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【 CASE REPORT 】

Ovarian Follicular Lymphoma Diagnosed Due to Hydronephrosis

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Abstract:
A 74-year-old woman presented with left lateral abdominal pain. Abdominal echography revealed left hydronephrosis and a pelvic mass. The patient underwent left adnexal resection of a suspected left ovarian tumor and was diagnosed with follicular lymphoma (FL) of clinical stage IIIA, grade 2. The patient was treated with rituximab-combined chemotherapy and achieved complete remission. The most common histological types of ovarian lymphoma are diffuse large B-cell lymphoma and Burkitt lymphoma, with FL being an extremely rare variant. We herein report a case of ovarian FL diagnosed as hydronephrosis.

Key words: primary ovarian lymphoma, follicular lymphoma (FL), ovarian follicular lymphoma

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Introduction

Primary non-Hodgkin's lymphoma of the ovary is extremely rare. The most common histologic types are diffuse large B-cell lymphoma and Burkitt lymphoma. Since follicular lymphoma (FL) is rarely reported, the clinicopathological characteristics of ovarian FL have not yet been fully elucidated.

We herein report a case of ovarian FL that was treated with surgical resection followed by chemotherapy.

Case Report

A 74-year-old woman visited her doctor because of left-sided abdominal pain that began in February 2021 and had gradually worsened. The patient was referred to our gynecology department in April 2021 due to suspicion of a left ovarian tumor, after an abdominal echocardiogram revealed left hydronephrosis and a left pelvic mass. Transvaginal ultrasonography revealed a 50-mm substantial tumor in the left adnexal region (Fig. 1A). No abnormalities were observed in her uterus. Computed tomography (CT) showed left hydronephrosis (Fig. 1B) and a mass approximately 50× 40 mm in size, with a marginal lobular shape and in contact with the left pelvic wall (Fig. 1C). On magnetic resonance imaging (MRI), T1-weighted images showed almost equal signal to that of the muscle, and T2-weighted images showed a mildly high signal, but there were areas of high signal intensity at the edges of the tumor that appeared to be cysts (Fig. 1D, 1E). Blood tests showed mild elevation of sIL-2R, positive M-protein, elevated IgM due to monoclonal immunoglobulinemia (IgM-κ), and decreased IgG and IgA levels (Table 1).

The patient consulted a hematologist regarding the possibility of an ovarian malignant lymphoma based on blood tests; however, a preoperative diagnosis was difficult to make. Left salpingo-oophorectomy was performed for suspected ovarian tumors or ovarian malignant lymphoma. The left adnexal tumor was adherent to the sigmoid colon and left pelvic wall. The uterus and right adnexa were normal, and the left adnexa was removed, after detachment of adhesions to the sigmoid colon and pelvic wall. Grossly, the left ovary was occupied by a yellow-white tumor that had also invaded the oviduct (Fig. 2A). A histopathological examination showed nodular hyperplasia of atypical lymphocytes

