FIBERS
WOOD-DUST PNEUMONITIS	OAK and MAHOGANY
HUMIDIFIERS and AIR-CONDITIONER PNEUMONITIS	THERMOPHILIC ACTINOMYCETE

* Katz and Kniker, NEJM 288:233, 1973

DECEMBER 6, 1981 - CASE NO. 13

ACCESSION NO. 24338

MODERATORS' DIAGNOSIS: ATYPICAL CARCINOID TUMOR, LUNG

CLINICAL HISTORY:

This 37 year-old woman had a two year history of hemoptysis, chronic cough, and recurrent left lower lobe pneumonias. Bronchograms showed a stenotic lesion in a segmental bronchus of the left lower lobe and a left pneumonectomy was performed. The gross specimen showed a 3.5 cm. hilar mass. The hilar lymph nodes appeared to be involved by tumor.

RADIOGRAPHS:

This 37 year-old female presented with a chronic nonproductive cough from left lower lobe infective episodes. This history in itself is strongly suggestive of a bronchial lesion. The patient presented with a rather large lobulated density seen near the left hilum and associated with peripheral obstructive pneumonitis. The plane film remains suspicious for central hilar mass effect with compression of the subsegmental bronchi and resulting in subsequent obstructive pneumonitis. This is nonspecific and is suggestive of malignancy but in view of the patient's age, bronchial tumors would be high on the radiological differential. When carcinoid bronchial adenomas present, often with hemoptysis, the plane radiographs are frequently normal. On rare occasions the endobronchial tumor mass is outlined on plane film by surrounding bronchial air. This is often better seen in the lateral view. At times even bronchoscopy has been regarded normal with no definitive lesion identified and subsequent careful bronchography has demonstrated a small bronchial adenoma more peripherally in the third or fourth generation bronchi.

MICROSCOPIC DESCRIPTION:

This hemorrhagic tumor extends from the submucosa of a large cartilage-bearing bronchus into the surrounding peribronchial tissues. Even though the tumor is poorly preserved, one can discern the following characteristic histologic features: a prominent nesting pattern of growth; tumor cells with a distinctly punctate nucleoplasm and ample pale eosinophilic cytoplasm; marked vascularity. These features, as well as the bronchial location of the tumor, support the diagnosis of bronchial carcinoid tumor. However, there is more prominent nuclear atypia with variation in nuclear size and a coarser nuclear chromatin pattern than is usually seen in "typical" carcinoid tumors. Therefore, despite the paucity of mitoses and the scarcity of necrosis, this tumor is best considered an atypical carcinoid. The reported involvement of the hilar lymph nodes is in keeping with this designation.

DISCUSSION:

Carcinoid tumors of the lung are low grade malignant neuroendocrine neoplasms arising from bronchi or bronchioles. They constitute approximately 80% of the so-called bronchial adenomas. Carcinoid tumors may be divided into categories according to location, e.g. central vs. peripheral, or histologic appearance, e.g. typical vs. atypical.

About 90% of pulmonary carcinoid tumors are central in location, arising in the larger bronchi and protruding into their lumens as smooth, polypoid masses. Their color varies from gray to cherry red, depending on the vascularity of the neoplasm. They typically invade beyond the bronchial wall. As would be expected, central carcinoid tumors tend to produce bronchial obstruction with its sequelae, i.e. cough, wheeze, atelectasis, recurrent pneumonias, or hemoptysis.

About 10% of carcinoid tumors are peripheral in location. They often fail to show an obvious connection to a bronchus. Peripheral carcinoids are usually circumscribed, tan or red, firm nodules. They are more likely to be asymptomatic than central carcinoids, and typically present as unexpected coin lesions on routine chest x-ray.

Carcinoid tumors usually consist of cells with uniform round nuclei, punctate nucleoplasm, and eosinophilic or clear cytoplasm. The tumor cells are disposed in a variety of patterns - nests, trabeculae, cords, glands, ribbons or combinations of these - and are typically very vascular. Oncocytic cytoplasmic features and interstitial calcification or bone formation have been reported in a minority of cases.

Peripheral carcinoid tumors frequently show spindling of tumor cells and a nesting pattern of growth, rather than glands, trabeculae, or ribbons of cells. Tumor cell spindling may also be seen in a few central carcinoids. Prominent spindling of tumor cells often leads to misinterpretation of a carcinoid as a mesenchymal tumor, i.e. a leiomyoma or fibroma.

The histochemistry of pulmonary carcinoids is summarized in Table 1. Extracellular mucin may be seen within glandular lumens of central carcinoids, but has not been reported in peripheral carcinoids. Intracellular mucin has not been seen in any type of pulmonary carcinoid tumor. Another striking feature of carcinoid neoplasms is the absence of glycogen. Cytoplasmic argyrophilia is present in about 80% of cases; argentaffin stains are usually negative.

Typical carcinoid is the term given to a carcinoid neoplasm, either central or peripheral in location, which shows cellular uniformity, absence of necrosis and lack of mitoses. Atypical carcinoids, conversely, show nuclear pleomorphism, variable numbers of mitoses and/or necrosis. These histologic features have been correlated with aggressive clinical behavior. Spindling of tumor cells is not an atypical feature. The clinical findings in patients with typical and atypical pulmonary carcinoids are compared in Table 2. Note that atypical carcinoids are on the average larger than typical ones, but a considerable degree of overlap in size exists between the two groups. Both typical and atypical carcinoid tumors may metastasize, but the incidence or metastasis, as seen in Table 3, is much higher for tumors with atypical features. The 5-year survival is 94% for typical carcinoids, but only 50-65% for patients with

atypical carcinoids. Rarely, a histologically typical carcinoid may metastasize widely, confounding prediction of a benign course.

