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PRIMARY MALIGNANT LYMPHOMA OF THE BREAST A Case Report and Review of the Japanese Literature

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SUMMARY : A 26-year-old pregnant woman was admitted to Nagasaki University Hospital complaining rapid enlargement of masses in the bilateral breasts and the right axilla. Biopsy of the right breast revealed malignant lymphoma. Simple mastectomy plus axillary node dissection on the right side (Br+Ax) and excision of the tumor in the left breast were performed. Histologically, the tumor was a diffuse lymphoma of the medium-size cell type according to the LSG classification, originated from B cells. After operation, Vincristine, Adriamycin, and Cyclophosphamide were administered, but chemotherapy was terminated because of marked leukopenia. The patient has remained asymptomatic for 7 years without any treatment, and there is no evidence of recurrence.

We have collected 79 cases of malignant lymphoma of the breast reported in the Japanese literature, including the present case, and examined factors that might affect the prognosis of patients. However, age, size of tumor, axillary lymph node involvement, histological findings, and type of therapy did not exert a significant influence. The most critical factor in a poor prognosis was the extramammary involvement of malignant lymphoma.

INTRODUCTION

Primary malignant lymphoma of the breast is rare. Among 25, 927 cases of histologically verified breast cancer collected for the 36th meeting of the Japan Mammary Cancer Society, only 45 cases (0.17%) were malignant lymphomas¹⁾. We have experienced a case of the disease in pregnancy. We report the case and discuss the prognosis of 79 cases collected from the Japanese literature.

CASE REPORT

A 26-year-old pregnant Japanese woman noticed a small 3 cm mass in the right breast

in the autumn of 1982. The mass enlarged progressively. Another small mass appeared in the left breast. She visited a hospital in Italy, where a biopsy was taken from the right breast. A diagnosis of malignant lymphoma was made. She returned to Japan and was admitted to Nagasaki University Hospital on October 13, 1982, complaining rapid enlargement of the right breast. There was no pain or discharge from the nipple. She was in the 35th week of pregnancy. The family and past histories were unremarkable.

On physical examination, the height was 164 cm and the body weight 63kg. Anemia was present. The right breast was almost completely occupied by a solid tumor, measuring 20×17cm (Fig. 1). There was fixation of the mass to the

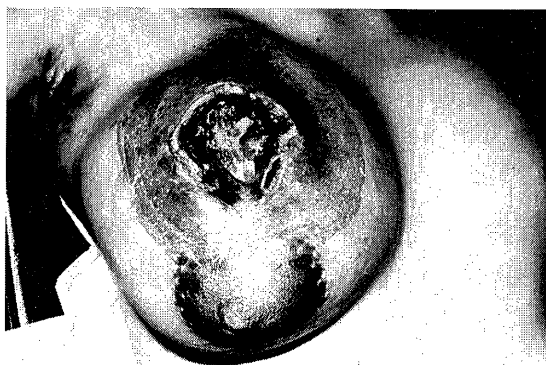


Fig. 1. A photograph of the right breast, showing a 20×17 cm solid tumor with the reddish and ulcerated overlying skin.

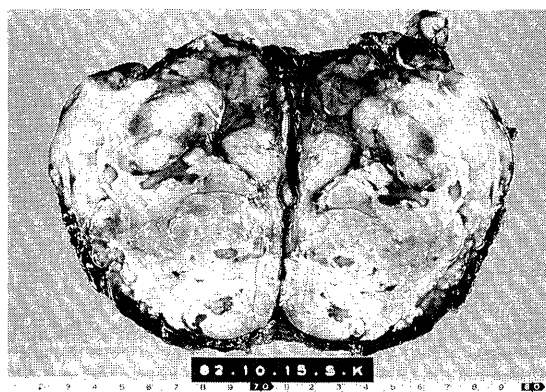


Fig. 2. The cut surface of the right resected breast tumor, which is nodular, solid, well-defined, yellowish-white, and partially hemorrhagic.

