AN UNUSUAL PULMONARY COMPLICATION IN ACUTE LYMPHOCYTIC LEUKEMIA

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Complications of acute leukemia in childhood have paradoxically increased since the development of modern chemotherapy and, in particular, since the introduction of the antimetabolites and the steroids. It is now well established that leukemia is more than a hematopoietic disorder and that it frequently involves infiltration of leukemic cells in various organ systems. Most commonly involved sites are the lymph nodes, liver, spleen, kidneys, bones, central nervous systems, pleura and the lungs, but infiltration of other organs is not unusual.

Pulmonary infiltration in leukemia is probably more common than it is generally thought to be. Because of the paucity of respiratory signs and symptoms in pulmonary leukemic involvement, this complication is most usually discovered only at autopsy.

According to various investigators, the incidence of parenchymal pulmonary involvement in leukemia ranges from 13 per cent to 40 per cent.

In Vieta and Craver's series,[1] among 158 lymphatic leukemia cases, parenchymal involvement was found in 24.6 per cent of cases, pleural involvement in 12 per cent and pleural effusion in 12 per cent. Postmortem examination of 31 cases revealed that the parenchyma was attacked in 19 per cent and the parietal pleura in 6 per cent.

Analysis of 52 cases of myelogenous leukemia skowed 7.6 per cent with parenchymal infiltration. Autopsy of 23 myelogenous cases indicated that the parenchyma was involved in 13 per cent.

Falconer and Leonard[2] reported pulmonary involvement in 30 per cent of their cases of lymphoblastic leukemia.

Kirklin and Hefke[3] discovered pulmonary involvement in 40 per cent of their cases by means of radiologic examination. Also using roentgen ray, Lamy, Debry, Gilgekrantz and Cherrier[4] report an

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incidence of 30 percent of patients with pulmonary involvement in their series of lymphatic leukemia cases.

Nathan and Saunders[5] reviewed 59 autopsied cases of all types of leukemia and noted pulmonary involvement in 23 per cent.

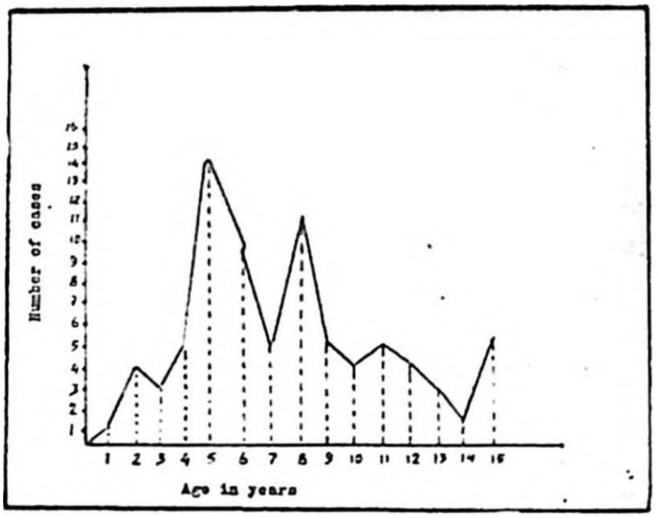

Figure 1. A breakdown by age and sex of the leukemia patients seen at Hacettepe Children's Hospital.

A recent review by Green and Nichol[6] mentions pulmonary infiltration in 27 per cent of a group of 109 autopsied leukemia cases. Infiltration of clinical significance was seen in 7 per cent.

A total of 81 cases of leukemia has been seen at Hacettepe Children's Hospital since its establishment five years ago. Fifty-nine of these patients were males, 22 were females and a breakdown by age is given in figure 1. Table 1 summarizes the types of leukemia involved.

TABLE 1

TYPE OF LEUKEMIA IN 81 CASES

TYPE	NUMBER	PER CENT
Acute lymphocytic	55	67.9
Acute myelocytic	22	27.1
Acute monocytic	1	1.2
Stem cell	3	3.7

