□ CASE REPORT □

Primary Malignant Lymphoma Originating from the Chest Wall without Preceding Pleural Disease

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Abstract

An 84-year-old woman presented to our hospital with dyspnea on exertion and left back pain. Chest X-ray and chest computed tomography (CT) revealed an irregular pleural mass invading her left chest wall with rib destruction and pleural effusion. CT-guided needle biopsy revealed diffuse large B-cell lymphoma. Low-dose oral etoposide produced a complete response, and she continued oral chemotherapy for one year after the diagnosis and maintained good performance status. We herein report a very rare case of non-pyothorax-associated lymphoma that nonetheless resulted in great recovery.

Key words: malignant lymphoma, primary chest wall tumor, pyothorax associated lymphoma

Introduction

Primary malignant lymphoma originating from the chest wall is often associated with preceding pleural disease, such as pleural tuberculosis or chronic pyothorax. It is classified as diffuse large B-cell lymphoma associated with chronic inflammation according to the 2008 World Health Organization (WHO) classification (1). We experienced a malignant lymphoma originating from the chest wall that differed in many respects from pyothorax-associated lymphoma (PAL), such as the presence of rib destruction, a good prognosis, and no preceding pleural disease. It is important to consider the possibility of malignant lymphoma when we see pleural masses, even if there is no preceding inflammatory disease. We have included the diagnosis and described the successful treatment regimen below.

Case Report

An 84-year-old woman presented to a local clinic with dyspnea on exertion and left back pain persisting for a month. She was admitted to our hospital because of left pleural effusion on a chest X-ray. She suffered hypertension and dyslipidemia but had no history of pleural tuberculosis or chronic pyothorax, nor a smoking history or dust exposure.

On examination, her vital signs and oxygen saturation were normal (SpO$_2$: 96% ambient air). A chest examination revealed a mass on the left side of her back with pain and decreased breathing sounds in the left lower-lung field. The rest of the examination findings were normal. Laboratory tests revealed elevated levels of C reactive protein, lactate dehydrogenase (LDH), and soluble interleukin-2 receptor (sIL-2R) (Table 1).

A chest X-ray (Fig. 1) showed left pleural effusion with mediastinal shift. On the first hospital day, an intercostal drainage tube was inserted, and after drainage, chest computed tomography (CT) (Fig. 2) revealed an irregular pleural mass invading her left chest wall with rib destruction and pleural effusion. The mass was adjacent to the posterior mediastinum, but the lateral side of the mass was thick and invading the chest wall, so we diagnosed this mass as a chest wall tumor.

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Table 1. Laboratory Data on Admission.

Hematology		
WBC	8,500	/μL
Neu	86.1	%
Eos	1.3	%
Bas	0.4	%
Mon	4.4	%
Lym	7.8	%
RBC	367×10^4	/μL
Hb	11.5	g/dL
Ht	33.5	%
Plt	21.9×10^4	/μL
Biochemistry		
TP	6.6	g/dL
Aib	3.4	g/dL
AST	22	IU/L
ALT	12	IU/L
T.Bil	0.8	mg/dL
LDH	274	IU/L
BUN	16.4	mg/dL
Cre	0.92	mg/dL
Na	142	mEq/L
K	4.2	mEq/L
Cl	101	mEq/L
Glu	120	mg/dL
Serology		
CRP	3.8	mg/dL
CEA	2.3	ng/mL
proGRP	58.9	pg/mL
CYFRA	1.2	ng/mL
sIR-2R	8,130	U/mL
Pleural effusion		
Cells	2,640	/μL
Neut	2.5	%
Lymph	81.7	%
Protein	4	g/dL
Glu	121	mg/dL
LDH	1,477	IU/L
ADA	79.9	IU/L
Hyaluronic acid	35,500	ng/mL
M.tuberculosis	Negative	
Bacteria	Negative	
Cytology	Class II	
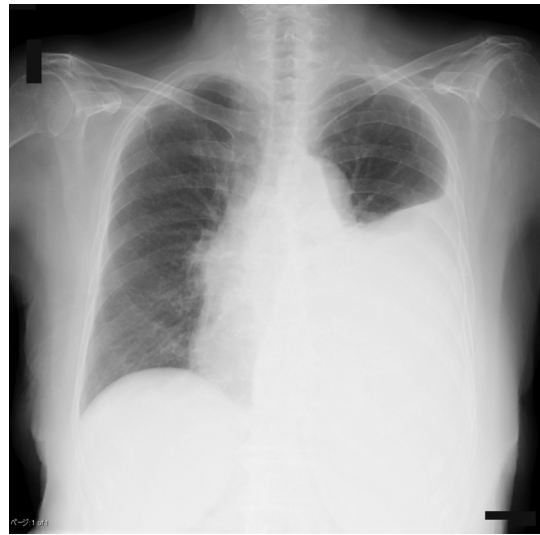
Figure 1. Chest X-ray on admission showing left pleural effusion.

mg/day d1-14, q28) was administered. Her pleural effusion disappeared within two weeks, her back pain disappeared, and her PS improved to 1 within a month. Chest CT performed four months later showed complete response (Fig. 4C and D). She continued oral chemotherapy and maintained a good PS for one year after the diagnosis.

