Review

Primary diffuse large B-cell lymphoma of uterine cervix diagnosed by cytology and concurrent cervical biopsy: a case report and literatures reviews since 1980

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Malignant lymphoma of the uterine cervix is rare with non-specific clinical presentation and is difficult to diagnose via cervical cytology. The current study presents a case of primary malignant lymphoma of the uterine cervix diagnosed via initial conventional smear cytology and subsequent cervical biopsy. We present a case of an 81-year-old woman with vaginal bleeding post-urination. The conventional smear cytology showed scattered large atypical lymphoid cells with necrotic debris. The concurrently biopsied specimen revealed large monotonous atypical lymphoid cells, which were immunoreactive for CD20 with high Ki-67 proliferative index, consistent with diffuse large B-cell lymphoma (DLBCL). Due to the transfer of the patient to another hospital, any other examinations associated with staging were not performed. Although rare, the likelihood of malignant lymphoma should be considered while screening for cervical cancer through cytology using Pap smear or conventional smear. Cytological screening may be useful for the early diagnosis of malignant lymphoma of the uterine cervix. Immediate and appropriate treatment can be initiated with a quick and accurate diagnosis. Herein, we report a case of primary uterine cervical DLBCL and review the literatures comprising 106 cases studies with 255 cases of primary cervical lymphoma reported since 1980 including clinical and histological characteristics through MEDLINE database.

Keywords

Uterine cervix; Lymphoma; Chemotherapy; Primary; B-cell

1. Introduction

Primary lymphoma of the uterine cervix (PLUCX) and corpus accounts for only 0.5% of extra-nodal malignant lymphomas, and among all cervical malignancies, the overall incidence of PLUCX is less than 1% [1]. Lymphomas of the female genital tract may be a primary manifestation of this area or may occur as genital recurrences or metastases that were initially diagnosed elsewhere. Kosari *et al.* [2] defined PLUCX as lymphomas localized in the uterine cervix without any myometrial involvement and without any evidence of leukemia at the time of diagnosis. When the uterine cervix is affected secondarily by malignant lymphoma in the setting of a systemic disease or when the biopsy specimen is encountered, the diagnosis is usually not difficult. However, when the uterine cervix is a primary site based on the clinical presentation or when the lesion is encountered on a cytological specimen (Pap smear or a conventional smear slide), diagnosis may be difficult. Herein, we report a case of diffuse large B-cell lymphoma (DLBCL) arising in uterine cervix which was diagnosed initially via cytology and confirmed by concurrently biopsied specimen. In addition, we review the 106 articles containing 255 cases of PLUCX available on PUBMED since 1980 and discuss the current knowledge on diagnosis, management, and of PLUCX. The study was approved by the ethics committee of Chosun university hospital (Institutional Review Board of Chosun university hospital, Gwangju, Korea), who waived the requirement for written informed consent due to the nature of the study.

2. Case presentation

An 81-year-old female patient with a history of hypertension and hyperlipidemia presented with vaginal bleeding for 3 months. Tele-cervicography revealed whitish hemorrhagic mass lesion with ulcerative surface occupying the uterine cervix (Fig. 1A). Pelvic ultrasound scan showed an irregular round hypoechoic mass approximately 7.0 cm in diameter. The abdominal computerized tomography scan showed a uterine mass of 6.7 cm size with intermediate to high signal intensity in T2-weighted image abutting upper to mid rectum suggesting rectal invasion. Moreover, pelvic magnetic resonance imaging scan revealed a heterogeneous enhancing mass, suggesting rectal invasion; however, there was no evidence of pelvic metastasis or uterine body involvement (Fig. 1B, arrow). Cervical cytological examination using conventional smear was performed. The slide revealed a necrotic background and scattered atypical cell clusters and single cells with "small round blue cells" with a high nuclear/cytoplasmic (N/C) ratio, scant cytoplasm, and hyperchromatism (Fig. 2A). Since there was no epithelial component detected, the lesion was suspected to be a nonepithelial malignant tumor, including malignant lymphoma, via cervical cytology. It was classified as "other malignancy" according to the Bethesda System 2001. A punch biopsy of the