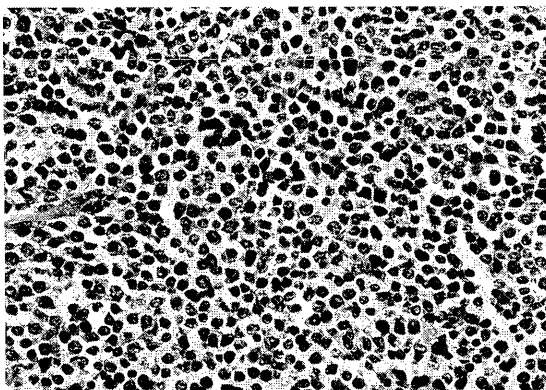


Fig. 3. The tumor is composed of diffusely infiltrated pleomorphic medium-sized lymphoblastic cells with large nuclei and scant cytoplasm. (H&E×400)

overlying skin but no retraction of the nipple. The overlying skin was reddish and ulcerated.

On the left side, a solid tumor, measuring 7.5×5cm, occupied the upper half of the breast. The tumors in both the right and left breasts were firm, elastic, nodular, and freely movable from the chest wall. In the right axilla, there was a firm, elastic, nontender, and movable lymph node measuring 7cm in diameter. No enlarged nodes were palpable in other sites. Hepatosplenomegaly was not apparent in the abdomen.

Examination of the blood showed a hemoglobin level of 9.5g and a white cell count of 7100/mm³ with normal differential cell count. The blood chemistry findings were within normal limits except for 1322mu/ml of LDH (normal : 146-382). Computed tomography of the chest and abdomen revealed neither hepatosplenomegaly nor enlarged nodes.

A right simple mastectomy, right axillary node dissection and excision of the tumor in the left breast were carried out on October 15, 1982, just after a Caesarean section.

The cut surface of the tumor in the right breast was nodular, solid, well-defined, yellowish-white, and partially hemorrhagic. Microscopically, the tumor was composed of diffusely infiltrated pleomorphic medium-sized lymphoblastic cells with large nuclei and scant cytoplasm. The disease was diagnosed as diffuse lymphoma of the medium-sized cell type according to the classification of the Leukemia-Lymphoma Study Group (LSG), and B cell originated.

After operation, a total dose of 4mg of Vincristine, 240mg of Adriamycin and 4800mg of Cyclophosphamide were administered from August 16 to November 10. Chemotherapy was terminated due to the development of marked leukopenia. The wound healed without incident. The white blood cell count returned to 2400/mm³ on November 29. The patient has remained asymptomatic for 7 years without any treatment, and there is no evidence of recurrence.

DISCUSSION

It is known that the breast contains periductal and intralobular lymphoid tissues²⁾. These tissues occasionally contain germinal centers that may be the site of origin of malignant lymphoma³⁾. In our case, microscopic studies

