MAJOR PAPER

Magnetic Resonance Findings of Primary Uterine Malignant Lymphoma

Noriko GOTO^{1*†}, Yumiko OISHI-TANAKA¹, Hajime TSUNODA², Hiroyuki YOSHIKAWA²,
and Manabu MINAMI¹

*Departments of ¹Radiology and ²Obstetrics and Gynecology, University of Tsukuba
2-1-1 Amakubo, Tsukuba, Ibaraki 305-8576, Japan*

(Received October 17, 2006; Accepted February 14, 2007)

To clarify the magnetic resonance (MR) characteristics of primary uterine malignant lymphoma, we identified 4 patients with primary uterine lymphoma in the MR database of our institute from 1994 to 2005 and evaluated their clinical and MR findings for tumor extension, size, shape, and signal intensity, multinodular growth pattern, preservation of normal endometrium, and lymphadenopathy. In all 4 patients, tumors extended to the uterus and vagina or parametrium, and uterine tumors showed relatively homogeneous intensity on both T₁- and T₂-weighted MR imaging. Two patients showed multinodular tumor growth; three revealed pelvic lymphadenopathy; and none had intact endometrium or normal uterine zonal structure. Thus, large tumors with relatively homogeneous signal intensity seemed to be a specific MR finding of uterine lymphoma, and findings of multinodular growth were considered a possible characteristic suggesting the uterine involvement of malignant lymphoma.

Keywords: *magnetic resonance imaging, uterus, malignant lymphoma*

Introduction

Malignant lymphoma rarely affects the uterus except in advanced stages. Favorable prognosis of uterine lymphoma has been reported with appropriate treatment in the earlier stages of the disease.^{1,2} Accurate imaging diagnosis is important because malignant lymphomas are unexpected in the female genital tract, and uterine involvement tends to be misdiagnosed as either inflammatory lesions or other types of malignant tumor, even by biopsied specimen. Only a few publications have addressed the radiological features of uterine lymphoma. Kawakami and associates³ reported diffuse symmetrical enlargement of the uterus without disruption of the endometrial and cervical epithelium to be one manifestation of uterine lymphoma. Kim's group⁴ reported that relatively homogeneous signal intensity in spite of large tumor size is a helpful finding for diagnosing this disease. However, these findings were observed in a limited

number of cases. Therefore, we evaluated the MR images of our own 4 cases of primary uterine malignant lymphoma to explore the specific MR findings in this entity.

Material and Methods

Patient population

We identified 4 women (65 to 69 years; mean, 67 years) with primary uterine lymphoma in the MR database of our institute from 1994 to 2005. All patients initially presented with vaginal bleeding and underwent MR examination of their pelvic organs, including the genital tract. The diagnosis of malignant lymphoma of the uterus was not confirmed in any case at the time of initial MR imaging. In all cases, transvaginal ultrasonography (TVUS), cervical or vaginal and endometrial smear cytology and biopsy, bone marrow biopsy, abdominal computed tomography (CT), and chest radiograph were performed for diagnosis and staging. Diagnoses from Papanicolaou smear of the endometrium or cervix were class 2 for one patient, class 3 for two, and class 4 for one. In the class 4 case, the presence of small round cells were suspicious for malignant tumor, such as malignant lymphoma. Histopathological diagnosis of malig-

*Corresponding author, Phone: +81-267-82-3131, Fax: +81-267-82-9602, E-mail: n-goto@umin.ac.jp

†Present address: Department of General Internal Medicine, Saku General Hospital, 197 Usuda, Saku-shi, Nagano 384-0301, Japan

Table 1. Clinical and imaging findings

Patient Number	Age (years)	Histological type	Stage (Ann Arbor)	Location	Symptom	Size (cm)
1	68	diffuse, large, B cell	stage IA	uterine body, parametrium	vaginal bleeding, abdominal mass	14.5
2	66	diffuse, large, B cell	stage IIB	vagina, cervix and body	vaginal bleeding	10.5
3	65	diffuse, midium, B cell	stage IIIB	vagina, cervix and body	vaginal bleeding, fever	14.5
4	69	diffuse, large, B cell	stage IIIA	vagina, cervix and body	vaginal bleeding	11

nant lymphoma was confirmed by transvaginal biopsy in 2 cases and by endometrial biopsy in two. In addition to vaginal biopsy, in one case, hysterosalpingo-oophorectomy after 4 courses of chemotherapy showed the remaining tumor to be uterine malignant lymphoma. The histological subtype of malignant lymphoma was diffuse large, B-cell type for 3 patients and diffuse medium-sized, B-cell type for one.

