Advances in Modern Oncology Research

doi: 10.18282/amor.v1.i1.33

CASE REPORT

Primary diffuse large B-cell lymphoma of the endometrium

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Abstract: This article was designed to analyze the prognosis and to explore the clinical characteristics and treatment of a case of primary diffuse large B-cell lymphoma (DLBCL) of the endometrium, through a detailed report. **Methods**: This report was done by analyzing a case through its clinical features, pathological examination and immunophenotyping. We believe that this would allow us to forecast the prognosis of the case. **Case Description**: The patient was admitted because of irregular postmenopausal vaginal bleeding for more than a month. She underwent a series of surgical procedures that included abdominal hysterectomy, bilateral adnexectomy, pelvic lymph node dissection and enterolysis owing to the assessed pathological results after uterine curettage. The postoperative pathological results showed that it was a DLBCL. **Conclusion**: Primary DLBCL of the endometrium is rarely reported. Its diagnosis and differential diagnosis mainly depends on pathological examination and immunophenotyping. Radical surgery combined with chemotherapy may be an ideal mode of treatment. The prognosis of the disease has a varied range but radical surgery combined with chemotherapy may improve her quality of life and prolong her survival period.

Keywords: endometrial cancer; diffuse large B-cell lymphoma; non-Hodgkin lymphoma (NHL)

Citation: Zou YQ, Zhao HM, Gao JH, et al. Primary diffuse large B-cell lymphoma of endometrium. Adv Mod Oncol Res 2015; 1(1): 36–40; http://dx.doi.org/10.18282/amor.v1.i1.33.

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Received: 3rd September 2015; **Accepted:** 18th September 2015; **Published Online:** 6th October 2015

Diffuse large B-cell lymphoma (DLBCL) is a high-grade invasive lymphoma. DLBCL accounts of about 30% of all non-Hodgkin lymphoma (NHL) cases and is the most common subtype of NHL. NHL rarely presents itself in a female genital tract. Only 0.2%–1.1% of all extranodal cases occur in a female genital tract. Its main distribution being in the ovary and uterine neck[1]. Fox et al. defined the primary uterine malignant lymphoma as: 1) one whose site is examined to be in the ovary, the first time; 2) it is the only lymphoma that can be found through a general checkup; 3) its incidence shows no evidence of leukemia in the peripheral blood test; 4) if a secondary lymphoma occurs where the hysterectomy was performed, it should be a few months between the date of the initial discovery of the primary lymphoma and the appearance of the secondary one[2].

Clinical data–general data

Patient: Female, 72 years old. **Chief complaint**: Bleeding irregularly for more than a month, 20 years post-menopause. **Personal history**: Regular menstruation started from 15 years old; 5–6/30 days; age at menopause was 52 years old; not addicted to tobacco or alcohol. **Past history**: Suffering from diabetes for more than 20 years and treated with insulin; blood glucose has been controlled effectively (fasting blood glucose 6.5 mmol/L; after breakfast 8.0 mmol/L; before lunch 7.1 mmol/L; after lunch 11.6 mmol/L; before supper 6.8 mmol/L; after supper 7.2 mmol/L; before sleep 5.9 mmol/L); suffering from coronary disease and rheumatoid for more than 20 years. **Pregnancy-labor history**: Pregnant four

times and gave birth four times. **Family history**: Parents deceased; sons and daughters are healthy; no family history of tumor. **History of present illness**: Irregular vaginal bleeding for a month before admission, small amount; bright red; no fever or stomach ache; examined with gynecological ultrasonography, indicated endometrial organic changes; curettage was performed; histopathology further revealed lymphoma; normal sleep, diet, bowel movement and urination without obvious weight changes during admission.

Materials and methods

Physical examination

No difference in general condition; free of spots; clear consciousness; stable life signs; heart and lungs are normal; flat abdomen; soft abdomen due to palpations; no tenderness or rebound pain. Gynecological examination: senile change of vulva; vagina patency and mild atrophy observed; anterior wall of vagina has one degree of expansion; fornix does not reach haphalgesia or nodules; humble vaginal mucosa; vagina is atrophic at cervical neck; flat fornix; cervical neck has one degree of erosion; bleeds when touched; uterus is anteversion and soft; uterus size is similar to that of one at 12 weeks of pregnancy; not active; no tenderness; bilateral accessory is normal.