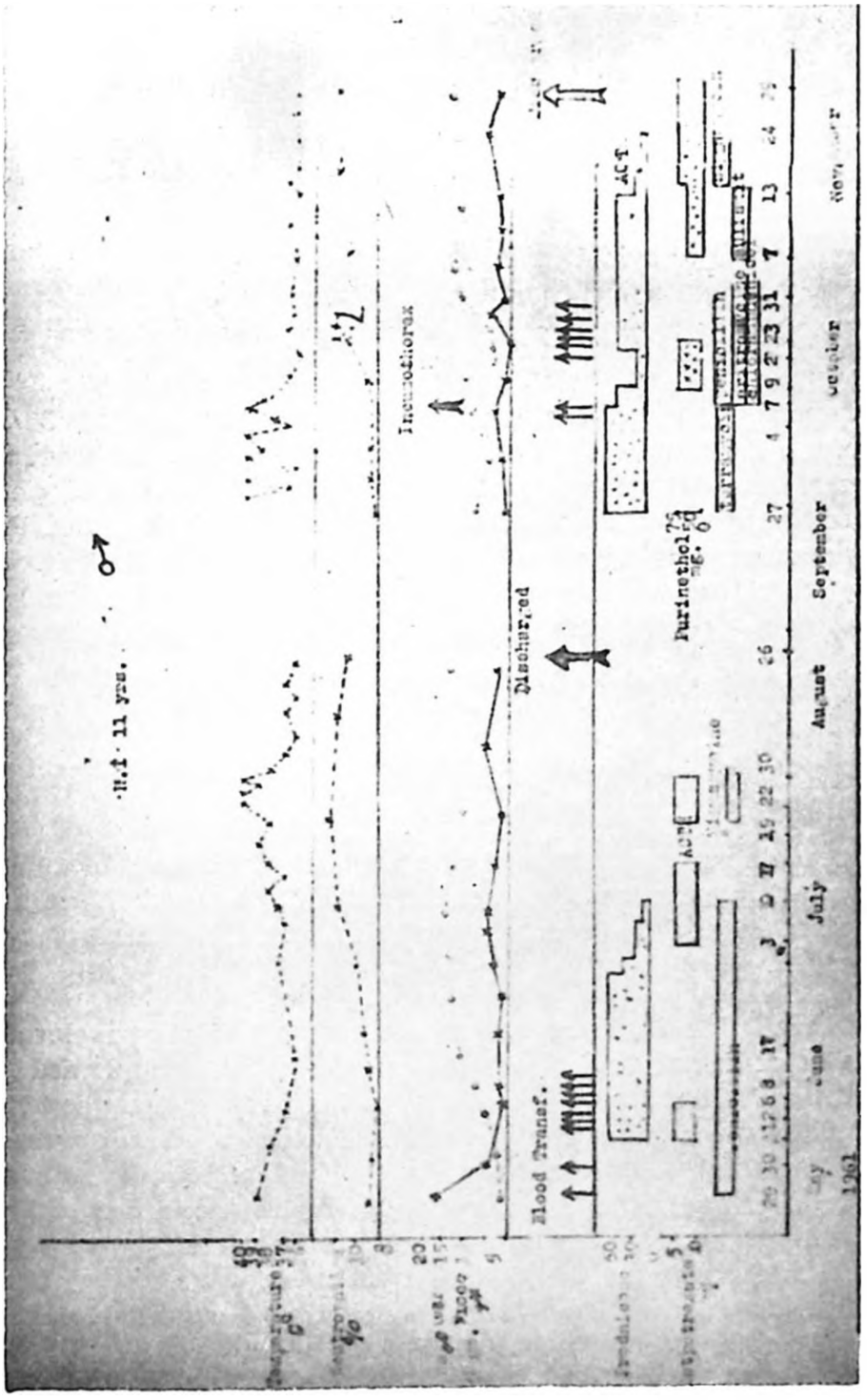

Figure 2. Clinical course of disease in a patient with acute lymphoblastic leukemia with pulmonary complications.

Thirty-six of these patients had chest films taken for one reason or another. In 11 cases roentgenography suggested pulmonary infiltration. An unusual pulmonary complication was noted in one of these children and his case will be described in this report.

Case Report

Patient was an 11 year old male whose illness had been diagnosed as acute lymphoblastic leukemia four months prior to this admission. After a steroid induced remission he was being maintained on 5 milligrams of methotrexate daily. On September 29, 1961, he was admitted to the hospital with complaints of fever, headache, respiratory difficulty, pain in the legs and swellings in the neck of three days duration.