Discussion

Primary malignant lymphoma originating from the chest wall accounts for about 0.3-1.0% of extranodal lymphoma. This lymphoma is mostly associated with underlying diseases, like tuberculous pleurisy or pyothorax after artificial pneumothorax, and is considered to be caused by chronic inflammation of the pleura. It is classified as diffuse large B-cell lymphoma associated with chronic inflammation according to the 2008 WHO classification (1). However, the present case shared none of these common features. We therefore consider this a non-pyothorax associated lymphoma (NPAL), originating from the chest wall without preceding pleural disease. The present case differs in many respects from PAL. The possibility of malignant lymphoma must be considered when pleural masses are observed, even if there is no preceding inflammatory disease. It is therefore important to distinguish NPAL from PAL.

While PAL tends to develop more than 20 years after chronic pyothorax and has male predominance, NPAL can occur in the relatively young (under age 50, about 24%) and without marked gender differences. Indeed, of the 21 reported NPAL cases in Japan, the average age is 64 (17-84) years, and the ratio of males to females is 4:3 (Table 2). In PAL, the average age is 70 (51-86) years, and the ratio of males to females is 8.8:1 (2).

The imaging features of primary malignant lymphomas originating from the chest wall are the tumor spreading along the pleura, sometimes involving the ribs but mostly

The pleural fluid was serous and not purulent. A fluid analysis showed it to be exudative, and 81% of the white blood cells were lymphocytes. The fluid culture was negative, and cytology did not show any evidence of malignancy (Table 1). CT-guided needle biopsy was performed. The histopathology results supported a diagnosis of diffuse large B-cell lymphoma (DLBCL) that was positive for CD10 and CD20 but negative for CD3 and CD5 (Fig. 3).

18-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) revealed high FDG uptake in the left chest wall mass without any other uptake (Fig. 4A and B), so we diagnosed her with primary malignant lymphoma originating from the chest wall. We reconfirmed her medical history, and she never had either tuberculous pleurisy or pyothorax.

Her performance status (PS) was 3 because of her back pain and fatigue. Owing to her bad PS and age, it was difficult to perform an operation or administer combination chemotherapy with Rituximab, so low-dose oral etoposide (50
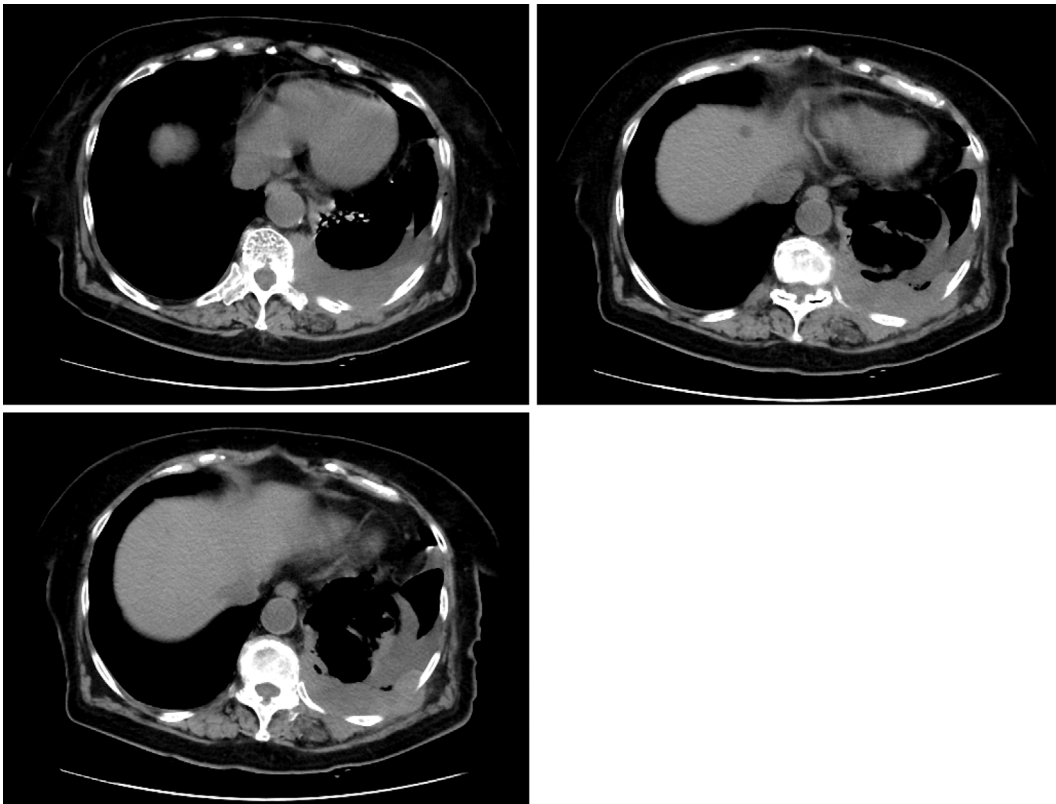
Figure 2. A chest CT scan exhibiting a mass invading the left chest wall with pleural effusion.