The ultrastructure and immunocytochemistry of carcinoid tumors has received increasing attention recently. Typical carcinoid tumors show numerous dense-core neurosecretory granules, usually measuring between 100 to 200 nanometers in diameter. Immunocytochemistry has served to identify a number of polypeptide hormones in typical carcinoids, including serotonin, bombesin, calcitonin, VIP, and leu-enkephalin. Atypical carcinoids, in addition to one or more of these hormones, may contain ACTH. In addition, atypical carcinoids are not richly granulated at the ultrastructural level.

Carcinoid tumors lie in the spectrum of neuroendocrine tumors, from which they must be distinguished. Undifferentiated small cell carcinoma in most histologic fields lacks the architectural features (trabeculae, cords, nests) of carcinoid tumors. Furthermore, the cytologic characteristics of the two lesions are different, carcinoid cells showing more cytoplasm and a more punctate nucleoplasm than the cells of small cell carcinomas. At the ultrastructural level, small cell carcinomas have far fewer neurosecretory granules than carcinoid tumors.

Tumorlets are now considered to be a variant of carcinoid tumors. The minute size of these lesions (usually less than 3 or 4 mm.) and the presence of a central "scar" about which the small nests of carcinoid-like cells arise distinguish tumorlets from carcinoid tumors.

Chemodectomas of lung consist of minute proliferations of spindle cells about interstitial vessels. The finely dispersed chromatin of the nuclei, swirled growth pattern of the cells, and absence of neurosecretory granules in these lesions (which are now known <u>not</u> to be related to paragangliomas) distinguish them from carcinoid tumors.

DECEMBER 6, 1981 - CASE NO. 13

ACCESSION NO. 24338

TABLE 1: HISTOCHEMISTRY OF PULMONARY CARCINOIDS

STAIN	RESULT
PAS (GLYCOGEN)	-
ARGYROPHIL	- TO +
ARGENTAFFIN	-
MUCIN	- TO + (EXTRA-CELLULAR)

- = NEGATIVE

+ = POSITIVE

TABLE 2: CLINICAL FINDINGS IN PATIENTS WITH PULMONARY CARCINOIDS

FEATURE	TYPICAL CARCINOID	ATYPICAL CARCINOID
% ALL CARCINOIDS	87	13
SEX RATIO (M:F)	1:1	2:1
MEAN AGE (YEARS)	45	51
SIZE OF TUMOR (CM)	2.2	4

DECEMBER 6, 1981 - CASE NO. 13

ACCESSION NO. 24338

TABLE 3: METASTASIS IN CARCINOID TUMORS OF LUNG

	% METASTASIZING
CARCINOID TUMORS (ALL TYPES)	12.9
"TYPICAL" FEATURES	5.6
"ATYPICAL" FEATURES	70
VASCULAR INVASION	12.5

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DECEMBER 6, 1981 - CASE NO. 14

ACCESSION NO. 24235

MODERATORS' DIAGNOSIS: LYMPHOMATOID GRANULOMATOSIS, LUNG

CLINICAL HISTORY:

The patient was a 29 year-old man with constitutional symptoms of fever and night sweats, bilateral nodular densities in lung by chest x-ray, and several renal nodules by CAT scan. He was treated with Prednisone, but was subsequently shown to have a large cerebellar mass. At autopsy, four months after open lung biopsy, he was shown to have tumorous involvement of lungs, liver, kidneys, spleen, cerebrum, meninges, and skin.

RADIOGRAPHS:

Not available.

MICROSCOPIC DESCRIPTION:

This lymphoid lesion infiltrates the walls of small muscular pulmonary arteries and veins, shows foci of coagulative necrosis, and is distinctly polymorphous. The polymorphous appearance is produced by admixed benign histiocytes (creating a granulomatous background in areas), scattered plasma cells, and a small lymphocytic infiltrate which comprises the bulk of the cell population. Many of the lymphocytes have elongated or serpentine cell shapes. Rare large multilobed lymphoid cells are present.

DISCUSSION:

Lymphomatoid granulomatosis (LYG), as originally described by Liebow, is an atypical lymphoreticular infiltrate in lung which is angiocentric and necrotizing. It shows a polymorphous cell population, including benign histiocytes (producing a granulomatous "background"), scattered plasma cells and numerous small lymphocytes with elongated or serpentine nuclei. Variable numbers of large multilobed lymphoid cells are also present. In addition to this unusual morphology, well demonstrated by our case, LYG shows a distinctive constellation of organ involvement. Skin and kidney (45% of cases each) and brain (22.5% of cases) are characteristic sites of extrapulmonary lesions in LYG, while lymph nodes and bone marrow are rarely involved. Between 12-15% of patients with LYG eventually develop "large cell" non-Hodgkin's lymphomas. Most patients show multiple bilateral nodules or masses in lung without hilar lymphadenopathy.

The prognosis of LYG is surprisingly poor. Approximately two-thirds of patients treated with corticosteroids and/or chemotherapy die, with a median survival of 14 months. Adverse prognostic findings include neurologic manifestations and the presence of abundant atypical lymphoreticular cells. Fauci et al. have recently advocated vigorous use of cyclophosphamide and Prednisone for LYG and have recorded remissions in 7 of 13 patients receiving this regimen.

The histogenesis of LYG has now been explored in a series of reports. Immunologic studies in one case showed more than 90% of the lymphoid cells to form E-rosettes, indicating a T-cell lymphoid proliferation. This finding is supported by immunopathologic studies in 6 other cases using antisera against OKT antigens. It is interesting to note that other T-cell lymphoid proliferations, such as T-cell lymphomas, may show admixed histiocytes and may involve unusual extranodal sites, such as skin and central nervous system.

