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CASE REPORT

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Primary large B-cell lymphoma of the cervix: A case report and review of literature

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Abstract

The primary diffuse large B-cell lymphoma (DLBCL) of the uterine cervix is extremely rare. In the present study, we described two cases of DLBCL of the uterine cervix in reproductive-aged women complaining of postcoital bleeding, recurrent vaginal discharge, and abnormal uterine bleeding.

KEYWORDS

female genital tract lymphoma, non-Hodgkin's lymphoma, R-CHOP chemotherapy, uterine cervix lymphoma

1 | INTRODUCTION

Primary lymphomas of the female genital tract are a quite rare entity, accounting for 0.2%–1.1% of all cases of extra-nodal lymphoma.[1] Extra-nodal non-Hodgkin lymphoma (NHL) affects the gastrointestinal tract and central nervous system; however, it is additionally sometimes recognized in the breast, thyroid, prostate, bones, and female genitalia tract.[2] Patients usually present with abnormal vaginal bleeding, and clinically, the cervix is expanded by a subepithelial mass without ulceration. Given the lymphoma is unexpected at the cervix, it might be not diagnosed by a pathologist in Papanicolaou (Pap) smear and also might be mistaken with other types of malignant neoplasms or inflammatory processes.[3] Due to the rarity of this diagnosis, management approaches are anecdotal and there is no clear consensus. However, general guidelines can be suggested.

Here, we reported two cases of diffuse large B-cell lymphoma (DLBCL) of the uterine cervix. The importance of presenting to these patients includes the following: (1) cervical lymphoma is a rare entity, (2) complaints of postcoital bleeding are important, and should be taken seriously, and (3) abnormal appearance of the cervix should be evaluated with colposcopy by a gynecology oncologist or experienced gynecologist.

2 | CASE PRESENTATION

2.1 | Case 1

A 38-year-old woman gravida 1, para 1, presented to the Department of Obstetrics and Gynecology in Firoozgar medical center in Tehran, Iran, in October 2018 with compliant of postcoital bleeding for the past 6 months. Her medical history and family history of cancer were completely uneventful. She was not immunologically compromised nor was taking any immune-modulating medication. Cervical cytology performed 1 year ago was normal. Physical examination revealed no abnormal finding on systemic examination. No palpable cervical, axillary, or inguinal lymphadenopathy was found. Pelvic examination revealed abnormal bulky

cervix with no parametrial involvement in rectovaginal examination.

Punch biopsy of the cervical mass was performed. Diffuse infiltration of the exocervical and endocervical stroma by monomorphic population of malignant lymphoid cells with intermediate-to-large, round-to-ovoid, and irregular nuclei surrounded by scanty neoplasm was observed. Neutrophilic infiltration and large foci of necrosis were also noted. In immunohistochemical study, the neoplastic cells were positive for B-cell markers and negative for pancytokeratin. A diagnosis of diffuse large B-cell NHL was made (Figure 1).

Chest computed tomography (CT) scan, bone marrow examination, serum tumor markers, and lactate dehydrogenase were unremarkable. Pelvic magnetic resonance imaging (MRI) showed infiltrative mass of the cervix measuring about 40 mm with mild enhancement and restricted diffusion without local invasion to the rectum or bladder. Contrast-enhanced axial abdominopelvic CT revealed cervical enlargement and some small lymph node with SAD = 6 mm in internal iliac vessels (Figure 2).

Staging was compatible with stage I (E) DLBCL of the cervix. The patient was discussed in a multidisciplinary session and she was candidate for systemic R-CHOP (rituximab, cyclophosphamide, adriamycin, vincristine, and prednisolone) chemotherapy. Chest and abdominopelvic PET scans were performed after completion of chemotherapy, which indicated complete remission (Figure 3).

