Localized ground-glass opacities with multiple pulmonary small cysts in adult T-cell leukemia or lymphoma: An "alloy wheel" appearance

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short title: **Localized GGOs with multiple pulmonary cysts in ATL/L**

Localized ground-glass opacities with multiple pulmonary small cysts in adult T-cell leukemia or lymphoma: An “alloy wheel” appearance

Summary

We herein report a case of adult T cell leukemia or lymphoma (ATL/L) demonstrating multiple lung cysts within a localized ground-glass opacity (GGO) on CT. The patterns of multiple localized GGOs having multiple small cysts were varied, including a large air space in the center of the localized GGO with surrounding small cysts, a solid part in the center of the localized GGO with peripheral small cysts, and clustered small cysts. These findings were considered to simulate the appearance of an "alloy wheel". Some of the central large air spaces had thickened walls. Based on the histopathological findings, the pathogenesis of multiple cysts formation was considered to be a combination of two main mechanisms as follows: a check valve mechanism due to stenosis or an obstruction by the tumor cells' infiltration along the bronchioli, a traction bronchiolectasis and ectatic alveoli by fibrosis.

Key words: adult T-cell leukemia or lymphoma**,** lung cysts, computed tomography

Introduction

Adult T cell leukemia or lymphoma (ATL/L) was first discovered and reported in Japan, where it has a high incidence in the southwest region [1]. It was reported that the computed tomography (CT) findings of lung involvement of ATL/L consisted mainly of ground-glass opacity (GGO), centrilobular nodules, and a thickening of the bronchovascular bundles in the peripheral lung. To our best knowledge, however, there have been no reports of ATL/L patients having multiple lung cystic lesions [2]. We herein report a case of ATL/L with multiple lung cysts within localized GGOs.

Case report

A 62-year-old male presented with a loss of appetite and a 12 kg weight loss over the past year. He had smoked about 50 cigarettes per day for 45 years. On admission the laboratory findings included the following: white blood cell count 9600/ μ l (73% neutrophils, 8% lymphocytes, 12% monocytes, and 0% eosinophils), red blood cell count 432 x 10^4 / μ l, C-reactive protein 7.50 mg/dl, lactic dehydrogenase 163 IU/l. The tumor marker levels were normal, except for cytokeratin fragments (CYFRA) 5.2 ng/ml.

Chest radiograph on admission demonstrated consolidation and GGO associated with cystic lesions in the left middle and lower lung zones. In the right lung, several ill-defined hazy nodules were also present (Fig. 1). Chest thin-section CT (TSCT) with 1mm collimation on the same day showed multiple cystic lesions within consolidation associated with the surrounding GGO in the left lung (Fig. 2). Bronchiectasis, bronchial wall thickening and centrilobular nodules were also observed. Furthermore, TSCT showed multiple cysts within localized GGOs in both lungs (Fig. 2).

The patterns of these cystic lesions were varied, and could be described as follows: a large air space in the center of the localized GGO with surrounding small cysts (Figs. 2A-C), a solid part in the center of the localized GGO with peripheral small cysts (Fig. 2D), and clustered small cysts (Figs. 2B, C). Some of the central large air spaces had thickened walls (Figs. 2A, B). Left pleural effusion and mild mediastinal lymph node enlargement were also identified. Abdominal CT on admission depicted bowel dilatation associated with thickened walls in the jejunum, and lymphadenopathy.

Bronchoscopy was performed, and atypical lymphocytes were present in the bronchial washing. The soluble interleukin-2 receptor concentration in the serum increased (5545U/ml), and human T-cell lymphotropic virus type 1 (HTLV-1) antibody was positive. These studies suggested the presence of ATL/L. The patient complained of ileus symptoms 10 days after the admission, and suffered from peritonitis associated with bowel perforation. Emergency surgery of partial resection of the jejunum was performed. A photomicrograph of the resected jejunum showed a proliferation of atypical lymphoid cells, which was phenotype T (lubiquitin-C-terminal hydrolase 1+).

Despite the emergency surgery, the patient had an anastomotic leak one month after the operation and died. A photomicrograph of the autopsy specimens of the lung demonstrated atypical lymphocytic infiltration into the alveolar wall and the alveolar spaces, and along the bronchi, bronchioles, and terminal bronchioles (Fig. 3A). According to the radiological –pathological correlation, the former pathological finding corresponded to consolidation associated with surrounding GGO, while the latter one corresponded to bronchial wall thickening and centrilobular nodules. Based on these pathological findings, the diagnosis of ATL/L was confirmed.

Multiple cystic lesions within consolidation or localized GGOs on TSCT were

also observed in the autopsy specimens of the lung. The most characteristic lesion showing a large air space in the center of the localized GGOs with surrounding small cysts, was seen in the right upper and lower lobes on TSCT (Figs. 2A-C). The central large air space was formed by bronchiolectasis by fibrosis, and its walls corresponded to a diffuse infiltration of atypical lymphocytes (Figs. 3B-D). The surrounding multiple small cysts had thickened alveolar septa infiltrated with lymphoma cells. These cysts were thought to be caused by a check valve mechanism due to stenosis or obstruction by tumor cells' infiltration along the bronchioli.

Discussion

ATL/L was first discovered and reported in Japan, where it has a high incidence in the southwest region [1]. ATL/L is caused by HTLV-1, which is diagnosed by a positive HTLV-1 antibody test and the presence of malignant T cells that have highly indented or lobulated nuclei in the peripheral blood or histological findings in biopsied tissues [2]. The infiltration of leukemia cells into the lung has been reported to be present in 54% of ATL/L [2].

ATL/L involving the lung parenchyma has varied CT findings [2]. Okada et al. [2] reported that the main CT findings of lung lesions included GGO, centrilobular nodules, and thickening of the bronchovascular bundles in the peripheral lung. Based on the correlation between CT and the pathological findings, the extent of GGO corresponded pathologically with that of atypical lymphocytic infiltration into the alveolar wall and the alveolar spaces. In addition, the extent of centrilobular nodules corresponded with that of atypical lymphocytic infiltration along the respiratory bronchioles. The thickening of the bronchovascular bundles corresponded to an

infiltration of atypical lymphocytes along the bronchovascular bundles. Furthermore, nodules, consolidation with an air bronchogram and mild lymphadenopathy were reported, but cavitating nodules were rare. In the present case, GGO and consolidation, centrilobular nodules, and bronchial wall thickening were predominantly observed.

Interestingly, multiple cystic lesions within localized GGOs were observed on TSCT in this case. The pattern of these lesions were varied, and these findings were considered to simulate the appearance of an “alloy wheel”, which is an automobile wheel made from an alloy of aluminium or magnesium metals. This wheel is used for improved driving performance as well as for cosmetic purposes, and has an intricate design (Fig. 4). Several reports have described the mechanism of development of the thin-walled cyst of the lungs in general as follows: a check valve mechanism based on stenosis or obstruction by tumor cells’ and inflammatory cells’ infiltration along the bronchioli [3-6], a traction bronchiolectasis and ectatic alveoli by fibrosis [5, 7]. Based on the pathological findings in the autopsy specimens of the lung, a combination of these mechanisms is thought to be the cause of the development of multiple cystic lesions in this case. In the characteristic cystic lesions shown in Figures 2A-C and 3B-D, the central large air space was formed by bronchiolectasis by fibrosis, and the surrounding multiple small cysts were thought to be caused by a check valve mechanism. The fact that the number of the surrounding multiple small cysts in the autopsy specimens was fewer in comparison to that on TSCT may support this hypothesis. In the autopsy specimens, it was suspected that a check valve mechanism disappeared and small cysts collapsed due to the incomplete inflation of the lung [8].

Other mechanisms for the development of the thin-walled cyst such as, the destruction of pulmonary parenchyma due to the tumor cells’ infiltration [4,5,7,8],

elimination or excretion of necrotic elements from the lesion through the bronchioli [5,7-10], growth of malignant cells along pre-existing air cysts [4,5,8], and traction ectasia of pre-existing cavity by surrounding normal parenchyma have been reported [4]. However, these mechanisms seem to be a less likely cause in the present case.

Multiple cystic lesions are observed in various lung diseases, which include bronchioloalveolar carcinoma, metastatic lung tumor, lymphocytic interstitial pneumonia, eosonophilic granuloma, lymphangioleiomyomatosis and some infectious diseases such as pulmonary tuberculosis and *Pneumocystis jiroveci* pneumonia [3, 5,7,9-12]. In particular, bronchioloalveolar carcinoma is one of the most important differential diagnoses from lymphoma involving the lung parenchyma in an actual clinical situation. However, unique pulmonary cystic lesions in the present case are atypical of bronchioloalveolar carcinoma.

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Figure legends

Figure 1

Chest radiograph demonstrates consolidation and GGO associated with cystic lesions in the left middle and lower lung zones. In the right lung, some ill-defined hazy nodular opacities are present (arrows).

Figure 2

TSCT shows multiple cysts within a localized GGO. The patterns of these cystic lesions are varied, which includes a large air space in the center of the localized GGO with surrounding small cysts (white arrows, A-C), a solid part in the center of the localized GGO with peripheral small cysts (arrow, D), and clustered small cysts (arrowheads B, C). Multiple cystic lesions within consolidation associated with surrounding GGO in the left lung are also observed.

Figure 3

A: Atypical lymphocytes infiltration (hematoxylin-eosion stain, ×400).

The cellular component consists of diffuse infiltration of large atypical lymphocytes with irregular nuclei (arrows), consistent with ATL/L.

B, C: Central large air space with thin wall and surrounding small cysts (B: hematoxylin-eosion stain, ×20, C: hematoxylin-eosion stain, ×100)

The central large cyst is formed by bronchiolectasis. The wall of the surrounding small cysts (＊) includes terminal bronchiole elements (arrows). The surrounding alveolar septa are thickened by the infiltration of lymphoma cells (arrowheads).

D: Central large air space with thick wall and surrounding small cysts

(hematoxylin-eosion stain, scanning view)

The central large cyst (※) is formed by bronchiolectasis, and its thick wall corresponds to thick connective tissue associated with a diffuse infiltration of atypical lymphocytes. The surrounding multiple small cysts are associated with alveolar septal lymphoma cells' infiltration (arrowheads).

Figure 4

Schematic drawing of an "alloy wheel".