A number of other diseases should be considered in the differential diagnosis of this case. Wegener's granulomatosis typically shows abundant multinucleated giant cells of Langhan's type and palisaded epithelioid histiocytes around zones of necrosis, features not seen in LYG.

Histiocytic lymphomas of lung are rare, but may show vascular invasion and zones of necrosis. In addition, they are usually monomorphic and contain abundant mitotic figures (features not present in LYG). However, Colby and Carrington have shown that some pulmonary lymphomas may contain admixed "reactive" cells, thereby simulating LYG. In our experience, the presence of elongated lymphoid nuclei ("squiggly" lymphocytes) is a marker for LYG and may be of use to distinguish it from lymphomas.

Hodgkin's disease secondarily involving lung may show atypical multilobed lymphoid cells, a polymorphous cellular infiltrate, and vascular invasion and necrosis. However, the Reed-Sternberg cell of Hodgkin's disease is not seen in LYG. Further, Hodgkin's disease usually involves the reticuloendothelial system, while a peculiar extranodal distribution of disease (lung, skin, brain, etc.) should point to LYG.

DECEMBER 6, 1981 - CASE NO. 14

ACCESSION NO. 24235

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DECEMBER 6, 1981 - CASE NO. 15

ACCESSION NO. 19610

MODERATORS' DIAGNOSIS: EOSINOPHILIC GRANULOMA, LUNG

CLINICAL HISTORY:

The patient was a 41 year-old woman who was noted to have bilateral pulmonary densities on chest x-ray, but who was otherwise relatively asymptomatic. The gross specimen obtained by wedge biopsy of the right lung showed numerous soft to firm rubbery nodules. Seven months after biopsy, chest x-ray revealed spontaneous clearing of the patient's pulmonary infiltrates.

RADIOGRAPHS:

This 41 year-old female was discovered to have abnormal chest film and admitted for appropriate work-up. The initial radiograph on 11-12-71 clearly demonstrates a diffuse small rounded and irregular interstitial opacities situated throughout all segments of lung. This somewhat reticular-nodular pattern had a changing radiographic appearance from 11-12-71 through the series of films available to the latest film of 1-13-81. This 10 year film span would indicate a nonmalignant nodular interstitial process associated with a reticular interstitial component. There was no evidence of effusion initially nor pneumothorax. However, on close examination many of the nodular lesions are somewhat stellate in nature. Stellate interstitial nodular disease with diffuse distribution in a young patient and a history of abnormal chest film for 10 year period is almost pathognomic of histiocytosis X. The changing pattern that was demonstrated in this patient over a period of the 10 years indicated the influence of therapy. Diffuse nodular metastases such as associated commonly with adenocarcinoma, while possible in a young patient, is much less likely. The radiographic appearance of this such lesions are usually more round than stellate often associated with an effusion and/or lymphangitic changes consistent with lymphangitic carcinomatosis. The size and discrete nature of the stellate nodular densities as seen in this patient involving all segments is not characteristic of eosinophilic pneumonia which usually tends more peripheral in nature, more alveolar in appearance and characteristically consists of a changing pattern with air space lesions that come and go without specifically being associated with therapeutic changes.

MICROSCOPIC DESCRIPTION:

The biopsy shows multiple small nodules scattered throughout the section. The nodules are composed of histiocytes and eosinophils, and in some areas show a distinctly interstitial and peribronchiolar location. The lung parenchyma between the nodules is relatively normal, except for intra-alveolar collections of macrophages. At high magnification, the characteristic histiocytes of this lesion are seen. They have cleaved and lobulated nuclei, with relatively poorly demarcated cytoplasmic borders. An occasional multinucleated giant cell is seen.

DISCUSSION:

The vast majority of patients with pulmonary eosinophilic granuloma have

disease limited to the lung. Usually, young to middle age adults are affected, but the age range may be quite wide (17 years to 71 years). The male to female ratio is about 2 to 1 in the AFIP experience (information kindly supplied by Dr. L. Hochholzer). Approximately a third of the patients are asymptomatic, and an additional 40% show mild nonspecific symptoms, as was the case in our patient. Chest pain due to pneumothorax occurs in 15% of patients. Patients with pulmonary eosinophilic granuloma generally have a good prognosis. In the majority of patients, the disease shows radiographic clearing over a 6-12 month time period, as was the case in this patient. In some individuals, there is relentless progression to end stage "honeycomb" lung. The course is unpredictable from the histology of the biopsy.

The pathology of pulmonary eosinophilic granuloma is characterized by multiple nodules scattered throughout both lungs, often with large areas of relatively normal intervening parenchyma. The eosinophil content of the lesions is variable; the histiocytes are the pathognomonic feature of the lesion. The nodules are typically interstitial in location, at least early in their natural history, and are centered around bronchioles. As the lesion becomes larger, the alveolar architecture in the center is obliterated.

Cystic lesions of two types may be found within eosinophilic granuloma of the lung. The destruction of bronchioles by the lesions leads to bronchiolectatic cysts. Rupture of a cyst may lead to spontaneous pneumothorax. In those cases that show progressive fibrosis, honeycombing fibrosis with numerous cysts may also occur.

The characteristic cell of eosinophilic granuloma shows by electron microscopy lobulated nuclei and Birbeck or Langerhans cytoplasmic granules. In this manner, they are similar to Langerhans cells found in the skin, oral mucosa and, more recently, within the epithelium of the bronchi. Langerhans cells are phagocytic, show C3 and Fc receptors, as well as OKT6 antigen on the cell surface. It is now known that these cells are associated with T cell lymphoid proliferations, but their exact function is still unclear.

The differential diagnosis of eosinophilic granuloma is lengthy. Between the nodular lesions of eosinophilic granuloma, there may be an outpouring of intra-alveolar histiocytes, resembling desquamative interstitial pneumonitis. However, the characteristic interstitial nodular lesions found in eosinophilic granuloma excludes a diagnosis of desquamative interstitial pneumonitis.