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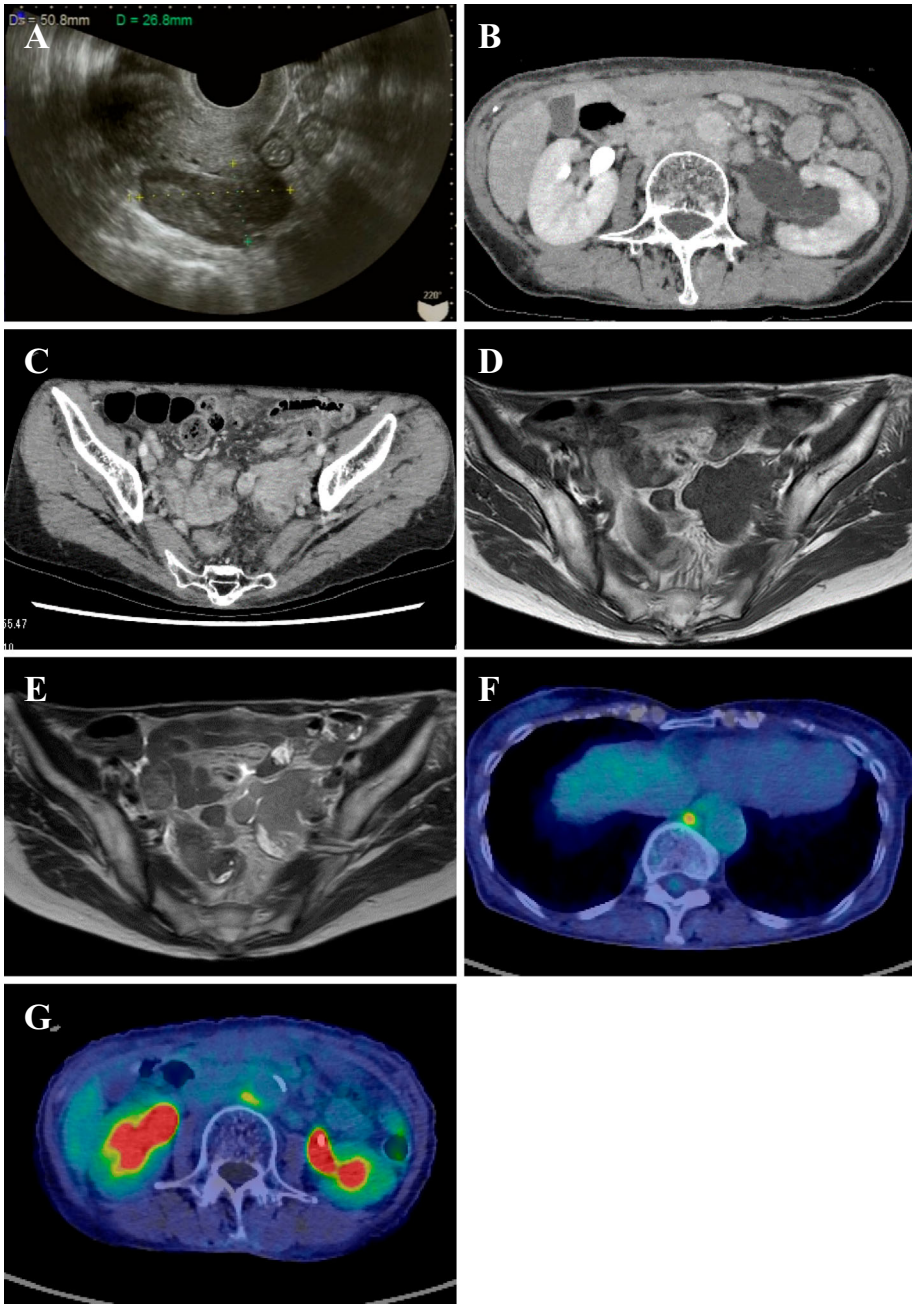

Figure 1. Transvaginal ultrasonography, CT, MRI, and PET/CT imaging findings. A) Substantial tumor in the left adnexal region. B) Left hydronephrosis due to left adnexal tumor. C) Left adnexal tumor. D) The left adnexal tumor is nearly equal in signal to the muscle on T1WI. E) The left adnexal tumor has a mildly high signal on T2WI, but there is an area of high signal intensity at the margin of the tumor, which appears to be a cyst. F) Posterior mediastinal lymphadenopathy. G) Para-aortic lymphadenopathy.

(Fig. 2B), and the centroblast count was 6-15 cells/high-power field (HPF). Immunostaining showed CD10+, CD20+, BCL-2+, BCL-6+, and MUM1-cells (Fig. 2C-G). Therefore, the patient was diagnosed with grade 2 FL. The MIB-1 index value was 5%. A G-band chromosome analysis showed t(14;18)(q32;q21) in four of the seven cells. Fluorescence in situ hybridization (FISH) showed an IgH/B-cell lymphoma-2 (BCL-2) fusion signal in 91.0% of the cells.

The patient was transferred to the Department of Hematology for postoperative chemotherapy. A physical examination revealed no superficial lymphadenopathy or B symptoms. Bone marrow aspiration and a biopsy showed no lymphomatous cell infiltration. Post-tumor resection positron emission tomography (PET)/CT showed the faint accumulation [maximum standardized uptake value (SUV_{max}) 1.92], which may be due to inflammatory changes associated with the surgery. Accumulation in the posterior mediastinal lymph nodes (SUV_{max} 4.51) and periaortic lymph nodes (SUV_{max} 3.81) was also observed, suggesting lymphomatous lesions (Fig. 1F, G).

Table 1. Laboratory Findings on Admission to Gynecology Department.