Auxiliary examination

Gynecological ultrasonography: Uterine empyema (endometrial neoplasm is to be excluded; exquisite dot and band echoes covering about 7 × 5 cm); small cysts in the left ovarian (3 × 3 cm) according to clinical features.

Pathologic findings of curettage: (Intrauterine substances) DLBCL, immune phenotype of germinal center. Immunohistochemistry: CA125(−), CK(−), EMA(−), Vimentin (portion of +), CD3(−), CD20(+), Ki-67(+, 80%), MPO(−), ER(−), P53(+), CD79a(+), CEA(−), CK20(−), TTF-1(−), CK19(−), CK7(−), CD34(−), CD56(−), CD43(+), CD10(+), α-inhibin(−), CD99(+), TdT(−), CD117(−), PR(−), CD5(−), CD7(−), MUM-1(+), Bcl-6(+), Bcl-2(+), desmin(−), SMA(−).

Surgical method and findings

The patient underwent a series of surgical procedures that included abdominal hysterectomy, bilateral adnexectomy, pelvic lymph node dissection and enterolysis. Uterus was observed to be enlarged in the shape of a sphere during operation, the size is close to one in 12 weeks of pregnancy. 12 × 9 × 6 cm, uterus profile presents gray and yellow like fish meat, pliable but strong, about 8 × 7 × 3 cm. Chemoinjections were administered into the internal iliac artery during operation (30 mg/side).

Postoperative chemotherapy

According to the result of the postoperative pathologic histology, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone were taken as R-CHOP chemotherapy step I one month after operation, the secondary reaction was so serious after chemotherapy that the patient was still in recovery two months after leaving the hospital.

Results

PET/CT result of the whole body (*Figure 1*)

1. The space occupying the lesion of the endometrium is accompanied by higher glycometabolism. It conforms to the image feature of malignant lesions. Thus, the primary lesion is taken into consideration.
2. The right basal ganglia shows softening focus, lacunar infarction.
3. The left sphenoid sinus is inflamed.
4. Higher glycometabolism was observed in the upper lobe of the left lung and the inferior lobe of the right lung. Optimum node is likely to be considered.
5. Higher glycometabolism was observed in the mediastinum and both hilus pulmonis lymphaden, thus inflammatory lymphonodus is likely to be considered.
6. Higher glycometabolism was observed in the chest, upside of the esophagus, inflammatory lesion or physiologic ingestion is taken into consideration.
7. Chronic cholecystitis.
8. Accessory spleen splenulus.
9. Calcification in both kidneys.
10. Cyst in the left accessory area.
11. Rarefaction of bone.
12. Degenerative change in several centrums.

Histopathologic examination after operation—general findings

The uterus and both accessories: the whole uterus V: 12 × 9 × 5 cm, gray and yellow goiter in intracavity V: 8 × 7 × 2 cm, takes up the whole uterine cavity. Cervical length is 2 cm, ectocervix d: 6.5 cm, 2 × 2 × 1 cm solid tumor in endostoma. Length of left fallopian tube is 6.5 cm, d: 0.4 cm, ovarian bursa V: 3.5 × 3 × 2.5 cm, length

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of right fallopian tube is 5 cm, d: 0.3 cm, ovary V: 3 × 1.5 × 0.8 cm, by the way, lymph gland is included. Microscopic examination (*Figure 1* and *Figure 2*): abnormally shaped, large cell diffuse infiltration and karyokinesis can be seen obviously.

