

Case Report

Expression of p63 in primary diffuse large B-cell lymphoma of the uterine cervix mimicking low differentiated squamous cell carcinoma

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Received July 11, 2016; Accepted September 21, 2016; Epub November 1, 2016; Published November 15, 2016

Abstract: Diffuse large B-cell lymphoma (DLBCL), a common type of non-Hodgkin lymphoma, is usually presenting in lymph nodes or extranodal sites. The most common extranodal site is the gastrointestinal tract. The occurrence in the uterine cervix is exceptional rare. Histologically, this tumor is characterized by a diffuse proliferation of large atypical B-cells. Occasionally the neoplastic cells are display features of signet ring cells. P63 was considered as commonly useful epithelial markers to distinguish carcinoma from lymphoma, but the expression of P63 had also been seen in some lymphoma. Herein, we present a case of DLBCL in a 64-year-old Chinese female. The tumor was predominantly composed of abundant large atypical B-cells with P63-positive and scattered T-cells and histiocytes, focally signet ring-like cells are presented reminiscent of low differentiated squamous cell carcinoma.

Keywords: Primary, diffuse large B-cell lymphoma, uterine cervix, low differentiated squamous cell carcinoma

Introduction

Diffuse large B-cell lymphoma (DLBCL), is a common type of non-Hodgkin lymphoma. It is usually considered malignancy, a highly aggressive lymphoma, can occur at any age, but usually in the elderly. The median age is in the 7th decade [1]. DLBCL is usually presenting in lymph nodes or extranodal sites including brain, bone, bone marrow, testis, spleen, Waldeyer ring, salivary gland, thyroid, liver, kidney, adrenal gland and breast [2-13]. But, cervical location is very exceptional rare [14, 15]. DLBCL is histologically characterized by a number of large B-cells with obvious atypia. Very rarely, tumor cells were suffusive, medial size, with intracytoplasmic vacuoles, second nucleolus and were display features of signet ring cells. Herein, we present a case of DLBCL in a 64-year-old Chinese female. Histologically, the tumor was predominately composed of suffusive atypical large B-cells, signet ring-like cells and scattered T-cells and histiocytes. This unusual histological appearance may pose a great diagnostic challenge. It may be easily mis-

diagnosed, especially if the specimen is limited.

Case presentation

Clinical history

A 63-year-old female referred to our hospital for complaining of postmenopausal bleeding. Blood examinations were in normal levels. No other tumors, lymphadenopathy, or hepatosplenomegaly were detected. There were no B symptoms. Magnetic resonance imaging (MRI) of the pelvis revealed a poor circumscribed, irregular shape, lobulated, low echo mass about 4.10×4.13×4.48 cm in the uterine cervix (**Figure 1**). The tumor was clinically diagnosed as a cervical carcinoma, and then cervical biopsy was performed in our hospital. According to the morphological and immunohistochemical findings, the tumor was diagnosed as a DLBCL.

Materials and methods

The resected specimens were fixed with 10% neutral-buffered formalin and embedded in



Figure 1. Magnetic resonance imaging (MRI) of the pelvis showed a solid tumor occupying the cervix.

paraffin blocks. Tissue blocks were cut into 4- μ m slides, deparaffinized in xylene, rehydrated with graded alcohols, and immunostained with the following antibodies: cytokeratin (pan), CK5/6, P63, P40, EMA, ER, PR, Vimentin, Actin (SM), MyoD1, CD34, CD99, CD3, CD5, CD20, PAX-5, CD21, bcl-2, bcl-6, CD10, mum1, CD15, CD30, ALK, CD68, CD163, c-myc, EBV and Ki67. Sections were stained with a streptavidin-peroxidase system (KIT-9720, Ultrasensitive TM S-P, MaiXin, China). The chromogen used was diaminobenzidine tetrahydrochloride substrate (DAB kit, MaiXin, China), slightly counterstained with hematoxylin, dehydrated and mounted. For the negative controls, the primary antibody was replaced with PBS.

Results

Gross features

Grossly, the biopsy masses were approximately 0.5×0.5×0.5 cm respectively. The cut face of the tumor was soft and greyish-white in color.

