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RPC¹ of the Month from the AFIP²

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Fig. 1 (AFIP Neg. 54-12078).

Fig. 2 (AFIP Neg. 64-4567-7).

Fig. 3 (AFIP Neg. 65-13009-2).

FIGURES 1, 2, and 3 are the chest films of 3 different patients. Figures 2 and 3 are presented as close-ups so that details can be studied and discussed. The field in Figure 2 is representative of all of the lung fields in the chest film of that patient. Figure 3 represents the only lesion in the chest film of that patient. Choose from the alternatives below and then turn to the discussion on the following pages.

1. Figure 1 is related to Figure 2 but not to Figure 3.
2. Figure 1 is related to Figure 3 but not to Figure 2.
3. Figure 2 is related to Figure 3 but not to Figure 1.
4. All are related.
5. None are related.

¹ RPC = Radiological-Pathological Correlation.

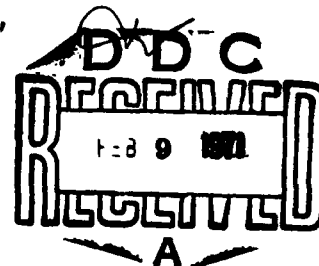
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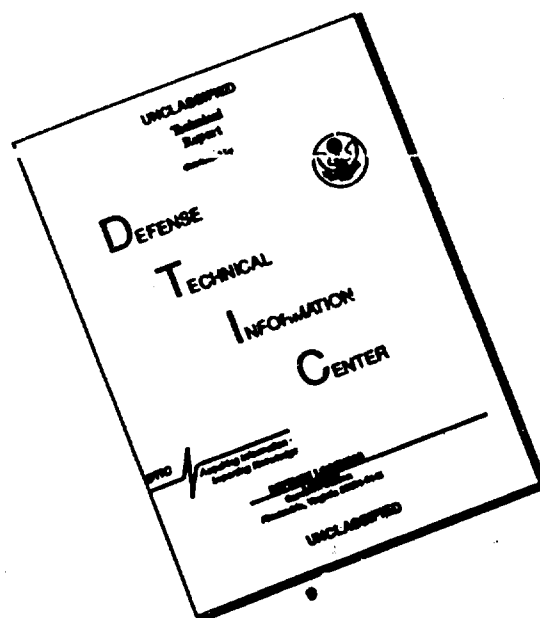
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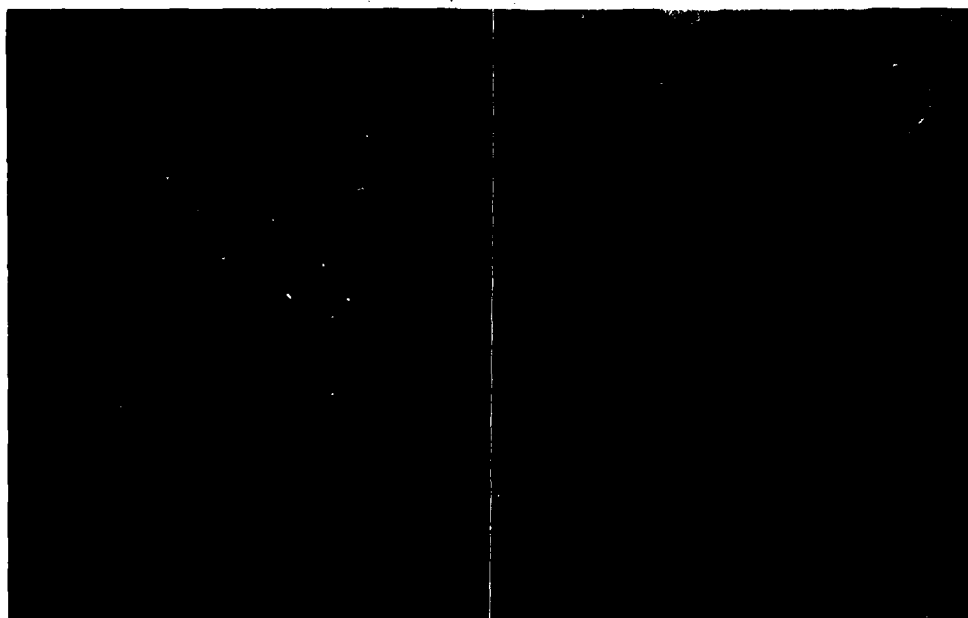