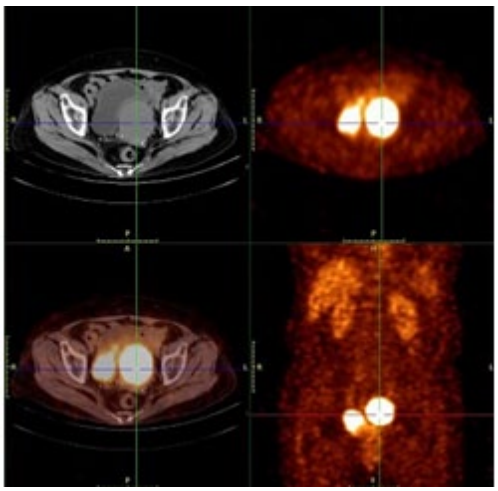

Figure 1 PET/CT results of the patient

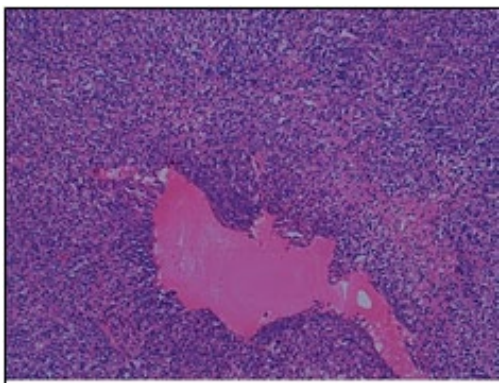

Figure 2 Pathological section after surgery, large cell diffuse infiltration is visible

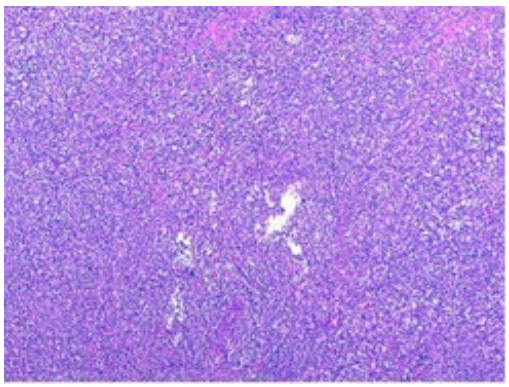

Figure 3 Similar to *Figure 2*, diffuse infiltration is seen among tumor cells in the same size, obvious atypia

Histopathology results

Uterus: Diffuse large B-cell lymphoma, germinal center immunophenotyping, leiomyoma, cervix uteri chronic inflammation: (left ovary) simple cyst, no change in right accessory and left fallopian tube, (left and right groin lymph gland, both obturator lymph gland, right ilium overall lymph gland, both internal ilium lymph gland, both external ilium lymph gland) 0/1, 0/2, 0/4, 0/2, 0/1, 0/1, 0/1, 0/1 and 0/2 are to be found without any change. (Left ilium overall lymph gland) soft tissue is seen without any change. Immunohistochemistry: CD3 (−), CD20 (+), CD79a (+), PAX-5(+), Ki-67 (>50%, +), CD10 (+), BCL-6(+), MUM-1 (+), p53 (individual cell+), CD5 (−), BCL-2 (+).

Discussion

Incidences of primary endometrial non-Hodgkin lymphoma are rare. There is little specificity of clinical manifestation. Therefore, it is difficult to clearly diagnose in the early phases, the diagnosis, however, mainly depends on the histopathologic examination and the immunohistochemistry phenotype. Diffuse large B-cell lymphoma always metastasizes in the early phase. Patients undergoing irregular treatment or no treatment at all, may survive for less than a year[3].

At present, there is no clear etiology for this kind of disease. There are, however, some factors that are taken into consideration these days:

1. There is no lymphoid tissue in genital organs, thus the lymphocytes in blood flow maybe the basis of the occurrence of endometrial non-Hodgkin lymphoma.
2. Chronic inflammation stimulates B-cell clone of NF-KB access mediated.
3. Endometrial non-Hodgkin lymphoma always manifests itself post-menopause, thus the morbidity may be related to female hormonal readiness.
4. Virus infection.
5. Immunodeficiency.
6. Occupational factors: long-term exposure to chemical coloring agents, dyestuff, etc.[4]

Primary endometrial non-Hodgkin lymphomas are rare. During diagnosis, it should be distinguished from myoma of uterus canceration, endometrial proliferation, inflammatory pseudotumors, primitive neuroectodermal tumors, endometrium mesenchymal tumors, and other small cellular tumors[5].