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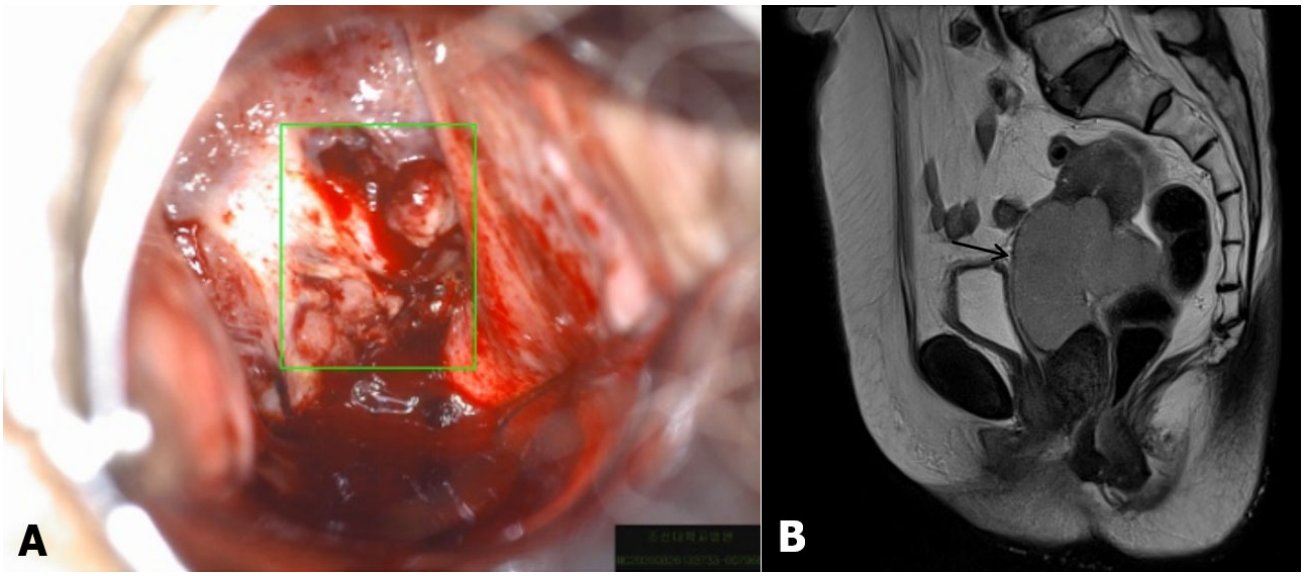

Fig. 1. Telecervicography showed whitish hemorrhagic mass lesion with ulcerative surface occupying the uterine cervix (A). Pelvic MRI revealed heterogeneous enhancing mass, suggesting rectal invasion (B, arrow).