Table 1. Reported cases of malignant lymphoma of the breast in Japan

No	Author	Year	Age	Sex	Site	Size (cm)	Ax.Lym. Invol	Histological findings	Therapy Operation	Radi.	Chemo.	Subsequent Involvement	Prognosis
1	Horiguchi	'50	20	F	B			Ret.cell sar.				General	
2	Hara	'53	29	F	B			Ret.cell sar.				General	
3	Tsuchiya	'58	20	F	R			Ret.cell sar.	Radical	+	+	Lung,Skin	Died 8mos.
4	Sakurai	'62	27	F	R	Fist		Ret.cell sar.	Radical		+		Liv. 2mos.
5	Asai	'63	16	F	B	7×4		Ret.cell sar.				General	Died 4days
6	Fujimori	'64	64	F	R	Thumb tip	-	Ret.cell sar.	Radical				Liv. 7.8yrs.
7	Shimura	'64	37	F	L	Bean	-	Ret.cell sar.	Radical	+			Liv. 2.5yrs.
8	Watanabe	'64	47	F	R	Pigeon egg	-	Ret.cell sar.	Radical	+			Liv. 1.5yrs.
9	Kondou	'65	58	F	R	Walnut	-	Ret.cell sar.	Radical				Liv. 10mos.
10	Inui	'65	46	F	L	Hen egg	+	Ret.cell sar.	Radical		+	Mediastinum	Died 4mos.
11	Satou	'66	50	F	L	4.5×4.5	-	Ret.cell sar.	Radical	+	+	General	Died 5days
12	Noda	'66	37	F	R			Ret.cell sar.	Radical	+	+	Leukemic	Died 10mos.
13	Noda	'66	47	F	R			Lymph.sar.	Radical		+	Leukemic	Died 4mos.
14	Yoshida	'70	16	F	L	6×5	+	Ret.cell sar.	Radical	+	+	Lung,Skin	Died 5mos.
15	Yoshida	'70	48	F	R	18×15	-	Ret.cell sar.	Radical			Ret.peri.	Died 7mos.
16	Nakagawa	'70	44	F	L	2.5×2.5	-	Lymph.sar.	Radical	+			Died 3mos.
17	Nakagawa	'70	32	F	R	10×9	+	Lymph.sar.	Radical		+		Died 6mos.
18	Miura	'70	19	F	L	4.6×4.2		Ret.cell sar.	Excision				Liv. 34mos.
19	Miura	'70	25	F	B	6.4×5.0	-	Ret.cell sar.	Radical	+		General	Died 11mos.
20	Tanaka	'70	52	F	R	Fist	+	Lymph.sar.	Radical	+			Died 3yrs.
21	Nishizawa	'70	37	F	R	8×8	+	Ret.cell sar.	Radical	+		Leukemic	Died 8mos.
22	Kinoshita	'70	46	F	L	Hen egg	+	Ret.cell sar.	Radical		+	Mediastinum	
23	Nakashima	'70	50	F	L	3×4		Ret.cell sar.					
24	Nakamura	'71	48	F	L	Goose egg	+	Ret.cell sar.	Radical	+			Liv. 2mos.
25	Yoshitani	'72	60	F	R	1×1	+	Ret.cell sar.	Radical				Liv. 1.3yrs.
26	Otowa	'73	33	F	B	Hen egg	+	Ret.cell sar.	Radical	+	+	Small intes.	Died 4mos.
27	Watanabe	'74	27	F	R	2.5×2.5	-	Lymph. sar.	Radical			General	Died 10mos.
28	Watanabe	'74	32	F	R	10×8	+	Ret.cell sar.	Radical		+	Rt.Neck	Died 2mos.
29	Watanabe	'74	32	F	R	2.5×2.5	+	Ret.cell sar.	Excision		+		Liv. 2.8yrs.
30	Shiromatsu	'74	13	F	L	9×9	-	Ret.cell sar.	Radical	+			Liv. 4mos.
31	Akao	'75	25	F	R	6×5	-	Ret.cell sar.	Radical		+		Liv. 3.6yrs.
32	Oomuro	'75	32	F	L	4.5×3	-	Ret.cell sar.	Radical	+	+		Liv. 11mos.
33	Mura	'76	58	F	L	3.5×3	-	Ret.cell sar.	Radical		+		Liv. 16mos.
34	Tanaka	'77	24	F	R	1.0	-	Ret.cell sar.	Br	+			Died 2yrs.
35	Tanaka	'77	66	F	L	5.8×5.2	-	Ret.cell sar.	Br	+		General	Died 6mos.
36	Tanaka	'77	38	F	R	1.5	-	Ret.cell sar.	Radical	+			Liv. 10.5yrs.
37	Tanaka	'77	67	F	R	2.4×1.4	-	Ret.cell sar.	Radical	+		General	Died 5mos.
38	Tanaka	'77	56	F	L	3.0	+	Lymph.sar.	Br	+	+	Heart,Spleen	Died 4mos.
39	Tanaka	'77	83	F	R	2.5×2.0	-	Ret.cell sar.			+		Died 14mos.
40	Tanaka	'77	79	F	R	1.5	-	Ret.cell sar.	Br				Liv. 15mos.
41	Marutani	'77	53	F	R	4×3	-	Ret.cell sar.	Radical	+	+		Liv. 2yrs.
42	Kawage	'77	25	F	R	14×13	+	Ret.cell sar.	Radical	+		Brain	Died 2mos.
43	Yamaguchi	'79	74	F	L	First	-	Ret.cell sar.	Radical	+	+		Liv. 3yrs.
44	Ikeda	'79	32	F	L	13.5×12		Ret.cell sar.	Excision	+		Brain	Died 2.7yrs.
45	Satou	'79	64	F	R	12×11	+	Ret.cell sar.	Radical		+		Liv. 1yrs.
46	Kosaka	'79	52	F	L	3×3	-	Lymph.sar	Radical		+		Liv. 5mos.
47	Oohashi	'80	56	F	L	3.5×3	-	Ret.cell sar.	Radical	+	+		Liv. 3.3yrs.
48	Seto	'81	45	F	R	21.5×20	+	Ret.cell sar.	Radical	+	+		Died 102days.
49	Kouno	'81	49	F	B	12×9	+	Lymph.sar			+		Died 15mos.
50	Yamashita	'82	54	F	R	4	+		Radical	+	+		Liv. 7mos.
51	Komaki	'83	14	F	R	6.5×5.5	+	Diffuse,Small		+	+	General	Died 10mos.
52	Nakamura	'83	38	F	R	Hen egg	-	Folli.,Medium	Radical		+	Leukemic	Died 8mos.
53	Koyama	'83	72	F	B	5.5×3.5	-				+		Died
54	Kawamura	'83	14	F	B	14×13	-	Lymph.sar.					
55	Suzuki	'83	72	F	R			Ret.cell sar.	Radical		+		Liv.6. 8yrs.
56	Keshigawa	'84	65	F	R			Ret.cell sar.	Radical		+		Died 69days
57	Yamamoto	'84	49	F	R	4×4	+	Diffuse,Large	Radical		+		Liv. 6mos.
58	Kawaba	'85	62	F	L	4.5	+	Diffuse,Medium	Br+Ax		+		

