Ground-glass opacities and a solitary nodule on chest in intravascular large B-cell lymphoma

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Keywords
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Abstract
A 74-year-old woman presented with dyspnea on exertion and nocturnal cough. Chest computed tomography (CT) revealed scattered bilateral ground-glass opacities without a zonal dominance. Bronchoalveolar lavage elicited increased lymphocytes, but transbronchial lung biopsies were not performed because of hypoxemia during the examination. She received steroid therapy because of her subsequent worsening respiratory condition, but her condition continued to deteriorate. The ground-glass opacities partially consolidated with the appearance of new ground-glass opacities and a nodular shadow. Hepatosplenomegaly was observed on CT while soluble interleukin-2 receptor was elevated. A biopsy of a Campbell de Morgan spot of the trunk yielded a diagnosis of intravascular large B-cell lymphoma. There was marked clearing of the pulmonary infiltrates and significant symptomatic improvement in response to systemic chemotherapy.

Introduction
Intravascular large B-cell lymphoma (IVLBCL) is a rare type of malignant lymphoma characterized by proliferation of neoplastic cells within the arterioles, capillaries, and venules [1]. IVLBCL cases with chest radiological findings are rare, and findings are nonspecific. Therefore, it is often difficult to diagnose these cases as IVLBCL in the lung. Here we present a case of IVLBCL with heterogeneous ground-glass opacities on chest computed tomography (CT), diagnosed by biopsy of the Campbell de Morgan spot.

Case Report
A 74-year-old woman, who had been complaining of dyspnea on exertion and nocturnal cough, presented to a community hospital. Bilateral heterogeneous ground-glass shadows of the entire lung fields were revealed by chest CT, and she was referred to our hospital for further examinations. The bronchoalveolar lavage fluid (BALF) elicited increased lymphocytes, while atypical cells, mycobacteria, or bacteria were not detected in the BALF. Transbronchial lung biopsy was not performed due to severe hypoxemia during the examination. She later received steroid therapy at another hospital due to deteriorating respiratory status after the examination. However, she was unresponsive to this treatment and progressive CT changes necessitated readmission to our hospital.

Blood examination on admission showed severe leukocytopenia, thrombocytopenia, renal dysfunction, and elevated lactate dehydrogenase (861 IU/L). The level of soluble interleukin-2 receptor was increased to 3220 U/mL (normal range 145–519 U/mL). Chest CT showed predominantly subpleural nonsegmental ground-glass shadowing, which had progressed, subpleural consolidations in both upper lobes and a subpleural nodule in the right lower lobe (Fig. 1). A differential diagnosis included pulmonary hemorrhage, hemosiderosis, and atypical pneumonia from these CT findings.
From the laboratory data and the presence of splenomegaly and hepatomegaly, intravascular lymphoma (IVL) was suspected, and biopsy of a Campbell de Morgan spot of the trunk was performed. Histologically, large atypical cells with hyperchromatic large nuclei with prominent nucleoli were packed in some vascular lumens of the Campbell de Morgan spot in the papillary dermis (Fig. 2). Intraepithelial or stromal infiltration was not obvious. As these pathological findings suggested IVL, immune histochemistry stains were performed to evaluate the atypical cell lineage. These were positive for CD5, CD20, Bcl-6, and MUM1, but negative for CD3, CD30, CD10, and cycline D1 (Fig. 2). Ki-67 labeling index was 70%, and EBER-ISH was negative. The final diagnosis was IVLBCL. She was treated with a pirarubicin/cyclophosphamide/vincristine/prednisolone regimen that resulted in improvement in her respiratory condition. After 2 weeks, most of the CT infiltrates had disappeared.

**Discussion**

The WHO classification of hematopoietic tumors defines IVLBCL as an extranodal diffuse LBCL characterized by the presence of neoplastic lymphocytes in the lumens of small vessels, particularly capillaries [1]. The clinical presentation of the disease in the Japanese patient population is distinct from that found in the West, where the majority of clinical presentations are characterized by symptoms related to skin or neurological involvement. In Japan, an Asian variant of IVL is characterized by bone marrow invasion, hemophagocytic syndrome, hepatosplenomegaly, and respiratory disturbances that account for more than 50% of all cases [2].

Chest CT findings in IVLBCL are nonspecific. In this case, ground-glass opacities were observed on presentation. These progressed partially to consolidation and were accompanied by new ground-glass opacities and nodular
All these shadows were thought to be derived from IVLBCL, because most of these shadows diminished after treatment.

In the present case, ground-glass opacities were heterogeneous and partially consolidated. It is possible that atypical cells may invade alveolar spaces, thus contributing to the consolidation in the CT scan. Although nodular shadows observed in IVLBCCL are rare, they were reported by Okada et al. [3]. The transbroncheal lung biopsy showed thrombi and recanalization in small vessels and pathogenic cells were filled in the small vessels. The nodular shadow in this case was well defined and may have derived from thrombi due to invasion of vessels by atypical cells.

A number of similar cases with aggressive clinical symptoms remain undiagnosed ante mortem. In the current case, a lung biopsy could not be performed because of thrombocytopenia and hypoxemia. This case was not diagnosed by random skin biopsy, which has been shown to be useful for diagnosis of IVLBCL [4], but through biopsy from a Campbell de Morgan spot on the trunk. Adachi et al. have suggested that biopsy from Campbell de Morgan spot is a useful method for diagnosing IVLBCL [5]. The present case further suggests that biopsy from Campbell de Morgan spot could be more useful for the accuracy of diagnosis for this type of lymphoma, rather than random skin biopsy, and that the former method is recommended.

In conclusion, IVLBCL of the lung could be considered in the differential diagnosis of cases with pulmonary infiltrates, systemic symptoms, and raised lactate dehydrogenase and interleukin 2.

Figure 2. (A) Campbell de Morgan spot biopsy revealed a low elevated skin lesion composed of a collection of thin-walled small or medium-sized vessels. Atypical cells are packed in some abnormal vessels (arrow) (hematoxylin and eosin staining, ×40). (B) Atypical cells having hyperchromatic large nuclei with prominent nucleoli are limited in vessels and do not infiltrate into perivascular stroma (hematoxylin and eosin staining, × 400). (C) Immunohistochemically, atypical cells in Campbell de Morgan spot revealed positivity for CD20 (×400).
Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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