Usual interstitial pneumonia (UIP) is an interstitial inflammatory process which may eventuate in honeycombing fibrosis. The later stages of eosinophilic granuloma and usual interstitial pneumonia can therefore appear histologically similar. Diagnosis of eosinophilic granuloma depends on finding typical Langerhans cells. Marked tissue eosinophilia also is not typical of usual interstitial pneumonia.

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Reactive eosinophilic pleuritis is a nonspecific reaction of the pleura to injury, usually following spontaneous pneumothorax. In this condition, the pleura is lined by histiocytes, eosinophils, giant cells and mesothelial cells. This mixture of cells resembles eosinophilic granuloma, but differs from it in two ways. First, it is limited to the pleura and the underlying bullae or blebs, and is not present within the remainder of the lung parenchyma. Furthermore, no Langerhans granules are seen within the histiocytes of this process.

Finally, chronic eosinophilic pneumonia may show eosinophils and histiocytes, but they are characteristically located within the alveoli of lung parenchyma, rather than within the interstitium, as in the case of eosinophilic granuloma.

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DECEMBER 6, 1981 - CASE NO. 16

ACCESSION NO. 23711

MODERATORS' DIAGNOSIS: PLEOMORPHIC (GIANT CELL) ADENOCARCINOMA, LUNG

CLINICAL HISTORY:

A 54 year-old white woman had a 3.5 cm. cavitary lesion demonstrated in the left upper lobe of lung by chest x-ray. A left pneumonectomy was performed, and a 3 x 2.5 cm. cystic, gray mass was found in the left upper lobe. A secondary bronchus of the upper lobe extended into the mass. The patient died one year later with widespread metastases.

RADIOGRAPHS:

This 54 year-old Caucasian female had a chest film in 1978 with a 3.5 cm. cavitary lesion in the anterior segment of the left upper lobe. The subsequent films confirmed the slight growth of this cavitary lesion and at all times it had an irregular thick wall, being suprahilar in projection with a lobulated internal cavitary wall and without the persistence of their fluid levels tends to raise the suspicion of malignancy and cavitating tumor mass rather than persistent abscess. When one reviews the patient's history and associates this with an enlarging left upper lobe cavitary mass that is associated with large amount of hemoptysis then cavitating tumor is high on the radiological differential list. Radiological features of this cavitary walls are strongly suspicious of malignancy. Overall these radiographic features are compatible with diagnosis of a giant cell adenocarcinoma.

MICROSCOPIC DESCRIPTION:

This well-defined but nonencapsulated tumor shows a number of significant histologic features. First, there is no evidence in the H&E stained sections of squamous or glandular differentiation; rather, the tumor is composed of sheets of spindled and multinucleated tumor cells. There are abundant mitoses, foci of necrosis, a distinct nesting pattern of growth in some areas, and extensive invasion of the walls and lumens of medium and small pulmonary arteries within the tumor mass. No obvious bronchus is seen. As the tumor cells undergo necrosis, they maintain cohesion, a feature suggestive of an epithelial neoplasm.

Intracytoplasmic vacuoles are noted within some tumor cells. A mucicarmine stain demonstrates the presence of unequivocal mucin within some of the tumor cells, supporting a diagnosis of adenocarcinoma.

DISCUSSION:

Pleomorphic carcinoma of lung is a carcinoma exhibiting either a prevalence of multinucleated giant tumor cells, spindle tumor cells, or a combination of these cell forms. At AFIP, it is accepted that pleomorphic carcinomas exhibit squamous differentiation (pleomorphic squamous cell carcinoma), glandular

differentiation or mucin secretion (pleomorphic adenocarcinoma), or no differentiation (pleomorphic carcinoma). The new WHO formulation of lung tumors is more restrictive in its definition: giant cell carcinoma is considered a variant of undifferentiated large cell carcinoma only, while spindle cell squamous carcinoma is viewed separately as a variant of squamous carcinoma. No mention is made at all of giant cell adenocarcinoma.

This disagreement concerning the definition of pleomorphic carcinoma manifests itself in published reports about these tumors. For example, the frequency of pleomorphic carcinoma in unselected series of pulmonary cancers varies from as little as one percent to as much as ten percent of lung cancers, depending on whether the authors accept squamous or glandular differentiation in the neoplasms. If only undifferentiated tumors are included, the frequency is one to two percent of cases.

Pleomorphic carcinomas typically present in middle and older age adults. The average age of patients in four series of cases ranges anywhere between 51 and 60 years. Pleomorphic carcinomas usually occur in heavy smokers, and manifest themselves as large, peripheral mass lesions in the lung. The clinical course is characteristically short, with an average survival of six months or less (Table 1), making pleomorphic carcinoma the deadliest of pulmonary cancers. In addition, metastasis at autopsy is more widespread and more frequent than in other forms of lung cancer (Table 2).

Histologically, pleomorphic carcinomas typically show numerous multinucleated giant tumor cells, with or without spindled tumor cells. There is also a background of large mononuclear tumor cells. One may find cytocohesive cell nests. A careful search of H & E sections for foci of squamous or glandular differentiation and of mucin stains for intracellular mucin should be performed as a matter of course.

A number of points of evidence suggest that pleomorphic carcinoma of lung is epithelial in type. The light microscopic demonstration of cytocohesive cell nests, the report of epithelial characteristics in tissue culture explants and the ultrastructural demonstration of cell junctions of desmosomal type and intracellular tonofilament-like fibrils are in keeping with an epithelial neoplasm.