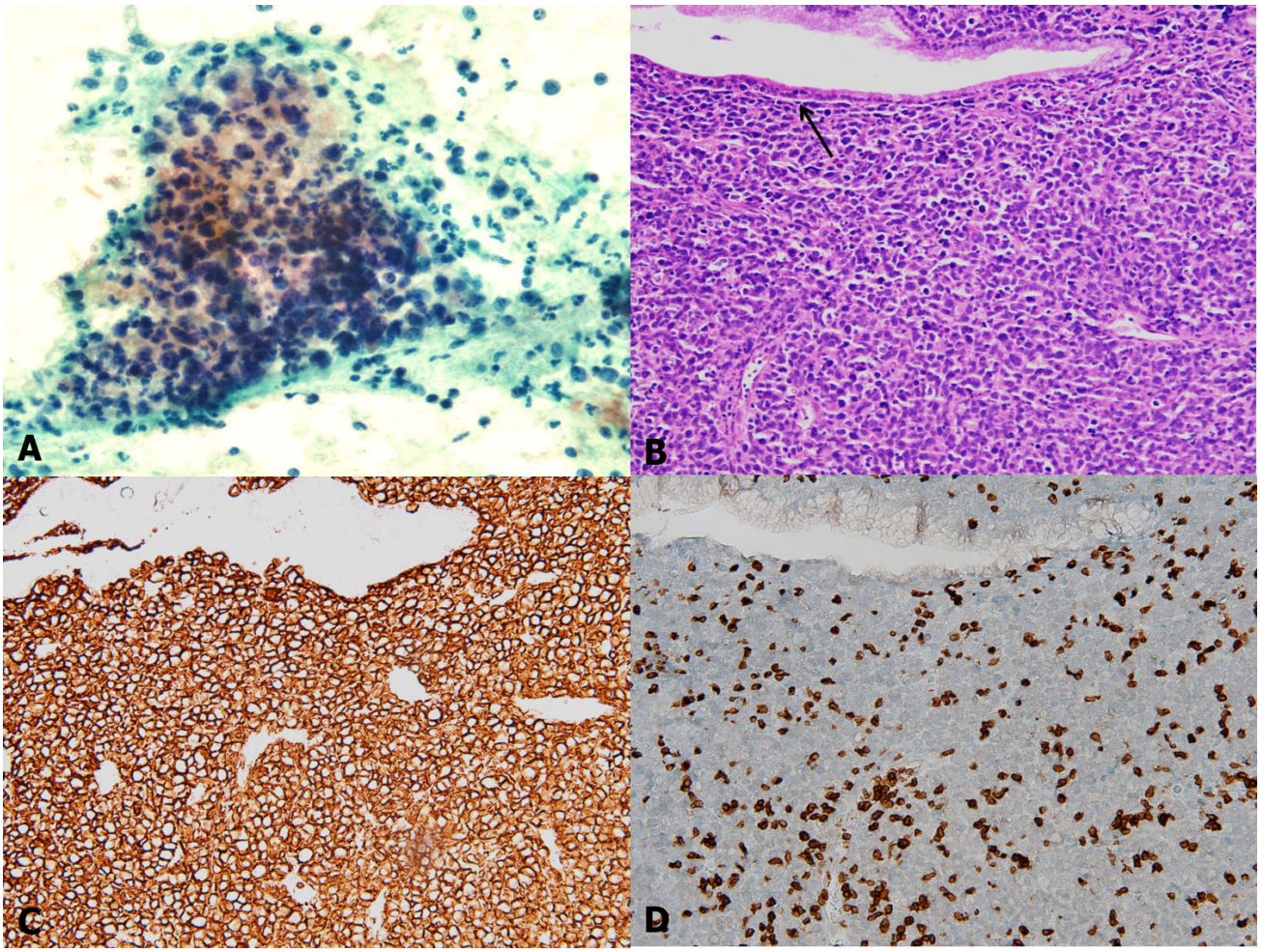

Fig. 2. Cytological examination using conventional smear demonstrated a necrotic background and scattered atypical cell clusters and single cells showing "small round blue cells (A, ×20). The cervical specimen filled with diffuse large and atypical lymphocytes with remnant endocervical glands (B, ×20). Immunohistochemically, the atypical cells were immunoreactive for CD20 (C, ×20) while CD3 (D, ×20) were negative.

uterine cervix was carried out concurrently, and the histological examination revealed diffuse large atypical lymphocytes with remnant endocervical glands (arrow) (Fig. 2B). Immunohistochemically, the atypical cells tested negative for epithelial marker, cytokeratin (CK). Most cells were strongly immunoreactive for CD45 (LCA) and CD20 (Fig. 2C) while only scattered, small T-cells were positive for CD3 (Fig. 2D), and staining was diffusely negative. On the basis of histologic and immunohistochemical findings, we diagnosed it as primary cervical DLBCL. The patient was discharged without any treatment in our hospital and lost to follow-up.

3. Discussion

Malignant lymphomas can also affect extra-nodal sites, approximately in one-third of the cases [3]; the most common sites are the gastrointestinal tract and skin [3]. In rare cases, it may affect the female reproductive organs, with the ovaries being the most common site [3], PLUCX is an extremely rare occurrence. As per MEDLINE, since the 1980s, about 250 cases of PLUCX have been reported. We reviewed 106 articles on PLUCX available on PUBMED since 1980 (search term: "uterine cervix", "lymphoma" (Table 1). The previous reports on cervical involvements in the systemic lymphomatous or leukemic conditions were excluded. Table 1 summarizes the characteristics and findings of these 106 articles with comprising 255 cases. In our literature review, the mean age of the patients was 51 years, and the most common clinical symptoms were vaginal bleeding including hypermenorrhea, menorrhagia, postcoital bleeding, atypical uterine bleeding, and dysfunctional uterine bleeding. Other symptoms included vaginal spotting, vaginal discharge, abdominal pain, pelvic pain, menolipsis, micturition pain, lower back pain, dyspareunia, hydronephrosis, and other urinary symptoms. Out of 168 cases, the most common histologic types were identified. The most common histologic type was DLBCL (53.6%, n = 90/168), followed by follicular lymphoma (18.3%, n = 4/168), unclassified B-cell lymphoma (7.3%, n = 13/168) and unclassified non-Hodgkin lymphoma. Rarely, mucosa-associated lymphoid tissue lymphoma, marginal zone lymphoma, peripheral T-cell lymphoma, NK/T-cell lymphoma, Burkitt lymphoma, small lymphocytic lymphoma were also reported. In the literatures of 1980's and 1990's, by classification by "Working formulation", diffuse pattern of lymphoma was common (14.2%, 24/168 cases).

