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Case report

Pulmonary intravascular large B-cell lymphoma accompanying synchronous primary pulmonary adenocarcinoma and benign interstitial lesions

Tsugumi Satoh,[1)] Eiichi Arai,[1)] Hidekazu Kayano,[2)] Hirozo Sakaguchi,[3)] Naoki Takahashi,[4)] Kunihiro Tsukasaki,[4)] Masanori Yasuda[1)]

Intravascular large B-cell lymphoma (IVLBCL) is a rare type of extranodal large B-cell lymphoma, and initial or predominant presentation in the lungs is uncommon. The synchronous occurrence of IVLBCL and malignant tumors is less frequent, and no such reports have described pulmonary presentations. We report a rare case of pulmonary IVLBCL accompanying lung cancer and interstitial lesions. A 73-year-old man with a history of pneumonia underwent a follow-up examination. Computed tomography revealed diffuse, bilateral ground-glass opacities (GGO) with a partial solid mass. Histologically, the mass consisted of adenocarcinoma. However, two other types of interstitial lesions were scattered throughout the resected lung: 1) peribronchovascular thickening with the aggregation of macrophages and anthracosis, and 2) alveolar septal thickening in the centrilobular area with atypical CD20-positive large cells in the capillaries. These two types of lesions were not mixed. Computed tomography and positron emission tomography demonstrated no other organ involvement. The patient was considered to have the synchronous occurrence of pulmonary IVLBCL and lung cancer (adenocarcinoma). After R-CHOP therapy, GGO on CT disappeared. Lung cancer often accompanies benign background lesions, and the combination of these lesions with lung cancer may make it difficult to detect the presence of pulmonary IVLBCL. However, the histological distribution pattern of IVLBCL may be a clue to the correct diagnosis.

Keywords: pulmonary intravascular large B-cell lymphoma, lung cancer, synchronous occurrence, distribution pattern, interstitial lesion

INTRODUCTION

Intravascular large B-cell lymphoma (IVLBCL) is a rare type of extranodal large B-cell lymphoma that selectively grows within vessels.[1] Pulmonary involvement of the disease is common; however, initial or predominant pulmonary presentation of IVLBCL is rarely reported.[2-4] The synchronous occurrence of IVLBCL with a malignant tumor in the same organ is markedly rare. Several previous reports revealed that IVLBCL can coexist with a malignant tumor,[5-9] but to the best of our knowledge, no reports to date have described lung involvement. We present a rare case of the synchronous occurrence of pulmonary IVLBCL and lung cancer (adenocarcinoma) in which IVLBCL accompanied synchronous adenocarcinoma and benign interstitial lesions. We also discuss the clinical and histopathological features together with a literature review.

CASE REPORT

Clinical history

A 73-year-old man who had developed pneumonia 1 year previously underwent a detailed pulmonary examination for an abnormal residual chest shadow. He was a taxi driver and had a history of smoking. Chest computed tomography (CT) revealed a solid lesion in the right lower lobe of the lung (approximately 2 cm in diameter) and multiple patchy ground-glass opacities (GGO) in the bilateral lungs (Fig. 1). As primary lung cancer was highly suspected, partial resection of the right lower lobe including the solid lesion was performed. The histological diagnosis of the solid lesion

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[1)]Department of Pathology, Saitama Medical University, International Medical Center, Saitama, Japan, [2)]Faculty of Health and Medical Care, School of Medical Technology, Saitama Medical University, Saitama, Japan, [3)]Department of Respiratory Surgery, Saitama Medical University, International Medical Center, Saitama, Japan, [4)]Department of Hematology, Saitama Medical University, International Medical Center, Saitama, Japan
Corresponding author: Tsugumi Satoh, MD, PhD, Department of Pathology, Saitama Medical University, International Medical Center, 1397-1, Yamane, Hidaka-shi, Saitama-ken, Japan. E-mail: tsugumig@gmail.com