Table 2. Report of Primary Malignant Lymphoma Originating from the Chest Wall without a History of Chronic Pyothorax in Japan.

Age, Sex	Radiographic features	Pathology	Treatment	Diagnostic operation	Survival time	EBV	Reference
67, F	mass, effusion	MZL, B	CT(CR)		unknown		13
72, M	mass, effusion	MZL, B	OP		unknown		13
76, M	mass	DLCL, B	CT+RT		death(5M)	(-)	13
82, F	mass, bone invasion	DLCL, B	CT→OP→CT→RT		alive(15M)	(-)	4
74, M	mass, effusion	DLCL, B	OP→RT→OP+CT+RT	○	alive(11M)	(-)	13
84, F	mass, bone invasion	DLCL, B	CT		death(4M)	(-)	13
63, M	mass, effusion	DLCL, B	CT		recurrece(8M over)		13
67, F	mass. bone invasion	DLCL, B	OP		alive(36M)	(-)	13
39, F	mass	DLCL, B	RT+CT		alive(15M)		13
22, M	mass	PTCL	CT(CR)		alive(17M)		13
80, M	mass	DMCL, B	RT→CT+RT(CR)		alive(24M)		13
72, F	mass	DMeCL, B	OP	○	unknown		13
17, M	mass, bone invasion	DLCL, B	OP+CT	○	alive(60M)	(-)	13
44, M	mass	DSCL, B	CT(CR)		unknown		14
83, M	mass, bone invasion	DLCL, A	RT→OP→CT+RT		death(19M)		13
48, F	mass, bone invasion	DLCL, B	OP+CT+RT	○	alive(47M)		10
54, M	mass, effusion	DMCL, B	CT→CT		death(14M)	(-)	13
55, F	mass, effusion	FL, B	CT(CR)		alive(36M)		13
77, M	mass	DMeCL, B	OP+CT		death(12M)		13
84, M	mass	MZL, B	OP+RT(CR)	○	alive(26M)		15
84, F	mass, effuion, bone invasion	DLCL, B	CT		alive(12M)		our case

RT:radiotherapy, CT:chemotherapy, OP:operation

MZL:marginal zone lymphoma, DLCL:diffuse large cell lymphoma, PTCL:peripheral T cell lymphoma, DMCL:diffuse mixed cell lymphoma

DMeCL:diffuse medium-sized cell lymphoma, DSCL:diffuse small cell lymphoma, FL:follicular lymphoma

B: B-cell type, A: anaplastic type

maintaining rib structure (3). In our case, invasion and destruction of the rib was observed, so we first considered lung cancer or mesothelioma. Of the 21 reported NPAL cases, bone destruction was seen in 6; pleural effusion was also seen in 6 of these 21 cases, but only 2 cases had lymphoma cells in the pleural fluid.