Of the 106 case studies analyzed in this review, treatment protocols were identified for 156 patients from 84 papers. No standardized therapy modality was found. Various treatments and treatment combinations were used. Surgery such as total abdominal hysterectomy (TAH) and bilateral oophorectomy (BSO), TAH, or radical hysterectomy (RH), radiotherapy (RTx), and various combination of chemotherapies (CTx) as well as combinations of these treatment modalities have been used. Of the 156 patients, 44 (28.2%) underwent hysterectomy with or without CTx or RTx. Additionally, most of the patients received CTx; Of the 156 patients, (96/156) underwent CTx, either alone or in combination with surgery or RTx. Combination CTx including cyclophosphamide, doxorubicin, vincristine with or without rituximab, is the most common treatment for patients with PLUCX. Hilal *et al.* [107] suggested that a specialized pathological assessment may be required for planning the treatment for PLUCX. They proposed that local surgery followed by a comprehensive staging is the most reasonable therapy for women with early stage PLUCX both for diagnostic and therapeutic reasons. In case of localized disease, there is no evidence for an adjuvant treatment; therefore, adjuvant RTx, CTx or targeted therapies cannot be recommended outside of clinical trials [106] .

Despite the wide variation in treatments carried out for patients with PLUCX in the previous studies, the prognosis of this disease was favorable. In the pooled analysis of our literature review, individual follow up data of 117 patients (70 studies) were reported, out of which 109 patients (93.2%) achieved complete remission or disease-free state. Moreover, several cases of successful pregnancy and delivery after treatment of PLUCX have beed reported [39, 55, 95]. Based on these post-treatment outcomes, we concluded that PLUCX has an excellent prognosis despite the lack of a standard treatment, therapeutic uncertainty, and a resulting variability of applied treatments. Hilal *et al.* [107] reviewed 246 cases of primary and recurrent cervical lymphomas and reported that most cases are occurring at an early stage, had the histological appearance of a DLBCL, and a good 5-year overall survival rate of $> 80\%$. This is consistent with the 5-year survival rate of 73% reported by Harris *et al.* [106] in a case series including 21 women with lymphoma of uterine cervix and with the 5-year survival rate of 86% reported by Ahmad *et al.* [30] in their case series including 9 women.

In cervical cytology, the detection rate for malignant lymphoma cells has been reported to be 30%–40% [9]. Some researchers described that unlike epithelial tumor, lymphomas arise from the stroma, and that cervical cytology is not sensitive enough to recognize them [3]. However, in our case, the classical cervical cytological features of a malignant lymphoma from the conventional smear were so prominent; that we were able to detect the malignant lymphoma at an early stage from the cervical cytology. As per Cahill *et al.* [108], in cervical cytology, the classical features of lymphoma cells are as follows: a dispersed monomorphic cell population, high N/C ratios, coarse granular nuclear chromatin, focally cleaved nuclei, and the presence of prominent nucleoli. Based on the morphological access, the important differential diagnosis includes chronic cervicitis with lymphoid hyperplasia, malignant melanoma, carcinosarcoma, small cell carcinoma, and so on. Usually, immunohistochemistry can effectively differentiate these tumors from cervical lymphoma. Also, subtype of lymphoma can be determined based on the morphology and immunohistochemical profiles.

Table 1. Summary of primary uterine lymphoma reported in the literature since 1980.

