Successful Treatment of Primary Vaginal Diffuse Large B-Cell Lymphoma Using Chemotherapy

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SUMMARY

Objective: Non-Hodgkin's lymphomas (NHL) rarely affect the vagina. As a result, a standard treatment has not been defined.

Case Report: A 34-year-old female virgin patient with a primary vaginal NHL stage IEA, diffuse large cell B lineage, showed an excellent response to cytotoxic chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone) without surgery or radiotherapy. She had experienced no recurrence after 40 months.

Conclusion: In young patients who wish to preserve their fertility, chemotherapy alone may be the treatment of choice for primary diffuse large B-cell NHL of the lower female genital tract. [*Taiwan J Obstet Gynecol* 2008; 47(3):334–337]

Key Words: chemotherapy, diffuse large B-cell, vaginal non-Hodgkin's lymphoma

Introduction

Lymphomas account for 3.5% of all malignant neoplasms in females. Non-Hodgkin's lymphomas (NHL) represent 70–80% of all lymphomas. NHL can involve extranodal sites, most often the gastrointestinal tract and skin [1]. Primary NHL of the vagina is extremely rare. Only 0.5% of extranodal lymphomas in women are likely to originate in the female genital tract [1,2].

We describe a case of primary NHL of the vagina (stage IEA) treated successfully using chemotherapy alone. The associated literature is also discussed.

Case Report

A 34-year-old female virgin presented with a 3-month history of irregular vaginal bleeding and pelvic pain. She had no fever, weight loss or night sweats. As the patient was a virgin, vaginal examination could not be been performed. Transabdominal ultrasonographic examination revealed a 7 × 6-cm solid, homogenous, regular-shaped mass confined to the cervicovaginal junction, with no extension to the pelvic wall or other related structures (Figure 1).

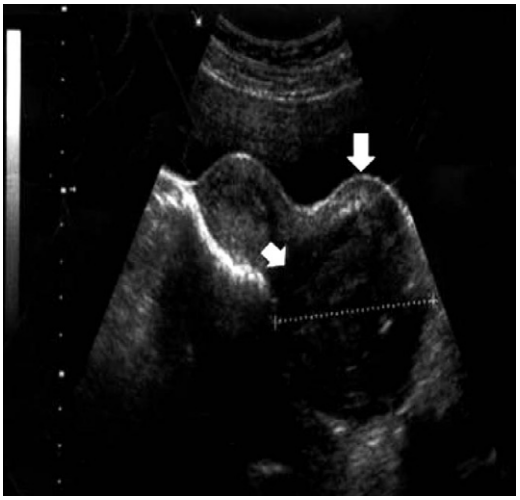

Figure 1. Ultrasound image of the pelvic mass (arrows).

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Abdominopelvic magnetic resonance imaging showed diffuse enlargement of the cervix and vagina, which exhibited homogenous intermediate signal intensity and internal necrosis, without destruction of the endometrial lining of the uterus. On admission, the following laboratory parameters were noted: white blood cell count 8.0×10^3/L (normal range, 4.5–11.0 $\times 10^3$/L), hemoglobin 15 g/dL (normal range, 13.5–18 g/dL), platelet count 240×10^3/L (normal range, 150–400 $\times 10^3$/L), segmented leukocytes 0.65 (normal range, 0.4–0.70), lymphocytes 0.30 (normal range, 0.29–0.44), sedimentation rate 8 mm/hr. The serum biochemistry profile was completely normal. Tumor markers were within the normal range. Based on the physical examination and laboratory findings, a surgical exploration was planned, with a suspected diagnosis of cervical myoma.

During laparotomy, the uterus and both ovaries were seen as normal in shape, but a bulky, solid, fixed, irregular mass was seen at the cervicovaginal junction, expanding throughout the whole vagina and parametrium, extending to the pelvic side walls. The uterine corpus and cervix were seen just above this mass. It was revealed that the tumoral mass originated from the cervicovaginal area and that all other visceral organs and the peritoneal area were normal. The mass had no obvious surgical cleavage, and after sharp and blunt dissection, it was determined to be unresectable and could not be removed completely. After multiple biopsies, the operation was stopped. Histopathologic diagnosis identified the tumor as a diffuse large B-cell NHL. There was no component of low-grade lymphoma suggestive of a mucosa-associated lymphoid tissue lymphoma origin (Figure 2).