A previous study detected Epstein-Barr (EB) viral DNA (EBV-DNA) in lymphoma cells, indicating that EB viral infection contributes to the pathogenesis of PAL (4). However, the findings on an evaluation of the presence of EBV-DNA
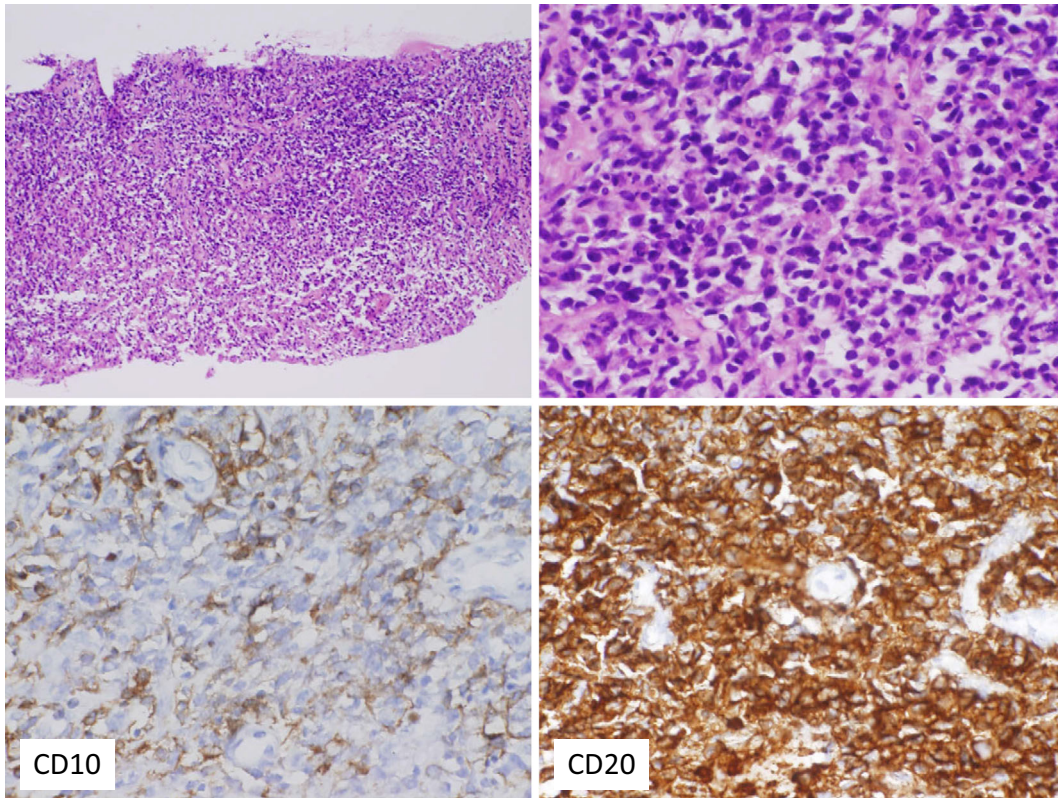
Figure 3. The histopathological findings of the tumor showing diffuse large cell, non-Hodgkins lymphoma, immunohistochemically stained positive for CD10 and CD20.
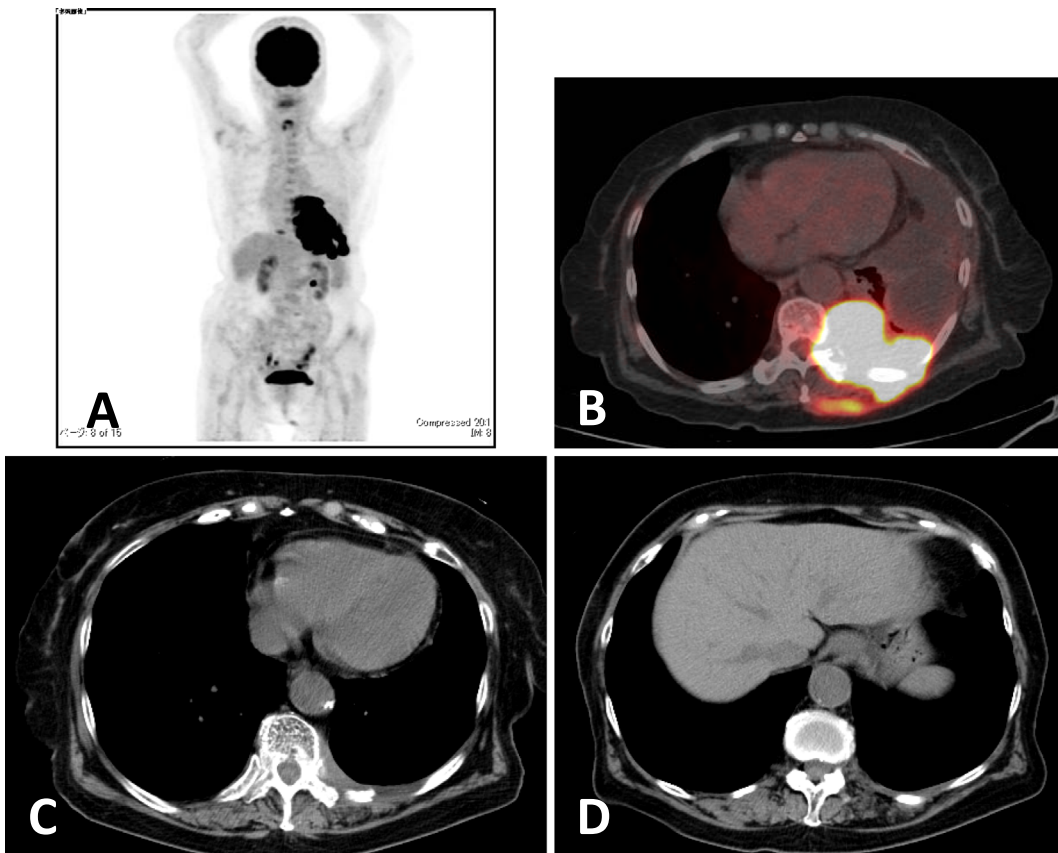

