

# Primary CD30-positive Diffuse Large B-cell Lymphoma in the Superior Vena Cava

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## Abstract

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Primary superior vena cava lymphoma originating from the endothelium of a large vein is very rare. A 70-year-old man was admitted to the hospital; computed tomography showed a tumor limited to the inside of the superior vena cava, completely occluding the vessel. A transjugular biopsy confirmed the diagnosis of diffuse large B-cell lymphoma, which was diffusely positive for CD30. Rituximab monotherapy followed by five courses of R-CHOP chemotherapy induced a complete remission. There was no recurrence after two years. The pathophysiology of lymphoma derived from large vessels may be different from intravascular large B-cell lymphoma, which usually involves small vessels.

**Key words:** superior vena cava syndrome, malignant lymphoma, CD30, intravascular lymphoma

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## Introduction

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Malignant lymphoma is likely to involve the vascular system. Intravenous large B-cell lymphoma is well known and is characterized by the invasion of relatively small vessels, which often results in a poor prognosis (1). However, most of the macrovascular components of lymphoma are caused by oppression from swollen lymph nodes or ectopic invasion, and other causes have not yet been clearly defined. We herein report a case of diffuse large B-cell lymphoma (DLBCL) localized in the superior vena cava (SVC) and complicated by SVC syndrome without oppression from outside of the SVC.

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## Case Report

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A 70-year-old man was admitted to our hospital in January 2007 complaining of progressive facial and upper limb edema and occasional chest pain over the past 5 months. He had no weight loss or night sweats. The patient had a 20-year history of surface antigen-positive chronic type B hepatitis. A physical examination showed no swelling of the su-

perficial lymph nodes. His vital signs were normal, as was his peripheral blood, with no evidence of abnormal lymphocytes. Blood chemistry showed normal lactate dehydrogenase and soluble interleukin-2 receptor levels. Hepatitis B virus (HBV)-DNA was undetectable. Bone marrow aspiration revealed no evidence of malignancy. Enhanced computed tomography of the chest showed a soft tissue shadow in the SVC with numerous collateral vessels in the upper limbs (Fig. 1A). Transesophageal echocardiography showed a high-echoic tumor in the SVC (Fig. 1B) with complete occlusion of the SVC. We suspected thrombosis, angiosarcoma, or lymphoma because the mass was in the vessels. Although it is rare for a tumor to originate from the large vessels, we conducted positron emission tomography, which showed abnormally high accumulation (SUVmax 24.3) around the SVC (Fig. 1C). We suspected SVC syndrome owing to the malignant tumor, and a biopsy was performed transvenously. A histological analysis revealed proliferation of large atypical lymphoid cells (Fig. 2A and B) with phenotypes of CD20 (+), CD30 (+) (Fig. 2C and D), CD3 (-), CD5 (-), CD10 (-), bcl2 (+), and MUM1 (+), which supported a pathological diagnosis of CD30-positive DLBCL.