Peripheral blood		Biochemistry		Immunology	
WBC	6,500 /μL	TP	7.1 g/dL	CRP	0.14 mg/dL
Neutro	66.20 %	ALB	4.5 g/dL	β2MG	2.1 mg/L
Eosino	2.30 %	AST	21 U/L	IgG	514 mg/dL
Baso	1.30 %	ALT	11 U/L	IgA	64 mg/dL
Mono	6.90 %	LDH	197 U/L	IgM	440 mg/dL
Lympho	23.30 %	ALP	194 U/L		
RBC	433×10^4 /μL	γGTP	17 U/L	Tumor marker	
Hb	13.5 g/dL	ChE	275 U/L	AFP	4.93 ng/mL
Ht	41.50 %	T-Bil	0.6 mg/dL	CA15-3	8.7 U/mL
PLT	27.0×10^4 /μL	BUN	15.1 mg/dL	CA19-9	12.7 U/mL
		Cre	0.77 mg/dL	CA72-4	<1.5 U/mL
Coagulation		UA	4.8 mg/dL	CA125	13.4 U/mL
PT-INR	1.01	Na	138 mEq/L	CEA	2.2 ng/mL
APTT	31.0 s	K	4.2 mEq/L	SCC	0.3 ng/mL
FIB	241 mg/dL	Cl	99 mEq/L	sIL-2R	505 U/mL
FDP	6.6 μg/dL	Ca	9.6 mg/dL		
D-dimer	2.25 μg/dL				

Based on the examination results, ovarian FL (clinical stage IIIA, FLIPI2 intermediate risk) was diagnosed. BR therapy (rituximab 375 mg/m^2 and bendamustine 90 mg/m^2) was initiated in June of the same year (Fig. 3). After six courses of treatment, CT showed a complete response, while PET/CT showed a complete metabolic response. Since then, the patient has been undergoing regular follow-ups at the outpatient clinic and has survived without recurrence.

Discussion

Ovarian non-Hodgkin's lymphoma (NHL) is an extremely rare disease, accounting for 1.5% of all ovarian tumors and 0.5-1% of all NHL cases (1). The most common histological types of ovarian NHL are diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma, while FL is an extremely rare subtype. Table 2 shows the reported cases of ovarian FL in our study. Patients with no apparent stage and those with histologically confirmed DLBCL, or without composite lymphoma or BCL-2 immunostaining, were excluded. The median age of the 19 cases was 63 years old, with 10 cases (53%) diagnosed at the localized stage. It is possible that all of the cases were diagnosed after oophorectomy. Cases were classified into types 1 and 2, according to their clinicopathological features. Six patients with type 1 and stage IE showed low BCL-2 expression by immunostaining. Other patients, including the patient in our case report, expressed BCL-2. The type 2 tumors were immunohistologically and genetically the same as the usual nodal FL. According to the diagnostic criteria of Fox et al. (2), primary malignant lymphoma of the ovary in a narrow sense is defined as follows: 1) no lesions other than those in the ovary, surrounding organs, and adjacent lymph nodes; 2) no lymphoma cells in peripheral blood and bone marrow; and 3) lesions in distant sites occurring more than several months after the discovery of the primary lesion. In our case, the possibility of secondary ovarian lymphoma due to the systemic dissemination of nodal FL cannot be ruled out. However, the unilateral ovarian lesion was almost entirely occupied by lymphoma cells. The tumor had a large volume, infiltrated the surrounding organs, and was not found to have other nodal lesions at the primary site (the left ovary). Thus, the patient was diagnosed with primary ovarian FL.

Ahmad et al. reported that the clinical manifestations of gynecological organ NHL are similar to those of gynecological malignancies, and it is difficult to distinguish them preoperatively. They recommended that surgery be performed for gynecological malignancies to confirm the pathological diagnosis, followed by chemotherapy (3). Ambulkar et al. suggested that chemotherapy should be administered even if staging does not show non-ovarian involvement (4, 5). As shown in Table 2, all patients underwent oophorectomy, but only 4 of the 19 patients underwent total abdominal hysterectomy (6-8). Regardless of the disease stage, chemotherapy was administered in all but two cases and was effective. Radiation therapy was performed in only one case (9). Although the long-term prognosis is unknown, a diagnosis by oophorectomy and chemotherapy is commonly performed for ovarian FL.