Fig. 4 (AFIP Negative 68-9286). Extensive infiltrates in the autopsy lung specimen result in an overall appearance similar to consolidating pneumonia. This correlates well with the radiograph findings in Figure 1.

Fig. 5 (AFIP Negative 67-7445). A selected field from the tissue in Figure 4 shows that the general architecture is relatively undisturbed. The lobules of the lung and the interlacing septa are clearly seen. Small end air passages of the lung tend to remain open unless filled with mucus or cellular debris.



Fig. 6 (AFIP Negative 53-13787). Higher magnification discloses that the alveolar walls are thickened by a lepidic growth of uniformly tall columnar cells which extend contiguously along the alveolar walls and use them as a scaffolding. Thus the alveolar spaces are partially filled by the papillary infoldings of lining tumor cells.

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RADIOLOGICAL FINDINGS

Figure 1 shows a diffuse mottled infiltrate throughout the lungs, tending toward coalescence. A large "fluffy" ill-defined consolidation has formed in the right lower lung field, and numerous air-bronchogram effects indicate an alveolar-filling process. No pleural reaction or effusion could be demonstrated, and the possibility of adenopathy cannot be properly evaluated because of the superimposition. The superior mediastinum appears somewhat widened, however. The cardiovascular silhouettes are not considered remarkable.

Figure 2 demonstrates multiple nodules throughout the lungs. The nodules vary greatly in size, but the larger ones are nearly 1.5 cm in diameter. The margins of the nodules are ill-defined and "fluffy," and there is a tendency for them to coalesce. Again, no associated abnormalities could be found on study of the chest films.

A solitary lesion seen on an otherwise normal chest film is noted in Figure 3. The lesion is a large, rounded mass, but the margins are "hairy" or "frayed" and poorly defined. Well-defined linear streaks appear to course into or through the rounded mass, and air-bronchogram effects are readily seen within it. In addition, there are ill-defined, soft linear densities streaking between the lesion and the hilus.

RADIOLOGICAL DISCUSSION

Although these three cases present dissimilar gross patterns, they all show the basic findings of alveolar or end-air-space filling processes: ill-defined margins, coalescence, consolidation, and air-bronchogram effects. The difference lies in the distribution of the alveolar infiltrates. Figure 1 shows pervasive deposits which have an almost miliary distribution; it may be postulated that there has been a generalized showering of the lungs, perhaps from the older area of consolidation in the right lower lung. The same pervasiveness is noted in Figure 2, but the foci are disparate in size and some are quite large.

Many of the foci are older, and the tendency toward coalescence is more striking. In the last case, an alveolar-filling process has involved a single area of the lung and become rather extensive without involving other areas. The well-defined linear streaks associated with the margins and the body of the mass suggest some chronicity, as though some fibrous reaction had taken place. The presence of fibrolinear changes and air-bronchogram effects within the same ill-defined mass is not consistent with most inflammatory infiltrates (with the possible exception of indolent granulomatous pneumonitis) or with most organizing infarcts. For this reason, we must propose a very slowly developing process to account for the radiographic signs in Figure 3; on the other hand, the morphological findings in Figures 1 and 2 may result from either acute or chronic insults, and clinical backgrounds are needed before a definite diagnosis can be offered. An intriguing question remains: Is there any process that can be represented by all 3 cases, in view of the chronicity implied in Figure 3? Perhaps a review of the clinical stories of our 3 patients will provide a further clue.