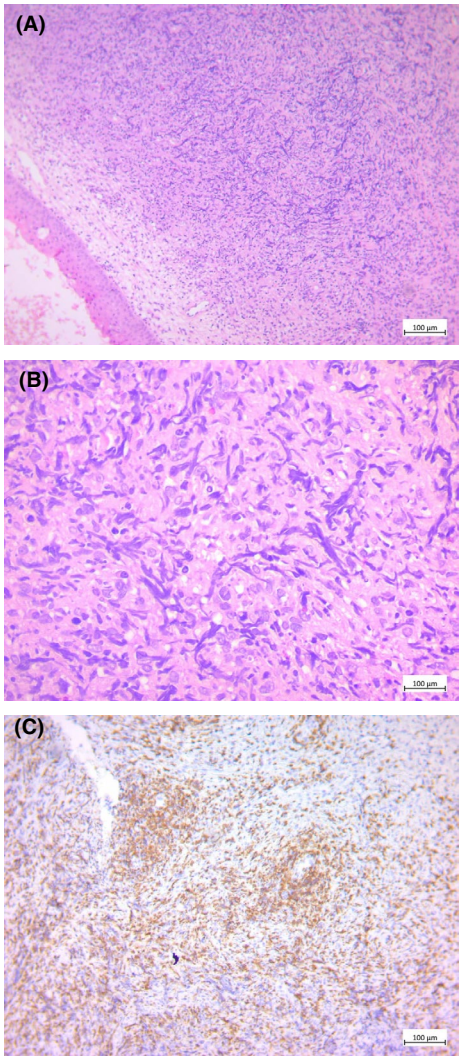

FIGURE 1 (A,B) Diffuse infiltration of the ectocervical and endocervical stroma by the monomorphic population of malignant lymphoid cells. The cells had intermediate-to-large, round-to-ovoid, and irregular nuclei surrounded by scanty neoplasm. The neutrophilic infiltration and large foci of necrosis were also noted. (C) Photomicrograph showing CD20 positive in immunohistochemical study

2.2 | Case 2

A 30-year-old woman gravida 1, para 1, with complaint of a 1-year history of postcoital bleeding, abnormal uterine bleeding, and recurrent vaginal discharge presented to the Department of Obstetrics and Gynecology in Firoozgar Hospital in Tehran, Iran in August, 2019. Her past medical history and family history for cancer was negative. High-risk subtypes human papillomavirus (HPV) testing was positive for HPV-16, although cervical cytology was negative for intraepithelial lesion or malignancy. No palpable cervical, axillary, or inguinal lymphadenopathy was found. Pelvic examination revealed a fixed hypertrophic cervix with abnormal consistency. There was parametrial involvement in rectovaginal examination.

Endometrial biopsy, endocervical curettage (ECC), and colposcopy were performed. Colposcopic evaluation revealed abnormal vessels. Pathology examination showed low-grade cervical intraepithelial neoplasia (CIN I). A month later, punch biopsy of the cervix was repeated due to the more severe and persistent vaginal discharge. A diagnosis of diffuse large B-cell NHL was

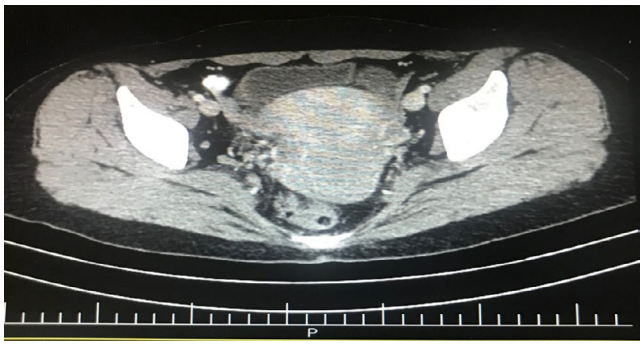

FIGURE 2 Axial section of CT scan showing the increase in size of the cervix with no cervical mass

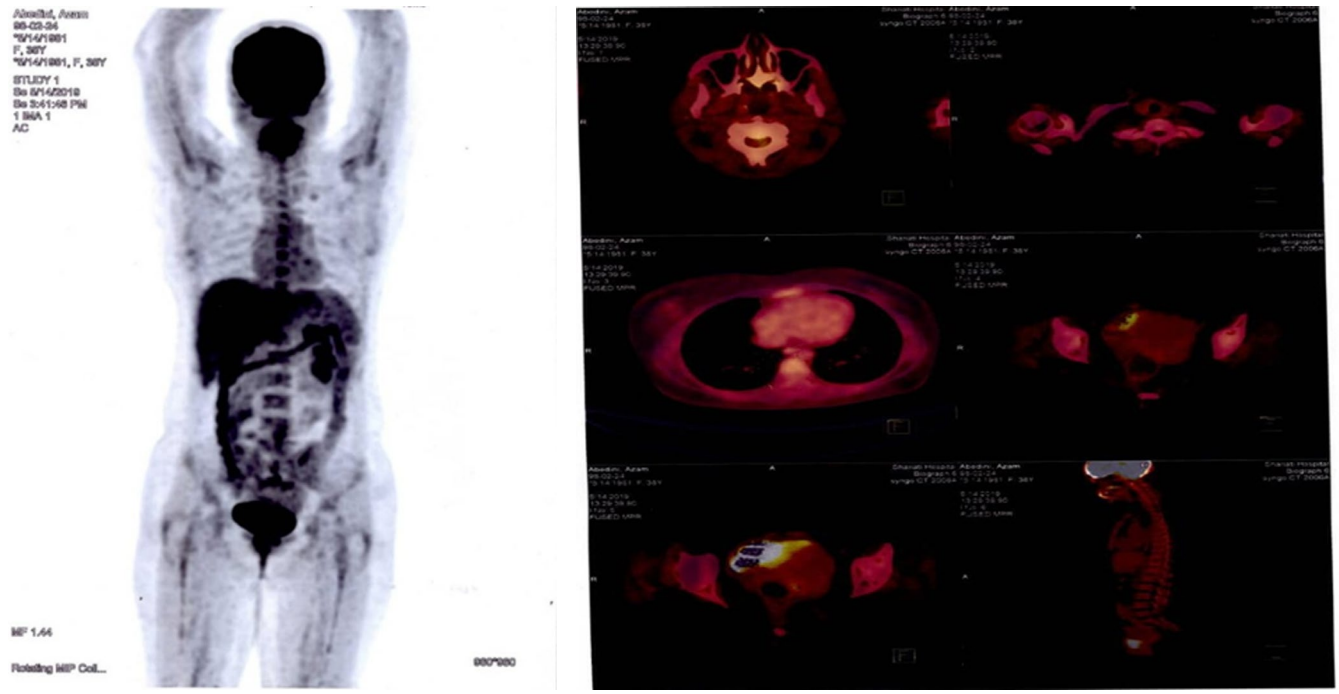

FIGURE 3 PET scan after eight cycles of chemotherapy showing almost complete regression of the cervical mass and its extensions

reported (Figure 4). Transvaginal sonography demonstrated a heterogeneous and infiltrative mass of the cervix measuring about 40*54 mm with increased vessels flow. Contrast-enhanced axial CT of abdominopelvic showed a 63*74 mm hypodense solid mass in cervix with heterogeneous enhancement and some pathologic lymph node in bilateral iliac vessels with SAD of 8 mm (Figure 5). Pelvic MRI revealed a 40 mm infiltrative circumferential mass of the cervix with vaginal wall involvement. The mass had restricted diffusion in diffusion-weighted imaging[4] and heterogenous post gadolinium enhancement. The liver, spleen, and para-aorta were normal. Diagnosis of large B-cell CD 20 positive lymphoma of the cervix was confirmed in a review by an expert pathologist. The stage of the tumor considered as II (E) using the Ann Arbor system. After discussion at tumor board, patient underwent R-CHOP-based chemotherapy. During one-year follow-up, there was no evidence of clinical recurrence in the chest and abdominopelvic PET scans and she delivered a healthy term baby. She was in a good condition during postpartum period.

3 | DISCUSSION

In this case report, we described two women presented to the Gynecology oncology clinic with symptoms of postcoital bleeding and negative cervical cytology ultimately diagnosed as diffuse large B-cell lymphomas (DLBCL). Primary female genital lymphomas are extremely rare neoplasms that make up 0.2% to 1.1% of all extra-nodal cases.[2] The age range at the time of the diagnosis is generally wide (20–80 years) with an average age of 40–59 years old.[5] The two presented cases in this article were younger than the mean age reported in the medical literature. In the literature review, DLBCL were the most frequent histologic type reported, as in the two cases introduced in the present article.[6] Others included follicular lymphoma, Burkitt lymphoma, and mucosal-associated lymphoid tissue lymphoma.[7] Table 1 depicts some cases of DLBCL of the uterine cervix reported in the literature.

A Study by Nasioudis et al. revealed most cases, similar to ours, are diagnosed at an early stage (I or II) according to the Ann Arbor classification. Unlike other gynecological malignancies, primary lymphomas of the genital tract have a good prognosis, even when diagnosed at an advanced stage.[7]

Due to the fact that lymphoma infiltrate the cervical stroma and the squamous and glandular epithelial lining is preserved in the early stages, the cervical cytology is nondiagnostic in most cases.[3] In a study conducted by Dursun et al.,[8] abnormal cervical cytology was observed in 41% of women affected with primary cervical lymphoma. Cervical cytology was reported to be negative for intraepithelial dysplasia or malignancy in the second presented case. Histologic diagnosis might be difficult, which occasionally necessitates histological review and immunohistochemical study by an experienced pathologist. Initially, the result of cervical biopsy with a guide by colposcopy in the latter case was incorrectly reported as CIN I only, which could be a concurrent

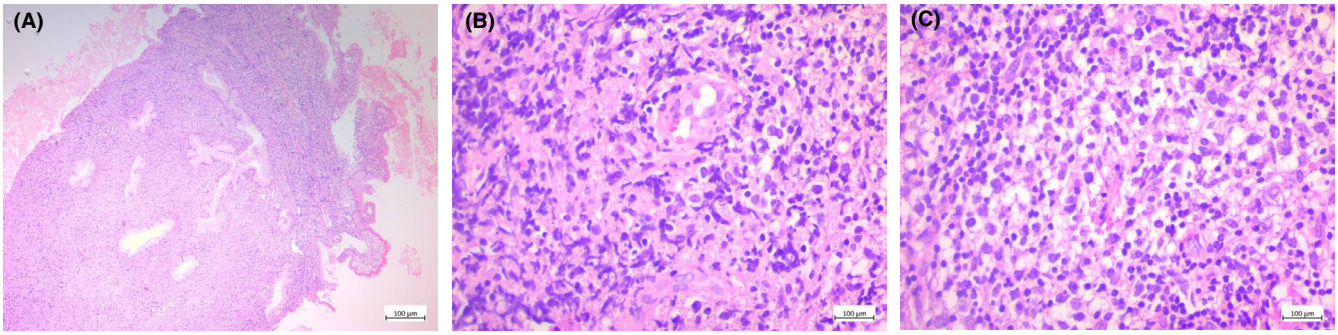

FIGURE 4 (A) Photomicrograph showing tumor cells infiltrate stroma without destroying glandular or squamous epithelium. (B,C) Round and loosely arranged neoplastic cells with scanty cytoplasm. Neutrophilic infiltration was also noted

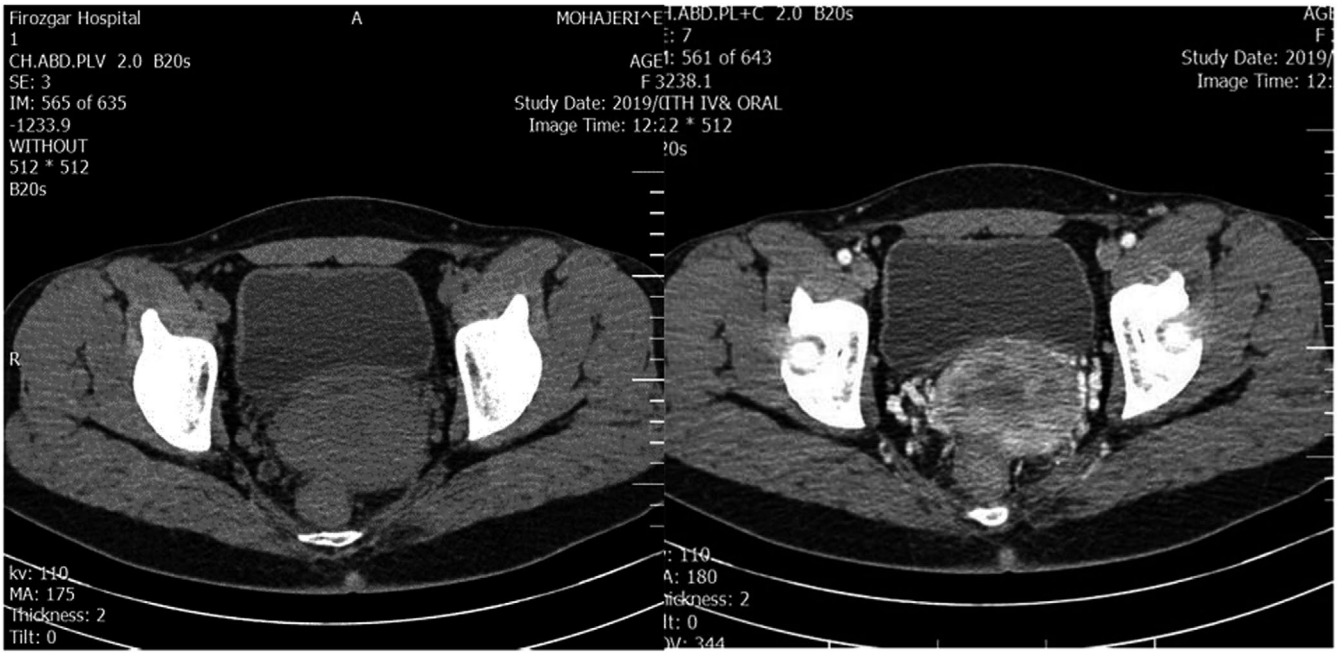

FIGURE 5 Axial section of computed tomography showing a 63*74 mm hypodense solid mass in cervix with heterogeneous enhancement

finding of HPV effect with undiagnosed cervical lymphoma. It is important to distinguish malignant lymphoma from undifferentiated cervical carcinoma, sarcoma, and small-cell neuroendocrine carcinoma because cervical lymphoma can be successfully treated in spite of locally advanced disease.[9]

The best standard treatment option for primary malignant lymphoma of the uterine cervix should be assigned to the individuals; however, treatment approaches include surgery, chemotherapy, or radiotherapy. Clearly, treatment with systemic therapy using combination chemotherapy regimens is indicated in the majority of cases.[6,7,9] The recommended regimen is R-CHOP, which is rituximab, a monoclonal antibody to CD20, cyclophosphamide, doxorubicin, vincristine, and prednisolone.

There is no evidence that radical gynecologic surgery is advantageous and should be avoided.[10] Surgery has been used as an adjunct to chemotherapy, either before or after chemotherapy, especially in patients with stage I or II disease. Radiation therapy following chemotherapy should be considered, particularly for bulky tumors (>10 cm) and residual disease, which does not completely respond to chemotherapy.[6,11]

Young patients who wish to preserve fertility can be counseled about the possibility of conization followed by chemotherapy and close follow-up. Conception has been reported in patients treated successfully, although the outcome of these pregnancies is unclear due to their overall rarity.[12] One of the reported cases in the present study had a successful pregnancy one year after the completion of treatment.

Masashi Ohe et al.[13] in 2012 reported a 71-year-old woman with DLBCL lymphoma, which was treated with clarithromycin and prednisolone along with radiotherapy, and complete remission was achieved after 6 months.

TABLE 1 Some cases of diffuse large B-cell lymphoma of the cervix in the literature review

Authors	Age (years)	Clinical presentation	Cervical cytology	Imaging finding	Treatment	Follow up
Aminimoghaddam, 2021	30	Postcoital bleeding, abnormal uterine bleeding, and recurrent vaginal discharge	Positive for HPV-16, NILM	A 4-mm infiltrative circumferential mass of the cervix with vaginal wall involvement	Six courses of R-CHOP	Delivered a healthy term baby and asymptomatic after 2 years
González-Mariño, 2021[16]	49	Pelvic pain, vaginal discharge and bleeding	ASC-H	Soft tissue lesion of homogeneous appearance measuring 5.7 × 7.5 × 5 cm in CT	R-CHOP chemotherapy	Asymptomatic after 10 years
P. D. Menon, 2021[17]	48	Abnormal vaginal bleeding, fixed mass in the left inguinal area measuring 8 × 8 cm	Numerous relatively monomorphic, intermediate-to-large lymphocytes with high nuclear to cytoplasmic ratio	Multilobulated hyperattenuating left inguinal lesion measuring up to 14.2 × 8.9 cm	Not mentioned in the article	Not mentioned in the article
Gengrong Liu, 2020[18]	74	Fever, night sweats, and a weight loss of 4 kg in the past year	Not performed	Enlargement of the cervix accompanied by increased metabolism in PET-CT	R-CHOP regimen	Patient refused to undergo a regular assessment
M. Del, 2020[19]	36	Vaginal bleeding, pelvic pain, dysuria and asthenia without fever	NILM one year ago	An 8-cm cervical mass right parametrium, compressing the right ureter and causing a unilateral hydronephrosis in MRI	Six courses of R-CHOP	Disease-free after follow-up of 15 months
H. Murata, 2020[20]	50	Asymptomatic, bulky cervix in examination	NILM	A 5 cm cervical mass with invasion of the left parametrium and vagina	Six courses of R-CHOP	Not mentioned in the article
H. Murata, 2020[20]	46	Abnormal genital bleeding	NILM	A 6-cm cervical mass with invasion of the right parametrium and right urinary tract	seven courses of R-CHOP	Free of recurrence after 3.5 years

Abbreviation: NILM, Negative for intraepithelial lesion or malignancy.

Maureen et al. in 2018 reported a 55-year-old woman with compliant of AUB and diagnosis of DLBCL. After multi-agent chemotherapy with 3 cycles of R-CHOP, remission was achieved.[14] Mousavi Seresht et al. in 2018 reported a 31-year-old woman with AUB and diagnosis of non-Hodgkin's B-cell lymphoma of the cervix. She received chemotherapy of CHOP regimen, and on the 14th month of follow-up, she was disease-free with no signs of a recurrence.[15]

4 | CONCLUSION

Patients with symptoms including vaginal discharge, postcoital bleeding, and abnormal uterine bleeding initially seek the gynecologists. It might be not diagnosed by a pathologist in Papanicolaou (Pap) smear and also might be mistaken with other types of malignant neoplasms or inflammatory processes. To prevent delays in diagnosis, it is important for gynecologists and pathologists to identify these cases as early as possible and take the appropriate management to improve therapy.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

S A was the surgeon involved in the case and contributed to writing of the article. E S contributed to writing the first draft. S NT contributed to writing the final draft and revision of the article.

ETHICAL APPROVAL

Informed consent was provided for the purpose of publication of images and other clinical information in this case report. In addition, no identifying personal details are included in this manuscript.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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