Alveolar Cell Tumor of the Lung

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Of the primary tumors of the lungs, the alveolar cell type is believed to be rare.1 Our case is of interest because of its rarity, duration and autopsy findings. The historical data and other pertinent facts, including etiology, signs, symptoms and pathology have been discussed in detail by Ikeda.1 According to Ewing the tumor occurs in two forms;2 the nodular and the more diffuse or pneumonic type. The lesions may be restricted to one or more lobes and they may be unilateral or bilateral. The bronchi are not involved except as result of invasion by the nodular areas. Metastases do take place to regional lymph nodes and on occasion to distant organs. Clinically the symptoms are most often atypical and misleading. Death in the reported cases is usually secondary to widespread involvement of the lungs creating asphyxia and rarely due to extensive visceral or cerebral metastases.

The first case of diffuse alveolar cell carcinoma, of the type we are reporting, was described in 1903 by Musser.3 This was a 47 year old man whose chief complaint was soreness of throat at night, expectoration of mucoid material in large quantities, progressive dyspnea and cough. His death occurred three weeks after a diagnosis of tuberculosis bronchopneumonia was made and the autopsy revealed the typical picture of primary carcinoma of the lung, originating in the alveolar epithelium. The only metastases found at the time of autopsy were in the regional lymph nodes.

The symptoms, which have been enumerated by some authors,4-6 are variable and usually those ascribed to carcinoma of the lung of bronchogenic origin. These are cough, presence of bloody sputum, pain in the chest, cyanosis, pleural effusion and loss of weight. In other cases fever, non-productive cough, prostration and other constitutional symptoms of an inflammatory lesion predominate. In the presence of diffuse involvement pneumonia is often suspected. Bronchoscopic examination usually furnishes no diagnostic information. The roentgenograms show a variable picture, depending upon the type of alveolar cell tumor present. In the nodular or miliary type there may be punctate infiltrations resembling the mottling of miliary tuberculosis or metastatic

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carcinoma. In the diffuse or pnemonic type the picture of lobar pneumonia is often simulated. The middle lobe syndrome\(^7\) or chronic atelectasis and pneumonitis\(^8\) may be confusing in the differential diagnosis of this condition. Treatment recommended for alveolar carcinoma of the lung is excisional surgery when possible and radiation therapy as an adjunct in palliation of the advanced case. The majority of reported cases have died within a year.

**Case History**

I.G.P., a 34 year old white male, first consulted one of us (J.N.W.) in March 1946, at which time he complained of a sudden onset of coughing of six days duration and which was productive of sputum streaked with blood. In addition there was an associated severe pain in the right lower chest, which resembled pleurisy. The past history dated to 1939 when he was first seen and treated in Longview, Texas; at that time a diagnosis of unresolved pneumonia of the right lower lobe was made (Figure 1). He continued to have intermittent attacks of cough, chest colds and fever until July 1941, when he was in an automobile accident and sustained an injury to the right side of his chest. There were no fractures at that time, however, x-ray films revealed a pneumatic type process in the lower portion of the right lung field. In January 1942 he was again hospitalized for an exacerbation of his pulmonary symptoms and the pathology which had been previously described in the right lower chest was still present but had become more extensive (Figure 2). The diagnosis of pneumonia, right lower lobe, type undetermined, was made. In December 1942, he was again hospitalized for the pulmonary condition, at which time symptoms and physical findings were essentially the same as before. He was treated with chemotherapy and oxygen and at the time of dismissal the diagnosis of unresolved pneumonia of the right lower lobe was again made. Sputum examinations were negative for tubercle bacilli, spirochetes or fungi. He was next hospitalized in December 1945 for an exacerbation of the pulmonary symptoms and again the diagnosis of pneumonia of the right

![FIGURE 1](image)

*Figure 1:* Original x-ray film taken December 1939, showing lesion in lower right lung field.

![FIGURE 2](image)

*Figure 2:* Same process increased in extent.
lower lobe was made. The disease, however, was more extensive in the right chest and at this time was first noted to involve the left lower lung field. His next admission was in March 1946, when he was first seen by one of us (J.N.W.). During the preceding year he had lost approximately 35 to 40 pounds in weight. X-ray film inspection revealed evidence of consolidation in the lower portion of the chest on the right and a probable pneumonic process in the lower lobe of the left lung. The diagnosis of bilateral pneumonia was entertained. He was treated with antibiotics and discharged after the acute exacerbation of his pulmonary symptoms had subsided. During the period of hospitalization he was raising copious amounts of thick, frothy, mucopurulent blood tinged sputum. A daily record of this sputum was kept and ranged from 830 cc. to 1200 cc. daily. Examination of the sputum showed no acid-fast organisms, spirella, or fungi. There were numerous pus cells and the sputum had an offensive odor. No organisms were found on gram stain. He was bronchoscooped by (L.K.T.) on March 20, 1946 and moderate narrowing of the openings into the right lower and middle lobes with reddening of the mucosa of both bronchi was noted. No tumor masses could be seen. The bronchoscopic diagnosis of bronchial stenosis, right lower and middle lobes was made.