Physical examination revealed a temperature of 39 C., respirations 36/minute and a pulse rate of 136/minute. Axillary, inguinal and cervical lymphadenopathy was noted, the nodes measuring 1 to 1.5 centimeters each. Scattered petechiae were present on the chest, on the abdomen and also on the soft palate. Pharynx and tonsils were moderately hyperemic. There was no significant positive respiratory finding other than an increased respiratory rate. The liver and spleen were palpable 3 and 7 centimeters, respectively, below the costal margin.

Laboratory studies showed the hemoglobin to be 9.25 Gm./100 ml. and the white blood cell count was 1500 per cubic millimeter. A differential count showed 2 per cent neutrophils and 98 per cent lymphocytes. Platelets were reduced in number.

The patient's illness was diagnosed as acute lymphoblastic leukemia complicated with acute upper respiratory tract infection. He was treated with 1 Gm. of tetracycline and 60 mg. of prednisone per day, and the clinical course may be seen in figure 2.

Soon after admission his temperature again rose and stayed elevated for the next three days. Urinalysis was normal and the patient complained only of pain in the extremities. Six days after admission his temperature was 38 C. and scattered folliculitis was observed on the skin. The clinical picture was suggestive of sepsis. Blood and throat cultures were taken and both subsequently produced pathogenic staphylococcus sensitive to erythromycin and chloramphenicol. Treatment with terramycin was stopped and the patient put on penicillin, chloramphenicol and erythromycin. A blood transfusion was given on October 6 to raise the hemoglobin level. Prednisone was continued at 40 mg./day and 75 mg./day of 6 mercaptopurine was started. Fever remained at about 40 C.

On October 7 the child was restless and seemed dyspneic. He was given a second blood transfusion. Moist and crepitant rales were heard in the right axilla. A chest roentgenogram disclosed the presence of pneumothorax on the left side together with perihilar infiltration and reaction in the fissure on the right (figure 3). Following a closed thoracotomy and drainage under water pump, dyspnea subsided.

Rales were subsequently heard on the right side and subcutaneous emphysema developed on the left. A control film taken on October 11 showed the presence of pneumothorax on the right side (figure 4). The left lung appeared

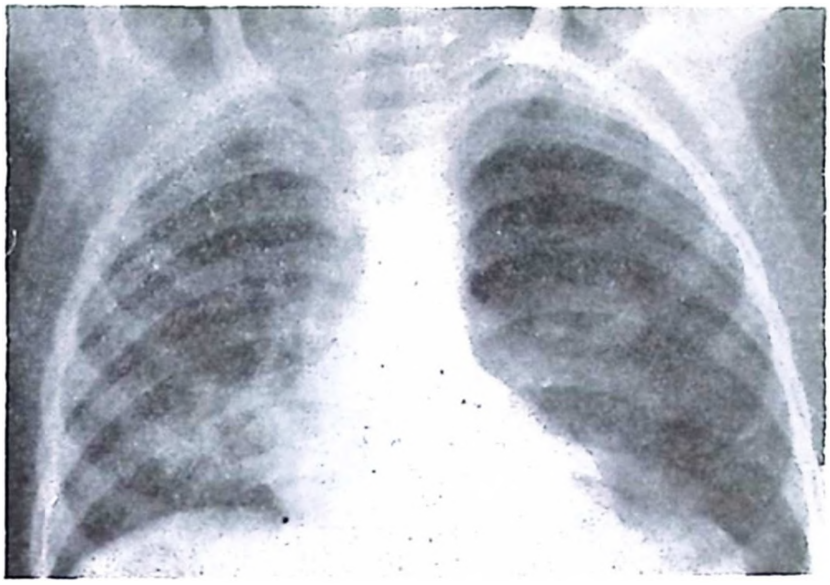

Figure 3. Chest roentgenogram showing pneumothorax on the left side. 10/7/62.

to be well expanded but there was widespread subcutaneous emphysema on the left. The air from the right thorax was emptied by syringe (open method). Films taken on the 12th and 13th showed no change but a roentgenogram on October