Microscopic features

Histologically

The normal structure of the uterine cervix is completely destroyed by tumor cells (**Figure**

2A). In focal area of the tumor, the tumor was predominantly composed of abundant atypical large B cells. The cells were diffusely arranged into solid sheets with little stroma (**Figure 2B**). The neoplastic cells had marked cellular atypia, with pale chromatin and second nucleoli, and even are display features of signet ring cells (**Figure 2C**). There was approximately 1 mitosis/10 high power in large B cells. In another focal area of the tumor, diffuse large B cells were present within the background of the scattered T-cells and histiocytes (**Figure 2D**).

Immunohistochemistry

Immunohistochemical staining showed that atypical large B cells were diffusely positive for CD20 (**Figure 3A**), PAX-5 (**Figure 3B**), bcl-6 (**Figure 3C**), P63 (**Figure 3D**), bcl-2 and Vimentin, negative for CK (**Figure 3E**), CK5/6, P40, EMA, ER, PR, Actin (SM), MyoD1, S-100, CD34, CD99, CD3, CD5, CD21, c-myc, mum1, CD10, CD15, CD30, ALK, CD68, CD163 and EBV. In contrast, T-cells were positive for CD3 (**Figure 3F**) and CD5, negative for CD20, PAX-5 and P63. Histiocytes were positive for CD68 (**Figure 3G**) and CD163, negative for CD20, PAX-5 and P63. Ki67 index was approximately 60% (**Figure 3H**). According to the morphological and immunohistochemical findings, the tumor was diagnosed as a DLBCL-germinal center B cell-like (GCB).

Discussion

Diffuse large B-cell lymphoma (DLBCL) is a common type of non-Hodgkin lymphoma which is considered malignancy, a highly aggressive lymphoma [1]. DLBCL can occur in lymph nodes and various organs including brain, bone, bone marrow, testis, spleen, Waldeyer ring, salivary gland, thyroid, liver, kidney, adrenal gland and breast [2-13]. Uterine cervix location is very exceptional rare [14, 15]. As the most common primary neoplasms in the uterine cervix were squamous cell carcinoma, the correct diagnosis of THRLBCL may be a hard work.

Histologically, DLBCL is characterized by large B lymphoid cells with a diffuse growth pattern replacing most of the normal cervical parenchyma. It is comprised of diffuse large B cells embedded in a background of small lymphocytes that represent T cells, and variable numbers of histiocytes. Usually, the tumor cells

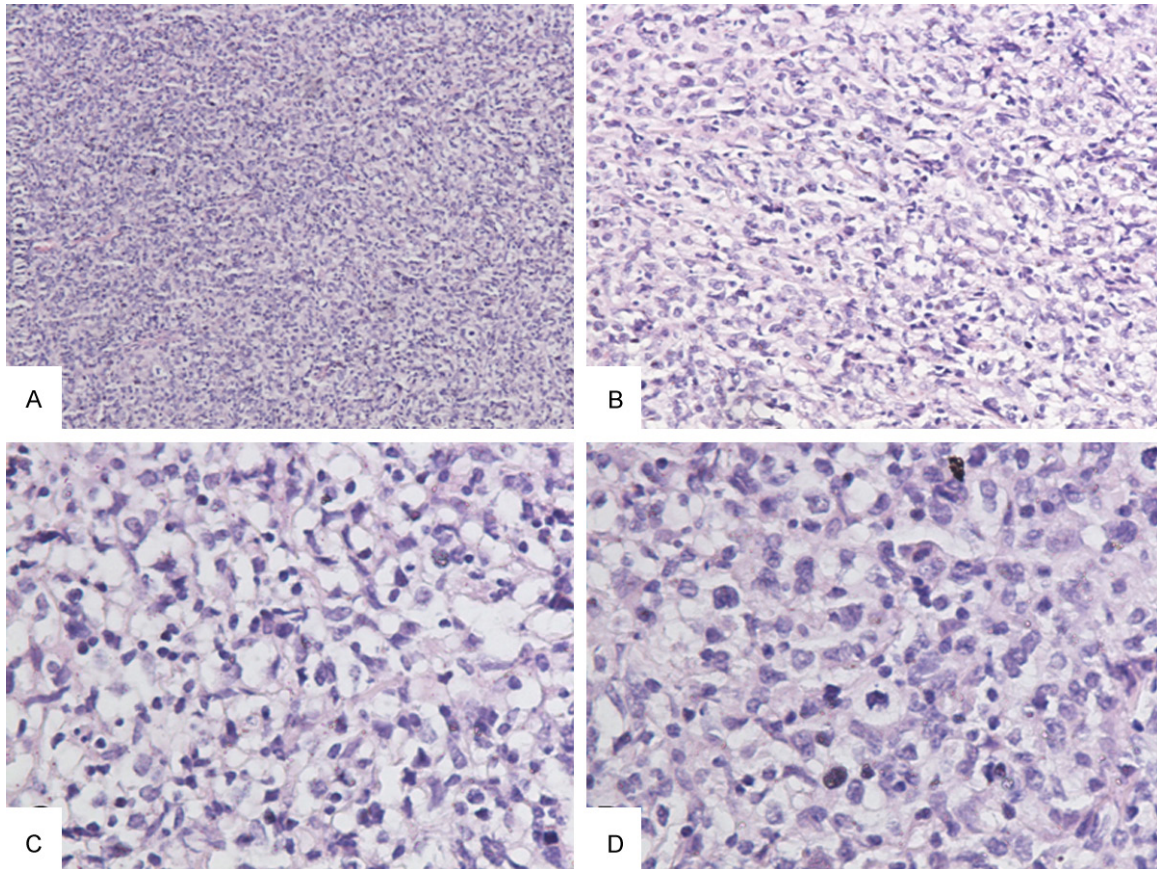


Figure 2. Morphological change of the tumor. A. The tumor was relatively poor circumscribed. B. Numerous large B cells were arranged into sheets patterns. C. The signet ring-like cells with intracytoplasmic vacuoles were focally present. D. The large B cells had marked cellular atypia, scattered T-cells were present around the large B cells.

show moderate to distinct atypia. Infrequently, the tumor cells may be focally expressed signet-ring like cells [16]. Our reported case show that extensive atypical large tumor cells change with small lymphocytes and histiocytes. We found diffuse p63 expression in the tumor cells. P63 was a p53 homolog that is expressed in various epithelial tumors [17]. Wooff JC [18] found that P63 was positive in all cases of squamous cell carcinoma. So, low differentiated squamous cell carcinoma is an important differential diagnosis. However, p63 inconsistently stained DLBCL [19]. The p63 expression in DLBCL represents a diagnostic pitfall. The presence of classic atypical large B cells with intracytoplasmic vacuoles or less cytoplasm in few hyaline stromas and the positive of expression CD20 and PAX-5 can usually favor the correct diagnosis and rule out low differentiated carcinoma. Histologically, the tumor focally was predominately composed of sheets of atypical large B cells and scattered T-cells and histio-

cytes. So, we secondly thought it might be a lymphoma such as T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL). Lymphomas containing B cells with a spectrum of cell size, morphology and distribution, should not be included within the category of THRLBCL, and may be considered a subtype of DLBCL, GCB. So, if the specimen is limited, and histologically lacks the classic histological structure, the correct diagnosis may be a great challenge.

In addition, the differential diagnosis also includes some other tumors, such as: extramedullary leukaemias, Burkitt lymphoma variants and blastoid mantle cells lymphomas. Based on the classic histologic structure and immunostaining, the correct diagnosis can be made. Moreover, some nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) can present as the neoplastic cells may exhibit a Hodgkin-like morphology and rich in reactive T-cells. Thus, NLPHL is also an important differential diagnosis.