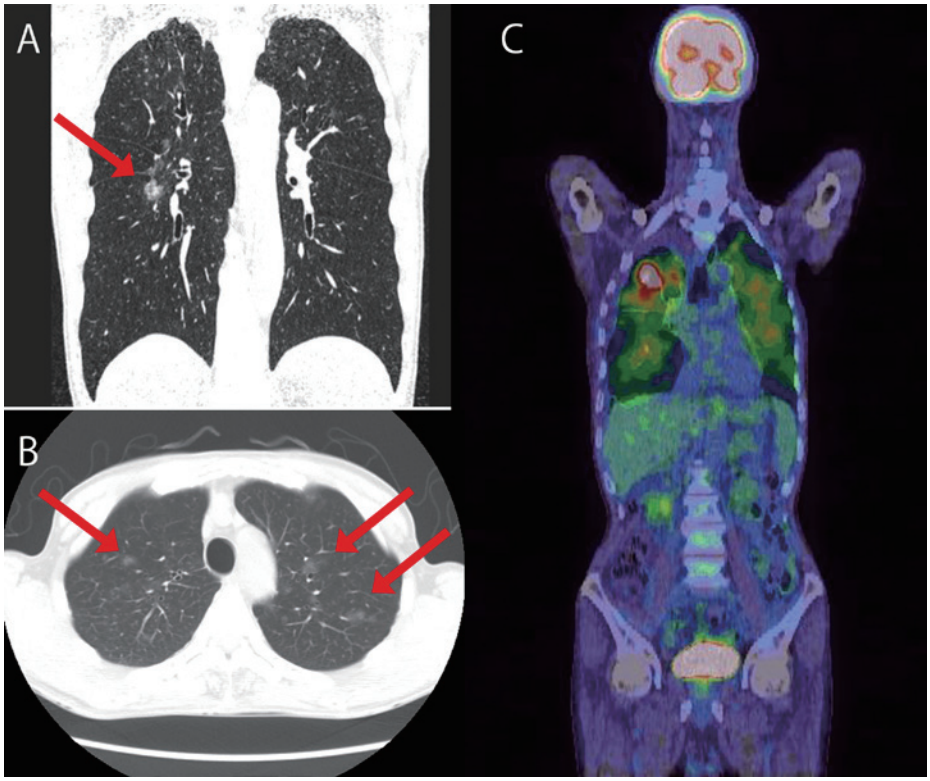

Fig. 1. Chest computed tomography (CT) imaging and positron emission tomography (PET)-CT scan. (***A***) Coronal plane. A solid lesion (arrow) was present in the right lower lobe (S6). (***B***) Transverse plane. Patchy ground-glass opacities were observed (arrow). (***C***) PET-CT scan performed after right partial lobectomy. Abnormal uptake of fluorodeoxyglucose was detected only in the bilateral lungs.

was invasive adenocarcinoma. The patient was discharged postoperatively but was readmitted a few days later because of severe dyspnea. No mass lesion was found in the lungs or other organs on CT. However, diffuse and patchy GGO remained and had worsened. Infection was suspected, but the lesion also exhibited the abnormal uptake of fluorodeoxyglucose (FDG) on positron emission tomography (PET). In addition, the serum levels of soluble IL-2 receptor and lactase dehydrogenase were high (2,098 U/mL and 645 U/L, respectively). Pulmonary malignant lymphoma was suggested, and the previously resected specimen was pathologically re-evaluated.

Pathological findings

In addition to the solid lesion, which consisted of invasive adenocarcinoma (papillary adenocarcinoma with a lepidic growth pattern), diffuse scattered pulmonary interstitial lesions were observed. In some areas around the solid lesion, adenocarcinoma and interstitial lesions were close, but they did not mix. Detailed observation revealed that the interstitial lesions were histologically divided into two types, although they looked similar at first: 1) lesions located along bronchovascular bundles, characterized by the aggregation of many macrophages and non-atypical small lymphoid cells with anthracosis, and 2) thickened alveolar septa in centrilobular areas, where small aggregates of inflammatory cells were found, but macrophage aggregation and anthracosis were not notable. Many atypical large lymphoid cells were identified in the capillaries of the alveolar septa of the second lesion. These atypical cells were also diffusely detected in the non-thickened alveolar septa (Fig. 2). Immunohistochemically, these atypical cells were positive for CD20 and CD5 (Fig. 3). They were also positive for CD79a, BCL2, and MUM1, and negative for CD3, CD10, and EBER-ISH (data not shown). Of note, these two types of interstitial lesions were not mixed, and no CD20-positive large atypical cells were found in the peribronchovascular lesions. No parenchymal invasion was histologically noted throughout the entire resected specimen. Bone marrow examination performed later for staging revealed CD20-positive large atypical lymphoid cells in small vessels; however, the area involved was limited, and only a few atypical cells were present. Thus, the lung was thought to be the predominant site of the IVLBCL.