Based on the Ann Arbor system used for staging NHL, the patient was diagnosed with IEA primary vaginal large B-cell NHL disease. She was treated with six cycles of a CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone)-containing chemotherapy regime. During the treatment period, no hematologic or other organ system-related side effects developed. She received no radiation therapy.

The patient was treated using this approach for 40 months post-diagnosis, after which the tumor had completely disappeared and there was no further clinical evidence of the disease.

Discussion

Although secondary involvement of the female genital organs can be seen in up to 40% of disseminated lymphomas, primary genital lymphomas are rarely encountered. They are most commonly localized in the ovaries (49%), uterus (29%) and Fallopian tubes (11%) [3]. Primary vaginal lymphomas are very rare. Chorlton et al reviewed 9,500 cases of lymphomas in women and found only four cases of primary vaginal lymphomas, i.e. an incidence of 1 in 2,375 cases [4]. Ten cases of primary vaginal diffuse large B-cell lymphomas were reported in the literature between 1994 and 2007 (Table).

Vaginal lymphomas may occur in patients of a wide range of ages (20–80 years). The most common histologic subtype is diffuse large B-cell lymphoma. Clinical symptoms usually include vaginal bleeding (70%), perineal discomfort (40%), and persistent vaginal discharge (20%). An abdominal or pelvic mass may be found on clinical examination. Fever, night sweats and weight loss are unusual symptoms. Cervical cytology is usually negative. Colposcopic biopsy may give false negative results [1,2]. Our patient was 34 years old and presented with abnormal vaginal bleeding and pelvic pain.

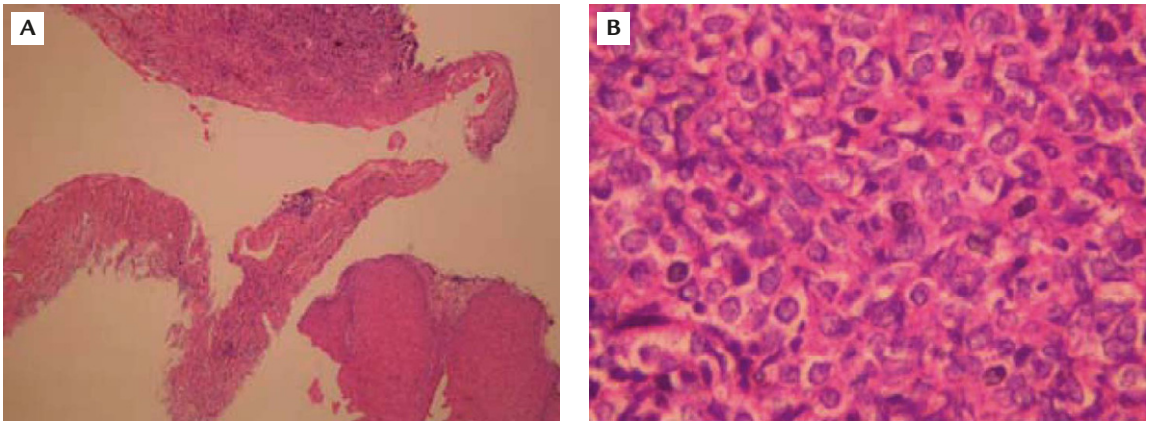

Figure 2. Histologic examination of the samples. (A) A low magnification photomicrograph of the infiltrate showing the distinct nodular architecture (original magnification ×40). (B) At high magnification the infiltrate is composed of a mixture of small cleaved and large lymphocytes (original magnification ×400).

