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CASE REPORT

A case report of double-protein expression in primary uterine cervical diffuse large B cell lymphoma and a review of the literature

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Abstract

Primary non-Hodgkin's lymphoma of the uterine cervix is rarely observed. Here, we report a case of "double-protein" expression in a primary uterine cervical diffuse large B-cell lymphoma that was detected based on cervical biopsies at Sichuan Cancer Hospital in December 2016 in a 53-year-old woman with a 1-month history of postmenopausal vaginal bleeding. She was diagnosed with stage IVA cervical cancer after workup and treated with six cycles of rituximab + cyclophosphamide + epirubicin + vindesine + prednisone. She showed a positive partial response after two cycles; however, response assessment revealed a progressive disease after six cycles. Based on the current condition, a treatment regimen comprising a combination of second-line chemotherapy and radiotherapy was advised for the patient. Unfortunately, she discontinued her treatment because of various factors. We conclude that "double-protein" expression in primary uterine cervical diffuse large B-cell lymphoma is difficult to treat and has a poor prognosis. Therefore, improving the diagnosis and treatment of this disease should be considered.

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Non-Hodgkin's lymphoma (NHL) involves the extranodal regions in approximately one-third of patients [1]. The most common extranodal sites are the gastrointestinal tract, nasal cavity, and skin. However, female genital tract lymphoma is an extremely rare disease, which accounts for 1.5% of extranodal NHL [2], and its clinical manifestation includes a lack of specificity, leading to misdiagnosis. A previous study identified that the most common subtype of uterine cervical lymphoma is diffuse large B-cell lymphoma (DLBCL), with abnormal vaginal bleeding being the most common presenting symptom [3]. DLBCL is a clinically and biologically heterogeneous disease and could be divided into prognostically important subgroups: germinal center subtype (GCB) and non-GCB [4]. Hence, the response of patients to therapy invariably differs. Currently, there is a growing interest in "double-protein" lymphoma that is defined as the co-expression of two oncogenes (MYC and BCL2 and/or BCL6) [5]. A recent study identified that MYC/BCL2 co-expression was a predictor of prognosis in DLBCL patients treated with rituximab + cyclophosphamide + epirubicin + vindesine + prednisone (R-CHOP) chemotherapy because most treatment failures were observed in "double-protein" DLBCL [6]. Therefore, a standard treatment has not yet been established. Here, we report a case of DLBCL with "double-protein" expression involving the uterine cervix treated with R-CHOP chemotherapy.

Case presentation

A 53-year-old postmenopausal woman presented with a 1-month history of vaginal bleeding, with the absence of fever, weight loss, night sweats, and an Eastern Cooperative Oncology Group performance status score of 1. She subsequently visited the Department of Obstetrics and Gynecology in our hospital. Gynecological examination showed a large exophytic mass in the cervix with necrotic and bleeding areas infiltrating the upper vagina and left parametria.

A cervical biopsy revealed a high-grade non-Hodgkin's DLBCL, GCB, and double-protein expression. Immunohistochemistry revealed the following results: creatine kinase (–), cluster of differentiation CD3 (–), CD5

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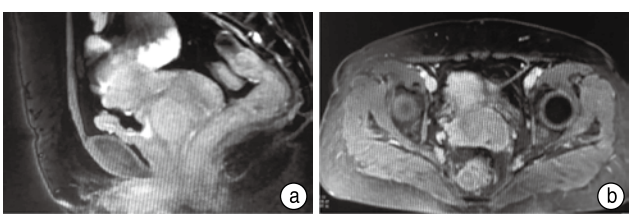
(–), CD10 (+), CD30 (–), CD20 (+), Lens culinaris lectin (+), PAX5 (+), myeloperoxidase (–), CD79a (+), CD138 (–), epithelial membrane antigen (–), vimentin (–), MUM-1 (–), BCL2 (+, 40%), BCL6 (–), c-MYC (+, 60%), P53 (–), EBER (–), and Ki-67 (+, 80%).

Contrast-enhanced magnetic resonance imaging (MRI) of the upper abdomen and pelvis revealed a solid tumor (4.9 × 6.1 × 4.0 cm) occupying the uterine cervix, extending to the upper part of the vagina and the left parametria. Multiple lymph nodes in the subcutaneous fat layer of the upper left abdominal wall, right perirenal space, left iliac fossa, presacral space, right rectum, and left inguinal groin were enlarged (largest 2.1 × 2 cm) (Fig. 1).

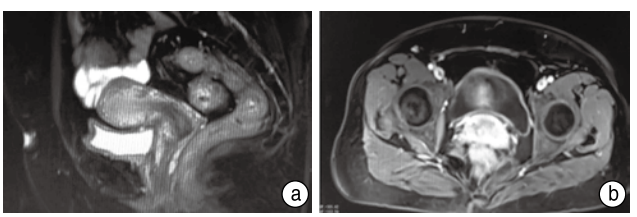
Contrast-enhanced computed tomography (CT) of the neck and chest revealed no evidence of lymphoma (figure not shown). Bone marrow and cerebrospinal fluid were uninvolved. Routine laboratory analysis showed an elevated serum lactate dehydrogenase level (174 U/L [normal value, 0–240 U/L]). Viral serological results for human immunodeficiency virus, hepatitis B surface antigen, hepatitis C, and syphilis were negative. Based on the clinical and imaging examination findings, the patient was diagnosed with DLBCL (GCB, BCL2/c-MYC double-protein expression, stage IVA, IPI score of 2).