MR examination

MR studies were obtained using a 1.5-Tesla superconducting magnet (Phillips, Gyroscan Intera, and Gyroscan Power Trak 1000, Best, The Netherlands). In all patients, sagittal or axial T₁- and T₂-weighted images (T₁WI, T₂WI) and additional coronal or axial T₂WI were obtained, and contrast-enhanced T₁WI was performed using intravenous administration of 0.1 mmol/kg (body weight) of gadopentetate dimeglumine (Magnevist®, Nihon-Schering, Osaka, Japan). T₁WI were obtained using spin-echo sequences (repetition time/echo time [TR/TE]=400 to 550/10 to 15 ms; slice thickness=5 to 7 mm; intersection gap=0.5 to 3.0 mm; matrix=256×192; and number of excitations [NEX]=2 to 4); T₂WI were obtained with fast spin echo (TR/TE=1600 to 2500/100 to 150 ms; slice thickness=5 to 7 mm; intersection gap=0.5 to 3.0 mm; matrix=256×256; NEX=2 to 4). The field of view (FOV) was 280 to 320 mm.

Two radiologists retrospectively interpreted the MR images. We evaluated tumor appearance, including size, location, shape, and signal intensity, presence of septal structures and necrosis, preservation of normal endometrium, and pelvic lymphadenopathy. Tumor size was measured as its maximum diameter. Location was classified as vagi-

na, cervix, corpus, or parametrium. We classified whether the tumor showed diffuse, uniform enlargement of the uterus with preserved normal endometrium. We defined normal endometrium as the innermost uterine layer showing linear high intensity on T₂WI and with strong enhancement, and we judged it to be preserved when we could recognize it without disruption. The signal intensity of the tumor was judged to be low on T₁WI when it showed a low signal, such as in the case of the iliopsoas muscle. On T₂WI, we classified the signal intensity as intermediate when it was higher than that of muscles and lower than that of normal endometrium. We defined the septal structure as the linear structure within the tumor that showed low intensity on T₂WI and contrast enhancement. We defined necrosis as an unenhanced area on T₁WI with contrast that had fluid-like high intensity on T₂WI with irregular borders. We defined lymphadenopathy as a lymph node larger than 1 cm in its minimum axis.

In one case with hysterectomy, we correlated MR and histopathological findings.

Results

Clinical and imaging findings are summarized in Tables 1 and 2.

On MR images, tumor extended to both the vagina and uterus in 3 patients and involved the parametrium in one of them. Both the uterine body and parametrium were involved in one.

All 4 tumors showed relatively homogeneous intermediate intensity on T₂WI and low signal intensity on T₁WI.

In none of the cases did the endometrium seem to remain intact.

Table 2. Clinical and imaging findings

Patient Number	Signal intensity T ₂ WI	Signal intensity T ₁ WI	Septal structure	Necrosis	Intact endometrium	Pelvic lymphadenopathy
1	intermediate	low	+	–	–	–
2	intermediate	low	+	–	–	+
3	intermediate	low	–	–	–	+
4	intermediate	low	–	–	–	+

Fig. 1. A 68-year-old woman with non-Hodgkin's lymphoma (diffuse, large, B-cell type)

A: Sagittal T₁-weighted image shows the large mass with homogeneous low intensity. The endocervical mucosa shows linear high intensity (arrow).

B: Sagittal T₂-weighted magnetic resonance image shows a large mass predominantly involving the anterior wall of the uterine body. The tumor is represented as a mass-forming pattern rather than as diffuse enlargement of the uterus. The uterine mass exhibits uniform intermediate intensity and has septal structures that show low intensity on T₂WI (arrow). Cervix seems to be normal.