CLINICAL BACKGROUNDS

The patient in Figure 1 was a 62-year-old Caucasian woman who had had progressive cough for many months before this radiograph was obtained. She had also reported increasingly severe dyspnea for many weeks, and weight loss was noted one month prior to work-up. Laboratory data, including sputum and skin tests, had been unremarkable. The overall clinical impression was sarcoidosis.

The patient in Figure 2 was a 56-year-old Caucasian man who was admitted to the hospital for work-up in early 1964 because of nodular lung infiltrates found on a chest film. On physical examination, the prostate gland felt suspicious; and, since "the chest x-ray appearance was consistent with metastases from prostatic carcinoma," a prostate work-up was performed but revealed only hyperplasia. A right lung biopsy was then performed in April 1964. Review of the patient's previous chest films showed a normal study in early 1958, but a few scattered small nodular densities were seen in late 1963. These had become more prominent and numerous by the time of admission in early 1964; they were considerably larger and had begun to coalesce by the time Figure 2 was taken in July 1964.



Fig. 7 (AFIP Negative 54-25957). In some areas the alveoli are filled with mucus and blood cells. Again the alveolar walls are lined by contiguous lepidic growth of the same uniformly tall columnar cells, which have a light clear cytoplasm filled in many cases with mucus vacuoles, thus revealing their mucus-producing nature. The findings in these sections led to the diagnosis of bronchioloalveolar carcinoma of the lung.

The patient in Figure 3 was an asymptomatic 54-year-old Caucasian man whose solitary lesion was found on a routine chest x-ray film in early 1965. A lobectomy was performed in April 1965. Past history was noncontributory.

The clinical backgrounds in these patients reveal no specific information and indicate an insidious disease of long standing in each case. Since the timetable is measured in months to years, chronic diseases must be postulated. There was no way of determining how long the solitary mass had been present in the patient in Figure 3. Similar cases in our files, however, have shown the development of such a nodule over a period of several years. The diagnosis in each of these cases was made only after tissue study.

PATHOLOGICAL CORRELATION AND DISCUSSION

Microscopic sections of the autopsy lung specimen (Figs. 4-7) from the case in Figure 1 present findings which led to the diagnosis of bronchioloalveolar-cell carcinoma of the lung.

When this type of tumor is fairly well

differentiated, it is likely to produce copious amounts of mucus, filling the alveoli over extensive areas of the lung with a water-density substance which forms a contrasting background against which open air-filled bronchi may be seen. This gives rise to the air-bronchogram effects noted in Figure 1, which indicate an underlying alveolar-filling process. The architecture-sparing behavior peculiar to this type of lung carcinoma allows preservation of open bronchi and permits conditions for air-bronchograms, just as we see them in acute alveolar-filling processes or in a chronic disease such as pulmonary alveolar proteinosis in which the lung architecture remains intact.

It is easy to correlate the massive consolidation in the right lower lung in Figure 1. Here mucus has so filled the end air spaces of the lung that the resultant picture is similar to that of a consolidating pneumonia in which the end air spaces have become filled with a water-density substance of a different nature. The same observations could be made for alveolar proteinosis, for example.



Fig. 8 (AFIP Negative 53-13783). One of the diffuse small "miliary" mottled nodules seen in the radiograph of Figure 1 is noted histologically at a relatively high magnification. Note the contiguous growth of tumor cells in a focal area of the alveoli while surrounding alveoli are free. This results in an irregular nodule and implies spread of disease by bronchogenous implants. Such an implant may continue to grow until it finally meets the spread of similar nearby implants and coalesces with them. On reviewing Figure 1, we do note that these "mottled" nodules tend to coalesce into larger masses. The same observations may apply to the larger coalescing nodules seen in Figure 2.