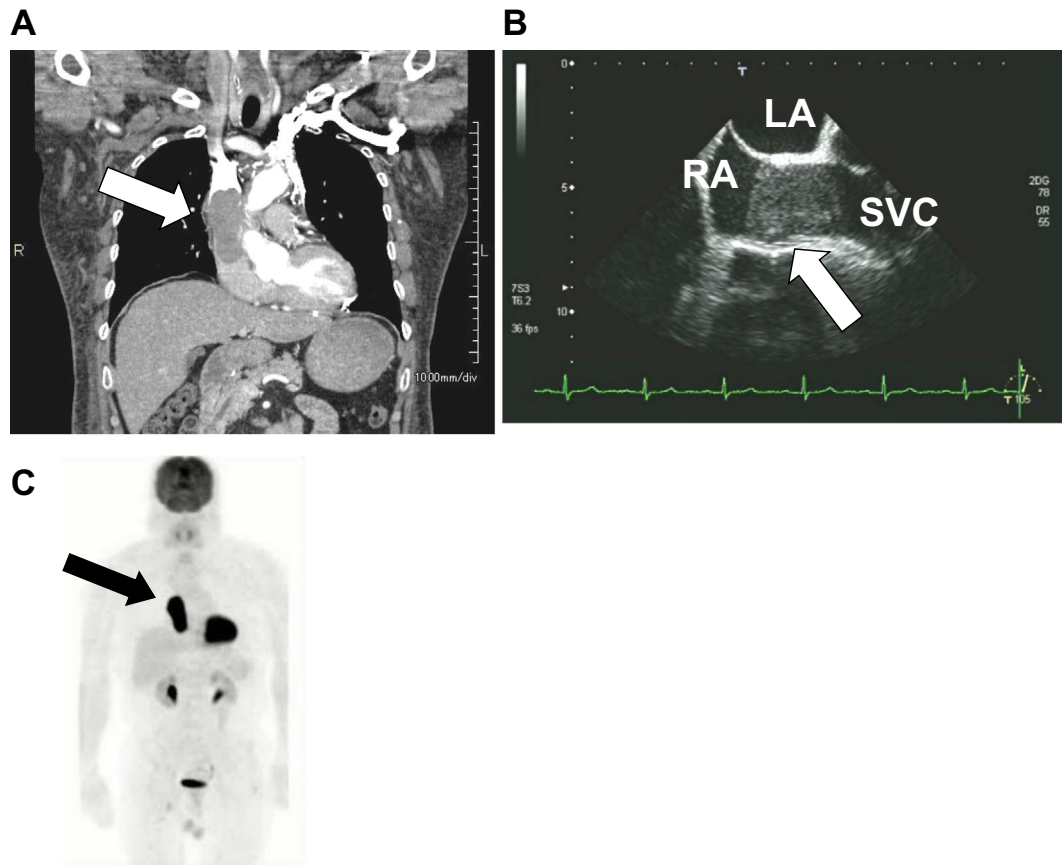
We were concerned about tumor lysis syndrome and pul-

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**Figure 1.** (A) Computed tomography image of the chest on admission. A tumor measuring approximately 6×3×3 cm was located in the superior vena cava (SVC) and had completely occluded the SVC (arrow). (B) Transesophageal echocardiogram on admission. The tumor occupied the superior vena cava near the right atrium (arrow). (C) 2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT) image on admission. Abnormal FDG accumulation was observed in the SVC (arrow).

monary thromboembolism after resolution of the SVC obstruction by systemic chemotherapy; therefore, we initiated chemotherapy rituximab monotherapy two times with a week interval in combination with prophylactic anticoagulant therapy. Subsequently, five courses of rituximab, cyclophosphamide, adriamycin, vincristine, and prednisolone (R-CHOP) combination therapy were administered with warfarin (an anticoagulant) and entecavir (an antiviral). As a result, the patient achieved complete remission (Fig. 3). Serious complications such as pulmonary thromboembolism were not observed. There was no subsequent recurrences for two years after chemotherapy; however, the patient died from hepatocellular carcinoma two years after discontinuation of chemotherapy and entecavir.