C: Sagittal contrast-enhanced T₁-weighted image reveals the enhanced mass. The septal structures are also enhanced more intensely (arrow), and the mass appears multinodular. There is an unenhanced region in the dorsal part of the mass, which was considered due to promontrial compression. Normal endometrium was not recognized.

Fig. 2. A 66-year-old woman with diffuse, large, B-cell lymphoma

A: Axial T₂-weighted image reveals a tumor with homogeneous intermediate intensity. The septal structures of the mass show slightly low intensity (arrow).

B: Axial contrast-enhanced T₁-weighted image reveals enhanced septal structures (arrow). Thus, the uterine tumor appears multinodular. The endometrial cavity is seen with strong enhancement (arrowhead); however, surgical specimen showed no remaining intact endometrium.

C: A photomicrograph of the specimen with hematoxylin-eosin stain obtained by total abdominal hysterectomy after chemotherapy reveals that the tumor has a nodular appearance. However, we cannot find any septal structures macroscopically.

The septal structures of the tumors were seen in 2 patients (Figs. 1, 2).

Only one case had an unenhanced area within the tumor (Fig. 1), which was attributed to promontrial compression. Thus, none of the cases showed necrosis.

In one patient, surgical and pathologic records corroborated these MR images. Grossly, a circumscribed white solid tumor occupied the lower portion of the corpus to the cervix and infiltrated to immediately beneath the serosa. Vaginal involvement seemed to disappear following 4 courses of chemotherapy. The tumor had lobulated contours and a nodular appearance (Fig. 2C) that reflected well on MR imaging. Microscopically, tumor cells proliferated diffusely. The surgical specimen showed stromal linear connective tissue within the tumor that was too small to be visible on MR imaging. In addition, there was no septal structure pathologically to be projected on MR imaging.

Focal areas of necrosis were observed, which may be attributable to chemotherapy.

Pelvic lymphadenopathy was seen in 3 patients.

Discussion

Malignant lymphoma rarely affects the uterus except in advanced stages. Charlton and colleagues¹ reported that one in 175 female extranodal lymphomas were likely to originate in the vagina or uterus. The prevalence in Western countries was reported at 0.008% in primary uterine cervical tumors and 2% in extranodal involvement of the malignant lymphomas in women.² The prognosis of uterine lymphoma has been reported to be favorable when appropriate treatment is performed in the earlier stages of the disease.² The most common presentation of cervical lymphoma is vaginal bleeding. Perineal discomfort or vaginal discharge is also reported.⁵ All our patients present-

Fig. 3. A 65-year-old woman with diffuse medium-sized, B-cell lymphoma
A: Sagittal T₂-weighted image shows the uterus to be diffusely enlarged. The tumor, with relatively homogeneous intermediate intensity, involves both the endometrium and myometrium (arrow). There are neither septal structures nor normal endometrium.
B: Sagittal contrast-enhanced T₁-weighted image reveals weaker enhancement of the tumor (arrow) compared to the outer myometrium.

Fig. 4. A 69-year-old woman with diffuse large B cell lymphoma
A: Sagittal T₂-weighted image shows diffuse tumor involvement of the vagina, uterine cervix and body, and parametrium. The tumor exhibits homogeneous relatively high intensity. Partly intact endometrium can be recognized (arrow).
B: Axial T₂-weighted image exhibits tumor involving not only the uterus, but also the parametrium. Right external iliac and obturator lymph node swelling are also seen.

ed with vaginal bleeding. Abdominal or back pain is also reported in cases with involvement of the uterine body,² and one of our patients showed abdominal mass caused by uterine lymphoma involvement. The age of the 27 reported patients with uterine lymphoma ranged from 20 to 80 years (mean 42.2 years).⁶ The average age of our patients was higher than that of the reported cases.

The cervix and vagina were reported to be more commonly affected than the uterine body.² In our series, however, none of the tumors was limited to one part; in three of 4 patients, both vagina and

uterus were involved, probably because of the tumor's aggressiveness. The histological subtypes of lymphoma of our cases were all diffuse, B-cell type, which was the common high-grade lymphoma.

