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Successfully Treated Massive Pulmonary Thromboembolism and Thrombus in the Right Atrium Due to Diffuse Malignant Lymphoma: A Case Report

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Abstract

A 40-year-old man presented with massive pulmonary embolism related to diffuse large B cell lymphoma. His hemodynamic state worsened rapidly to shock after sudden onset of dyspnea. Echocardiography and thoracic computed tomography indicated pulmonary thromboembolism due to deep venous thromboembolism, associated with a mass in the anterior mediastinum and a 5×8cm mass in the left pelvis compressing the left femoral vein. He underwent emergent surgery to remove a huge thrombus from the right atrium through the bilateral pulmonary arteries. Soon after this surgery, his hemodynamic state recovered and excision of the left cervical lymph node revealed diffuse large B cell lymphoma. Venous compression by the lymphoma mass had caused hemostasis and thrombus formation in the present case.

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Key Words
■**Neoplasmas (lymphoma)** ■**Thromboembolism (pulmonary)** ■**Thrombus**

INTRODUCTION

Cancer is a well-recognized risk factor for venous thromboembolism which may lead to a life-threatening pulmonary thromboembolism. We treated a patient with acute massive pulmonary thromboembolism related to malignant lymphoma. A huge thrombus from the superior vena cava had passed through the pulmonary arteries, which devastated his hemodynamic state. We evaluated his state quickly and successfully performed surgical removal of the thrombi, followed by appropriate chemotherapy for the malignant lymphoma. After the surgery, a huge thrombus appeared in the left femoral vein to the inferior vena cava because of venous obstruction compressed by the lymphoma mass although we had continued adequate anticoagulation therapy. A venacaval filter was placed in the inferior vena cava.

CASE REPORT

A 40-year-old man was admitted to our hospital because of sudden onset of severe dyspnea. He had been well until he noted easy fatigue and appetite

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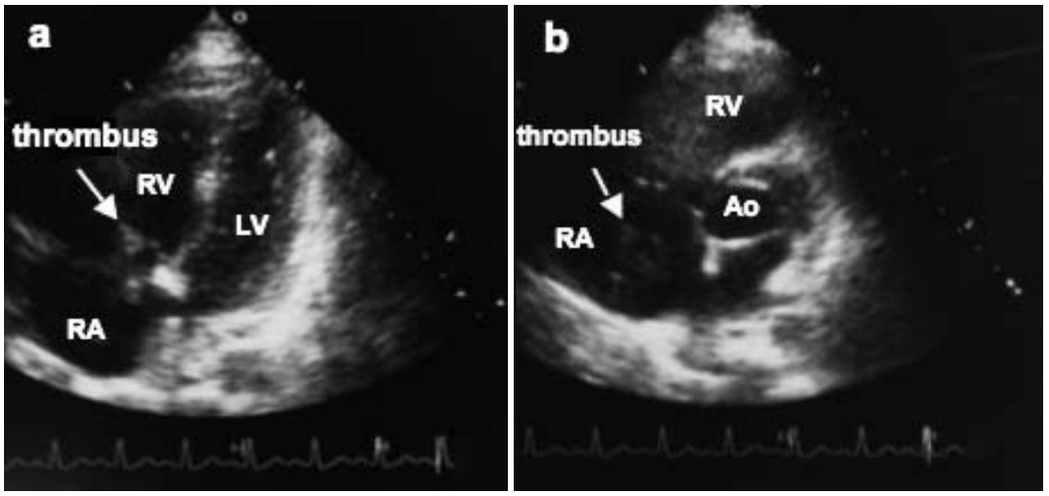

Fig. 1 Transthoracic two-dimensional echocardiograms from apical four-chamber view (*a*) and parasternal short-axis view (*b*) on admission
Mobile string-like mass in the dilated right atrium prolapsed into the right ventricle during the diastolic phase. The right ventricle showed moderate dilation and diffuse hypokinesis. Left ventricular size and function were normal except for septal compression.
RV = right ventricle; LV = left ventricle; RA = right atrium; Ao = aorta.

loss with gradual weight loss 1 year before admission. Four weeks before admission, he had spiking fever above 38 ℃ for several days. He consulted a nearby hospital 1 week before admission. Chest radiography showed no abnormalities except for a mass in the left upper anterior mediastinum. On day 2, he collapsed just after sudden onset of severe dyspnea during walking. Tachypnea and hypoxemia were refractory to oxygen administration. He was transferred to our hospital for advanced treatment for acute pulmonary thromboembolism.

The patient was a barber and had no exposure to occupational diseases. He had smoked one pack of cigarettes daily for 20 years and had drunk alcohol occasionally. On admission, blood pressure was 90/64 mmHg, body temperature was 38.8 ℃, pulse was regular and 132/min, and respiration rate was 35/min. Physical examination showed no crackles in the lungs, no murmurs in the heart sound, flat and soft abdomen without tenderness, no hepatosplenomegaly, and no costovertebral tenderness. An elastic soft lymph node with a diameter of 3 cm was palpable in the left supraclavicular region. The arms and legs were intact except for mild edema in the left leg.