She originally planned to receive six cycles of 3-weekly R-CHOP chemotherapy followed by involved-field radiotherapy. After two cycles, an MRI of the upper abdomen and pelvis revealed a positive partial response in all lesions (Fig. 2). After four cycles, an MRI revealed a stable disease (Fig. 3). After the completion of six cycles, an MRI revealed the progression of the cervical mass (Fig. 4). Meanwhile, contrast-enhanced chest CT revealed a lymphoma of the right breast (Fig. 5), which was confirmed by a lumpectomy of the right breast. Her family refused involved-field radiotherapy and second-line chemotherapy because of various factors. Finally, she discontinued treatment.



MRI scan pretreatment

Fig. 1 Contrast enhanced magnetic resonance imaging (MRI) of pelvic scan pretreatment shows that enhancing lesion is seen involving the cervix and invading the left parametria. (a) sagittal; (b) coronal

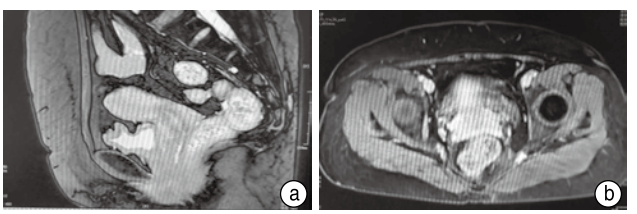


MRI scan after two cycles

Fig. 2 Contrast enhanced MRI scan after two cycles of chemotherapy showed partial response of the cervical mass and its extensions. (a) sagittal; (b) coronal

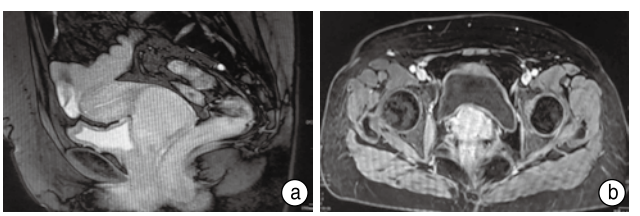
Discussion

A lymphoma can occur in every tissue; however, a primary lymphoma of the uterine cervix is a rare disease. Most cases of lymphoma have nonspecific clinical symptoms, such as vaginal bleeding, perineal discomfort, and persistent vaginal discharge. Moreover, signs of lymphoma are similar to uterine cervical cancer [1, 3]. Therefore, establishing the diagnosis of lymphoma is considered difficult, and it is often misdiagnosed because of its rarity and non-specific clinical presentation.



MRI scan after four cycles

Fig. 3 Contrast enhanced MRI scan after four cycles of chemotherapy showed stable disease of the cervical mass. (a) sagittal; (b) coronal



MRI scan after six cycles

Fig. 4 Contrast enhanced MRI scan after six cycles of chemotherapy progressive disease of the cervical mass. (a) sagittal; (b) coronal

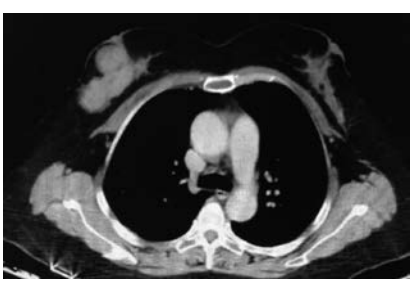


Fig. 5 Contrast enhanced CT of chest scan showed lymphoma of the right breast (coronal)

Primary cervical lymphoma is predominantly observed in postmenopausal women, and the median age of patients diagnosed with stage III or IV cervical lymphoma is 58 years (range, 22–75 years) [7]. Our patient was a 53-year-old postmenopausal woman with abnormal vaginal bleeding without evidence of B symptoms. As concluded in a previous study, the disease was confirmed by cervical biopsy, and occasionally, repeat biopsies may be required to prove the definitive diagnosis [8], similar to our case. In our study, a contrast-enhanced CT of the neck and chest revealed that the bone marrow and cerebrospinal fluid were uninvolved. However, a contrast-enhanced MRI revealed a solid tumor occupying the uterine cervix, extending to the adjacent tissue and organs. Hence, in this case report, the patient was diagnosed with primary uterine cervical DLBCL with "double-protein" expression defined by immunohistochemistry. Generally, cervical lymphoma has a good prognosis, and the 5-year survival rates of patients with early-stage and high-stage cervical lymphomas are 83% and 29%, respectively [7]. Although the optimal treatment of this condition remains unknown, patients diagnosed with cervical lymphoma can select chemotherapy, radiotherapy, and surgery, alone or in combination [9–10]. To date, according to some reported studies, the R-CHOP regimen chemotherapy followed by radiotherapy has been recommended [11]. Consistent with a previous study, in the present case report, the patient received R-CHOP chemotherapy. Unexpectedly, after the patient completed the six cycles, she showed progressive disease of the primary cervical lesion, and a clinically detectable lymphoma was observed in the right breast, which was confirmed by lumpectomy of that breast. Some explanations have significant prognostic effects as follows: (1) the patient was diagnosed with stage IVA cervical cancer with a heavy tumor load associated with poor survival, as concluded in a previous study. (2) the histological subtype showed a lymphoma with "double-protein" expression. Several groups have shown that the "double-protein" lymphoma has a poor prognosis with R-CHOP chemotherapy [12–15]. We can conclude that the co-expression of MYC and BCL-2 was significantly associated with the poor outcome.

Conclusion

In summary, a primary cervical "double-protein" expression lymphoma is a rare disease, which has a poor clinical outcome. Improving the recognition of the disease, establishing the accurate diagnosis of the disease, and initiating a timely therapy are considered important in the treatment of a cervical lymphoma. For "double-protein" expression DLBCL, the standard treatment is not yet established. Therefore, a novel treatment for patients diagnosed with DLBCL is urgently required.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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