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Letter to the Editor

Primary non-Hodgkin lymphoma of cervix successfully treated with rituximab: Positron emission tomography images before and after therapy: A case report

Primary non-Hodgkin's lymphoma (NHL) of the genital tract is extremely rare (0.5%) and mostly originates from the ovary [1,2]. The cervix lymphoma is 0.008% of the all cervix tumors and 2% of the all extranodal lymphomas in the females [3,4]. The most common histological type is diffused large B cell lymphoma (DLBCL) [1,2,5]. Primary cervical carcinoma, sarcoma or benign inflammatory conditions are kept in mind in differential diagnosis [1,6]. Histopathological and immunohistochemical examinations of cervix biopsy specimen are required for definitive diagnosis [1]. In staging, computerized tomography (CT) of the pelvis, abdomen and thorax or position emission tomography (PET–CT) can be used. There is not any established treatment protocol for primary cervix lymphoma (PCL) due to rarity of disease. Radiotherapy (RT), chemotherapy, immunotherapy, surgery, either alone or in combination can be applied [3,7]. Herein we report a case of PCL that was staged and re-evaluated after treatment by using PET–CT. The patient was treated successfully with combination of R-CHOP (Rituximab, cyclophophamide, doxorubucin, vincristine, prednisone) and RT.

A 65-year-old postmenopausal woman presented with vaginal bleeding, fever, weight loss for 4 months. Her past medical and family history was unremarkable. Gynecological examination revealed a diffused enlargement of the cervix without ulcer. Papanicolaou (PAP) smear was normal. CT of pelvis was 9 cm × 8 cm in size mass in the cervix which did not extend through pelvis. The cervix biopsy was performed. Histopathological examination revealed that stroma infiltrated by large cell with scant clear cytoplasm convoluted large nuclei, dispersed chromatin and peripheral nucleoli. The immunohistochemical staining was positive for CD20 and LCA and negative for CD3, HMWCK, LMWCK, vimentin, consequently the diagnosis of DLBCL of the cervix was confirmed. At the systemic evaluation of patient, biochemical tests including LDH and complete blood counts were normal. PET–CT was performed for full staging and any malign uptake except for primary cervix mass (SUVmax 11.2) was detected (Fig. 1A). Bone marrow biopsy was also negative for lymphoma. The patient was staged as IEB according to Ann Arbor staging system. ECOG performance status of patient was 1 and she was in low group with respect to international prognostic index (IPI). After she was treated with six cycles of R-CHOP chemotherapy, PET–CT was repeated and complete response was achieved (Fig. 1B). After that she was treated with external RT to the whole pelvis. A total dose of 3600 Gy in 18 fractions was applied. She well tolerated the therapy without any toxicity. During 10 months of the follow-up, she was well and in the remission.

The presentation may mostly include symptoms of gynecological malignancy such as vaginal bleeding, and the B symptoms including fever, weight loss and night sweat are not usually seen [1,3,6,7]. Incompatible with the literature, she presented with vaginal bleeding, weight loss, fatigue and fever. The diagnosis of early-stage PCL may be confusing because differential diagnosis of systemic disease with local involvement or primary tumor of cervix is difficult [3]. The biopsy of cervix and immunophenotyping is necessary to differentiate lymphoma from malign or benign disease of the cervix because early-stage PCL has better survival than primary cervix malignancy [1,6]. Pap smear is not a reliable tool for diagnosis because it may be negative for malignancy because of absence of mucosal surface ulceration as in our case [5,6].

The majority of PCL are B cell lymphoma and DLBCL [3]. In our case, while CD20 was positive, CD3, HMWCK, LMWCK, vimentin were negative by immunohistochemical staining, consequently the diagnosis of DLBCL of the cervix was confirmed. Staging work-up of NHL consists of CT of chest, abdomen and pelvis, and bone marrow biopsy. PET–CT imaging has also been used in staging and follow-up of patients [6,8]. Delbeke showed that PET–CT and CT was comparable in staging of lymphoma and PET–CT was superior in treatment monitoring especially to differentiate viable tumors from fibrosis [9,14]. We made staging by using PET–CT. Because of tumor located in only cervix as extranodal site, it was classified as stage IEB according to Ann Arbor staging system.

Several methods have been proposed for treatment of patients with PCL [3,7,12]. In the literature, combination chemotherapy with RT was suggested as the best modality because 5-year survival rates were up to 83% to 100% [1–3,13]. Rituximab is monoclonal antibody that binds specifically to the B cell surface antigen CD20 and is used for both CD20 positive NHL and PCL [6]. Trials combining rituximab with CHOP chemotherapy have reported an improved response rate compared to chemotherapy alone [8,14]. In the English literature 21 cases of PCL were reported, 8 of them were treated with surgery followed by RT [2], 3 of cases with chemotherapy alone [7]. There are 9 cases of DLBCL treated with chemotherapy (4 of them with CHOP) and pelvic external RT, only 3 of them received rituximab in combination with chemotherapy and radiotherapy [1] (Table 1). Here, we report 4th patient with PCL who was treated with 6 cycles of R-CHOP followed by pelvic RT without surgery. After treatment, response to treatment was re-evaluated by PET–CT. Also our case is noteworthy because of pre- and post-treatment PET–CT images.