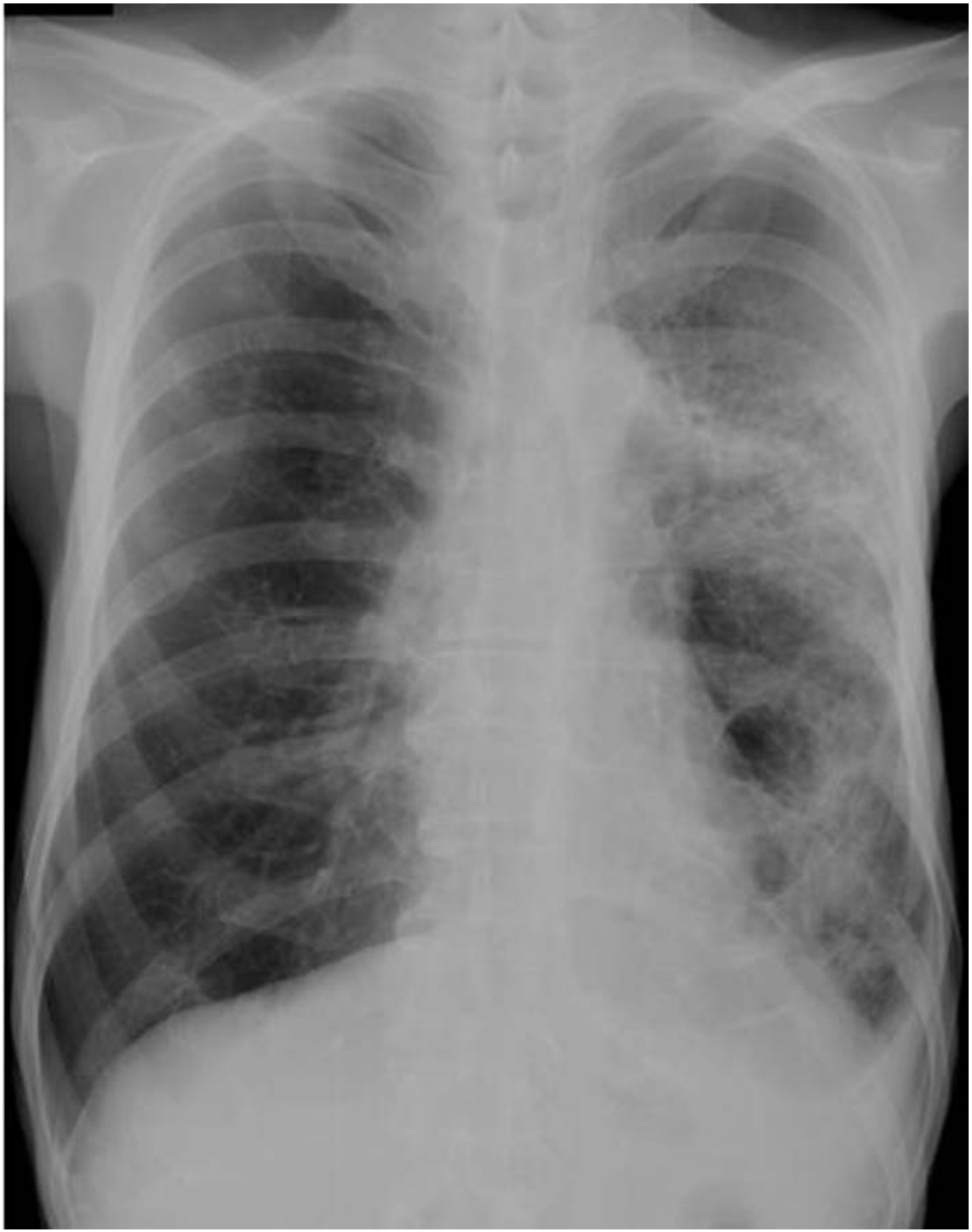

Figure 1

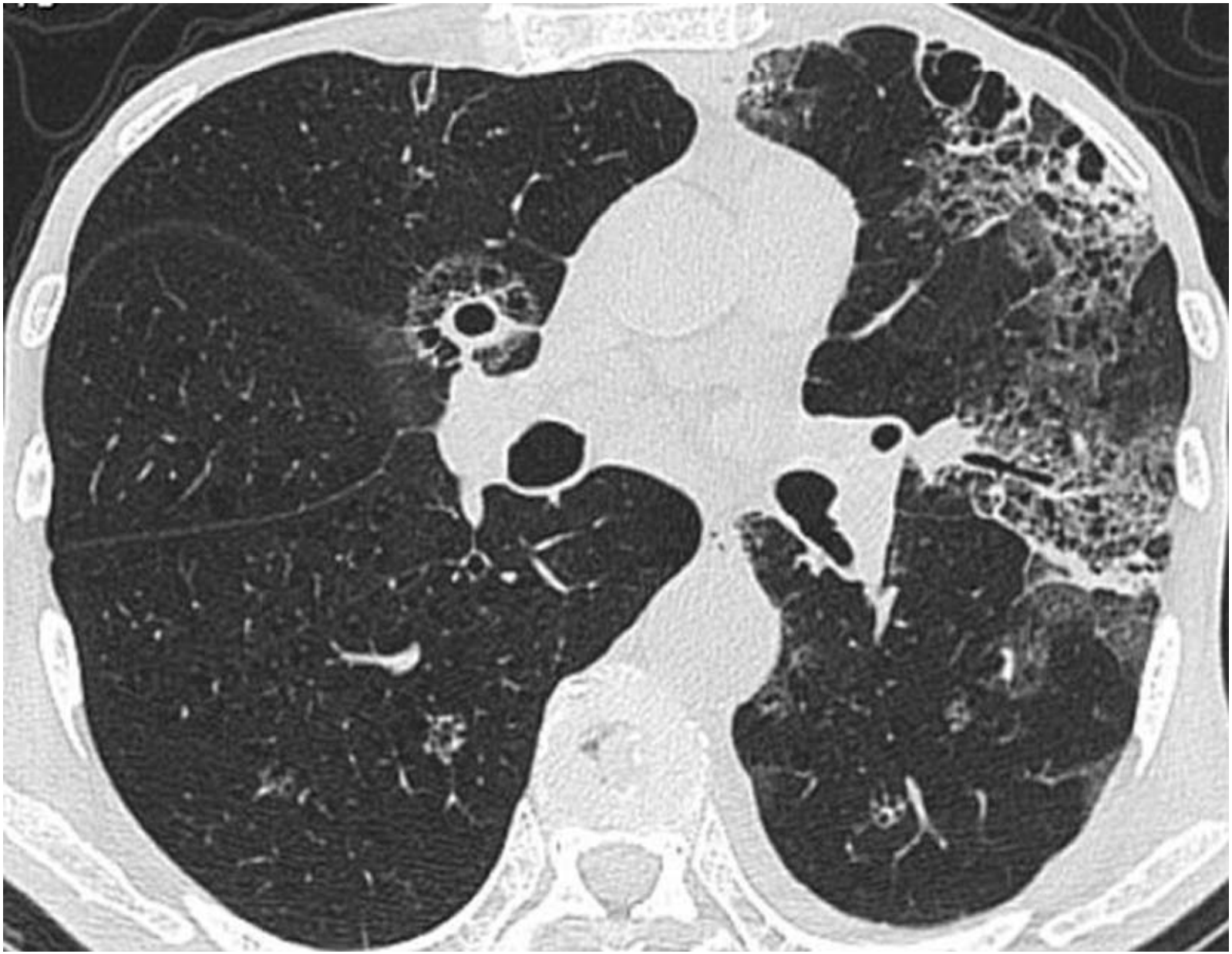