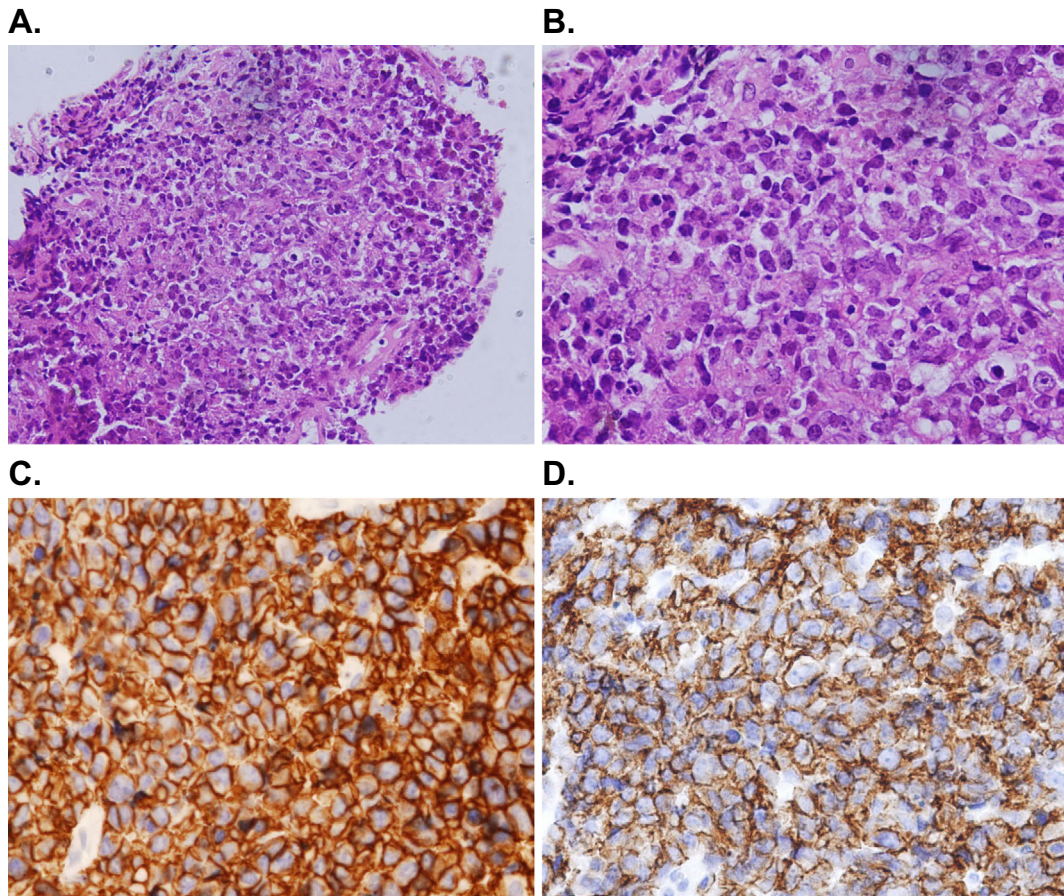
## Discussion

We herein report a case of CD30-positive malignant B-cell lymphoma localized in the SVC with SVC syndrome. To our knowledge, there are only a few reports of primary malignant lymphoma limited to the SVC (2-4). We diagnosed our patient using a non-invasive transjugular biopsy and administered systemic combination chemotherapy, in-

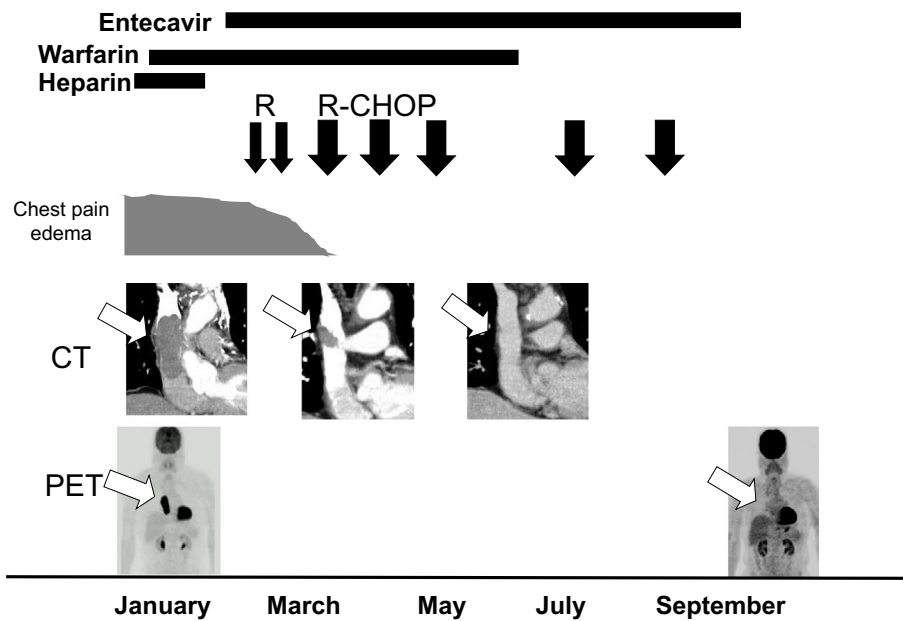
cluding rituximab, without thoracotomy. No serious complications, such as pulmonary embolism, occurred as a result of warfarin therapy during chemotherapy.

The prevalence of SVC syndrome due to malignant causes is reported to be up to 60-80%. Non-malignant causes include thrombosis, fibrosing mediastinitis, infection (tuberculosis, fungal infection), sarcoidosis, and aortic aneurysm. Among the malignant causes, lung cancer is the most common cause of SVC syndrome and accounts for about 75% of cases, while lymphoma accounts for 10% (5). However, these statistics were based on the prevalence of SVC oppression from outside of the SVC. Because the SVC in our case was occluded intravascularly by a tumor in the SVC, not by a tumor outside of the SVC, our case does not seem to be similar to the previously described cases of SVC syndrome in the context of the mechanism of SVC syndrome development.