Correct diagnosis is important in order to avoid radical gynecologic surgery, which is not helpful in improving the survival rate [6,7]. Chemotherapy and immunotherapy with external RT seem to be most effective treatments. In the differential diagnosis of the gynecological malignancies, PCL should be kept in mind because it has a favorable outcome if diagnosed properly.

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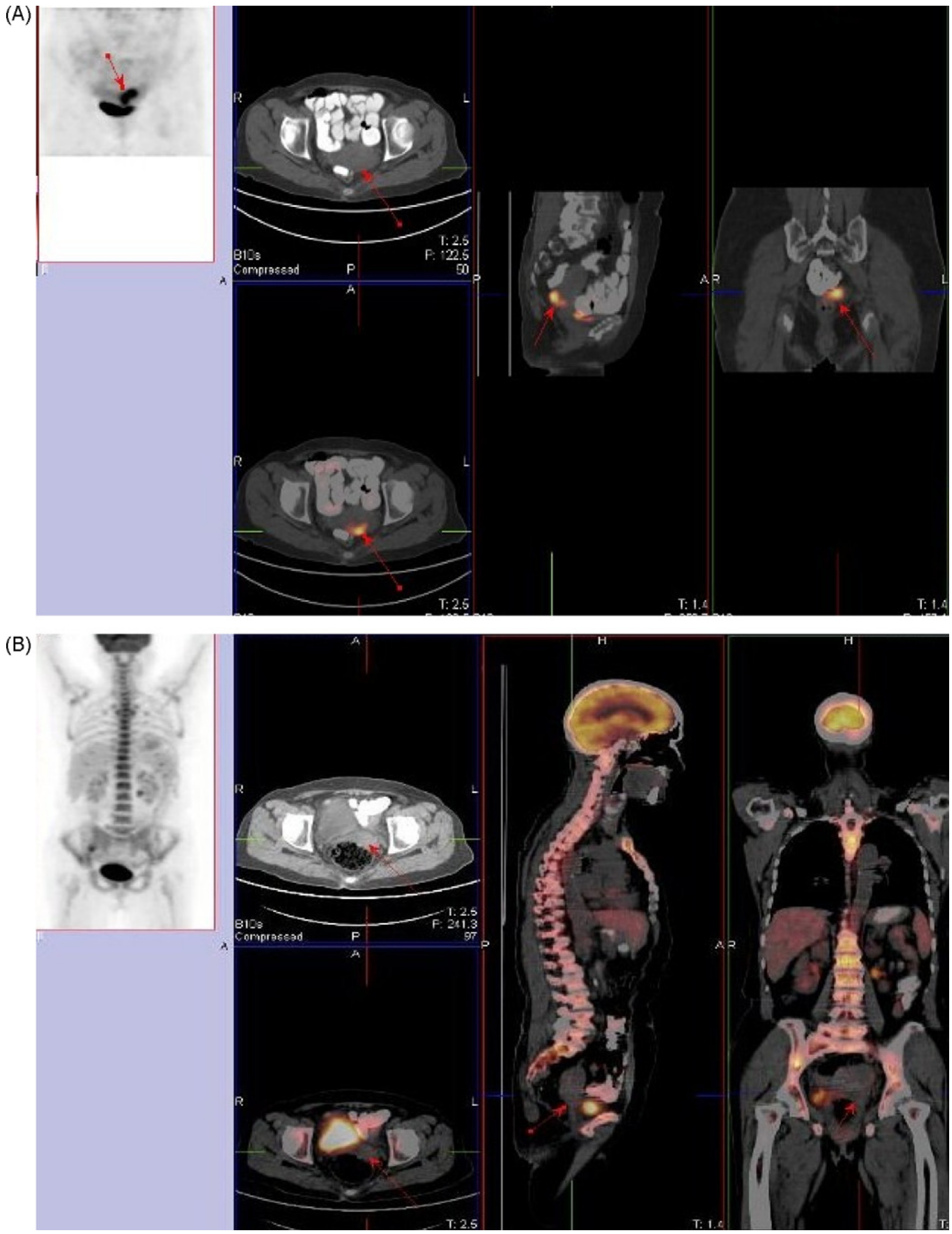

Fig. 1. (A) PET–CT images before treatment of cervix lymphoma. (B) PET–CT images after treatment of cervix lymphoma.

Table 1
Primary cervix diffuse large B cell lymphoma treated with chemotherapy and radiotherapy without surgery.

Number	Age (yr)	Ann Arbor stage	NHL type	Treatment	Follow-up (mo)	Response	References
1	52	IEA	DLBC	CT-RT	12	NED	[2]
2	67	IEA	DLBC	CT-RT	60	NED	[2]
3	56	IIE	DLBC	CHOP-RT	6	CR	[3]
4	22	IEA	DLBC	CHOP-RT	14	NED	[6]
5	64	IE	DLBC	CHOP-RIT-RT	13	CR	[6]
6	47	IE	DLBC	CHOP-RT	13	NED	[9]
7	32	IEA	DLBC	CHOP-RIT-RT	10	CR	[10]
8	57	IIEA	DLBC	CT-RT	120	CR	[11]
9	55	IIEA	DLBC	CT-RT	10	CR	[15]
Present case	65	IEB	DLBC	CHOP-RIT-RT	10	CR	

yr: year, NHL: non-Hodgkin's lymphoma, mo: month, DLBCL: diffuse large B cell lymphoma, CR: complete response, DED: death of disease, NED: no evidence of disease, CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone, RIT: rituximab, PERT: pelvic external radiotherapy.

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