59	Tanada	'85	51	F	L	3.5×2.5	-	Diffuse, Large	Radical		+	General	Died 4mos.
60	Hori	'85	67	F	L			Ret. cell sar.	Radical		+		Liv. 7mos.
61	Sou	'85	57	F	R	5.5×5	-	Diffuse, Small	Radical	+	+	General	Died 1yr.
62	Sai	'85	81	M	R	4×4	-	Lymph. sar.	Br				Liv. 4mos.
63	Yamakawa	'86	14	F	R	6.5×5.5	+	Diffuse, Small		+	+	Liver, Bone	Died 9mos.
64	Yamakawa	'86	45	F	L	5.5×3.5	-	Diffuse, Large	Radical	+	+	Brain	Died 9mos.
65	Yamakawa	'86	58	F	L		+	Diffuse, Large			+		Liv. 17mos.
66	Yamakawa	'86	50	F	R	3.3×2.5	-	Diffuse, Large	Radical		+		Liv. 14mos.
67	Yamakawa	'86	62	F	R	3.7×2.8	-	Diffuse, Large	Radical		+		Liv. 9mos.
68	Biwata	'86	74	F	B	5.6×2.7	+	Diffuse, Small	Radical		+		Liv. 1.7yrs.
69	Hirata	'86	74	F	R	5.5×5		Diffuse, Medium	Radical		+		
70	Masuda	'86	65	F	R	3.5×4	-	Diffuse, Medium	Radical		+		Liv. 6mos.
71	Saitou	'86	68	F	R	10.5×9.5	+		Radical		+		
72	Takahashi	'87	23	F	R	5.5×5		Diffuse, Mixed	Br+Ax		+		Liv. 3yrs.
73	Goushi	'87	48	F	L	3×3	+	Diffuse, Medium			+		Liv. 1yrs.
74	Kawaguchi	'88	78	F	L	8×4	-	Diffuse, Large	Br+Ax	+	+	Leukemic	Died 205days
75	Yamoto	'88	20	F	L	6×4	-	Folli., Medium			+	Leukemic	Died 14mos.
76	Komatsu	'88	65	F	L	4×3.5	-	Diffuse, Midium	Br+Ax		+		Liv. 110days
77	Katsuki	'89	34	F	R	6.5×5.5	+	Diffuse, Mixed	Radical	+	+	General	Died 11mos.
78	Nakano	'89	34	F	B			Burkit's Lym.	Br+Ax+Sc	+	+	Brain	Died 20mos.
79	our case	'90	26	F	B	20×17	+	Diffuse, Medium	Br+Ax, Exc		+		Liv. 7yrs.