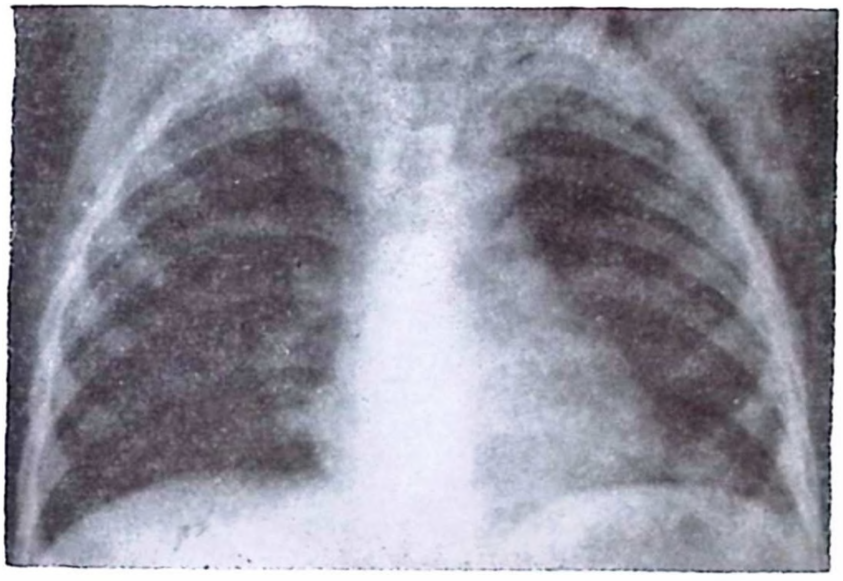

Figure 4. Roentgenogram of same patient showing pneumothorax on the right. 10/11/62.

17 disclosed a reduction in the pneumothorax on the right and no pneumothorax on the left (figure 5). There was still some mediastinal emphysema but subcutaneous emphysema was considerably reduced. On October 19 the intrathoracic tube was removed and a roentgenogram on that date showed that the pneumo-

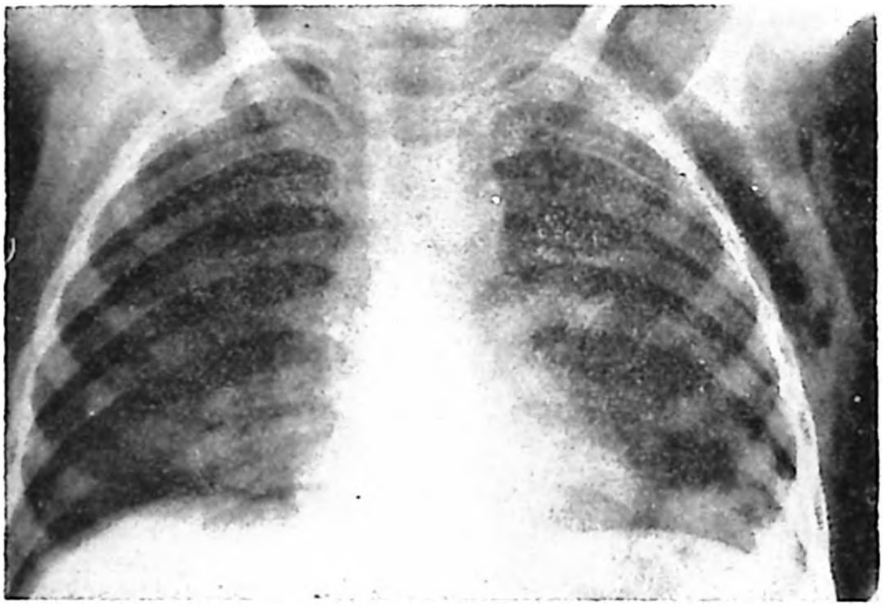

Figure 5. Same patient. Roentgenogram on 10/17/62 indicating reduction of pneumothorax on the right and disappearance of pneumothox on the left.