Figure 2A

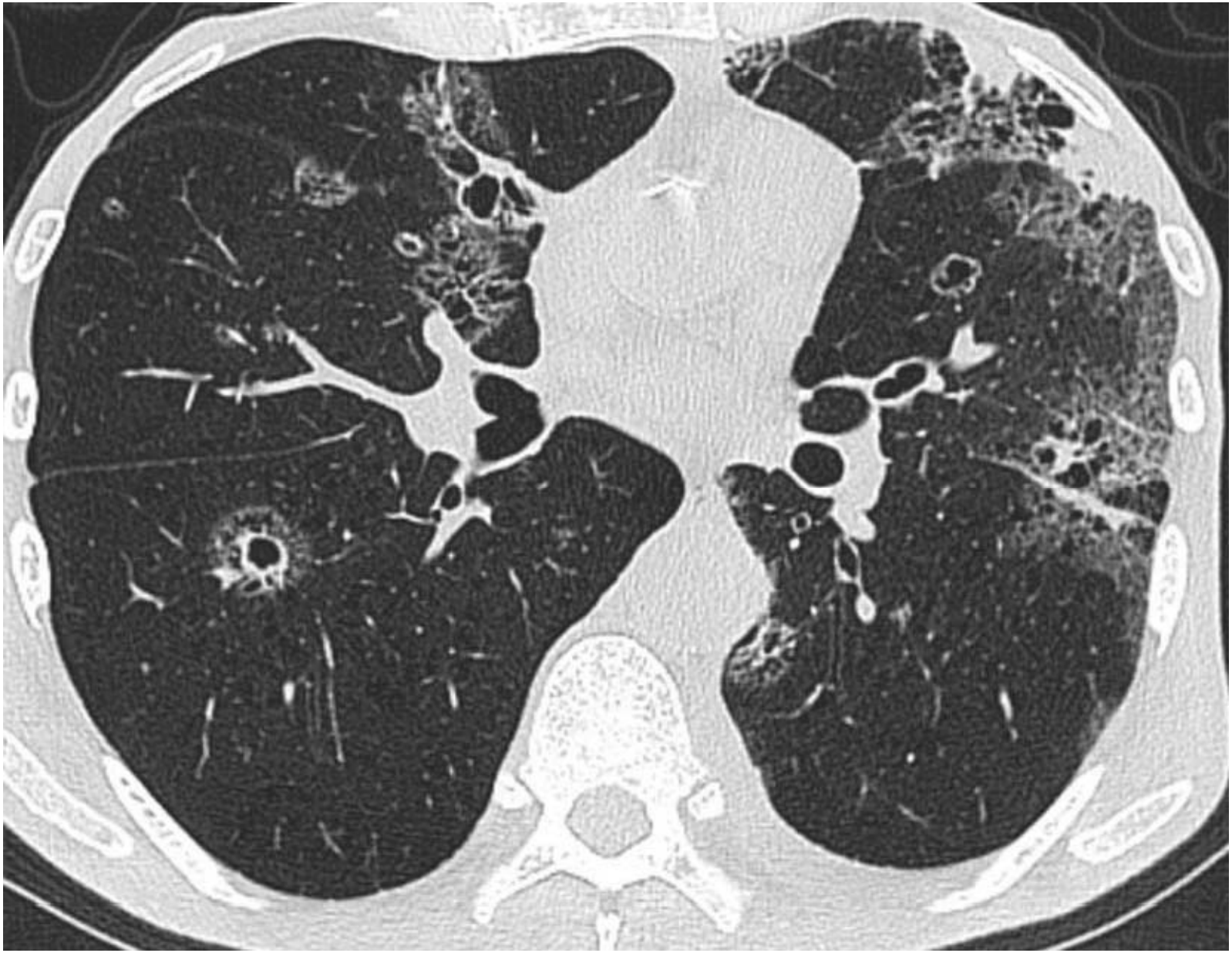

Figure 2B