The diffuse "miliary" mottled nodules found throughout the lung fields in Figure 1 can be understood by studying Figure 8. The details of the large nodules in Figure 2 are more easily appreciated and show ill-defined borders consistent with the contiguous alveolar-filling characteristics of this disease. It should be noted by contrast that nodules which result from hematogenous spread in most diseases nearly always have sharply defined borders. The bronchogenous implant theory in bronchioloalveolar-cell carcinoma is favored, but there are still many proponents of lymphogenous or hematogenous spread or possible multifocal origin.

The lesion in Figure 3 is another example of bronchioloalveolar carcinoma: the solitary-nodule type, less notorious than the so-called "adenomatosis" or pneumonitis type, but nevertheless occurring frequently enough to make up about 30% of the cases of bronchioloalveolar-cell carcinoma in the AFIP files. Armed with

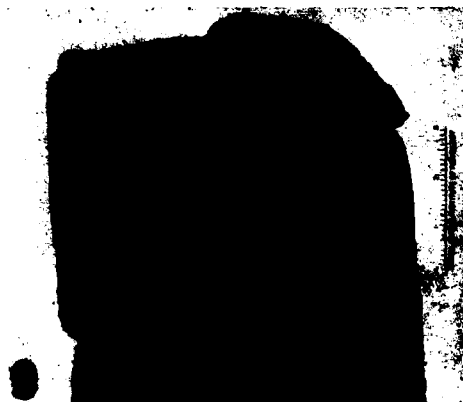
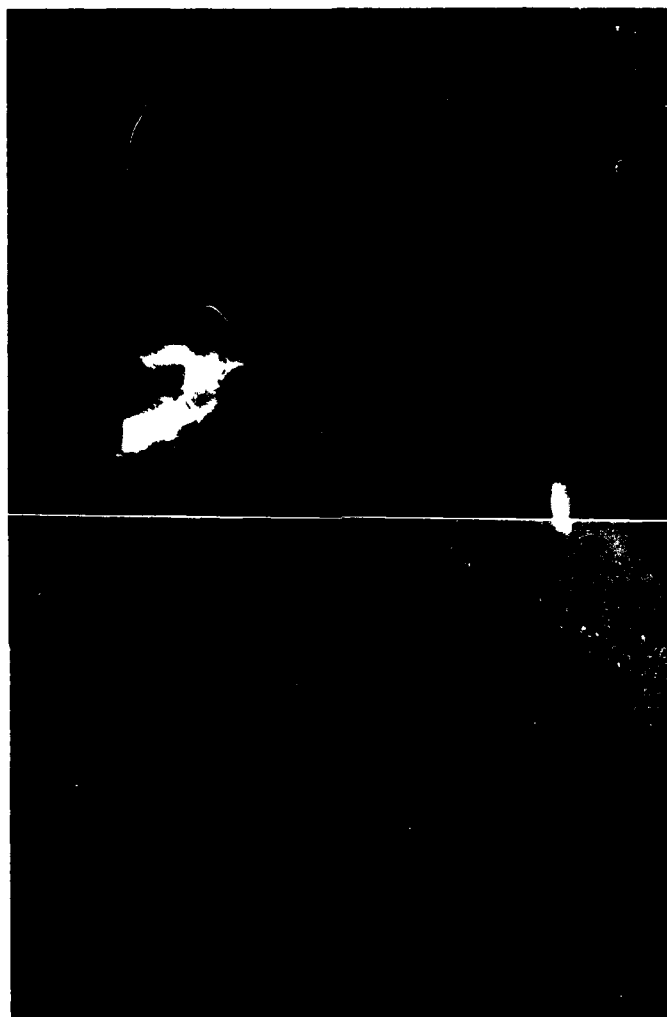


Fig. 9 (AFIP Negative 57-4116-2). A representative gross specimen in the solitary-nodule type of bronchioloalveolar-cell carcinoma shows that this type of tumor causes a marked fibroplastic reaction in surrounding lung tissue. Scarring with retraction causes the tissue around the site of the lesion to be drawn in and puckered. On the radiograph, as in Figure 3, we see the resultant strands extending into the surrounding lung, thus giving the impression of "hairy" margins and of fibrolinear streaks coursing through the mass.