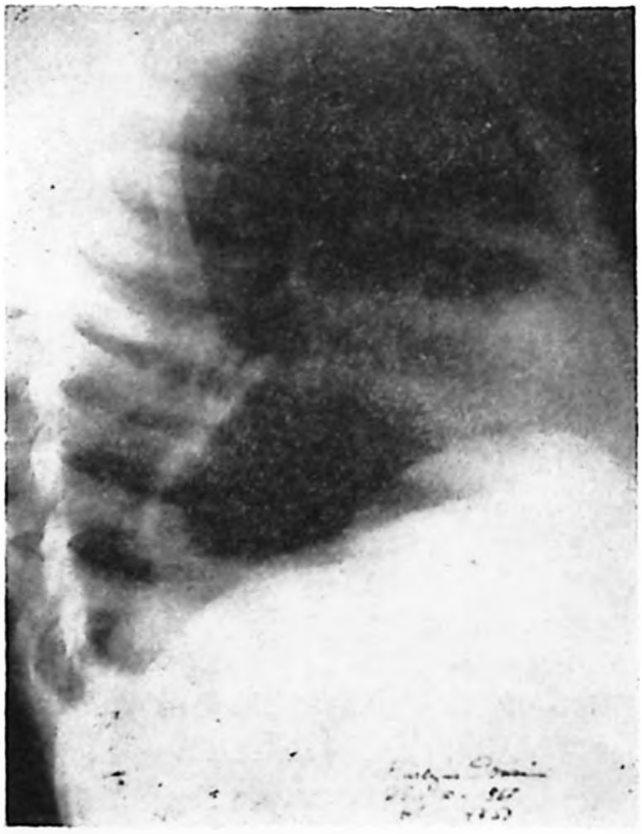

Figure 6. Film taken on 10/25/62, showing cystic development over the diaphragm in the lower left lung field with infiltration around it.

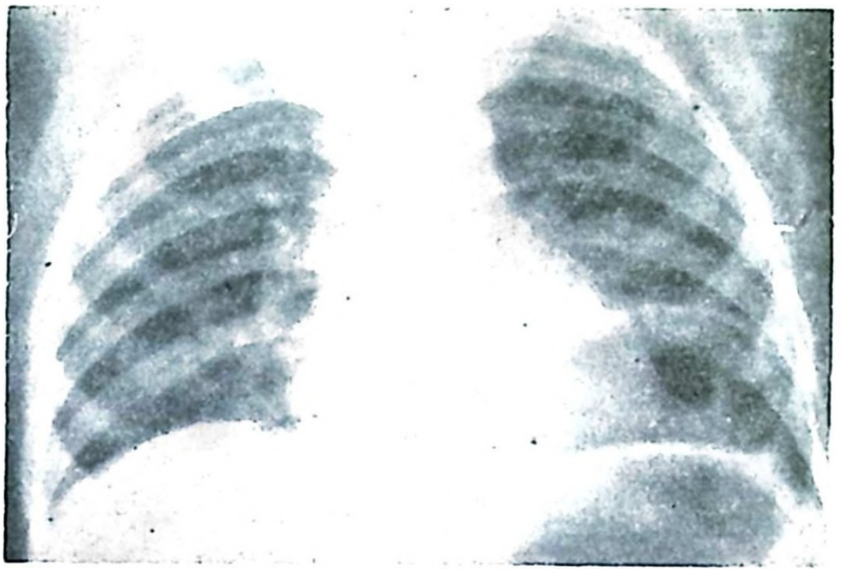

Figure 7. Second film taken on 10/25/62, showing cystic development over the diaphragm in the lower left lung field with infiltration around it.

