Case report

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

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Intravascular large B-cell lymphoma (IVL BCL) is a rare type of extranodal large B-cell lymphoma, and initial or predominant presentation in the lungs is uncommon. The synchronous occurrence of IVL BCL and malignant tumors is less frequent, and no such reports have described pulmonary presentations. We report a rare case of pulmonary IVL BCL 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 IVL BCL 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 IVL BCL. However, the histological distribution pattern of IVL BCL 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 (IVL BCL) 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 IVL BCL is rarely reported.2-4) The synchronous occurrence of IVL BCL with a malignant tumor in the same organ is markedly rare. Several previous reports revealed that IVL BCL can coexist with a malignant tumor,5,6) 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 IVL BCL and lung cancer (adenocarcinoma) in which IVL BCL 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

Received: March 23, 2019. Revised: June 13, 2019. Accepted: June 24, 2019. J-STAGE Advance Published: August 8, 2019
DOI:10.3960/jslrt.19012

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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 lepidoic 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
autopsy cases. However, initial or predominant presentation involving the lung is rare. 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. 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 the bronchi and pulmonary arteries. The potential sites for IVLBCL are the perivascular area and the interstitium of the lung. The histological findings of the resected right lower lobe are shown in Fig. 2. (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.
bronchovascular structures, and pulmonary veins in the septa and pleura. The lymphatics do not extend into alveolar walls.\textsuperscript{13} IVLBCL selectively grows within vessels and spreads through them;\textsuperscript{4} 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,\textsuperscript{3,10-12,14-16} the lymphatics and aorta have been involved in a few cases.\textsuperscript{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,\textsuperscript{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.\textsuperscript{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 non-specific as the IVLBCL lesion expands.

ACKNOWLEDGMENT

We thank Angela Morben, DVM, ELS, from Edanz Group (www.edanzediting.com/ac), for editing a draft of this manuscript.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES