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Vaginal Lymphoma with Immune Thrombocytopenic Purpura: An Unusual Case Report

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Key Words

Non-Hodgkin's lymphoma · Immune thrombocytopenic purpura · Vagina · Transvaginal ultrasonography · Magnetic resonance imaging

Abstract

The female genital tract is rarely the initial site of presentation in lymphoma or leukemia. We report a case of non-Hodgkin's lymphoma (NHL) presenting initially in the vagina. The patient, a 75-year-old woman, had a history of immune thrombocytopenic purpura (ITP). She presented with a chief complaint of genital bleeding and introital pain. On transvaginal ultrasonography, a vaginal tumor with an irregular wall was detected, and the internal echo showed a hypoechoic and echogenic pattern. Ultrasonography and magnetic resonance imaging (MRI) suggested that the vaginal tumor was likely to be a hematoma or a hemorrhagic tumor arising from ITP. Incision and resection for a hematoma or a hemorrhagic tumor were carried out in response to genital bleeding, introital pain, and pathological diagnosis. Postoperative microscopic examination confirmed that the tumor was a vaginal NHL. The final diagnosis using the Ann Arbor staging system was high-stage (stage IV) NHL. The patient received chemotherapy, and she remains in remission for 42 months after treatment.

Introduction

Lymphoma and leukemia can both affect the female genital tract [1–7]. However, involvement of these organs usually arises as a secondary manifestation of a systemic

disease [1, 2]. Clinically unrecognized lymphoma or leukemia in the gynecologic area at initial presentation is rare [1–7]. Although there have recently been a few reports on lymphoma or leukemia of gynecologic organs, the number of case reports remains small. Additionally, to our knowledge, vaginal non-Hodgkin's lymphoma (NHL) with immune thrombocytopenic purpura (ITP) has not been reported previously. Here we report such an unusual case.

Case Report

A 75-year-old postmenopausal woman had consulted a gynecologic clinic with a chief complaint of slight genital bleeding and introital pain. She had no gravida, and her medical history included a supra-abdominal hysterectomy due to myoma uteri at the age of 48 years. She was referred to our institution to be evaluated and to receive treatment for her complaint. Upon pelvic examination, an egg-sized and slightly firm tumor was visible at the posterior aspect of the left vaginal wall. It became apparent that the genital bleeding was due to a breach in the surface of the vaginal tumor. Magnetic resonance imaging (MRI) of the pelvis also revealed the tumor on the left posterior vaginal wall. On T1-weighted images, the approximately 30 mm-long tumor showed a high-intensity signal in comparison with urine and isointensity to subcutaneous fat (fig. 1a). On T2-weighted images, the tumor showed a low-intensity signal in comparison to urine and a high-intensity signal in comparison to the uterine cervix (fig. 1b). Cytological examination of a uterine cervical smear was negative. A pathological examination of tissue fragments obtained from the breach of the bleeding tumor revealed inflammation with abundant lymphoid cells. A definitive diagnosis of malignant lymphoma was difficult to establish. The results of the initial laboratory examination were normal except for thrombocytopenia ($4.3 \times 10^9/l$) and slight increases in blood glucose and C-reactive protein (CRP) levels (table 1). The patient was diagnosed with ITP and received prednisolone 20 mg/day orally. Pathological and aspiration cytology samples obtained from bone marrow showed no abnormalities. Chromosomal analysis of the peripheral blood also showed normal results.

The patient postponed treatment because of a fracture of her left wrist. Four months later, when she consulted our institution again, the vaginal tumor had increased to the size of a small fist. On transvaginal ultrasonography, the tumor had a diameter of about 71×57 mm and the internal echo had a predominantly hypoechoic area with an irregular thin layer of echogenic material. The tumor wall was irregular and slightly thickened. In addition, the cystic lesion was poorly demarcated (fig. 1c). Because her platelet count was low, the patient received a blood transfusion of platelets on the eve of the operation and on the operation day. Our preoperative diagnosis of the vaginal tumor was left vaginal hematoma or hemorrhagic tumor derived from ITP. An operation was carried out for the purpose of tumor resection and pathological diagnosis. Several firm, rough and over thumb-sized white masses were obtained from the blood in the vaginal tumor (fig. 2). A drain was placed in the vaginal wound, so as to avoid the possibility of hematoma formation, and the cavity was closed. The total amount of blood lost during resection was 268 g. On transvaginal ultrasonography on the 4th day after the operation, the tumor was visible again in the posterior aspect of the left vaginal wall. It appeared to be heterogeneous and sponge-like. In addition, it contained thick irregular septations. Solid areas probably represented synechiae or clotted blood. The margin of the tumor was remarkably irregular. Echo findings indicated again that the tumor was a hematoma or a hemorrhagic tumor (fig. 3a).

Postoperative microscopic findings revealed numerous atypical lymphoid cells (fig. 3b; i, ii). The majority of these lymphoid cells had large and round cleaved cytoplasm with round nuclei of various sizes and predominant nucleoli. Immunohistochemical staining of the lymphoid cells was positive for CD20 and CD79a. The cells were negative for CD3, CD5, and CD10. Staining for Ki-67 was also positive (fig. 3b; iii–v). These results of immunohistochemical examination indicated a diagnosis of infiltration of B-cell origin (table 2). Postoperative histological examination confirmed the diagnosis of diffuse large B-cell lymphoma (DLBCL). Staging was undertaken with thoracoabdominal computed tomography (CT). The enlarged left external iliac and paraaortic lymph nodes are shown. However, the superficial nodes were not involved. The final diagnosis using the Ann Arbor staging system was high-stage (stage IV) NHL. The patient received chemotherapy with cyclophosphamide, adriamycin, vincristine and prednisolone (CHOP) as an initial therapy. She remains in remission for 42 months after treatment.

Discussion

Several authors have reported lymphoid neoplasms such as lymphoma and leukemia manifesting in gynecological organs [3–10], but the total number of such cases remains small. In autopsy studies of patients with NHL, the uterus was found to be involved in approximately 0.5% of cases and the vagina in 2% [4]. NHL more commonly involves multiple peripheral nodes and extranodal sites [1, 2]. Although NHL originates often at a particular tissue site, the tumors are usually widely disseminated by the time of diagnosis [1]. The distinction between a primary extranodal lymphoma and secondary involvement of an extranodal site by a lymphoma originating in a lymphoid organ is not easy [6]. Additionally, in late-stage disease, it is usually not possible to determine whether the lymphoma originated in the genital tract and spread to the lymphoid tissues or vice versa [6].

DLBCL is one of the more common subtypes of NHL, accounting for 45% of all lymphomas [2, 4], and the mean age of patients with DLBCL is about 60 years [2]. In addition, DLBCL is the most frequent type occurring in the female genital tract, including the vagina, irrespective of the primary and secondary site of the lymphoma [1, 2, 4]. It may manifest in lymph nodes or in extranodal sites [1, 2]. Common extranodal sites of involvement include bone, skin, the thyroid, the gastrointestinal tract, and lung. Lactate dehydrogenase (LDH) is elevated in more than 50% of patients [2]. The most frequent primary symptom of vaginal malignant lymphoma is vaginal bleeding; other symptoms include abdominal pain, introital mass, and urinary complaints [5, 6]. The most common clinical finding is a vaginal, cervicovaginal or pelvic mass [5]. The mean age at presentation of vaginal lymphoma is 65 years [5]. In previously reported cases, vaginal lymphoma resulted in ill-defined thickening or induration of the vaginal wall [5, 7]. In our previous report of a case of uterine cervical acute lymphoblastic leukemia (ALL) extended into the vagina, the vaginal wall was macroscopically thickened [8], but in the present case, the vaginal wall was not hard or thickened.

ITP is one of the most common causes of acquired thrombocytopenia, and has been estimated to affect about 1 in 10,000 people in the general population [11]. The initial symptoms of ITP include gingival bleeding, hematuria, or genital bleeding [11]. ITP occurs in up to 1% of patients with Hodgkin's lymphoma (HL), and is often diagnosed after HL in these patients [11].