Occasional giant cells or foci of spindling may be seen in anaplastic or poorly differentiated carcinomas of many types. Their prognostic significance is unclear. Distinction between such tumors and pleomorphic carcinomas is often difficult since it depends on a subjective impression of the relative abundance of giant or spindle cells. Thus, there are those who might argue that the present case is better classified as anaplastic (poorly differentiated) adenocarcinoma. Clearly, however, if the bulk of the tumor cells exhibit pleomorphic features, the term pleomorphic adenocarcinoma is best employed.

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The distinction between pleomorphic carcinoma and malignant fibrous histiocytoma of lung may be difficult. The latter is a rare primary tumor in lung. Both neoplasms characteristically show giant and spindle cells, often with a storiform pattern, but pleomorphic carcinomas differ from malignant fibrous histiocytomas in having cytocohesive cell nests and in some cases intracytoplasmic mucin. Abundant cytoplasmic glycogen is not seen in malignant fibrous histiocytoma (except adjacent to necrotic areas), while pleomorphic carcinoma may show glycogen. Extensive sampling of tumor may demonstrate a small focus of glandular or squamous differentiation. In general, pleomorphic carcinomas of lung are far more frequently encountered than malignant fibrous histiocytomas, a factor which should be taken into account before making a diagnosis of malignant fibrous histiocytoma. Finally, electron microscopy may demonstrate cell junctions of desmosome type and intracellular tonofilament-like fibrils, thereby supporting the diagnosis of pleomorphic carcinoma.

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TABLE 1: CLINICAL COURSE OF PLEOMORPHIC CARCINOMA

AUTHORS	NO. PATIENTS	DURATION ILLNESS (MOS.)
HELLSTROM AND FISHER	17	4.6 (AVERAGE)
HERMAN ET AL.	63	6.1 (AVERAGE)
GUILLAN AND ZELNA	11	3 - 10
FLANAGAN AND ROECKEL	4	2 - 6

TABLE 2: PLEOMORPHIC CARCINOMA - INCIDENCE OF METASTASIS BY ORGAN

SITE	GIANT CELL CA. (%CASES)	ALL LUNG CA. (%CASES)
REGIONAL LYMPH NODES	100	72
ADRENAL	54	20
BONE	33	21
BRAIN	27	16
HEART AND PERICARDIUM	24	12

DECEMBER 6, 1981 - CASE NO. 17

ACCESSION NO. 22369

MODERATORS' DIAGNOSIS: FAVOR MALIGNANT THYMOMA, EPITHELIAL TYPE

CLINICAL HISTORY:

This 37 year-old white man presented with chest discomfort. Chest x-ray showed a mediastinal mass. At thoracotomy, an 11 cm. tan, nodular tumor mass involving the mediastinum and adherent to the pericardium was excised. The patient died nine days after operation.

RADIOGRAPHS:

This 37 year-old white male presented with a discomfort in the central upper chest and on the radiograph was found to have approximately 11 cm. large anterior mediastinal mass that had no intralesional calcification. This lesion is very large for thymoma but as in the previous case No. 5 the radiological features were nonspecific are consistent with the diagnosis. Computerized tomography in this situation would be helpful to estimate tumor tissue density, identify the presence or absence of fat, and estimate the radiodensity of the tumor tissue. While this latter feature is still in the experimental stage, work by Siegelman from Baltimore is encouraging. His work as clarified that pulmonary lesions greater than 170 Hounesfield units in radiodensity have all been found to be benign. We should immediately caution that this does not necessarily translate into mediastinal but is an interesting addition to pulmonary nodule assessment.

In this case at hand, it is interesting that such a large mass of tumor tissue and does not significantly distort the adjacent mediastinal structures on the plane radiograph. This would be suggestive of a softer tissue type such as usually found in the thymoma.

MICROSCOPIC DESCRIPTION:

The histologic sections show neoplasm bounded by a thick fibrous capsule. The neoplasm shows the following pertinent characteristics: A sheet-like and, in some areas, nesting pattern of growth; relatively monotonous tumor cells with single nucleoli, moderate amounts of cytoplasm and ill-defined cell borders; collections of lymphocytes, predominantly around vessels and within small fibrous septae; and cystic areas in which small vessels are surrounded by eosinophilic material (possibly edematous perivascular spaces).

DISCUSSION:

Thymoma, seminoma and histiocytic lymphoma need to be considered in the differential diagnosis of this case. About 4% of thymomas are monophasic lesions, consisting solely of malignant thymic epithelial cells, while another 20% show a scant lymphoid infiltrate. The cytological appearance of thymic epithelial cells under the circumstances is surprisingly polymorphous. Ovoid or round cells, vesicular nuclei, and prominent nuclei may suggest malignant lymphoma or seminoma; spindle cells may simulate fibrous histiocytoma or

hemangiopericytoma; rosettes may bring to mind neuroectodermal neoplasms, and glands or squamous epithelium may suggest adenocarcinoma or squamous cell carcinoma respectively. In these cases, certain light microscopic and ultimately electron microscopic features support the diagnosis of thymoma. The former include a thick fibrous capsule, fibrous septae, edematous perivascular spaces and neoformation of Hassall's bodies. The latter include the presence of desmosomes, cytoplasmic tonofibrils, and elongated cellular processes. Unfortunately, we do not have electron microscopy to aid in differential diagnosis in this case. However, by light microscopy, the thick fibrous capsule and suggestive perivascular spaces seen in this tumor are most in keeping with thymoma.

Seminoma may occur as a primary tumor involving the thymus gland. It is typically found in young adults, and is restricted to men. In all such cases, of course, a testicular primary must be excluded. Microscopically, a granulomatous and/or lymphoid infiltrate is characteristically present in the fibrous septae of the tumor. Further, a nesting pattern is usually found, a suggestion of which is seen in our slides. My chief objection to this diagnosis lies in the absence, in this case, of the typical coarse nuclear chromatin stippling and aboundant cytoplasmic glycogen typical of seminoma. Further, edematous perivascular spaces of the type present in this case are not seen in seminomas.