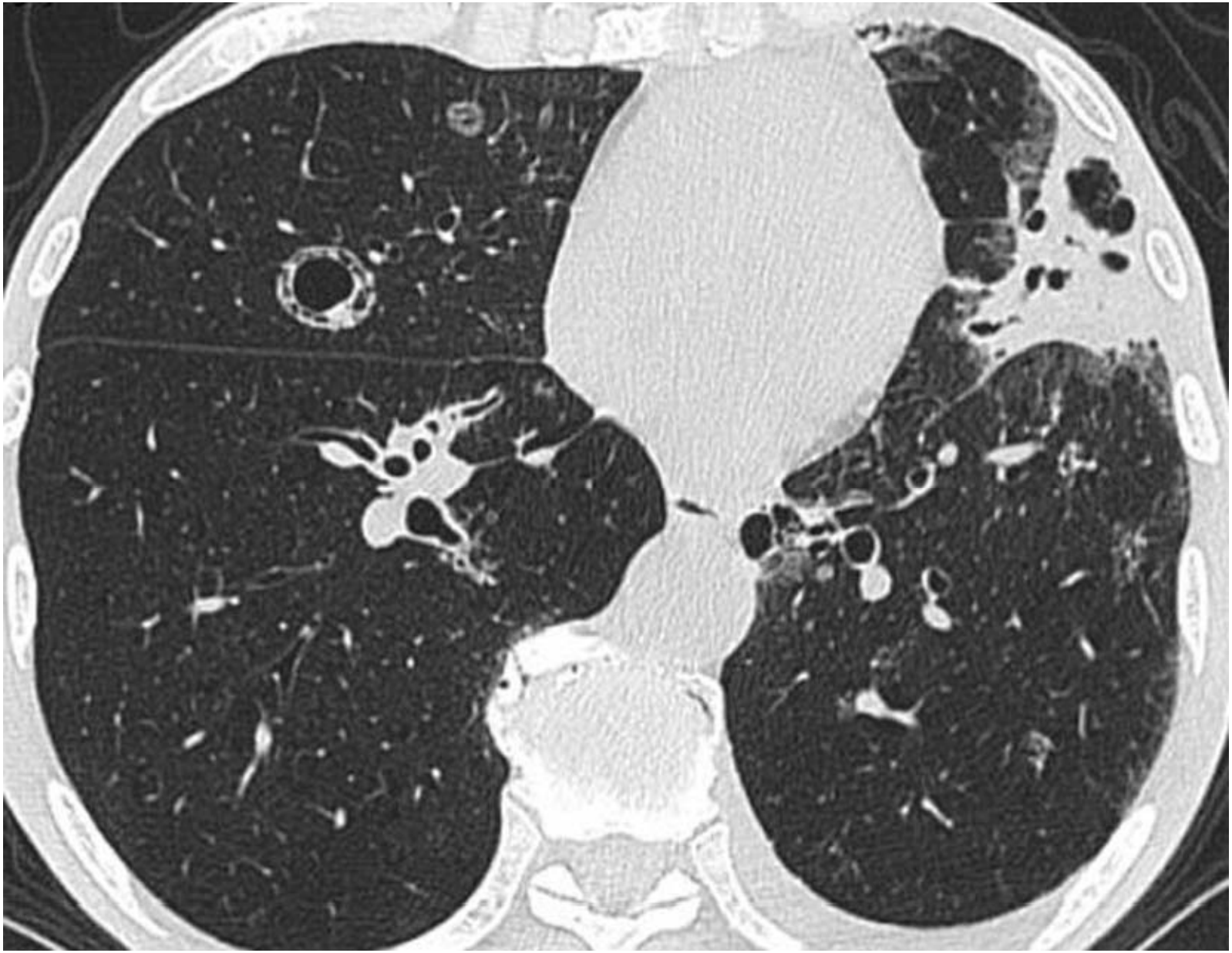

Figure 2C

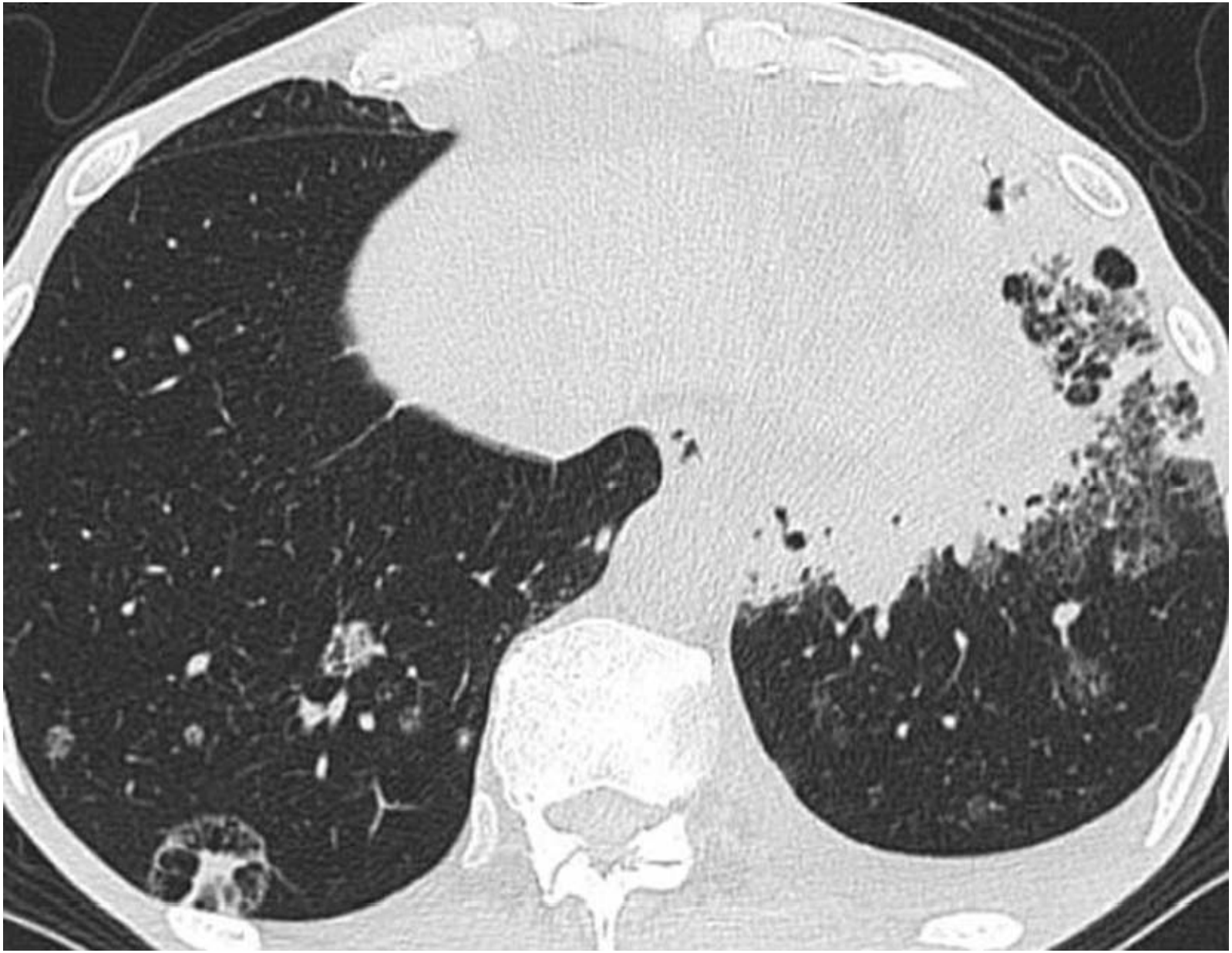

Figure 2D