Endometrial primary non-Hodgkin lymphoma has no specific characteristics in terms of clinical symptoms. It usually occurs among post-menopausal women, which

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may be related to excessive endometrial proliferation that is caused by hormone level changes after menopause. The most common symptom is irregular post-menopausal vaginal bleeding or drainage. Endometrial primary non-Hodgkin lymphoma is diagnosed using information from the pathological and histological diagnosis of preoperative diagnostic curettage, but since this disease is rare, it sometimes fails to receive enough attention from doctors in the department of obstetrics and gynecology. A majority of patients are diagnosed according to the result of intraoperative and postoperative pathologic histology. Using the pathological histology report from this case and related literature reports, we can say that most primary non-Hodgkin lymphomas of the uterus belong to type B lymphocyte lymphomas, mostly diffuse large B-cell lymphoma tumors. Heterotypic large B-cell diffuse infiltration can be seen through a microscope, but only confined to the shallow endometrium. It can erode the endometrial glands and go far into the deep muscle layer. It grows diffusely in muscle tissue, characterized by pleomorphism. The types of form of the tumor can be divided into polyps, erosion and nodular types, generally in the shape of a fishes together with a small amount of hemorrhage and necrosis[6,7].

A lot of research and data show that p53, Ki-67, part of the CD family and expressions of other genes have changed in a variety of tumor which include endometrial carcinomas and lymphomas. Therefore, research of the related gene expression changes has important significance to predict diseases in the future.

Tumor suppressor gene p53, encoding p53 protein, which are called "genome guardian", were discovered by Linzer[8] in 1979, p53 can be divided into wild type and mutant type. Under normal circumstances, p53 usually exists in wild-type, maintaining a low level state within cells and is nonfunctional. When DNA suffers damage or other stimuli, p53 can be activated, and participates in regulating the cell cycle and promoting apoptosis. The p53 mutations lose normal biological function of tumor suppressing genes and p53 protein lose vitality for tumor suppressing. The p53 is a tumor suppressor gene and excessive expression of p53 means that the survival rate is low, studies show that excessive expression of p53 exists in most type II endometrial carcinomas. In this case, immunohistochemical prompts ER (−), PR (−) and p53 (+) are in conformity with type II endometrial cancer. Immunohistochemical, female and progesterone negative receptors suggest that hormone therapy does not promote good effects, high expression of p53 suggests easy relapse and low survival rate.

Ki-67, namely the nuclei associated antigen, is associated with cell proliferation and reflects cell proliferation activity, studies have shown that Ki-67 is closely related with the development, transfer and prognosis of a variety of malignant tumors[9], the positive expression rate of Ki-67 can be used to determine the strength of the tumor. Ki-67 has a short half-life, it can reflect the activity of cell proliferation more accurately. High Ki-67 expression rate indicates a stronger degree of tumor malignancy. Ki-67 is in lower expression in normal endometrium tissues. Relevant literature data shows[10]: in normal endometrium tissues, endometrial hyperplasia tissues and endometrial polyps, the positive expression rate of Ki-67 showed a trend of increasing (12.00%, 37.33%, 17.33% and 82.00% respectively), these differences are statistically significant (p <0.05). The research results of Yoon, et al.[11] showed that DLBCL patients with high expression of Ki-67 often faced tumor recurrence even after receiving recent satisfactory curative effect and this resulted in the decrease of long-term efficacy and shortened lifetime. In this case, the preoperative diagnostic curettage pathological immunohistochemistry shows Ki-67 (+80%), postoperative pathological immunohistochemistry showed Ki-67 (+, >50%), both Ki-67 showed high expressions, which means tumor cells proliferate actively. There is a high degree of tumor malignancy, they grow invasively, progress fast, and hence easily fall into relapse.