Lymphoma is excluded with equal difficulty. As Rosai and Levine have eloquently pointed out: "the problem that confronts the pathologist is whether the cells of a clearly malignant mediastinal tumor, characterized by large vesicular nuclei, prominent nucleoli and relatively abundant cytoplasm, are lymphoreticular cells or epithelial cells of a malignant thymoma... The distinction is usually difficult and may be impossible, because we know of no constant criteria by which to differentiate these two cell types." The light microscopist is left only with those architectural criteria noted above to suggest thymoma. In this case, I believe that the presence of a fibrous capsule and perivascular spaces somewhat favor a diagnosis of thymoma over lymphoma. Electron microscopy (see Table 5, case 6), cell culture, or B and T cell markers are useful aids in arriving at a definitive diagnosis. In summary, this case points out the difficulty of distinguishing in some instances thymoma from malignant lymphoma and seminoma, and suggests the need for ancillary techniques, particularly electron microscopy, to allow the pathologist to reach a final conclusion.

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DECEMBER 6, 1981 - CASE NO. 18

ACCESSION NO. 24342

MODERATORS' DIAGNOSIS: RHEUMATOID NODULES, LUNG

CLINICAL HISTORY:

The patient was a 57 year-old woman with a four year history of rheumatoid arthritis, treated with steroids. She was admitted to the hospital for hyperthermia and hypertension; blood cultures subsequently grew Staphylococcus aureus. The patient eventually died of sepsis. At autopsy, the right lung showed four peripheral, yellow-white nodular lesions measuring up to 2 x 2.5 cms.

RADIOGRAPHS:

This patient presented with multiple round nonhomogenous nodules situated in the right lower zone and with a known history of rheumatoid arthritis and therapy with steroids. The acute clinical situation of presentation with the left cerebral vascular accident and hypothermia did not necessarily aid in the differential of these cavitating nodular lesions. However, from radiological point of view cavitating well rounded nodular lesions often more peripheral, in a patient with known rheumatoid should automatically include cavitating rheumatoid pulmonary nodules in the differential. Abscess formation or cavitating tumors, particularly squamous cell metastases are also a radiological differential concern. It is not uncommon with the rheumatoid nodular expression in the chest to have an increased association with pneumothorax. In these cases because of the nonspecific nature of the radiographic findings, it is the remainder of the patient's history and the presence of rheumatoid that heightens suspicions that any pulmonary rounded cavitating densities would be those related to rheumatoid nodules.

MICROSCOPIC DESCRIPTION:

The histologic section shows a necrotizing granuloma, consisting of a central necrotic core bounded by spindled mononuclear cells and occasional giant cells. A fibrous capsule containing lymphoid aggregates and numerous plasma cells is present. In one area, a small artery adjacent to the necrotizing granuloma shows vasculitis. The remainder of the lung shows pulmonary edema and scattered perivascular lymphoid aggregates.

DISCUSSION:

The presence of pulmonary necrotizing granulomas in a patient with a history of rheumatoid arthritis should raise the possibility of rheumatoid nodule. Rheumatoid nodules are the least common pleuro-pulmonary manifestation of rheumatoid arthritis. They may appear as solitary or, more often, multiple lesions in the lung, and are typically associated with elevated rheumatoid factor titers and rheumatoid nodules in the soft tissues. Although the clinical history of rheumatoid arthritis should raise suspicion of the diagnosis, rheumatoid nodules may on occasion precede the onset of clinical rheumatoid arthritis

by as long as several years. Even in these exceptional cases, an elevated rheumatoid factor titer will usually be found and will support the diagnosis.

Rheumatoid nodules are characteristically subpleural, yellow-white, well-demarcated lesions measuring up to 7 cms. in diameter. Cavitation and eruption of the nodule through the pleura with subsequent pleural effusion or broncho-pleural fistula are common complications.

The histology of the rheumatoid nodule is characteristic, although not pathognomonic. As in the present case, there is a necrotic center surrounded by a band of partially necrotic polymorphonuclear cells and a palisade of epithelioid histiocytes with occasional giant cells. The external capsule of the rheumatoid nodule is usually fibrotic and contains lymphoid aggregates and plasma cells. Although vasculitis is not a prominent component of rheumatoid nodules, one may occasionally see inflammation of vessels adjacent to the necrotic nodule.

Rheumatoid arthritis may be associated with a number of other manifestations in the thorax (see Table 1).

Chest x-rays demonstrate pleural effusion in up to 10% of patients with rheumatoid arthritis. Histologically, these effusions are often associated with nonspecific pleural inflammation or with the presence of palisaded spindled histiocytes resembling a rheumatoid nodule on the pleural surface.

Diffuse interstitial fibrosis affecting the lower lobes of the lung is found by chest x-ray in 1-2% of patients with rheumatoid arthritis. The histology of these infiltrates resembles usual interstitial pneumonia, differing only in the presence of large-interstitial lymphoid aggregates and follicles, particularly around the airways, in some cases.

Caplan's syndrome consists of multiple rheumatoid nodules in lung occurring in a patient with pneumoconiosis. The first cases were described by Caplan in coal miners, but other pneumoconioses, such as asbestosis, may be associated.

The clinical course of rheumatoid nodules is variable. They may wax and wane in size, or disappear completely. The effect of corticosteroids on the clinical course is not established. Since rheumatoid nodules are usually asymptomatic, they are often not treated unless they become infected or cavitated. Thoracotomy is usually performed to exclude an infectious or malignant process.