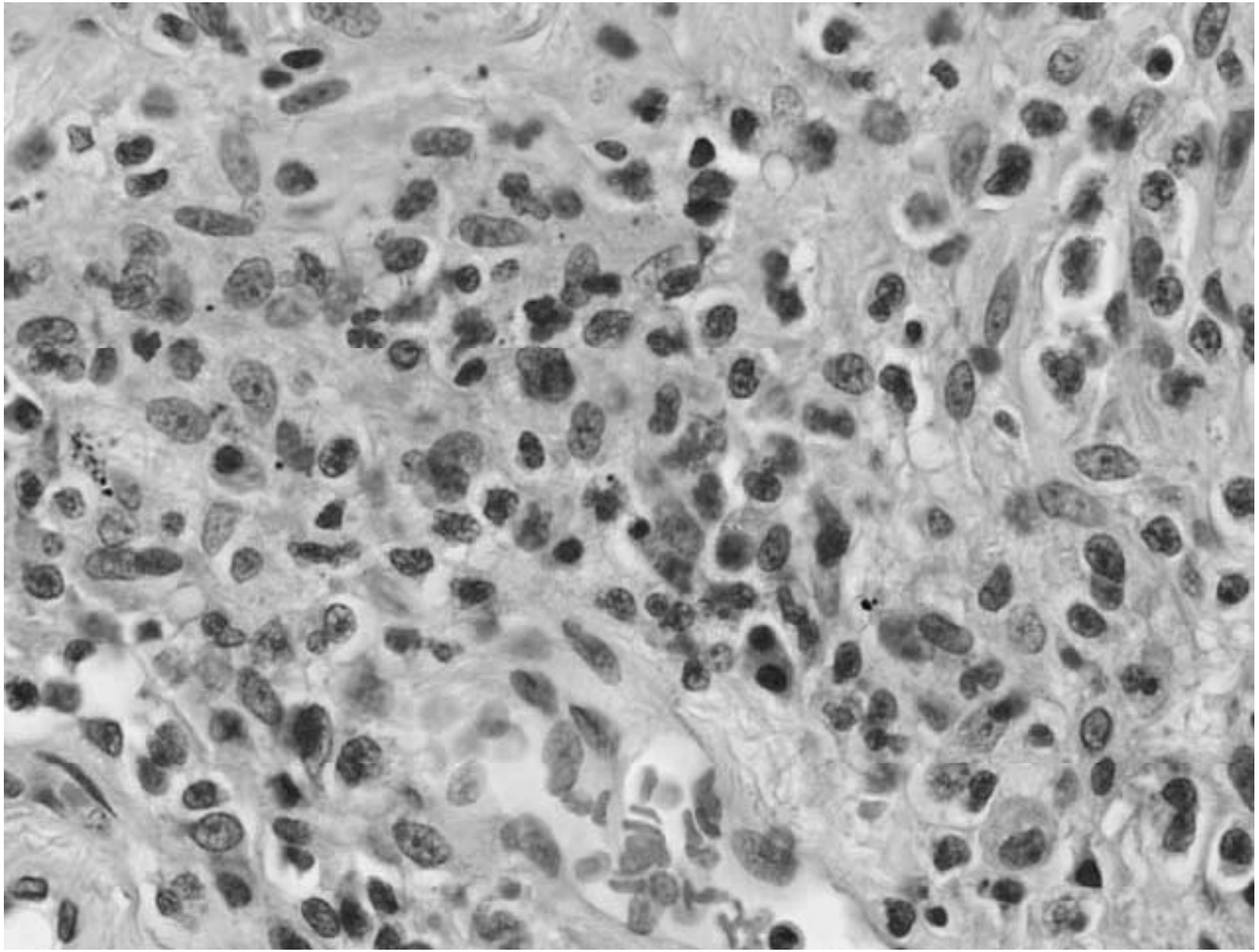

Figure 3A

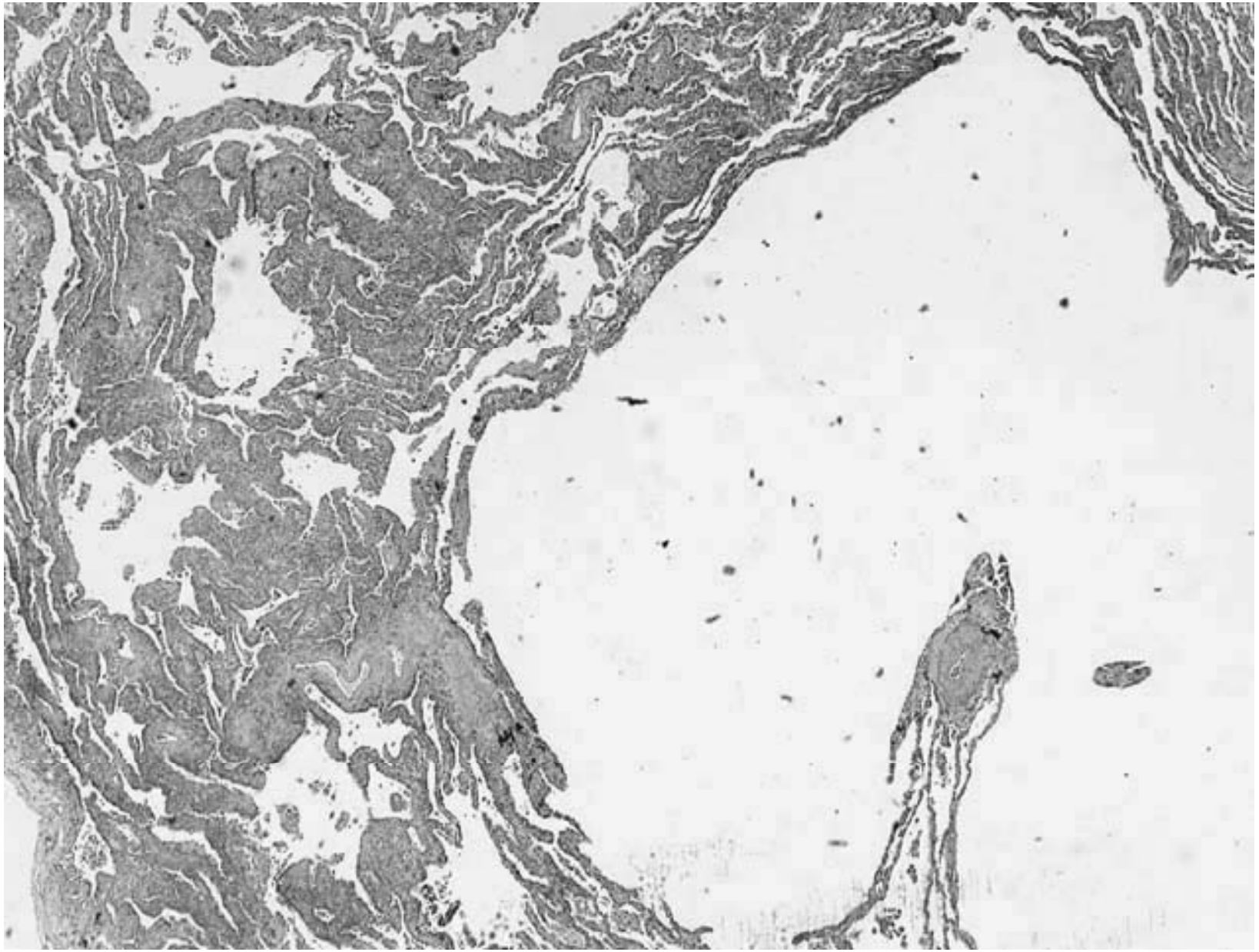