Many cases of primary cardiac lymphoma (PCL) have been reported (6-9); however, they rarely involve the SVC (10). Our case did not meet the definition of PCL, which presents as a cardiac disease, particularly as the bulk of the tumor was intrapericardial (11). Therefore, this is a fairly rare case.



**Figure 2.** (A and B) Hematoxylin and Eosin staining of the specimen obtained using a transjugular biopsy. Many large atypical lymphoid cells were observed (A:  $\times 100$ , B:  $\times 400$ ). (C) CD20 immunostaining of the specimen obtained using a biopsy. CD20 was diffusely positive ( $\times 400$ ). (D) CD30 immunostaining. CD30 was diffusely positive on the surface of the tumor cells ( $\times 400$ ).



**Figure 3.** The clinical course. The patient received rituximab twice weekly followed by five courses of R-CHOP combination therapy alongside anticoagulant therapy. The malignant lymphoma localized in the SVC immediately diminished in size. The abnormal FDG accumulation detected using FDG-PET/CT around the right mediastinum completely disappeared after systemic chemotherapy.

Lymphoma is rarely observed as a mass in the major vessels. Thus far, malignant lymphoma proliferating in vessels has been classified as intravascular large B-cell lymphoma (IVLBCL), a subtype of non-Hodgkin's lymphoma characterized by proliferation only in the lumina of small (not large) vessels (12). IVLBCL is considered a variant of lymphoma characterized by the loss of adhesion molecules, such as beta-1 integrin, intercellular adhesion molecule-1 (ICAM-1), and E-cadherin. This is based on the fact that IVLBCL rarely extravasates (13, 14). Our case demonstrated lymphoma localized in SVC as a mass that exerted adhesion to the vascular endothelium with no evidence of extravasation. Such a discrepancy might result from residual expression or incomplete deficiency of certain adhesion molecules. The quantity of the biopsy specimen was limited; therefore, expression of these adhesion molecules in our case could not be analyzed. Furthermore, our patient may have had a better prognosis than those with typical IVLBCL. Taken together, these findings indicate that our case was different from typical cases of IVLBCL with regard to the pathogenesis, clinical manifestation, and prognosis.

With respect to the phenotypical characteristics, the presence of CD30-positive diffuse large B-cell lymphoma also differentiated our case from previous cases. CD30 belongs to the tumor necrosis factor receptor superfamily and is a functional marker expressed on the surface of activated lymphocytes with high positivity in Hodgkin's lymphoma and anaplastic large cell lymphoma (15). CD30-positive DLBCL is relatively rare, and its significance is not well known. It has been reported that CD30 expression in DLBCL is observed in up to 14% of *de novo* DLBCL patients, and CD30-positive DLBCL has a superior 5-year overall survival rate (79% vs. 59%,  $p=0.001$ ) to CD30-negative cases (16). In addition, the frequency of localized tumors is not markedly different between patients with CD30-positive DLBCL and those with CD30-negative DLBCL (16). Therefore, our case may represent a subgroup of DLBCL with a favorable prognosis. CD30 expression in IVLBCL has been reported, but its frequency, characteristics, and association with the prognosis are largely unknown (17). In our case, the response to chemotherapy was good, so a CD30-positive phenotype might be associated with a relatively good prognosis.

Brentuximab vedotin, an anti-CD30 antibody-drug conjugate, has been approved for the treatment of patients with relapsed/refractory Hodgkin's lymphoma or anaplastic large cell lymphoma in Japan. Jacobsen et al. reported a phase II clinical trial in patients with relapsed/refractory CD30-positive DLBCL or other CD30-positive B-cell lymphoma treated with brentuximab vedotin or its combination with rituximab (18). In that study, 49 patients with DLBCL and 19 with other B-cell lymphoma were enrolled. The objective response rate was 44% for DLBCL, including 8 (17%) complete remissions. In 13 treated patients, the combination of brentuximab vedotin with rituximab was well tolerated, and the overall response was 46%. Other types of CD30-positive B-cell lymphomas also responded to brentuximab vedotin,

yielding an overall response rate of 26%. Although our patient was successfully treated with R-CHOP, brentuximab vedotin appeared to be promising and should be considered a second-line therapy for patients with relapsed/refractory CD30-positive DLBCL.

In conclusion, we herein report a case of CD30-positive DLBCL originating from the SVC with SVC syndrome. To understand the pathophysiology and establish a standard therapeutic strategy, further clinical experiences are warranted.

**The authors state that they have no Conflict of Interest (COI).**

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