Ref. No.	Author	Journal	Year	No	age	Sx.	histology	Tx.	Px.
[4]	Murata *et al.*	Gynecol Oncol Rep	2020	2	48 (m)	R-E/VB	DLBCL (2)	R-CHOP (2)	CR (2)
[5]	Mohammed *et al.*	Cureu	2020	1	51	VS	CHL	CTx	Recur
[6]	Mathilde *et al.*	Gynecol Oncol Rep	2020	1	36	1)	DLBCL	R-CHOP	NED
[7]	Gui *et al.*	Oncol Lett	2019	3	48 (m)	VB	DLBCL (2) MALTL	R-CHOP CHOP (2)	CR (3)
[8]	Roberts *et al.*	Gynecol; Oncol Rep	2018	1	55	VB	DLBCL	R-CHOP →LAVH, BSO	CR
[9]	Koyanagi *et al.*	Oncol Lett	2018	1	74	R-E	DLBCL	R-CHOP	CR
[10]	Yang *et al.*	Diag Cytopathol	2017	1	69	2)	H/G BCL	R-CHOP	F/U -1
[11]	Takimoto *et al.*	Oncol Lett	2017	1	71	VB	MZL	R-CHOP	CR
[12]	Mutoh *et al.*	Rinsho Ketsueki	2017	1	37	aSx	DLBCL	4)	CR
[13]	Kosari *et al.*	Int J Gynecol Pathol	2017	1	49	VB	PTCL	CHOP + RTx	DOD
[14]	Cubo *et al.*	Medicine (Baltimore)	2017	1	51	VB	DLBCL	R-CHOP	NED
[3]	Sharma *et al.*	Case Rep Hematol	2016	1	61	VB	DLBCL	R-CHOP,+ MTX	CR
[15]	Zhou *et al.*	Clin Nucl Med	2016	1	31	menolipsis	DLBCL	R-CHOP	NED
[16]	Singh *et al.*	J Obstet Gynaecol India	2016	2	56 (m)	AP (2)	DLBCL (2)	RTx. + R-CHOP CHOP + RTx	NED (2)
[17]	Regalo *et al.*	BMJ case Rep	2016	1	40	pain	DLBCL	R-CHOP	NED
[18]	Omori *et al.*	Diag Cytopathol	2016	1	65	VB	NK/T-CL	CHOP	DOD
[19]	Kojs *et al.*	Ginekol Pol	2016	1	54	VD,VP	DLBCL	CHOP, R-CHOP	CR
[20]	Fratoni *et al.*	Int J Gynecol Pathol	2016	1	-	-	DLBCL	-	-
[21]	Dorosavljevic *et al.*	J Obstet Gynaecol	2016	1	-	-	FL		
[22]	Wang *et al.*	Taiwan J Obstet Gynecol	2015	1	54	pain	NK/T-CL	TAH, USO	RF
[23]	Pather *et al.*	Int J Gynecol Pathol	2015	6	-	-	H/G BCL	-	-
[24]	Li *et al.*	Clin Case Rep	2015	1	43	VB	NLHPL	CTx	NED
[25]	Mouhajir *et al.*	J Obstet Gynaecol India	2014	1	49	VB	DLBCL	CHOP, RTx	CR
[26]	Mandato *et al.*	Anticancer Res	2014	1	44	VB	DLBCL	Mc→R-CHOP	CR
[27]	Igwe *et al.*	Gynecol Oncol Rep	2014	1	22	edema	DLBCL	R-CHOP	NED
[28]	Cao *et al.*	Ann Hematol	2014	1	-	-	BCL	CTx + RXT	NED
[29]	Bellevicine *et al.*	Diagn Cytopathol	2014	1	79	VB	DLBCL	-	-
[30]	Ahmad *et al.*	Int J Gynecol Cancer	2014	9	-	-	DLBCL	R-CHOP	-
[31]	Hashimoto *et al.*	Gan To Kagaku Ryoho	2013	1	45	VB	DLBCL	CHOP + RTx	CR
[32]	Groszman *et al.*	J Ultrasound Med	2013	1	25	R-E	DLBCL	R-CHOP	CR
[33]	Bull *et al.*	Int J STD AIDS	2013	1	47	VD	DLBCL	R-CHOP	CR
[1]	Calli *et al.*	J Cytol	2012	1	65		DLBCL	R-CHOP	CR (3)

Table 1. Continued.