Clinical course

Therapy for IVLBCL was prioritized. The patient underwent six courses of rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone (R-CHOP) therapy. His dyspnea, GGO on CT, and abnormal lung uptake of FDG on PET subsequently dissipated.

DISCUSSION

IVLBCL can involve any organ. Lung involvement is relatively frequent, being present in approximately 60% of

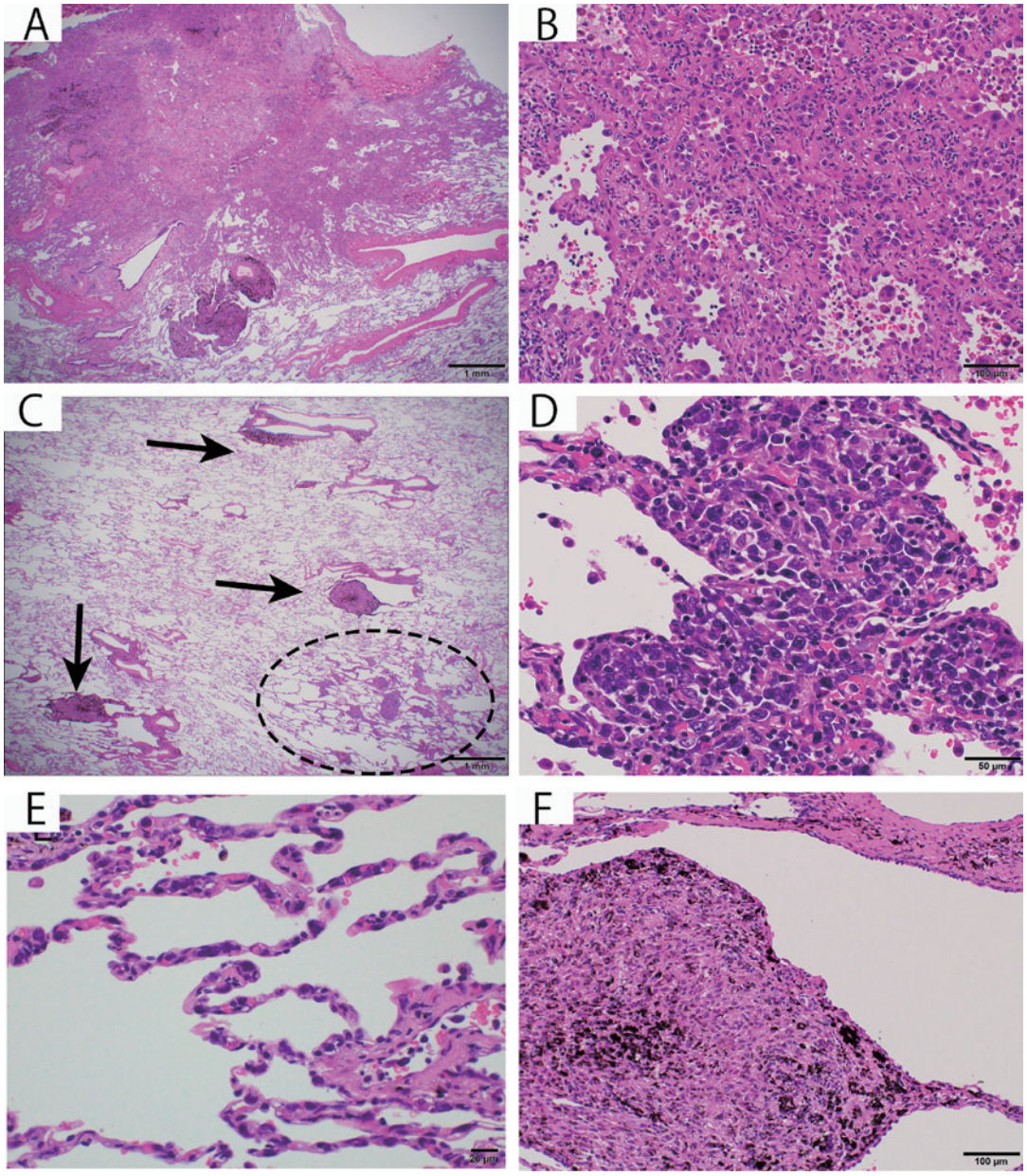

Fig. 2. Histological findings of the resected right lower lobe. (***A***) Lesion of adenocarcinoma. (***B***) Higher magnification of the solid lesion. The invasive adenocarcinoma was mainly composed of a papillary component. (***C***) Two types of diffusely scattered lesions were present in the background: 1) thickening of the peribronchovascular area with anthracosis (arrows) and 2) alveolar septal thickening in the centrilobular area (circle). (***D***) Higher magnification of the alveolar septa in the thickened centrilobular area revealed numerous large atypical lymphoid cells in the capillaries. Small inflammatory cells were also found in the background. (***E***) Atypical lymphoid cells were diffusely detected in non-thickened alveolar septa around thickened septa. (***F***) Higher magnification of a perivascular lesion. Many macrophages were observed, but large atypical lymphoid cells were not detected. Marked anthracosis was present.

autopsy cases.[2] However, initial or predominant presentation involving the lung is rare.[2-4,10-12] In our case, the lung was the only organ with clinical involvement. No abnormal uptake of FDG in other sites was observed on PET, although minimal bone marrow involvement was present. Therefore, we considered the patient to have pulmonary IVLBCL.

IVLBCL can coexist with other malignant tumors. Several cases have been reported, including those involving breast cancer and kidney cancer.[5-9] However, our literature search revealed no previous case in which IVLBCL and another malignant lung tumor were detected at the same time.

Lung cancer often accompanies benign background lung lesions such as inflammation or changes due to smoking. In the present case, in addition to the adenocarcinoma, interstitial lesions of perivascular area thickening with anthracosis were diffusely scattered throughout the lung tissue, and they were similar in appearance to IVLBCL lesions with focal inflammatory changes, making another interstitial lesion of IVLBCL difficult to find.