Based on the presence of hydronephrosis, which corresponded to a high tumor volume, we administered rituximab combination chemotherapy after surgery in this case. The patient remains in complete remission. We hope that the accumulation of future cases will clarify the differences in treatment responses and the long-term prognosis by stratifying primary ovarian FL based on BCL-2 expression.

Conclusion

In this study, we diagnosed a patient with ovarian FL with hydronephrosis. It is important to recognize that FL can occur in the ovary, although it is extremely rare. Surgical resection should be performed for the differential diag-

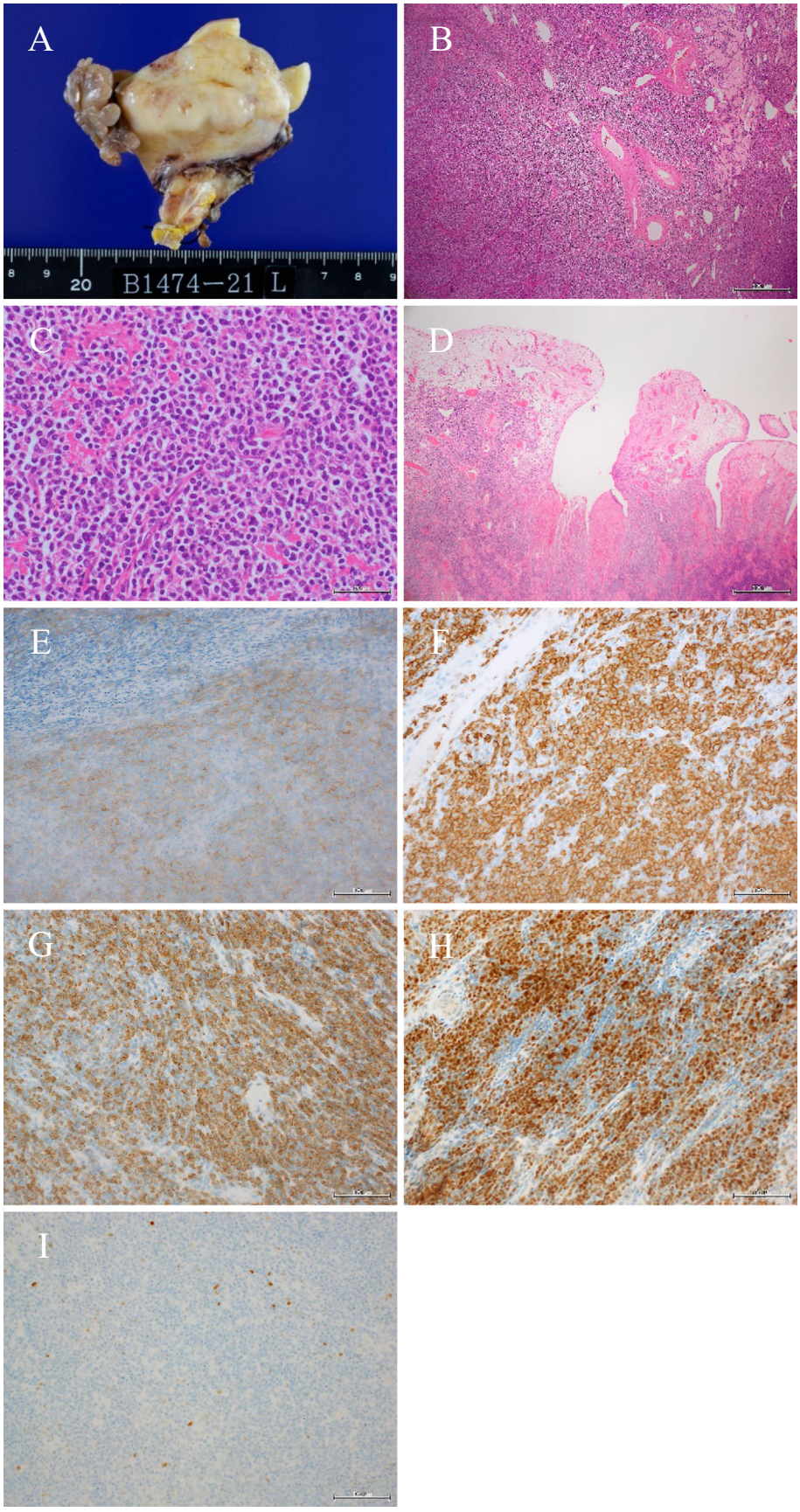

Figure 2. **Appearance and pathological findings of the tumor. A) Left adnexal tumor. B) Left ovary, Hematoxylin and Eosin (H&E) staining (×40). C) Left ovary, H&E staining (×400). D) Left oviduct, H&E staining (×40). E) CD10 immunostaining (×200). F) CD20 immunostaining (×200). G) BCL-2 immunostaining (×200). H) BCL-6 immunostaining (×200). I) MUM-1 immunostaining (×200).**