Ref. No.	Author	Journal	Year	No	age	Sx.	histology	Tx.	Px.
[34]	Yalta *et al.*	J Cytol	2012	1	56	-	BCL	TAH USO PL	-
[35]	Vasudev *et al.*	Online J Health Allied Sci	2012	1	52	VB	DLBCL	TAH BSO	CR
[36]	Parnis *et al.*	Case Rep Hematol	2013	1	54	VB	DLBCL	R-CHOP + RTx	NED
[37]	Daniel *et al.*	Radiologia Brasileira	2012	1	80	LBP	DLBCL	CTx	-
[38]	Binesh *et al.*	BMJ Case Rep	2012	1	85	VB	DLBCL	R-CHOP	DOOD
[39]	Upanal *et al.*	Aust N Z J Obstet Gynaecol	2011	2	50 (m)	VD, /pain, dyspareunia	DLBCL (2)	R-CHOP (2)	CR (2)
[40]	Parva *et al.*	J Obstet Gynaecol Can	2011	1	21	DUB	DLBCL	CHOP	NED
[41]	Dyer *et al.*	Br J Haematol	2012	2	25 (m)	R-E/VB	DLBCL (2)	CHOP, R-CHOP	CR (2)
[42]	Ustaalioglu *et al.*	Leuk Res	2010	1	65	VB	DLBCL	R-CHOP + RTx	CR
[43]	Naki *et al.*	Turk J Haematol	2010	1	82	VD	DLBCL	TAH BSO→R-CHOP	NED
[44]	Baijal *et al.*	J Can Res Ther	2009	1	44	VB	DLBCL	R-CHOP + RTx	CR
[45]	Amna *et al.*	BMJ Case Rep	2009	1	46	VB	DLBCL	RCVP + RTx	NED
[46]	Okudaira *et al.*	Gan To Kagaku Ryoho	2008	1	68	VB	FL	CHOP	NED
[47]	Köhler *et al.*	Rev Bras Ginecol Obstet	2008	2	44 (m)	aSx/VD	NHL-B (2)	CHOP + RTx (2)	NED (2)
[48]	Hanprasertpong *et al.*	Asian Pac J Cancer	2008	1	25	VB, VD	DLBCL	CHOP	CR
[49]	Coon *et al.*	J Clin Oncol	2008	1	56	VS	MALT	TAH BSO→ RTx + R	NED
[50]	Ab Hamid *et al.*	Singapore Med J	2008	1	43	VB	DLBCL	CHOP	NED
[51]	Signorelli *et al.*	Gynecol Oncol	2007	10	47 (m)	-	DBCL (10)	CHOP (5)/CVP + CHOP/TAHBSO (3)	NED (10)
[52]	Lu *et al.*	Zhonghua Bing Li Xue Za Zhi	2007	16	58	-	DLBCL (12) FL (4)	-	
[53]	Lorusso *et al.*	Oncology	2007	1	29	-	NHL	CTx→Surgery	NED
[54]	Korcum *et al.*	Ann Hematol	2007	1	67	VB	FL	CHOP, RTx	NED
[55]	Jiang *et al.*	Zhonghua Fu Chan Ke Za Zhi	2007	10	-	-	-	-	
[56]	Semczuk *et al.*	Pathol Res Pract	2006	1	43	R-E	DLBCL	CHOP	CR
[57]	Gonzalez-Cejudo *et al.*	Eur J Obstet Gynecol Reprod Biol	2006	1	26	VB	DLBCL	TAH	
[58]	Frey *et al.*	Leuk Lymphoma	2006	4	46 (m)	VB	DLBCL (3) MZL (1)	CTx→TAH(1)/TAH→CTx (2)/TAH (MZL)	NED (4)
[59]	Cantu DL *et al.*	Int J Gynaecol Cancer	2006	1	56		DLBCL	CTx + RTx	
[60]	Van Renterghem *et al.*	Eur J Gynaecol Oncol	2005	2			DLBCL		
[61]	Murad *et al.*	J Coll Phys Surg Pak	2005	1	62	VB	NHL	-	-
[2]	Kosari *et al.*	Am J Surg Pathol	2005	16			DLBCL (11); FL (4)		

Table 1. Continued.