Transvaginal ultrasonography and MRI are effective examinations for evaluating the status of tumors in gynecologic organs. In the literature, the most common ultrasound findings of malignant lymphoma are a hypoechoic mass with a homogeneous internal echo structure [12, 13]. If the internal echo pattern of the tumor changes from a homogeneous to a heterogeneous pattern, this indicates cystic change associated with necrosis of part of the tumor [12]. On the other hand, in the early stages of formation, the hematoma appears as a hypoechoic mass, but it becomes moderately echogenic after a reorganization within the hematoma has occurred [14]. In the current case, the patient had bleeding due to ITP, and the internal echo pattern of the tumor, which contained irregular septations and solid areas probably representing clots, seemed to be based on ITP. On MRI, lymphoma of the uterine cervix has been reported to be isointense to muscle on T1-weighted images. Mixed intermediate- and high-intensity signals are suggesting necrosis on T2-weighted images [9]. Another report on MRI of lymphoma in the vagina showed low-intensity signal on T1-weighted images, and relatively high-

intensity signal with respect to muscle on T2-weighted images [10]. It was difficult to distinguish the vaginal tumor from common vaginal hematomas based solely on the findings of ultrasonography and MRI, because there were no specific findings as lymphoma and tumor appeared to be modified by hemorrhage in the tumor due to ITP.

Although lymphomas affecting the female genital tract are uncommon, evidence is accumulating that such tumors may be underdiagnosed, both because they are unexpected in these sites and because they may be misdiagnosed as either inflammatory lesions or other types of malignant tumor [4]. In our case, a preoperative pathological examination of the obtained tissue fragments from the bleeding vaginal tumor revealed inflammation with many lymphoid cells. The etiology of lymphomas involving the female genital tract is essentially unknown [6]. However, some causal relationship between chronic inflammation and cervical lymphoma may be present, as suggested by the observation that a benign reactive infiltrate often surrounds the lymphoma [6].

In conclusion, we have described an unusual case of vaginal lymphoma (NHL) with ITP. In this patient, it was difficult to distinguish between lymphoma and hemorrhagic tumor before operation, and the definitive diagnosis was based on the results of the postoperative histological examination.

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Table 1. Laboratory data on initial examination

Peripheral blood count	
RBC	$4.09 \times 10^{12}/l$
Hb, g/dl	13.5
Ht, %	39.1
PLT	$4.6 \times 10^9/l$
WBC	$6.8 \times 10^9/l$
Neu, %	66.5
Eos, %	1
Baso, %	0.5
Lym, %	25
Mono, %	6
Biochemistry	
TP, g/dl	7.4
ALB, g/dl	3.9
AST, U/l	19
ALT, U/l	18
LDH, U/l	200
ChE, U/l	314
ALP, U/l	255
T-Bil, mg/dl	0.7
BUN, mg/dl	13
CRE, mg/dl	0.64
UA, mg/dl	3.7
Na, mEq/l	142
K, mEq/l	4.1
Cl, mEq/l	106
Ca, mg/dl	9.2
Glu, mg/dl	113
CRP, mg/dl	0.51
Blood coagulation	
APTT, s	30.3
PT, %	98

Table 2. Immunohistochemical staining

CD20	(+)
CD79 α	(+)
CD3	(–)
CD5	(–)
CD10	(–)
Ki-67	(+)

Fig. 1. Preoperative findings. **a** MRI of the pelvis (T1-weighted images at the sagittal plane). An approximately 30 mm-long tumor (arrows) showing a high-intensity signal in comparison with urine and isointensity to subcutaneous fat. The uterine corpus was already extirpated. **b** MRI of the pelvis (T2-weighted images at the sagittal plane). Tumor showing a low-intensity signal in comparison to urine and a high-intensity signal in comparison to the uterine cervix. **c** Transvaginal ultrasonography of the vaginal tumor. Ultrasonography revealed a tumor of about 71 × 57 mm in diameter with an irregularly shaped cyst wall and heterogeneous internal structure.

Fig. 2. Macroscopical findings. Contents of the vaginal tumor. Several firm white masses were obtained from the blood.

Fig. 3. Postoperative findings. **a** Transvaginal ultrasonography findings at 4 days after the operation. The internal echo revealed a heterogeneous, sponge-like interior suggesting an intratumoral hemorrhage. **b** Microscopical findings of the vaginal tumor. i, ii: Hematoxylin and eosin staining (HE) (i $\times 100$, ii $\times 200$). Numerous atypical lymphoid cells can be seen. iii–v: Immunohistochemical staining ($\times 200$). Lymphoid cells showed findings positive for CD20 (iii), CD79 α (iv) and Ki-67 (v). The cells were negative for CD3, CD5, and CD10.

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