In the lung, lymphatic channels are located along

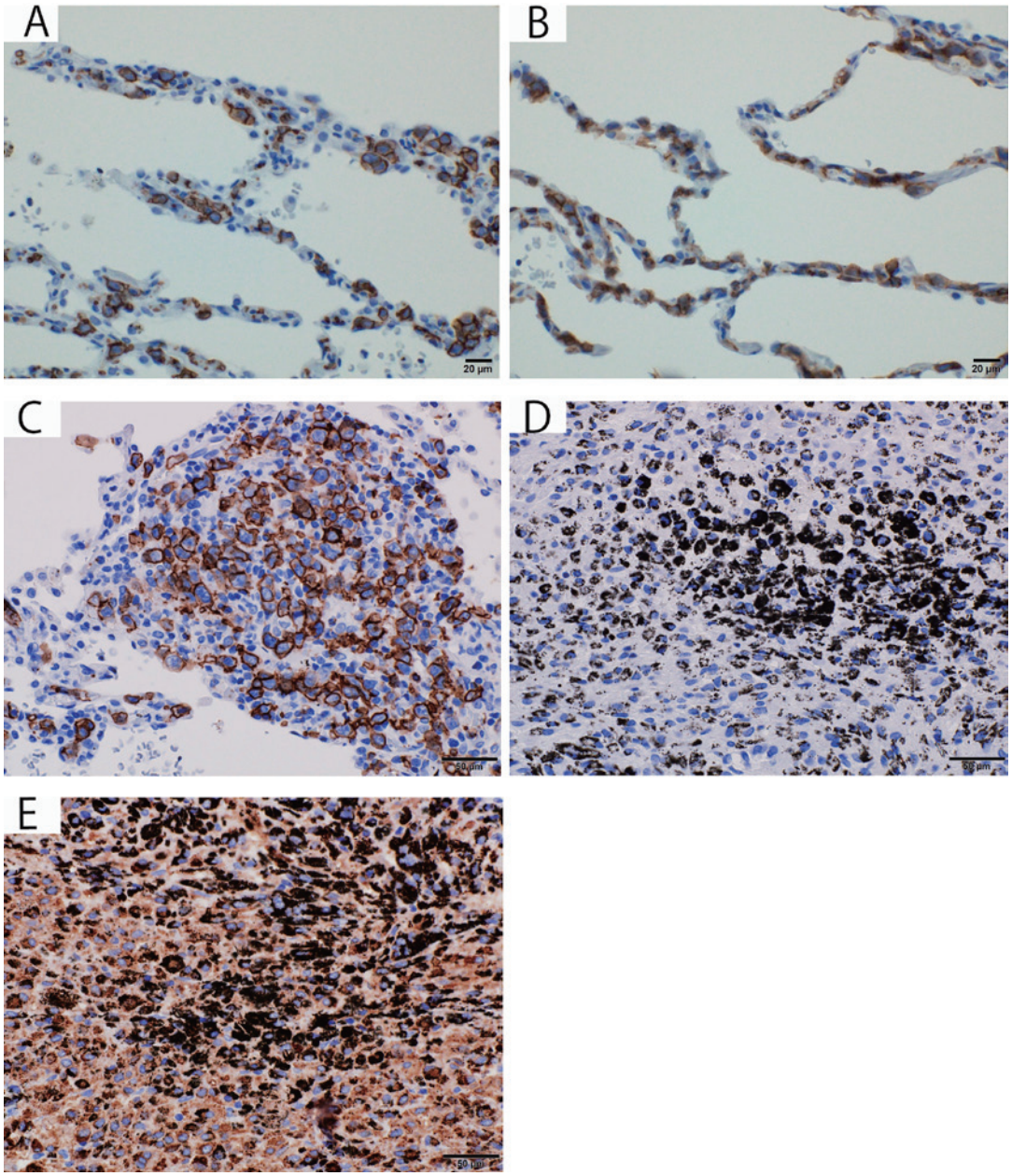

Fig. 3. Immunohistological analysis. (***A***, ***C***, ***D***) CD20. (***B***) CD5. (***E***) CD68. In the alveolar septa of the centrilobular area, large atypical cells were positive for CD20. Non-thickened alveolar septa (***A***) and thickened septa (***C***). These atypical cells were also positive for CD5 (***B***). On the other hand, in the peribronchovascular area, no CD20-positive cells were detected (***D***), but numerous CD68-positive macrophages were found (***E***).

bronchovascular structures, and pulmonary veins in the septa and pleura. The lymphatics do not extend into alveolar walls.[13] IVLBCL selectively grows within vessels and spreads through them;[1] therefore, the pattern of tumor expansion in the lungs may differ from that of other lesions that expand through the lymphatics or respiratory tract. Previous reports revealed that pulmonary IVLBCL cells most often affect capillaries in the alveolar septa and may involve small pulmonary arterioles or venules;[3,10-12,14-16] the lymphatics and aorta have been involved in a few cases.[12,17] However, unlike the size and type of the vessels, the distribution pattern of pulmonary IVLBCL in the lungs has not been fully histologically described to date.

A radiodiagnostic report on the distribution pattern of IVLBCL stated that the most common abnormal finding of pulmonary IVLBCL is bilateral GGO,[18] although changes in the parenchyma or lymphatic areas may also be observed on CT. However, parenchymal or lymphatic alterations can result from secondary changes due to the progression of IVLBCL based on the CT and histological findings.[18] In the present case, CT demonstrated a diffuse GGO pattern, as previously reported. Histologically, IVLBCL cells were detected in alveolar septa of the centrilobular region, but not in almost all interlobular septa or the peribronchovascular area. The presence of anthracosis highlighted the difference in the distribution pattern of these two types of lesions. In

addition to these histological findings, as GGO disappeared after R-CHOP therapy, the GGO lesion detected on CT may represent IVLBCL.

In conclusion, the present case demonstrated that pulmonary IVLBCL can coexist with lung cancer, but that the presence of IVLBCL can be concealed by comorbid lesions. Although the histological distribution pattern may be a clue to the correct diagnosis, it can become ambiguous and nonspecific as the IVLBCL lesion expands.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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