Ref. No.	Author	Journal	Year	No	age	Sx.	histology	Tx.	Px.
[62]	Huang *et al.*	Pathol Res Pract	2005	1	42		Burkitt L	surgery	DOD
[63]	Goker *et al.*	Int J Gynecol Cancer	2005	1	-	-	BL	CTx	-
[64]	Garavaglia *et al.*	Gynecol Oncol	2005	3	37	aSx. (2).	DLBCL (3)	MACOP-B (2) TAHBSO→CHOP	NED (3)
[65]	Dursun *et al.*	Gynecol Oncol	2005	2	50 (m)	VD/R-E	DLBCL FL	CHOP	NED (2)
[66]	Thyagarajan *et al.*	Br J Radiol	2004	1	41	VB	H/G BCL	CTx + RTx	CR
[67]	Mikami *et al.*	Gynecol Oncol	2004	1	52	VB	CLL/SLL	RH + RTx + CTx	DOD
[68]	Szantho *et al.*	Gynecol Oncol	2003	1	56	VD	DLBCL	CHOP→RH BSO LND	NED
[69]	Kahlifa *et al.*	Int J Gynecol Pathol	2003	1	32	VB	DLBCL	CTx+RTx	CR
[70]	Hu *et al.*	Zhonghua Zhong Liu Za Zhi	2003	28	-	-	-	-	
[71]	Au *et al.*	Am J Hematol	2003	1	45	VD	DLBCL	CTx	CR
[72]	Rossi *et al.*	Arch Pathol Lab Med	2001	1	46	VB	MALTL	CTx→TH+	NED
[73]	Liro *et al.*	Ginekol Pol	2001	1	58	VD	DLBCL	RH BSO LND→CTx	-
[74]	Vang *et al.*	Mod Pathol	2000	9	57 (m)	VB, AP, aSx, R-E, AUB (5)	DLBCL (7) MZL,FL	CTx + RTx (3)/TAHBSO/ Cone/CTx + RTx/CTx /Cone + CTx/Cone+ CTx + RTx	NED (7) DOD(2)
[75]	Pomares *et al.*	An Med Interna	2000	1	-	-	TCL	RTx	
[76]	Kostopoulos *et al.*	Pathol Res Pract	2000	1	64	VB	DLBCL	TAH BSO	
					(m)	VB		CHOP	
[77]	Wang *et al.*	J Reprod Med	1999	1	35	aSx	L/G BCL	RH	
[78]	Grace *et al.*	Eur J Gynaecol Oncol	1999	2	44 (m)	aSx	FL/DLBCL	CHOP + RTx	
[79]	Nasu *et al.*	J Obstet Gynaecol Res	1998	1	64	VD	DLBCL	CTx (THP-COP)	CR
[80]	Lee *et al.*	Austral Radiol	1998	2	66 (m)	VB (2)	NHL (2)	RH→RTx/RH→RTx	CR/NED
[81]	Kaito *et al.*	Rinsho Ketsueki	1998	1	80	VB	DLBCL	CHOP + RTx	
[82]	Chandy *et al.*	J Obstet Gynaecol Res	1998	1	59	VB	NHL	CHOP RTx	NED
[83]	Biswal *et al.*	J Indian Med Assoc	1997	2			-	-	
[84]	Dhimes *et al.*	Cytopathology	1996	1	69	aSx	DLBCL	TH	-
[85]	Al-Talib *et al.*	Cytopathology	1996	2	-	-	H/G BCL	CTx	
[86]	Abbas *et al.*	Am J Roentgenol	1996	1	25	VB	PLL	embolization→CTx→mass removal	NED
[87]	Winer *et al.*	J Gynecol Obstet Biol Reprod (Paris)	1995	1	78		CBL	TH→CTx + RTx	
						VB,AP, aSx, R-E, AUB (5)	DLBCL (7)	CTx + RTx (3)/TAHBSO/	NED (7)
[74]	Vang *et al.*	Mod Pathol	2000	9	57 (m)		MZL, FL	Cone/CTx + RTx/CTx /Cone + CTx/Cone + CTx + RTx	DOD (2)
[75]	Pomares *et al.*	An Med Interna	2000	1	-	-	TCL	RTx	
[76]	Kostopoulos *et al.*	Pathol Res Pract	2000	1	64	VB	DLBCL	TAH BSO	

Table 1. Continued.

Ref. No.	Author	Journal	Year	No	age	Sx.	histology	Tx.	Px.
[88]	Reynaud *et al.*	J Gynecol Obstet Biol Reprod (Paris)	1995	1			-	-	
[89]	Makarewicz *et al.*	Clin Oncol	1995	3			NHL		
[90]	Figuera *et al.*	Sangre (Barc)	1994	1					
[91]	Rodier *et al.*	J Chir (Paris)	1993	1			NHL		
[92]	Maryniak *et al.*	Eur J Gynaecol Oncol	1993	3			BCL	-	
[93]	Aozasa *et al.*	Cancer	1993	4	53 (m)	VB	DL/DLNC DLC/DMix	CTx + RTx/TH + RTx TH SO + RTx/TH + RTx	DOD (3) DOOD
[94]	Bou Saba *et al.*	J Med Liban	1992	1	45	R-E			
[95]	Pasini *et al.*	Eur J Gynaecol Oncol	1991	1	-	VB	NHL-B	TAHBSO→CHOP	CR
[96]	Muntz *et al.*	Cancer	1991	5	51 (m)		DL (3)/DS/FS	RTx (3)/TAHBSO +RTX/RTx + TAHBSO &LND	NED (5)
[97]	Sandvei *et al.*	Gynecol Oncol	1990	1	22	VB VS	NHL	CHOP	NED
[98]	Ohta *et al.*	Nihon Sanka Fujinka Gakkai Zasshi	1990	3					
[99]	Murotsuki *et al.*	Gan No Rinsho	1989	1	85	VB	DS	TAH	CR
[100]	Khoury *et al.*	Eur J Surg Oncol	1989	2	-	-	-	RTx + CTx	NED
[101]	Cardillo *et al.*	Eur J Gynaecol Oncol	1987	1	-	-	PLL	-	-
[102]	Cardillo *et al.*	Eur J Gynaecol Oncol	1987	1	-	-	PL	-	-
[103]	Taki *et al.*	Acta Cytol	1985	1			BCL		
[104]	Gharpure *et al.*	Indian J Cancer	1985	2	-	-	-	-	-
[105]	Komaki *et al.*	Cancer	1984	3	40 (m)	AP,PD Men&LBP	DL (2) D&S L	RTx (3)	Recur NED (2)
[106]	Harris *et al.*	Cancer	1984	20	42 (m)	VB (11) hematuria, R-E/pain	DL (9) FL (3) DM (3)/IBL (3)/FSC (1) FC (1)	TAHBSO/TAHBSO + RTx/TAH + RTx/TAHBSO + CTx/RTx/RH + RTx//RT + CTx/No	NED (14) DOD (4) Re-cur (2)