The gross manifestations of uterine lymphoma have been reported to be various, ranging from small lesions localized in the endometrium to large tumors involving the entire uterus. There are 2 common classifications of developing uterine lymphomas, uniform uterine enlargement and mass formation, and in the latter type, the masses

formed are subcategorized as multinodular mass, endocervical polyp, and submucosal mass.⁷ According to literature on pathology, the most common gross manifestation of uterine lymphoma is diffuse symmetrical enlargement of the uterus without mucosal abnormality.^{3,6,8} Suzuki and associates also suggested that an intact junctional zone was a specific feature of uterine lymphoma because lymphoma cells might infiltrate the entire layer of the uterus without destroying the normal uterine architecture.⁷ However, in all our cases, both normal uterine endometrium and junctional zone were indistinct on MR imaging. Our one case of surgically proven uterine lymphoma revealed diffuse infiltration by tumor cells beneath the serosa without intact endometrium. As Kawakami's group mentioned, diffuse uniform enlargement of the uterus without mucosal abnormality might be seen in limited cases of primary uterine lymphoma. Diffuse uniform enlargement of the uterus without intact endometrium was seen in our one case. Like this case, when endometrium or cervical epithelium was involved, it was difficult to differentiate uterine lymphoma from other carcinoma, such as endometrial or cervical carcinoma.

Kim and colleagues⁴ reported large tumor size with relatively homogenous signal intensity on MR imaging to be a useful finding for diagnosing uterine lymphoma. The average tumor size of our patients was 10 cm, and the signal intensity of the tumors was also relatively homogenous on both T₂WI and T₁WI in all cases. It is reported that hemorrhage and necrosis were rare in uterine lymphoma in pathological literature.^{6,9} This relatively homogenous signal intensity seems to be the result of these pathological features. However, tumoral necrosis of lymphoma is infrequent but can occur when the mass is sufficiently large.⁹

T₂-weighted and contrast-enhanced MR images of 2 patients demonstrated septal structures within the tumors. The tumors seemed to consist of multiple nodules divided by the septal structure. One of these patients underwent hysterosalpingo-oophorectomy after chemotherapy. Macroscopically, the surgical specimen revealed the tumor to have a lobulated contour and nodular appearance. However, septal structure within the tumor was not proved histologically. Masses formed where lymphoma cells clustered comparatively densely, and the aggregative formation of these masses made them appear large and multinodular. We speculate that the septal structures on MR imaging reflect the extracellular matrix separating blocks of the lymphoma cells. Harris's group⁶ reported that the cut surface of the uterus involved by lymphomas was

firm, often multinodular, and fairly demarcated from the adjacent tissue. Follicular lymphoma tends to form follicle and often appears multinodular, but the lymphoma subtypes of our cases were all diffuse large- or medium-sized, B-cell types. Therefore, the reason why lymphoma cells produce multinodular growth patterns is unclear. To our knowledge, this growth pattern of uterine lymphoma on MR imaging has not been previously reported. It may be another finding that suggests lymphomas involving the uterus.

Yamamoto and colleagues reported that small-cell carcinoma of the uterus showed symmetrical uterine enlargement of the uterus with inhomogeneous enhancement on MR imaging.¹⁰ Except for the enhancement pattern, the MR findings of uterine small-cell carcinoma resemble those of uterine lymphoma. Histopathological characteristics of small-cell carcinoma, such as diffuse monotonous proliferation without hemorrhage or necrosis, also resemble malignant lymphoma. Therefore, small-cell carcinoma may mimic uterine malignant lymphoma on images.

In addition, metastatic disease to the uterus is rare, but its appearance on MR can resemble that of primary uterine lymphoma. The most common primary sites are the breast and stomach. On MR images, metastatic disease to the uterus shows diffuse enlargement and abnormally high or low signal intensity throughout the myometrium on T₂WI.¹¹ If the lesion exhibits high signal intensity, it is difficult to differentiate metastatic disease from uterine lymphoma.

Conclusion

Although our study population is limited, we conclude that large uterine mass with relatively homogeneous signal intensity is one of the MR characteristics of uterine lymphoma, as previously reported. In addition, the multinodular appearance seems to be another MR characteristic that suggests uterine lymphoma.

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