

An autopsy of intravascular large B-cell lymphoma with hemophagocytic syndrome

Hisanori Fukunaga^{1,2}, Kazumasa Kawashima³, Hiromi Kumakawa¹, Yuko Hashimoto⁴ and Yuta Takahashi¹

¹Soma General Hospital, Fukushima 976-0011, Japan

²Department of Nuclear Medicine and Radiology, Institute of Development, Aging and Cancer, Tohoku University, Sendai 980-8575, Japan

³Department of Gastroenterology and Rheumatology, Fukushima Medical University School of Medicine, Fukushima 960-1295, Japan

⁴Department of Diagnostic Pathology, Fukushima Medical University School of Medicine, Fukushima 960-1295, Japan

Corresponding author: Yuta Takahashi. Email: yuta5034@yahoo.co.jp

Lesson

Intravascular large B-cell lymphoma presents with highly variable symptoms caused by the occlusion of small vessels by neoplastic cells in a variety of organs.

Keywords

intravascular large B cell lymphoma, hemophagocytic syndrome, autopsy, fever of unknown origin, cough

Case report

A 51-year-old Japanese man visited a general practitioner with chief complaints of dry cough and fever. The clinical diagnosis at that time was common cold; however, his condition did not improve after taking an oral cold medicine. A blood test and abdominal ultrasound revealed liver dysfunction, thrombocytopenia and hepatosplenomegaly. The patient was referred to Soma General Hospital for treatment. Physical examination on admission revealed diminished breathing sounds in the right thorax. Oxygen saturation was 95% (3 L of oxygen), and body temperature on admission was 38.2°C. Blood values on admission indicated thrombocytopenia ($1.1 \times 10^4/\mu\text{L}$), and abnormal WBCs were not detected in repeated peripheral smears. Other laboratory data results are as follows: aspartate aminotransferase, 142 IU/L; alanine aminotransferase, 133 IU/L; lactate dehydrogenase, 1898 IU/L; alkaline phosphatase, 3594 U/L; γ -glutamyl transpeptidase, 710 IU/L; C-reactive protein, 9.4 mg/dL; ferritin, 2962 ng/mL; and soluble IL-2 receptor, 5390 U/mL. The test for Epstein-Barr virus antibody to detect nuclear antigen IgG was positive. Chest and abdominal CT showed pleural effusion and hepatosplenomegaly but no swelling of the lymph nodes. Although no similar diseases were detected among his family members after clinical

examinations, physicians strongly suspected malignant lymphoma and hemophagocytic syndrome from the patient's clinical characteristics. Soon after hospitalization, the patient's general condition deteriorated. A bone marrow biopsy was performed for advanced diagnostic purposes; however, the pathological diagnosis was not in time for the treatment. Despite treatment for hemophagocytic syndrome, the patient died 24 days after the onset of the symptoms. The patient's family requested an immediate autopsy of all organs to obtain a definitive diagnosis.

The autopsy identified severe pleural effusion and lymphatic obstructions on the pulmonary pleura which was responsible for dry cough and was one of the first symptoms (Figure 1). Hepatosplenomegaly, renal congestion, myocardial necrosis and gastric mucosa necrosis were also identified. Immunohistochemical examination showed that these findings were caused by the occlusion of small vessels by neoplastic cells (Figure 2). Immunohistochemical analysis using antibodies against common leukocyte antigen and the B-cell marker CD-20 revealed intense staining of neoplastic cells. The summary of the immunohistochemical findings is as follows: CD-3 (–), CD-5 (+), CD-10 (–), CD-31 (+), Bcl-6 (+), MUM-1 (+) and Bcl-2 (+). A previous study from Japan detected the expression of CD5, CD10, Bcl-6, MUM1 and Bcl-2 in 38%, 13%, 26%, 95% and 91% of intravascular large B-cell lymphoma (IVLBCL) tumor cells, respectively.¹ Therefore, the final pathological diagnosis of this case was Asian-variant IVLBCL.

Discussion

IVLBCL, which is an exceptionally rare and fatal disease with an aggressive course and short survival, is a

Figure 1. Autopsy of the lung. Pleural effusion and lymphatic obstructions on pulmonary pleura were severe but were not accompanied by diffuse alveolar hemorrhage and pulmonary edema. The weights of right and left lungs were 600 and 724 g, respectively, and the volumes of pleural effusion from the right and left lungs were 500 and 350 ml, respectively. (a) Right and (b) left lungs.