The patient was referred to one of us (G.F.M.) in April 1946, and after examination, including AP and PA and lateral films of the chest, as well as bronchoscopy, a tentative diagnosis of carcinoma or chronic pneumonia and atelectasis was entertained with disease involving the right middle and lower lobes, as well as the left lower lobe. Because of the duration of the disease and the severity of the cough with hemoptysis and marked expectoration, it was felt that an exploration was indicated and this was accordingly carried out by one of us (G.F.M.). At the time of exploration the pathologic process was found chiefly in the right middle and lower lobes but also was present in the right upper lobe (Figures 3 and 4. The exact nature of the lesion was not determined. Frozen sec-
tions were not obtained. Had we known that the underlying process was malignant any operative procedure carried out to effect a cure would have required a total right pneumonectomy, as well as a left lower lobectomy. This, however, would have been too extensive because of his already limited respiratory reserve. Because the chief pathology in the right chest involved the middle lobe, a right middle lobectomy was done and he did well post-operatively. He was seen as an out-patient in the summer and fall of 1946, when he gained rapidly in weight to a maximum of 152 pounds. The sputum was reduced from a maximum of 1200 cc. to an average of 150 cc. of clear, frothy sputum daily. His condition remained satisfactory for two and one-half years and he returned to work. In the latter part of 1948 he had a gradual decline in general condition. He had been given x-ray therapy post-operatively but had not returned for his full course of treatment. In March 1949 the patient developed some numbness and weakness of the left arm and left leg. The diagnosis of possible cerebral metastasis was made. X-ray film inspection showed the pulmonary process to have become more extensive. Bronchoscopic examination done elsewhere (University of Texas) showed nothing startling save the excessive amount of secretion which was mucopurulent. There was no tumor tissue seen which was possible to obtain by biopsy. The patient’s weight had reduced to 129 pounds in June 1949. In the fall of 1949 he developed visual difficulties which developed almost to a point of total blindness and the numbness and pain in the left arm and left leg progressed. He was dyspneic and cyanotic most of the time. His condition was progressively downhill until January 1950, when he became delirious and died.

*Surgical Specimen*: Submitted by G.F.M. on April 20, 1946, consisted of the middle lobe of the right lung. No detailed record was made of the size, weight, or appearance of this lobe. Microscopic sections showed neo-

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**FIGURE 5**: The surgical specimen showing the diffuse involvement of the lung alveoli. (x150).
plastic changes involving all of the alveoli. The pattern of the alveoli was moderately well preserved. The lining carcinoma cells were tall columnar, with nuclei placed near the base. No cilia were present. The nuclei stained densely and in areas showed pleomorphism. In some alveoli these neoplastic cells were present as a single layer, while, in others, they had proliferated to form both solid nests and papillary projections. The cells had produced a marked amount of mucin as demonstrated by Azure-A. This mucin was present in the form of globules in the cytoplasm of some neoplastic cells and also filled most of the alveolar spaces (Figure 5).

**Autopsy:** On January 16, 1950, this study revealed alveolar carcinoma involving the entire remaining right lung, the left lower lobe, and about one-half of the left upper lobe. Metastatic deposits of alveolar carcinoma were found in the right cerebral hemisphere, in two tracheobronchial nodes, in one preaortic node (celiac node), and in the liver. No additional pathology of importance was noted in the remainder of this post mortem examination except dense pleural adhesions. The right lung was so adherent to the chest cavity that it could not be removed as a complete organ. The left lung weighed 1000 grams. On the pleural surface numerous nodules were seen that appeared slightly elevated and grayish-yellow in color. On cut section this same nodular pattern was observed but the nodules were confluent. There was no evidence that the carcinoma had its origin from any of the bronchi. Glairy mucus could be scraped from the cut surface. The main bronchi also contained this type of secretion.

The tumors in the right cerebral hemisphere were about three centimeters in diameter and were found in the superior pre-frontal area and in the superior parietal lobule. The tumors were made up of mucus for the most part (Figure 6).

The metastatic deposits in the lymph node and in the liver were more solid in character (Figure 7).

The microscopic appearance was similar to that described in the surgical specimen. However, one interesting thing was noted in the lung concerning the distribution of the neoplastic tissue. There were areas

**FIGURE 6**

*Figure 6:* Right cerebral hemisphere, showing the two metastases. They are seen as projecting tumors over the convexity of the cerebral hemisphere. (Reduced to one-fifth actual size.)

**FIGURE 7**

*Figure 7:* Liver, showing the two metastatic deposits, one subcapsular and the other slightly below the surface. (Reduced to one-fifth actual size.)
where all of the alveoli were definitely involved by carcinoma, and then other areas where small, discrete nodules could still be detected. In the latter areas, occasionally, only one-half of an alveolus would show tumor tissue.

The intervening lung appeared normal, thus ruling out pulmonary adenomatosis. The amount of mucus produced was marked in the lung and in the brain. The metastases in the lymph nodes and in the liver showed both gland formation and solid strands of tumor cells.