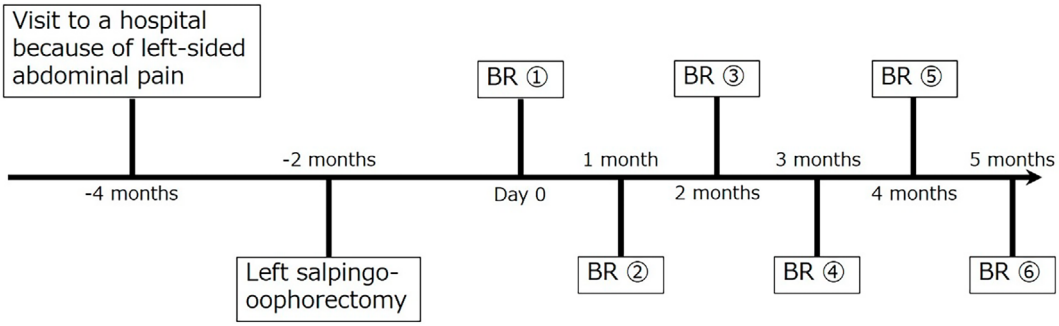

Figure 3. **Clinical course in this case. BR: bendamustine, rituximab**

Table 2. **Reported Cases of Ovarian Follicular Lymphoma.**

No	Type	Age	Ovary	Lymph-adenop-athy	Stage	Grade	CD10	CD20	BCL-2	BCL-6	MUM-1	IGH/ BCL-2	SO	TAH	RT	CT	Outcome	Ref. No.
1	1	50	Right	-	IE	2	+	+	-	+	NA	NA	+	+	-	+	A	7
2	1	51	Right	-	IE	3	+	+	-	+	NA	NA	+	+	-	+	A	7
3	1	43	Left	-	IE	3a	dim	+	dim	+	-	NA	+	-	-	+	A	9
4	1	67	NA	-	IE	3a	-	+	-	+	-	NA	+	-	-	+	A	9
5	1	68	Right	-	IE	2	-	+	-	+	-	NA	+	-	-	-	A	9
6	1	73	Left	-	IE	3a	dim	+	dim	+	+	-	+	-	-	-	A	9
7	2	54	Right	+	IIE	1	+	+	+	NA	NA	+	+	+	-	+	A	6
8	2	66	Both	-	IIE	1	+	+	+	NA	NA	-	+	-	-	+	A	10
9	2	42	Both	-	IIE	1	+	+	+	+	-	+	+	-	-	+	A	9
10	2	66	Both	-	IIE	2	+	+	+	+	-	NA	+	-	-	+	D	9
11	2	61	Both	+	III	1	+	+	+	+	-	+	+	-	+	+	D	9
12	2	62	Right	-	III	2	+	+	+	+	-	NA	+	-	-	+	A	9
13	2	55	Right	+	III	1	+	+	+	+	-	+	+	-	-	+	A	9
14	2	71	Left	+	III	3a/3b	+	+	+	+	NA	NA	+	+	-	+	A	8
15	2	59	NA	-	IV	1/2	+	+	+	NA	NA	-	+	-	-	+	A	10
16	2	64	Left	-	IV	1	+	+	+	+	-	+	+	-	-	+	A	9
17	2	63	Both	-	IV	1	+	+	+	+	-	+	+	-	-	+	D	9
18	2	63	Left	+	IV	1	+	+	+	+	-	+	+	-	-	+	NA	9
This case	2	74	Left	+	III	2	+	+	+	+	-	+	+	-	-	+	A	

NA: not available, SO: salpingo-oophorectomy, TAH: total abdominal hysterectomy, RT: radiation thrapy, CT: chemotherapy, A: alive, D: dead

nosis of ovarian cancer. Rituximab combination chemotherapy can provide a long-term survival in ovarian FL, as well as nodal FL.

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

Shinsuke Noguchi and Yuiko Kimura contributed equally to this work.

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