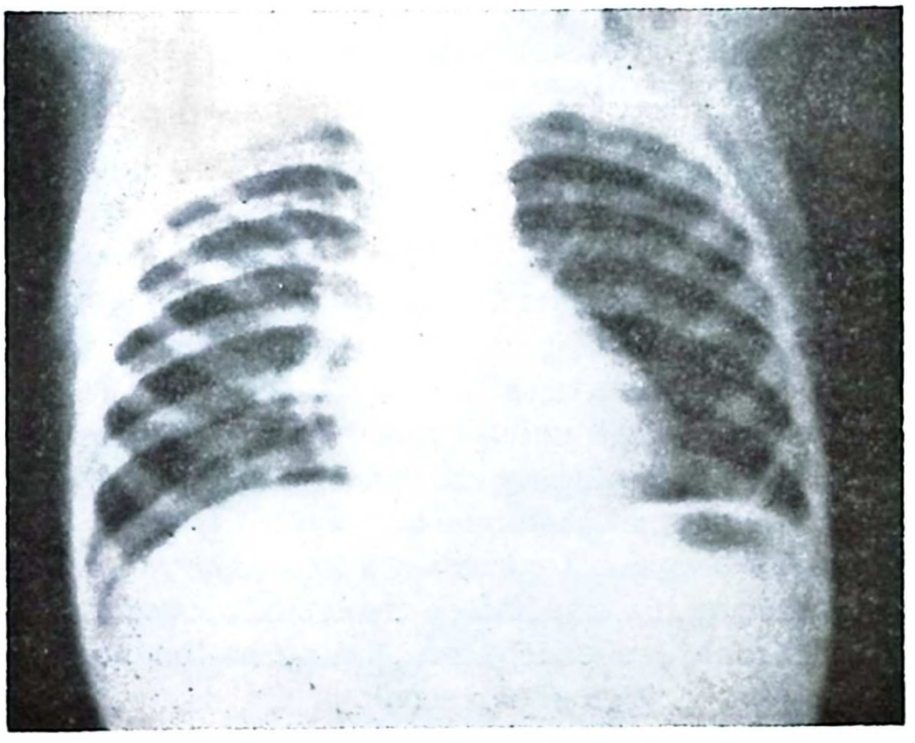

Figure 8. Pneumatocele-like lesions on the left side in a film taken on 11/3/62.

thorax on the right side had disappeared. A chest film on October 25 (figures 6 and 7) showed a cystic development over the diaphragm in the lower left lung field with an infiltration around it. On November 3 many pneumatocele-like lesions on the left side were observed roentgenographically (figure 8).

By November 29, pulmonary infiltration had been reduced and the patient was considered to be well clinically. He was discharged on that date in good condition, being maintained at home on 75 mg./day of 6 mercaptopurine.

Discussion

As indicated by the figures presented at the beginning of this paper, the incidence of respiratory system involvement in leukemia is much higher than might be expected. Green and Nichols[6] have classified the various types of pulmonary leukemic involvement and this classification is presented in table 2.

TABLE 2

CLASSIFICATION OF PULMONARY LEUKEMIC INVOLVEMENT

A. Parenchymal (diffuse interstitial or nodular)
   1. Alveolar septa
   2. Alveolar spaces

B. Non parenchymal (massive or focal)
   1. Bronchial or peribronchial
   2. Perivascular
   3. Pleural or subpleural
   4. Diffuse (combined)

C. Pulmonary infarction.

Leukemic pulmonary lesions may be rather silent clinically, producing minimal or negligible physical signs and symptoms. There fore only by frequent radiological examination of the chest can they be detected. Most of the time the clinical picture and physical signs are variable and do not correspond to the radiological findings,[7] but it seems that significant clinical involvement occurs with greater frequency in chronic leukemia than it does in the acute form (10 per cent as compared with 4 per cent).

Diffuse leukemic infiltration of the parenchyma, vascular throm botic lesions, necrotic infarcts caused by proteolytic enzymes of myeloid elements and aseptic cavity formation are the various well-known forms of pulmonary lesions in leukemia. Fiessinger and Fau-

vet[8] claim that proteolytic activity of the leukocytes is elevated in acute leukemia, particularly in the myeloid forms, whereas no such elevation is observed in lymphoblastic types.

Green and Nichols[6] found that one-third of their patients with diffuse pulmonary infiltration had bronchopneumonia, with or without areas of abscess formation, at the time of death.

The main difficulty in dealing with this condition lies in making a differential diagnosis of the pulmonary infiltrations seen on chest roentgenograms. Such infiltrations may be pure leukemic infiltrations or they may be the result of diffuse pulmonary infection. Leukemic infiltrations usually respond to antileukemic drugs; infiltrations due to pulmonary infection can usually be treated with antibiotics, but one cannot sharply differentiate between these two conditions since infection can be superimposed on leukemic infiltration of the lungs.

In our case it was rather difficult to differentiate the true etiology of the pneumothorax since we had no histopathological examination. The pneumothorax was revealed only by roentgen ray examination. Clinical evidence of infection with continuous fever, confirmed by positive cultures of pathogenic staphylococci, might make one consider the possibility of pneumothorax resulting from pure staphylococcus infection. However neither closed drainage nor roentgen ray examination disclosed any true empyema, leading us to the conclusion that this could not have been solely a case of pure staphylococcus infection and suggesting that leukemic infiltration of the pulmonary tree was involved. Furthermore the pneumothorax was bilateral and disappeared in two days with the closed drainage method. It is true that the roentgenograms themselves did not suggest leukemic infiltration but we feel that it is highly probable that our case represented a combined form of disease in which multiple staphylococcal lesions were superimposed on scattered foci of small leukemic infiltrates. The possibility of rupture of part of an infiltrated and inflamed lung as a result of proteolytic enzymatic activity, as suggested by Fiessinger, cannot be ruled out but it is our opinion that such a process was not involved here.

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