The problem of differentiating pulmonary adenomatosis from alveolar cell carcinoma is real but the recent work by Laipply and Fisher11 with their illustrations has helped define the two diseases. As they stressed, pulmonary adenomatosis shows "... alveoli lined with epithelium-like cells, marked fibrosis, and lymphocytic infiltration of interalveolar septums, lining alveolar cells are columnar or cuboidal, are usually nonciliated, and are uniform in size, shape, and staining reaction. Mitotic figures are few and there is no invasion of adjacent tissue."

In contrast alveolar carcinoma, as demonstrated by this case, shows diffuse and nodular involvement of the lung, essentially normal intervening lung tissue when present, cellular pleomorphism, and metastases. If these differences are kept in mind, the two diseases can be microscopically differentiated.

**Final Diagnosis:** Alveolar cell carcinoma of the lung with metastases to lymph nodes, liver and brain.

**Discussion**

The tumor in this patient was undoubtedly present for at least 11 years. Although the patient was seen throughout this period by a number of physicians, the most frequent diagnosis entertained was unresolved pneumonia. Congenital atelectasis with pneumonitis and carcinoma were considered at the time of his hospitalization in 1946. The chief symptom was productive cough and on some occasions it amounted to 1200 cc. of sputum daily. The patient was given considerable palliation by surgical excision of the right middle lobe and subsequent x-ray therapy. We feel that the tumor variety we are dealing with was that of a pneumonic type of alveolar cell carcinoma of the lung. The tissue has been studied by one of us (L.R.H.) and Dockerty,10 both of whom concur in the diagnosis. This case is another example of how closely carcinoma of the lung can simulate both clinically and roentgenographically other pulmonary lesions. It also demonstrates the fallacy in adopting the policy of waiting, watching, and taking frequent roentgenograms. Had this lesion been more localized at the time of exploration, the possibility of a cure could have been entertained, however, the extensiveness of the lesion was such...
that total extirpation of the entire pathology was impossible. We believe this to be the longest case on record in which the disease, which was first noted in the lung in 1939, persisted by roentgenographic evidence for a period of 11 years before death ensued. The patient had exacerbation of symptoms when an inflammatory process was superimposed on the existing lesion, however, the acute symptoms responded to antibiotics and oxygen therapy. He was never completely free of symptoms following his original illness in 1939. Successive x-ray films during the 11 year period showed extension of the process. This lesion should have been subjected to exploratory thoracotomy much earlier in its course. In addition, it demonstrates the slow growth of the neoplasm and the palliation which resulted from the removal of a portion of the involved lung followed by x-ray therapy. The case of Delarue and Graham⁵ would seem to substantiate this contention. In addition, it is an example of alveolar cell carcinoma of the lung which metastasized widely.

SUMMARY

1) Alveolar cell tumors of the lung are rare and present symptoms which are often atypical and misleading.

2) This tumor occurs in two forms, i.e. nodular or miliary variety and a diffuse or pneumonic type.

3) A case is reported in whom an alveolar cell tumor existed for a period of 11 years before death occurred. Symptoms had been attributed to unresolved pneumonia throughout the major part of its course.

4) Excisional surgery, where possible, is the treatment of choice but roentgen therapy is of aid in the inoperable case.

5) Metastases usually occur only to regional lymph nodes. In the case presented, distant metastases were also found.

RESUMEN

1) Los tumores de celdillas alveolares del pulmón son raros y presentan síntomas que son a menudo atípicos y engañosos.

2) Estos tumores ocurren en dos formas: nodular o miliar y una forma difusa de tipo neumónico.

3) Se refiere un caso en el que el tumor alveolar existió por 11 años antes de descubrirse. Los síntomas se atribuyeron a neumonía no resuelta durante la mayoría del tiempo de su evolución.

4) La cirugía de excisión es el tratamiento de elección cuando es posible pero la roentgenterapia es útil en los casos inoperables.

5) Las metástasis ocurren generalmente solo en los ganglios regionales. En el caso relatado también había metástasis a distancia.
RESUME

1) Les tumeurs du poumon d'origine alvéolaire sont rares et se présentent souvent sous un aspect symptomatique atypique et trompeur.

2) Ces tumeurs se présentent sous deux formes: la forme nodulaire ou miliaire, et la forme diffuse ou pneumonique.

3) Les auteurs rapportent une observation dans laquelle une tumeur à cellules alvéolaires évolua pendant onze ans avant l'apparition de la mort. Pendant la plus grande partie de l'évolution, des symptômes furent attribués à une pneumonie à résolution incomplète.

4) Le traitement de choix est l'exérèse chirurgicale quand elle est possible, mais dans les cas inopérables, le traitement radiothérapique est un auxiliaire précieux.

5) En général, les métastases se font dans les lymphatiques régionaux. Dans le cas rapporté, il y avait également des métastases à distance.

REFERENCES

10 Docketry, M. B.: Mayo Clinic, Rochester, Minn.