The primary DLBCL of the endometrium was treated by radical surgery combined with postoperative R-CHOP chemotherapy, which enabled a lower relapse rate than treatment by means of radical surgery combined with radiotherapy[6]. The primary diffuse large B-cell lymphoma of the endometrium is a highly malignant tumor with poor prognosis; however, the quality of life of patients with lymphoma can be improved by using rituximab combined with chemotherapy. According to Jones, et al.[12], the complete remission rates of R-CHOP21 and CHOP-21 are 76% and 63% respectively (p = 0.0005), and the 2-year survival rates are 70% and 57% respectively (p = 0.007); it can be concluded that the effect of the R-CHOP method is superior to that of the CHOP method, which is confirmed by five and 10 years follow-ups[13]. The prognosis is improved by radical surgery combined with R-CHOP chemotherapy and some patients' survival period can be prolonged by this method, although some patients may still suffer a poor prognosis. The selected case underwent radical surgery and one course of R-CHOP chemotherapy which caused serious side effects, so she failed to undergo chemotherapy. According to the aforementioned information, the selected case suffered from a highly malignant tumor and the progression was fast. There was also a slight possibility of tumor recurrence. We conclude that if she could

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successfully undergo chemotherapy, the survival period post-surgery may be prolonged but further follow-up would be necessary.

Conclusion

To conclude, the primary DLBCL of the endometrium is rare and its diagnosis and differential diagnosis mainly depends on pathological examination and immunophenotyping. The prognosis is poor, but radical surgery combined with chemotherapy may improve the life quality of patients and prolong their survival period.

Conflicts of interest

The authors declared no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

References

1. Kosari F, Daneshbod Y, Parwaresch R, et al. Lymphomas of the female genital tract: a study of 186 cases and review of the literature. Am J Surg Pathol 2005; 29(11): 1512–1520.
2. Fox H, More JR. Primary malignant lymphoma of the uterus. J Clin Pathol 1965; 18(6): 723–728.
3. Fisher RI, Miller TP, O'Connor OA. Diffuse aggressive lymphoma. Hematology Am Soc Hematol Educ Program 2004; 2004(1): 221–236.
4. Zou H, Fu J. Advances of primary lymphoma in the female genital system. J Pract Obstet Gynecol 2011; 5: 339–341.
5. Qing XY, Yao WX, Xu YQ. Prospect on research and development of B-DLCL. Chin J Clin 2012; 6: 983–985.
6. Cheng H, Zhang B, Xie Y, et al. Two cases of uterine B-DLCL. Chin J Clin 2013; 7(3): 1352–1353.
7. Wang LY, Su LP, Guo YR. One case of primary ureteral lymphoma and review of the literature. J Leuk Lymphoma 2010; 19: 244–245.
8. Linzer DI, Levine AJ. Characterization of a 54K Dalton cellular SV40 tumor antigen present in SV40-transformed cells and uninfected embryonal carcinoma cells. Cell 1979; 17(1): 43–52.
9. Ozaki K, Yamagami T, Nomura K, et al. Prognostic significance of surgical margin, Ki-67 and cyclin D1 protein expression in grade II canine cutaneous mast cell tumor. J Vet Med Sci 2007; 69(11): 1117–1121.
10. Wen HQ, Geng YY, Hu HJ, et al. Expression of Bc1-2 and Ki-67 in the endometria diseases. Chin Clin Oncol 2009; 14(7): 614–618.
11. Yoon DH, Choi DR, Ahn HJ, et al. Ki-67 expression as a prognostic factor in diffuse large B-cell lymphoma patients treated with rituximab plus CHOP. Eur J Haematol 2010; 85(2): 149–157.
12. Jones SE, Miller TP, Connors JM. Long-term follow-up and analysis for prognostic factors for patients with limited-stage diffuse large-cell lymphoma treated with initial chemotherapy with or without adjuvant radiotherapy. J Clin Oncol 1989; 7(9): 1186–1191.
13. Zhang LJ, Wang FW. Progress of diffuse large B-cell lymphoma. Chin J Clin 2014; 8(11): 2127–2132.

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