Figure 3B

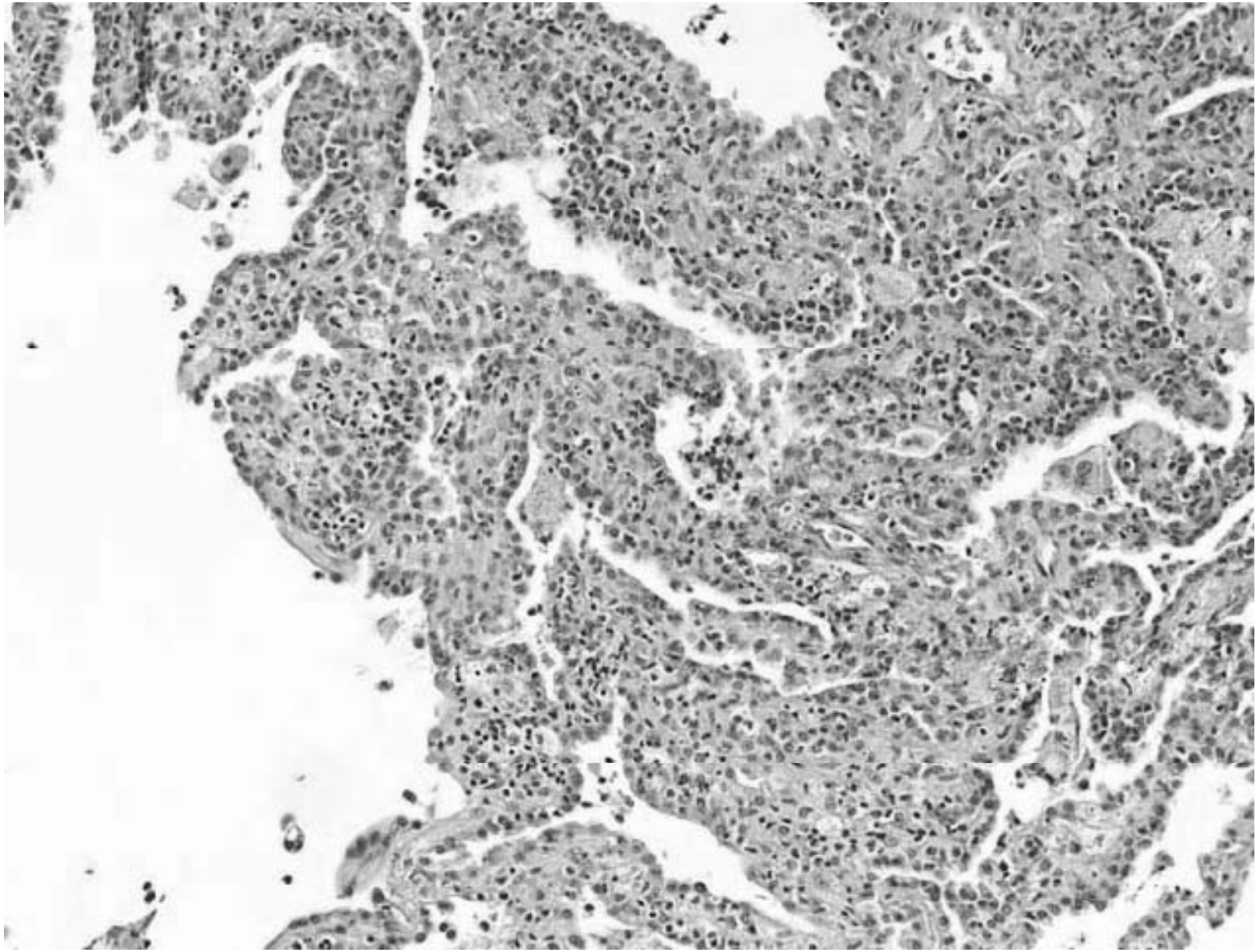

Figure 3C