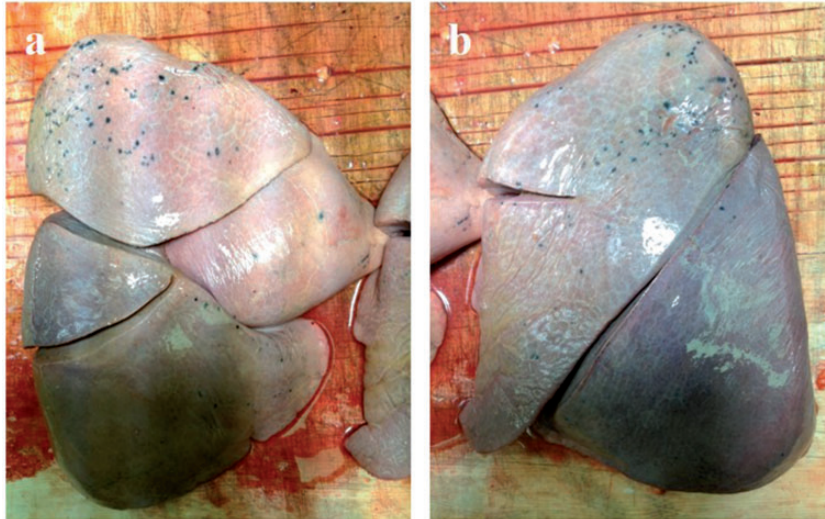
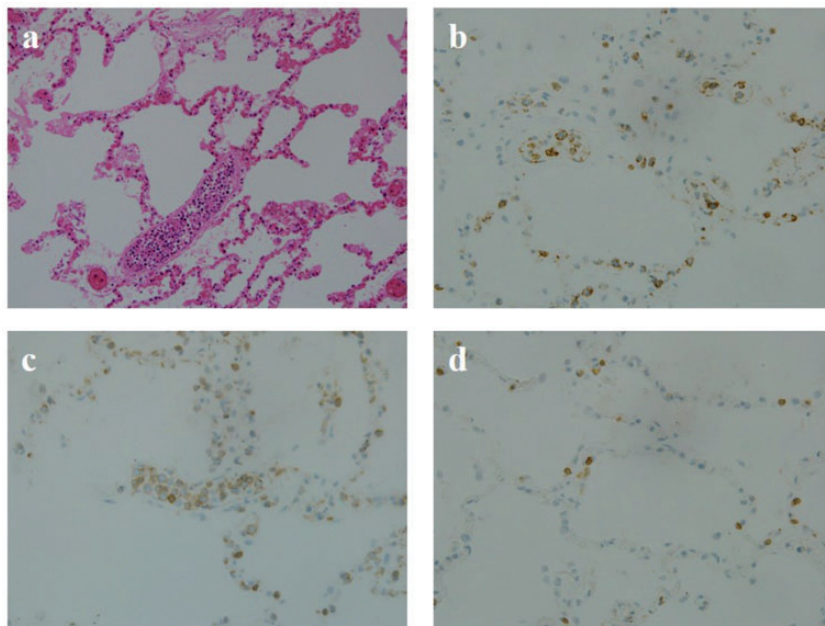


Figure 2. Immunohistochemical analysis of the neoplastic cells within capillary vessels in the lung: (a) HE, (b) CD-20, (c) CD-5, and (d) CD-3.



non-Hodgkin's lymphoma characterized by the selective growth of neoplastic cells within blood vessel lumina.¹⁻³ IVLBCL presents with highly variable symptoms caused by the occlusion of small

vessels by neoplastic cells in a variety of organs, and it displays some differences in clinical presentation among patients residing in diverse geographical areas, particularly between patients diagnosed in

Western and Eastern countries. For example, patients diagnosed in Western countries display a relatively high frequency of neurological and dermatological signs,⁴ whereas patients from Asian countries, mainly Japan, preferentially show hemophagocytic syndrome, bone marrow involvement, fever, hepatosplenomegaly and thrombocytopenia.⁵ Despite more than 50 years of research, IVLBCL remains an aggressive and systemic disease with a frequently fatal course, and little is known about the precise mechanisms responsible for this distinctive behavior as well as the most effective treatment options. It is imperative that continued research be promoted to better understand this unique malignancy.

Although the first symptoms of a cold are often cough and fever, patients may indicate an inapparent serious disease. Patients with hemophagocytic syndrome should be suspected with IVLBCL. IVLBCL patients can present with wide clinical variability; therefore, suspicion should be raised when patients' symptoms are cough, fever, headache, skin abnormalities, hepatosplenomegaly or hemophagocytic syndrome. If a timely diagnosis is made and an anthracycline-based chemotherapy is instituted, then many patients achieve 60% complete response and >30% survive for approximately 3 years.^{2,6} We recommend that clinicians should always keep in mind to take a timely and accurate diagnostic approach for IVLBCL.

Declarations

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