The count of white blood cells and the level of CRP were elevated to 11,000 and 3.1 mg/d*l*, respectively. GOT, GPT and LDH levels were 276, 308, and 1,262 IU/*l*, respectively. The protein S and protein C activities were in the normal range [97% (reference range: 65−135), 69% (reference range: 55−140), respectively]. The titer of anticardiolipin antibody was not significantly elevated. Transthoracic echocardiography (**Fig. 1**) disclosed a mobile string-like mass in the dilated right atrium, prolapsing into the right ventricle during the diastolic phase. There were no thrombus or tumor images in the inferior venae cava. The right ventricle showed moderate dilation and diffuse hypokinesis. Doppler imaging showed mild tricuspid regurgitation with pressure gradient of 30 mmHg between the right ventricle and right atrium. Left ventricular size and function were normal (ejection fraction of 62%) except for septal compression. Chest computed tomography (CT) with contrast medium revealed a large thrombus in the main pulmonary artery (**Fig. 2−a**) to bilateral pulmonary arteries, and a mass with a diameter of 5 cm in the anterior mediastinum (**Fig. 2−b**). Abdominal CT with contrast medium showed a large mass with a size of 5 × 8 cm in the left side of the pelvis, which compressed the left femoral vein (**Fig. 3**).

Oxygen (15*l*/min) was administered and bolus heparin (3,000 U) was given intravenously followed by continuous heparin drip infusion (20,000 U/day). In spite of the intensive medical treatment including catecholamine, his hemodynamic state aggravated into the shock state 4 hr

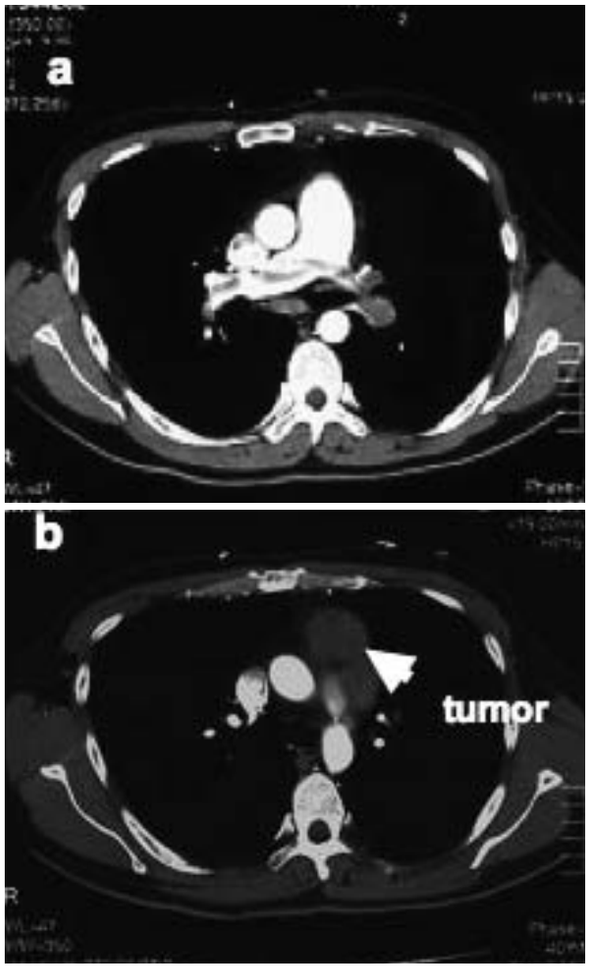

Fig. 2 Chest computed tomography scans with contrast medium on admission showing large thrombus in the main pulmonary artery to bilateral pulmonary arteries (*a*), and a lymphoma mass in the anterior mediastinum and a thrombus in the superior vena cava (*b*)

after admission. He underwent emergent surgery 5 hr after admission. Thrombectomy was performed from the right atrium and bilateral pulmonary arteries. A fibrotic thrombus string with a length of 7–8 cm from the right atrium and two pieces of thrombus from the bilateral pulmonary arteries were removed. Microscopical examination revealed no neoplastic cells in the thrombus. Immediately after the surgery, his hemodynamic condition recovered.