Figure 4. FDG-positron emission tomography (PET)/CT revealing significant accumulation of FDG in the left chest wall mass (A, B). Chest CT after 4 months exhibiting complete response (C, D).

in 7 of the 21 reported NPAL cases were all negative, so NPAL pathogenesis might differ from that of PAL. In our case, EBV-DNA was seen in the pleural effusion, but we could not check the EBV-DNA status in the biopsy specimen because of insufficient sample volume.

The 2008 WHO classification of tumors of hematopoietic and lymphoid tissues has recognized a new provisional entity: EBV-positive DLBCL of the elderly (1). This tumor is defined as an EBV-positive monoclonal large B-cell lymphoproliferative disorder arising in immunocompetent patients over 50 years of age. Patients with this disease often have constitutional symptoms, such as fever, malaise, and weight loss, and extranodal involvement like the skin, lungs, pleural effusion, stomach, and tonsils. However, the present patient did not show any such symptoms (5, 6). In addition, the histological features like extensive necrosis, lymphoid infiltration, and R-S cell like giant cells characterized in EBV-positive diffuse large B-cell lymphoma (DLBCL) of the elderly were also not seen in this case. While we cannot exclude the possibility of this disease because we could not assess the EBV-DNA status of the tumor, we suspect that the present case is a DLBCL not otherwise specified in the WHO classification.

The prognosis of PAL is generally poor, with a 2-year survival rate of 31.4% and median survival time (MST) of about 9 months (7). NPAL prognosis is slightly better: 5 of the 21 historical patients died, 1 recurred after remission, and the remaining 15 experienced remission following operation, chemotherapy, or radiation therapy (RT). We suppose these differences occurred because PAL patients tend to have low PS and low respiratory function due to preceding disease or are difficult to operate on due to chronic inflammation. Another possibility is that the grade of malignancy or biochemical features are different between these two pleural lymphomas (8).

No standard treatment regimen for primary pleural lymphoma has been established, and combination or monotherapy of operation, chemotherapy, and RT was performed for each case. Of the 21 historical NPAL cases, 8 received operation for the first treatment, but 5 of those 8 patients were not diagnosed before surgery. In the 15 patients who were diagnosed before treatment, the first treatment was chemotherapy in 8 patients, surgery in 3, a combination of chemotherapy and RT in 2, and RT only in 2. In two cases, surgery was performed for the remaining tumor after chemotherapy or RT. Nakajima et al. reported that surgery was a prognostic factor of PAL (9), and Nagata et al. recommended operation on NPAL because recurrence often happened with chemotherapy or RT (10). However, in the 21 reported NPAL cases, there were no significant differences in the remission rate and survival rate between the operated and the non-operated group. No fatal cases were reported among the patients with diagnostic operation, but there is some bias, because these cases were able to undergo complete resection due to their small size or low degree of invasion. Surgery may therefore not be a first choice in elderly patients or patients with substantial invasion.

The guidelines of hematopoietic malignancy in Japan do not recommend any specific treatment for elderly or poor-PS patients. In particular, there is little evidence available regarding the optimum treatment for the patients over 80 years of age. We therefore administered low-dose oral etoposide, which is considered a salvage therapy for malignant lymphoma, taking into account the patient's age and poor PS. Its safety for elderly patients (11) and a case with long-term survival (12) have been reported.

The present patient exhibited a complete response and maintained good PS for longer than one year, experiencing only partial remission. Our case represents a compelling treatment option, particularly in elderly or poor-PS patients who might not tolerate surgical resection or extensive chemotherapies. Low-dose oral etoposide was able to produce a remarkable response in just such a patient. To improve the patient's quality of life and chance of survival, it is important to consider the possibility of NPAL, even with a chest wall tumor with rib destruction and no history of preceding pleural disease.

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