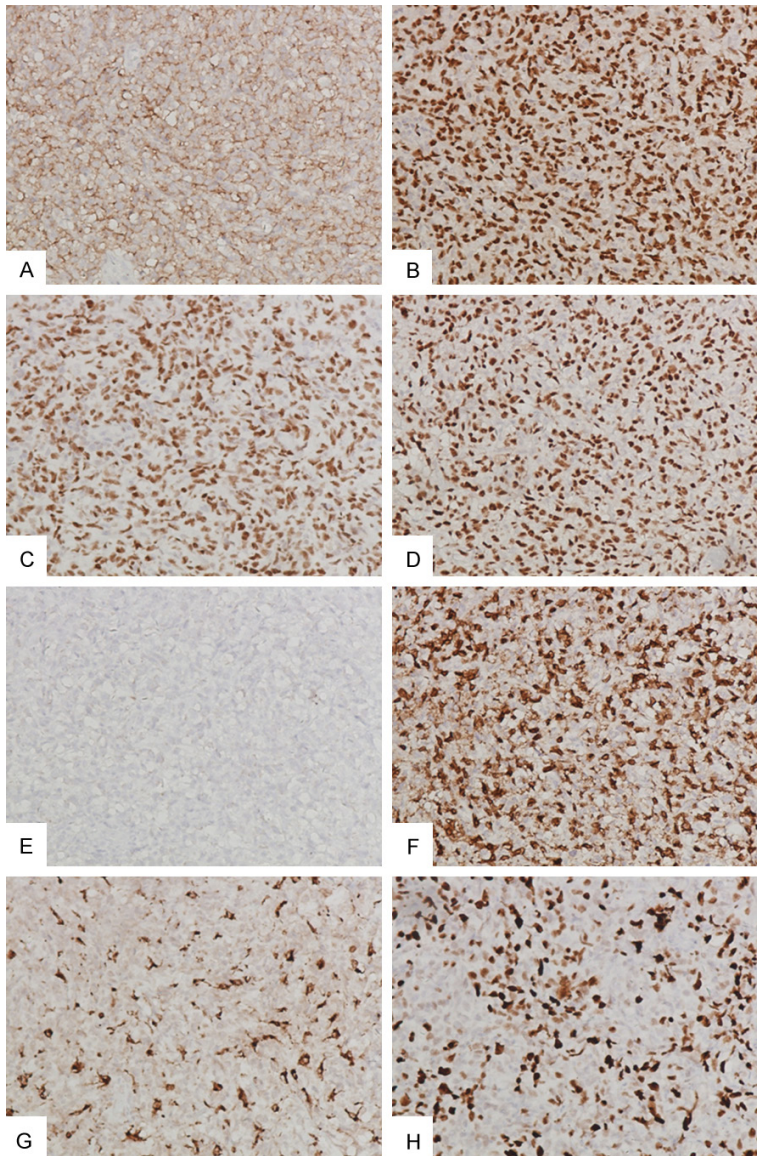


Figure 3. Immunohistochemical staining of the tumor. A. Diffuse and strong expression of CD20 could be seen in the large B cells. B. The large B cells were also positive for pax-5. C. Diffuse and strong expression of bcl-6 could be seen in the large B cells too. D. The large B cells were positive for p63. E. The tumor cells were negative for CK. F. The CD3 staining highlighted the presence of T-cells. G. The CD68 staining highlighted the presence of histiocytes. H. Ki67 proliferative index was approximately 60%.

DLBCL is an aggressive disease with considerable heterogeneity reflected in the 2016 World Health Organization classification. It is still unclear whether the presence of T-cells and histiocyte cells is associated with prognosis. According to Chang C [20], the majority of T-cells in blood are considered a poor prognostic factor. There are many conflicting reports on the prognostic impact of features of tumor cells, ki67 index and TP53 mutations [21].

According to Xu-Monette et al. [22], p63 was an independent favorable prognostic factor in DLBCL, which was most significant in patients with International Prognostic Index (IPI) >2, and in activated-B-cell-like DLBCL patients with wild-type TP53. And, further follow up should be made to investigate their significance.

Conclusion

We reported a case of uterine cervix DLBCL displays features of focally signet ring cells and with P63-positive. The unusual histological appearance may pose a great diagnostic challenge, especially if the specimen is limited.

Acknowledgements

This work was supported by the Program for Liaoning Innovative Research Team in University (No. LC2015029), the Natural Science Foundation of Liaoning Province of China (No. L2015598), and the Program of Science and Technology Department of Liaoning Province (No. 2013-225021).

Disclosure of conflict of interest

None.

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