The differential diagnosis of any necrotizing granuloma should include an infectious etiology first and foremost. Special stains for fungi and bacteria, cultures, and skin tests are therefore obligatory. In general, a necrotizing granuloma with few giant cells and with a prominent palisade of histiocytes in a patient with rheumatoid disease suggests rheumatoid nodule over an infectious process.

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Both Wegener's granulomatosis and rheumatoid nodule may show necrotizing granulomas and vasculitis. The presence of a disorderly and poorly demarcated granulomatous lesion with abundant giant cells should suggest Wegener's granulomatosis. Upper respiratory tract symptoms or glomerulonephritis are common in Wegener's disease, while extension of the lesion through the pleura is more typical of rheumatoid nodule.

Pulmonary necrotizing granulomas similar to that seen in rheumatoid nodule may also be found in patients infected with Dirofilaria immitis (the dog heart worm). The presence of mild eosinophilia surrounding the necrotic granuloma should provoke a search for the dead worm within a vessel of the necrotic tissue.

TABLE 1: PULMONARY MANIFESTATIONS OF RHEUMATOID DISEASE

1. PLEURAL EFFUSION
2. DIFFUSE INTERSTITIAL FIBROSIS
3. RHEUMATOID NODULES (CAPLAN'S SYNDROME)
4. PULMONARY ARTERITIS

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DECEMBER 6, 1981 - CASE NO. 19

ACCESSION NO. 23682

MODERATORS' DIAGNOSIS: PROBABLY BRONCHOCENTRIC GRANULOMATOSIS, LUNG

CLINICAL HISTORY:

This wedge biopsy of lung was performed in a 57 year-old white woman who complained initially of shortness of breath, and in whom a chest x-ray showed evidence of an irregular, marginated lesion in the left upper lobe. The gross specimen demonstrated multifocal zones of consolidation, whose central areas contained purulent yellow-white material. The patient was alive and well 4 months after biopsy, with no other lesions in lung.

RADIOGRAPHS:

This patient presented with a left upper lobe pneumonia and a history of being a heavy smoker. She was an antibiotic treatment failure. While her specific films were not available, radiographic features consistent with the diagnosis include that of irregular densities in the lung parenchymal tissue, usually associated without the presence of an effusion. There is often a changing growth pattern and the lesions are nonhomogeneous, sometimes with active air fluid levels. These irregular nodules often situated peripherally and there is an increase incidence of the presence of pneumothorax. Cavitating irregular pulmonary nodules associated with other classical features of this syndrome lead to the radiological differential that should have a high suspicion of bronchocentric granulomatosis.

MICROSCOPIC DESCRIPTIONS:

The biopsy shows multifocal necrotizing granulomas, many of which are contiguous to pulmonary arteries. The granulomas are characterized by palisades of epithelioid histiocytes around central necrotic zones containing few cells. A few of the adjacent pulmonary arteries show mild vasculitis, which is probably secondary to their physical proximity to the granulomatous inflammation. Fibrous connective tissue surrounds some of the granulomatous lesions, and there is a prominent obstructive pneumonia, characterized by numerous intra-alveolar foamy macrophages. Tissue eosinophilia is not seen. Special stains for fungi and acid fast bacilli fail to demonstrate organisms, while elastic tissue stains confirm the proximity of the necrotizing granulomas to the pulmonary arteries. These histologic findings suggest the diagnosis of bronchocentric granulomatosis rather than Wegener's granulomatosis.

DISCUSSION:

Bronchocentric granulomatosis (BCG) is a term coined by Liebow to describe a pulmonary lesion in which numerous necrotizing granulomas are limited to and destroy bronchi and bronchioles. The bronchocentric location of the lesion is demonstrated by continuity of the granulomas with the respiratory epithelium of the airway or by contiguity of the lesion to pulmonary arteries (i.e. the normal location of the airways). Elastic stains may be of use to demonstrate the proximity of the granulomas to arteries. The granulomas are typically composed of

a palisade of epithelioid histiocytes arrayed about a necrotic core which may contain either eosinophils, polymorphonuclear cells or caseous-like material. Surrounding lung may show obstructive or eosinophilic pneumonia or occasional interstitial giant cells. Large bronchi may demonstrate mucoid impaction or small necrotizing granulomas in their walls. Finally, pulmonary arteries may show a mild vasculitis, which is thought to be an "overflow" phenomenon from the contiguous inflamed airways, rather than a primary arteritis.

Patients with BCG may be divided into two groups on the basis of histologic features and clinical symptoms. The first, consisting of individuals with numerous eosinophils in the necrotic lesions, constitutes one-third to one-half of patients. This tissue eosinophilia is usually associated with asthma, peripheral blood eosinophilia, mucoid impaction of large airways, fragmented hyphae (usually resembling Aspergillus) in the granulomas or mucus, and/or positive skin tests or sputum cultures for Aspergillus. The known association between Aspergillus on the one hand, and eosinophilic hypersensitivity reactions in lung (allergic bronchopulmonary aspergillosis) and microgranulomatous reactions ("extrinsic allergic alveolitis") on the other, suggests that BCG is a novel form of hypersensitivity to intrabronchial fungi combining pathologic features of both these other lesions. Corticosteroids are the treatment of choice.

Between one-half and two-thirds of patients with BCG are non-asthmatic (as in the present case). This group constitutes of a more heterogeneous population both morphologically and clinically. The necrotizing granulomas usually contain polymorphonuclear cells or merely necrotic debris rather than eosinophils. Blood eosinophilia and mucoid impaction are rare, and fungi have never been demonstrated in the necrotic lesions. These cases of BCG may be caused by hypersensitivity to an as yet unknown antigen, but the possibility of a microscopically occult infectious agent cannot be excluded. Surgical resection of the lesion usually suffices to treat this form of BCG. The present case falls into this category.