Table. Clinical characteristics of the reported primary vaginal diffuse large B-cell lymphoma cases between 1994 and 2007

Author	Age (yr)	Gynecologic symptom	Ann Arbor stage	Therapy	Follow-up
McNicholas et al [15]	39	Vaginal bleeding	NR	Pelvic RT-CT*	NED 6 mo
Höffkes et al [16]	20	Postcoital bleeding	IEA	CHOP	NED 36 mo
Skinnider et al [17]	67	Vaginal bleeding	IIEA	ACOP-Pelvic RT	NED 29 mo
Pham et al [18]	76	Asymptomatic	IEA	Pelvic RT-CT†	NED 51 mo
Engin et al [10]	30	Vaginal mass	IEA	CHOP	NED 28 mo
Domingo et al [19]	45	Asymptomatic	IEA	Pelvic RT-CT‡	NED 28 mo
Garavaglia et al [11]	38	Vaginal mass	IEA	MACOP-B	NED 120 mo
Signorelli et al [12]	57	NR	IEA	CHOP	DOOD 146 mo
	56	NR	IEA	CHOP	NED 40 mo
	54	NR	IEA	Pelvic RT-CHOP	NED 36 mo

**Cyclophosphamide, vincristine, etoposide, prednisone; †cyclophosphamide, vincristine, mitoxantrone, prednisone; ‡cyclophosphamide, doxorubicin, vincristine, prednisone. NED = no evidence of disease; DOOD = dead of other disease; CT = chemotherapy; RT = radiotherapy; NR = not reported; CHOP = cyclophosphamide, Adriamycin, vincristine, prednisone; MACOP-B = methotrexate, Adriamycin, cyclophosphamide, vincristine, prednisone, bleomycin.*

Histopathologic evaluations can be used to diagnose NHL. Computerized tomography and magnetic resonance imaging are also useful for diagnosis and staging, but their specificities are low [9].

Malignant mixed Müllerian tumor, epithelioid leiomyosarcoma, degenerative myoma, endometrial stromal tumors including endometrial stromal sarcoma, melanoma and extra-osseous Ewing's sarcoma/primitive neuroectodermal tumor should be kept in mind in the differential diagnosis of vaginal NHL [6]. In our case, we performed laparotomy with the suspected diagnosis of cervical myoma, but morphologic and phenotypic features supported a diagnosis of a diffuse low-grade malignant NHL, consistent with a diffuse large B-cell lymphoma.

Because of its rarity, there is no established treatment protocol for primary NHL of the vagina. According to the literature, the mainstay of the treatment for primary genital lymphomas is radiotherapy alone, or in combination with surgery and/or chemotherapy [7,8]. The efficacy and safety of chemotherapy as first-line therapy is still debatable. Höffkes et al reported a complete pathologic and clinical response in one case of NHL of the vagina stage IEA after CHOP chemotherapy [16]. Similar results were obtained by Engin et al [10]. Garavaglia and colleagues reported on a patient with stage IEA NHL of the vagina who underwent complete remission with MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, prednisone, and bleomycin) alone [11].

The destruction of reproductive organs and resulting infertility is a significant disadvantage of radiotherapy in young women. Therefore, cytotoxic chemotherapy should be considered for these patients who wish to preserve their fertility. Even if the tumor does not respond to cytotoxic chemotherapy, salvage radiotherapy has been shown to be successful in the majority of cases [12]. Signorelli et al treated three patients with NHL of the vagina using a CHOP regime and observed two complete responses, though one patient with persistent disease after chemotherapy needed external beam radiotherapy to obtain a complete clinical response [12]. In this report, the patient underwent CHOP chemotherapy (six weekly cycles) which was well tolerated and completed without adverse effects. Radiation therapy was not given.

The prognosis for extranodal lymphomas is usually poorer than that for nodal lymphomas because of inaccurate or delayed diagnoses [1]. However, if pelvic lymphomas are diagnosed at earlier stages, the prognosis can be excellent compared with other gynecologic malignancies, with a 5-year survival rate ranging from 80–90% [13,14].

In conclusion, because of the rarity of primary NHL of the vagina, the optimal therapy is unknown. For young patients with primary large B-cell NHL of the lower female genital tract who wish to retain their fertility, chemotherapy alone may be the treatment of choice.

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