Pulmonary angiography 3 days after the surgery showed small defects in the left lower pulmonary arteries. On the following day, a Greenfield venacaval filter was placed in the inferior vena cava because CT showed appearance of thrombus in the left femoral vein to inferior vena cava in spite of

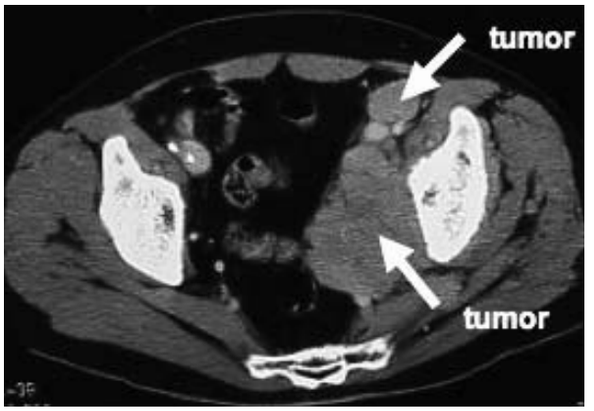

Fig. 3 Abdominal computed tomography scan with contrast medium on admission showing a large mass with a size of 5 × 8 cm in the left side of the pelvis, which compressed the left femoral vein, but no intravenous thrombus was found

adequate anticoagulation therapy by warfarin. Excision of the left cervical lymph node revealed diffuse large B cell lymphoma. Chemotherapy with cyclophosphamide, doxorubicin, vincristine and prednisone resulted in reduction of lymphoma size. The patient was discharged on foot on the 90th day. He had no recurrence of venous thrombosis for the next 6 months.

DISCUSSION

The present case involved a successfully treated massive pulmonary embolism, thrombus in the right atrium, and recurrence of venous thrombosis in the femoral vein related to diffuse large B cell lymphoma. CT and echocardiography showed massive thrombus in the main pulmonary artery and moving thrombus in the right atrium. Percutaneous thrombolytic therapy or thrombus-aspiration may worsen the situation by peeling the thrombus off from the right atrium. Right ventricular dysfunction by echocardiography indicates poor prognosis in patients with pulmonary thromboembolism.[1)] In this patient, the pressure of right atrium was expected to be 20 mmHg or higher, because of the uncollapsed inferior venae cava with a diameter of 22 mm.[2)] In fact, his hemodynamic state worsened quickly after admission. Emergent operation was essential to rescue the patient.

Venous thromboembolism is not a rare complication of malignant diseases. About 10% of patients presenting with idiopathic venous thromboembolism subsequently have diagnoses of cancer over

5－10 years, and the diagnosis is established within 1 year of presenting of venous thromboembolism in＞75% of the cases.[3－8] Among hematological malignancies, about 10% of patients with Hodgkin's lymphoma[9] or non-Hodgkin's lymphoma[10] develop venous thromboembolism. In our case, the mass of the lymphoma grew in the mediastinum and pelvis, and compressed the superior vena cava and the left femoral vein. The thrombus in the superior vena cava reached the right atrium. Thrombus also appeared in the left femoral vein in spite of adequate anticoagulation therapy.

Pathological mechanisms for venous thromboembolism related to lymphoma include hypercoagulability due to tumor activating of clotting, vessel wall injury, and venous stasis due to mechanical compression by mass. Venous stasis caused by venous obstruction predisposes to venous thromboembolism by preventing dilution and clearance of activated coagulation factors. Among 593 patients with non-Hodgkin's lymphoma, the incidence of venous thromboembolism was 6.6%.[10] Compression of veins by tumor and hypercoagulability may lead to venous thromboembolism.[10]

In our case, he noted transient left leg swelling with pain 6 months before admission, which may have been caused by vessel compression by the mass in the left pelvis. Hemostasis by bulky tumor was a strong factor for venous thrombosis. Activities of protein S and protein C, and anticardiolipin antibody level were within normal values in this patient. One case of massive pulmonary embolism caused hyperviscosity due to hypergammaglobulinemia with multiple myeloma.[11]

In general, patients with cancer who develop venous thromboembolism have poor prognosis.[12] Patients with cancer and thrombosis have a lower survival rate compared with those with cancer without thrombosis.[12] Patient with diffuse large B cell non-Hodgkin's lymphoma associated with venous thromboembolism had increased mortality and died early compared to patients without venous thromboembolism.[10] In particular, Ann Arbor stageⅣ (relative risk 2.5)and mediastinal clear B cell lymphoma(relative risk 5.1)are independent risk factors for venous thromboembolism.[10] Quick diagnosis and appropriate intensive treatment are essential to rescue patients from such a life-threatening complication with malignant neoplasm.

要　　約

悪性リンパ腫により生じた肺血栓塞栓症と右房内血栓に対して有効に加療しえた1例

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呼吸困難を主訴として当院集中治療部に搬送となり，急性肺血栓塞栓症と診断された40歳，男性の症例を提示する．右房内にも血栓を認め，さらに前縦隔に径5cm大，左骨盤内に5×8cmの腫瘤を認めた．緊急手術により血栓を除去したところ，血行動態の改善を得ることができた．本例においては凝固線溶系に特記すべき異常所見は認められず，血栓形成の機序として腫瘍による血管の圧迫がもたらした血流うっ滞が第一に考えられた．

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