(1) hydronephrosis, (2) irritative urinary voiding, (3) urinary incontinence and menometrorrhagia, Men, menorrhalgia; P/D, pelvic discomfort; A/P, abdominal pain; VB, vaginal bleeding; VS, vaginal spotting; VD, vaginal discharge; R-E, routine exam; LBP, lower back pain; aSx, asymptomatic; AUB, abnormal uterine bleeding; DUB, dysfunctional uterine bleeding; CTx, chemotherapy; RTx, radiotherapy; CHOP, combination chemotherapy including cyclophosphamide; doxorubicin; vincristine; prednisone R, Rituximab; (4) Chlamydia trachomatis eradication; CR, complete response; NED, no evidence of decease; DOD, dead of decease; DOOD, dead of other disease; Mc, myomectomy; RS, radical hysterectomy and bilateral salpingo-oophorectom; PL, pelvic lymphadenectomy; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MZL, Marginal zone lymphoma; MALTL, MALT lymphoma; NHL, Non-Hodgkin lymphoma; BCL, B-cell lymphoma; PLL, Plasmacytoid lymphoma; CBL, centroblastic lymphoma; DL, diffuse large; FSC, follicular small cleaved; FC, follicular cleaved; IBL, immunoblastic lymphoma; D&S L, diffuse and small lymphoma; DM, diffuse mixed; DIB, diffuse immunoblastic.

Accurate diagnosis for malignant lymphoma is important to prevent inappropriate gynecological surgeries such as RH and BSO. The clinical diagnosis of cervical lymphoma may be difficult because of the lack of specific symptoms. The most common clinical symptoms have been reported to be vaginal bleeding followed by vaginal discharge, abdominal or pelvic pain, among other symptoms. However, some patients were found to be asymptomatic, which were also identified in the present review. Consequently, the correct diagnosis is often delayed or the condition is misdiagnosed as a solid tumor in the cervix, which results in the disease diagnosed at an advanced stage or that the tumor is initially treated by wide surgical resection followed by CTx with or without RTx.

Since most cervical lymphomas are located subepithelially, unless ulceration is observed, the cervical cytology can be negative. However, cytological test screening may be useful for the early diagnosis of PLUCX. Although rare, the likelihood of malignant lymphoma should be considered while screening for cervical cancer using Pap smear or conventional smears for immediate and accurate diagnosis, and as a result, radical surgery may be avoided.

4. Conclusions

In conclusion, we presented a case of an 82-year-old woman with a primary DLBCL of the uterine cervix, which was initially diagnosed via conventional smear cytology and confirmed via concurrently biopsied surgical specimen. Moreover, we reviewed 106 articles with 255 cases and discussed the clinical and histological characteristics, treatment strategies, and survival outcomes in patients with PLUCX. Accurate and timely diagnosis through cytology and early biopsy can lead to immediate treatment without the need for surgeries such as RH and BSO. Despite its rarity, the differential diagnosis of malignant lymphoma should be included when screening for cervical cancers using cervical cytology.

Author contributions

RH designed and supervised the study. SAK and TKA collected and organized datm and wrote and revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the ethics committee of Chosun University Hospital (Institutional review Board of Chosun university hospital, Gwangju, Korea), who waived the requirement for written informed consent due to the nature of the study.

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Conflict of interest

The authors declare no conflict of interest.

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