BCG is not associated with clinically significant extrapulmonary disease, a feature which separates it from angiocentric granulomatoses such as Wegener's granulomatosis or Churg-Strauss syndrome. The prognosis of BCG is excellent, no patient yet being reported to have died of disease.

BCG must be distinguished from infectious granulomas and other forms of angiitis and granulomatosis. Tuberculosis, histoplasmosis and coccidiodomycosis may produce necrotizing granulomas involving airways. Usually, the bronchocentric granulomas in these infectious diseases are accompanied by extrabronchial necrotizing lesions (BCG is <u>strictly</u> limited to the airways). Rarely, patients with tuberculosis or histoplasmosis may show disease restricted to the airways, but special stains usually suffice to exclude these lesions.

The granulomas of Wegener's granulomatosis may involve airways, but also engulf extrabronchial sites as well. Further, there is usually a striking

vasculitis, which can be brought out in special stains for elastica. If necrotizing granulomas are uniformly seen adjacent to arteries, as in the present case, bronchocentric granulomatosis is the preferred diagnosis. Of course, involvement of extrapulmonary sites should suggest Wegener's granulomatosis over BCG.

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DECEMBER 6, 1981 - CASE NO. 20

ACCESSION NO. 23319

MODERATORS' DIAGNOSIS: CARCINOSARCOMA, LUNG

CLINICAL HISTORY:

This 72 year-old white man developed hemoptysis three months prior to admission. Resection of the right lung demonstrated an 8 x 4 x 3.5 cm. lobulated, pink, unencapulated mass containing areas of hemorrhage and necrosis in the lower lobe. The tumor extended as a polypoid lesion into the lower lobar bronchus and right main stem bronchus, and also involved the middle lobar bronchus. The patient died four months after surgery of bronchopneumonia and emphysema. A 1 cm. tumor nodule was noted in the left lung at autopsy.

RADIOGRAPHS:

This patient presented with a chest x-ray that primarily showed emphysematous changes with no obvious mass. There is some segmental atelectasis in the right lower zone and as this is a very common radiological feature, it would not raise any untoward suspicion. There was no definite mass lesion identified on the chest film but at times an endobronchial component of the tumor mass in the region of the bronchus intermedius is seen on plane films as a filling defect in the air column of the bronchus. This is not so in this case although the patient did have a lesion in this area.

MICROSCOPIC DESCRIPTION:

The tumor protrudes into the lumen of a bronchus and extends into the surrounding lung parenchyma. In one area, the neoplasm appears to arise from the epithelium of the bronchus. This tumor shows two components: unequivocal carcinoma with basaloid and glandular differentiation and intraglandular mucin, and a hyaline and myxoid stroma containing numerous atypical spindle and oval cells. In one area, in some sections, malignant cartilage is seen. The surrounding lung parenchyma shows peribronchiolar fibrosis, with numbers of birefringent silica-like particles in the fibrotic foci, and at least two ferruginous bodies.

DISCUSSION: See also discussion of Case No. 8

Carcinosarcomas of lung are neoplasms composed of intimately mixed epithelial and mesenchymal elements of a type ordinarily seen in malignancies of adults. Less than 40 of these rare lesions have been reported in the literature. They occur twice as often in men as in women, and commonly present in middle or old age (35 to 77 years), with an average age of 60 years.

Carcinosarcomas are typically bronchogenic mass lesions, a feature which accounts for their hilar location in most cases. Indeed, about one-half of

cases present as endobronchial polypoid masses, as in the present case. At resection, they average 5 cm. in diameter and are usually white-grey with or without hemorrhage.

Eighty-five percent of carcinosarcomas show squamous cell carcinoma, while the remainder may have adenocarcinoma, adenosquamous carcinoma or undifferentiated large cell carcinoma as their epithelial component. The most common combination of epithelial and mesenchymal elements (seen in about one-half of reported cases) is squamous cell carcinoma and fibrosarcoma. However, the ability of squamous cell carcinoma to spindle, thereby simulating a fibrosarcoma, suggests that in at least some of these cases the diagnosis of carcinosarcoma must be accepted with caution. Indeed, the World Health Organization classification demands that differentiation other than fibrosarcoma (malignant bone, cartilage, or muscle) be present before a lesion be considered carcinosarcoma. The second most frequently encountered stromal component is chondrosarcoma, while osteogenic sarcoma and rhabdomyosarcoma have also been reported.

The prognosis of carcinosarcoma is poor, 80% of patients dying of widely disseminated disease, usually within two years of presentation. It has been suggested that endobronchial location and lack of metastases to peribronchial nodes favor survival, but exceptions to both of these statements have been reported.

In the differential diagnosis of this lesion, we must include adenoepidermoid carcinoma with marked spindling of tumor cells. Ultrastructural studies of squamous cell carcinoma demonstrating spindle cell metaplasia have shown that tumor cells may have simultaneously fibroblastic and epithelial characteristics. It is therefore not difficult to conceive of a continuous spectrum of differentiation of tumor cells, from purely epithelial to purely mesenchymal. It is theoretically possible that carcinosarcomas represent a manifestation of such a process. For the moment, however, the presence of cartilage or bone in the malignant stroma should lead one to classify a biphasic tumor as carcinosarcoma, rather than spindle cell carcinoma.

Biphasic mesothelioma is readily distinguished from carcinosarcoma on the basis of location and distribution of tumor. Mesotheliomas may invade the underlying lung parenchyma, but are predominantly pleural in location. Localized biphasic mesotheliomas are very rare; diffuse biphasic mesotheliomas are more frequent, but their diffuse nature and pleural location readily distinguish them from carcinosarcoma.

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ACCESSION NO. 23319

REFERENCES: See Case No. 8

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