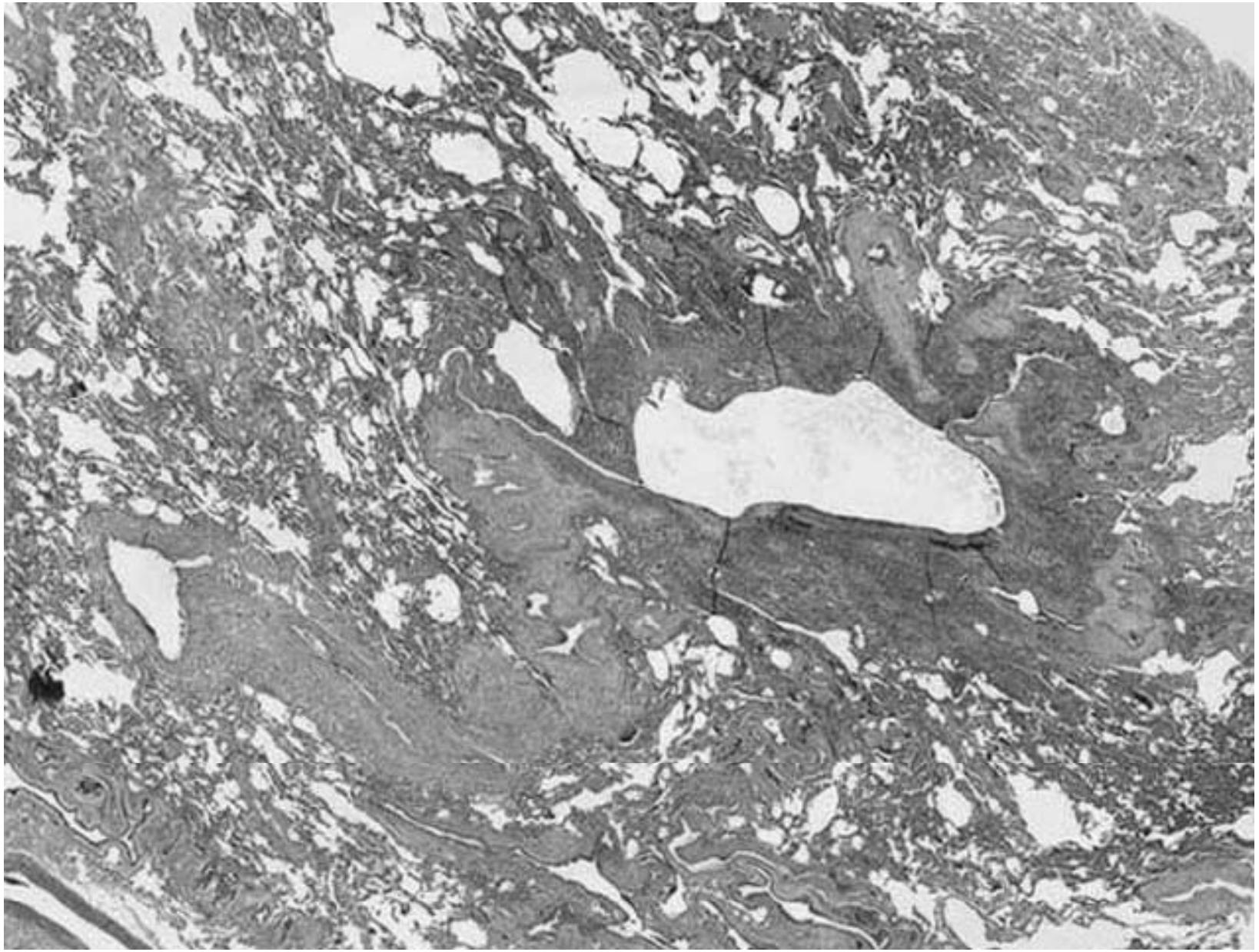

Figure 3D

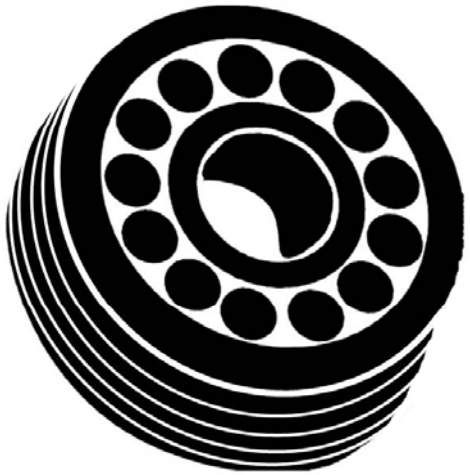

Figure 4