Site (B=Bilateral, R=Right, L=Left), Ax. Lym. Invol.=Axillary lymph node involvement Classification of common use (Ret. cell sar.=Reticulum cell sarcoma, Lymph. sar.=Lymphosarcoma), LSG's classification (Diffuse=Diffuse lymphoma, Folli.=Follicular lymphoma, Small=Small cell type, Medium=Medium sized cell type, Mixed=Mixed type, Large=Large cell type), Radi.=Radiation therapy, Chemo.=Chemotherapy, Ret. peri.=Retroperitoneum, Small intes.=Small intestine Liv.=Living

revealed diffuse lymphoma of the medium-sized cell type. The lymphomatous infiltrates were closely associated with the mammary tissues. Except for a right axillary lymphnode, no extramammary involvement was found clinically. From the above findings, our case can be accepted as primary malignant lymphoma of the breast according to Wiseman's criteria⁴⁾.

We collected and analyzed 79 cases of malignant lymphoma of the breast, among which 78 had been reported in the Japanese literature between 1950 and 1989, including our own case. A summary of these cases is presented in **Table 1**. Ages ranged from 13 to 83 years with a mean age of 45.9 years. Only one male suffered from this disease. Three cases were associated with pregnancy. Lymphoma, it is said, tends to involve the right breast⁵⁾. In our series, the initial involvement was right in 41 patients, left in 27, and bilateral in 11. The size of the tumor varied from a bean size to 20cm in diameter. Axillary lymph node involvement was found in 27 of the 63 cases (42.8%) for which lymph node findings had been recorded. Histologically, so-called reticulum cell sarcoma was the most common type in the past. By LSG's classification, diffuse lymphoma of the large cell type was common. Radical mas-

tectomy was performed in 57 cases. Twenty-six patients received supplementary radiotherapy, and adjuvant chemotherapy was employed in 40 cases.

The clinical course was usually rapid and fatal. Oberman reported that 5 of 6 patients died within one year⁶⁾. Similarly, Wiseman reported that 10 of 16 patients died within 2 years, and only 3 patients were alive after 5 years. In our series, 34 patients died within two years, and 15 patients lived more than 2 years.

An investigation was conducted into what factors might have prognostic values. The patients were divided into 2 groups, namely, those who died within 2 years and those who survived 2 years or more, but no significant difference was observed in the age or the size of the tumor between the two groups. There was also no significant difference in axillary lymph node involvement between the two groups. DeCosse also reported that the presence or absence of axillary lymph node involvement did not seem to affect the prognosis and stated that the most important factor in prognosis was the histological type of malignant lymphoma⁷⁾. In our series, however, there was no significant difference in the histological findings between the two groups. It has also been reported that

radical mastectomy combined with supplementary radiotherapy is useful in the treatment of primary malignant lymphoma of the breast^{8,9}. Again, however, the prognosis in our series was not significantly affected by the type of therapy. Only 4 patients lived longer than 5 years, and the longest survival was 10.5 years.

In a review of the long-term survivors, we were unable to find any influential factors for lengthy survival. However, the most critical factor in poor prognosis was considered to be the extramammary involvement of malignant lymphoma.

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