Figs. 10 and 11 (AFIP Negatives 67-7707 and 70-8625). In the above fields we observe that the lung lobules are separated by fibrous septa containing chronic inflammatory infiltrates and scattered lymphoid masses. The details are shown in Figures 12 and 13. Figures 10 and 11 show densely fibrous and highly vascular strands coursing through the tumor and extending to the pleural surface above. Note that the strands are surrounded by dilated air spaces (focal emphysema secondary to scar retraction) which form an air-contrast envelope around them. The air contrast throws these water-density strands into bold relief and permits their visualization within and around the tumor nodule on the radiograph. It must be realized that this can only occur in tumors which tend to spare the underlying normal lung architecture so that air passages which are still open can permit the flow of air into such dilated smaller air spaces. The bronchioloalveolar-cell carcinomas, and uncommonly the bronchogenic adenocarcinomas, are practically the only tumors that would permit such circumstances, just as they are practically the only types which would permit air-bronchogram effects within the tumor mass, because of the same architecture-sparing behavior. Epidermoid carcinomas and bronchogenic adenocarcinomas usually destroy the normal lung structures and strangle the air spaces (even the larger bronchi) in their encroachment.



Figs. 12 and 13 (AFIP Negatives 70-8626 and 70-8627). In the higher magnifications above, we note that the fibrous septa and interstitial structures show entrapped anthracotic pigment and chronic inflammatory infiltrates. Note also in Figure 13 the previously described tall columnar cells of the mucus-secreting type which line the irregular alveolar spaces.

the foregoing discussion, the reader will quickly appreciate the air-bronchogram effects in this nodule as well as the other alveolar-filling characteristics, since here again the lepidic, architecture-sparing growth of this tumor predominates. Figures 9-13 explain the well-defined fibro-linear markings associated with the nodule.

Bronchioloalveolar-cell carcinoma and so-called "alveolar-cell carcinoma" are adenocarcinomas of the lungs which are most frequently very indolent in their growth patterns; only 50% metastasize to the hilar nodes or beyond them. However, the mucus production of these tumors may rarely be so extensive that a patient brings up 2 liters of watery sputum or more a day. In fact, great numbers of these patients die in respiratory failure, literally from drowning. These tumors are not apt to invade the pleura or chest wall, despite their peripheral location. The nodules or masses seldom cavitate, and atelectasis is rarely seen, since the process does not involve the larger bronchi.

The radiographic patterns are quite distinctive. The lesion may be a single nodule, multiple nodules, a coalescing large circumscribed mass associated with nodules, or even a pattern resembling pneumonitis ("adenomatosis"). The majority of the hundreds of cases in the AFIP collection are either solitary nodules (30%) or a combination of masses and nodules (30%). The pneumonitis pattern represents 20% of our material, and the balance are a mixture.

This form of lung adenocarcinoma may be very insidious (as our previous clinical histories indicate) and easily confused with other infiltrative diseases, sometimes for long periods of time. There is no sex predilection, and the average age of involvement is less than in other pulmonary carcinomas, tending to center around the age of fifty years.

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RECOMMENDED READINGS

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Bronchioloalveolar-Cell Adenocarcinoma

RPC of the Month from the AFIP

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ABSTRACT—Three cases of bronchioloalveolar-cell carcinoma are presented. The lesions are vague, ill-defined, and coalescent and show air-bronchogram effects (even within the solitary-nodule type). Selected gross and histological specimens are used to explain the mechanisms underlying the radiographic signs. The fibroplastic reaction in the presence of this tumor results in the visualization of well-defined streaks of density in and around these tumors in long-standing cases.

INDEX TERMS: Armed Forces Institute of Pathology • Lungs, cancer • Lungs, diseases

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