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Case Reports

MALIGNANT LYMPHOMA OF THE UTERUS: REPORT OF A CASE AND LITERATURE REVIEW

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ABSTRACT

Uterine lymphoma is a rare disease; therefore, information regarding histologic type, immunophenotype of tumor cells and etiologic factors are limited. although secondary involvement of the genital tract occurs in up to 40% of cases of disseminated lymphoma, lymphoma presenting with primary female genital tract symptomatology is very unusual. We report a case of B-cell lymphoma in the uterine corpus of a 27-year-old white female and review the literature.

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Keywords: Malignant lymphoma, Uterus, Immunohistochemistry, B-lymphocyte, Burkitt.

INTRODUCTION

Malignant lymphoma of the female genital tract is a rare disease. Its frequency in Western countries was reported to be 0. 008% among primary cervical tumors[1] and 2% among extranodal lymphoma in women. The frequency (1.6%) among Japanese female patients with extranodal lymphoma was close to that in North America. Because of the differences in clinical and pathologic findings between cases with uterine and ovarian lymphoma, they have been reported separately.[2] Among the uterine lymphomas the cervix and vagina have been more prevalent sites than the corpus (85% of Japanese and 78% of North American cases).[6] The rarity of uterine lymphoma made a study of a large series of cases difficult, and single or a few sporadic cases of uterine lymphoma have been reported.[7, 10, 12, 15] Therefore, information on uterine lymphoma including its histologic type, immunophenotype of tumor cells and important etiologic role of chronic inflammation of the autoimmune or non-autoimmune nature for development of extraintestinal B-cell lymphoma[18,19] such as thyroid, salivary, gastrointestinal and pleural lymphoma has been suggested.[16, 17] Recently, the presence of lymphocytic mastopathy in patients with breast lymphoma was confirmed by histologic findings together with immunohistochemical corroboration showing positivity of duct epithelium for anti-HLA-DR antibody. In this article, the histologic and immunohistologic findings such as immunophenotype of uterine lymphoma cells are described.

CASE REPORT

The patient was a 27-year-old white female mother of

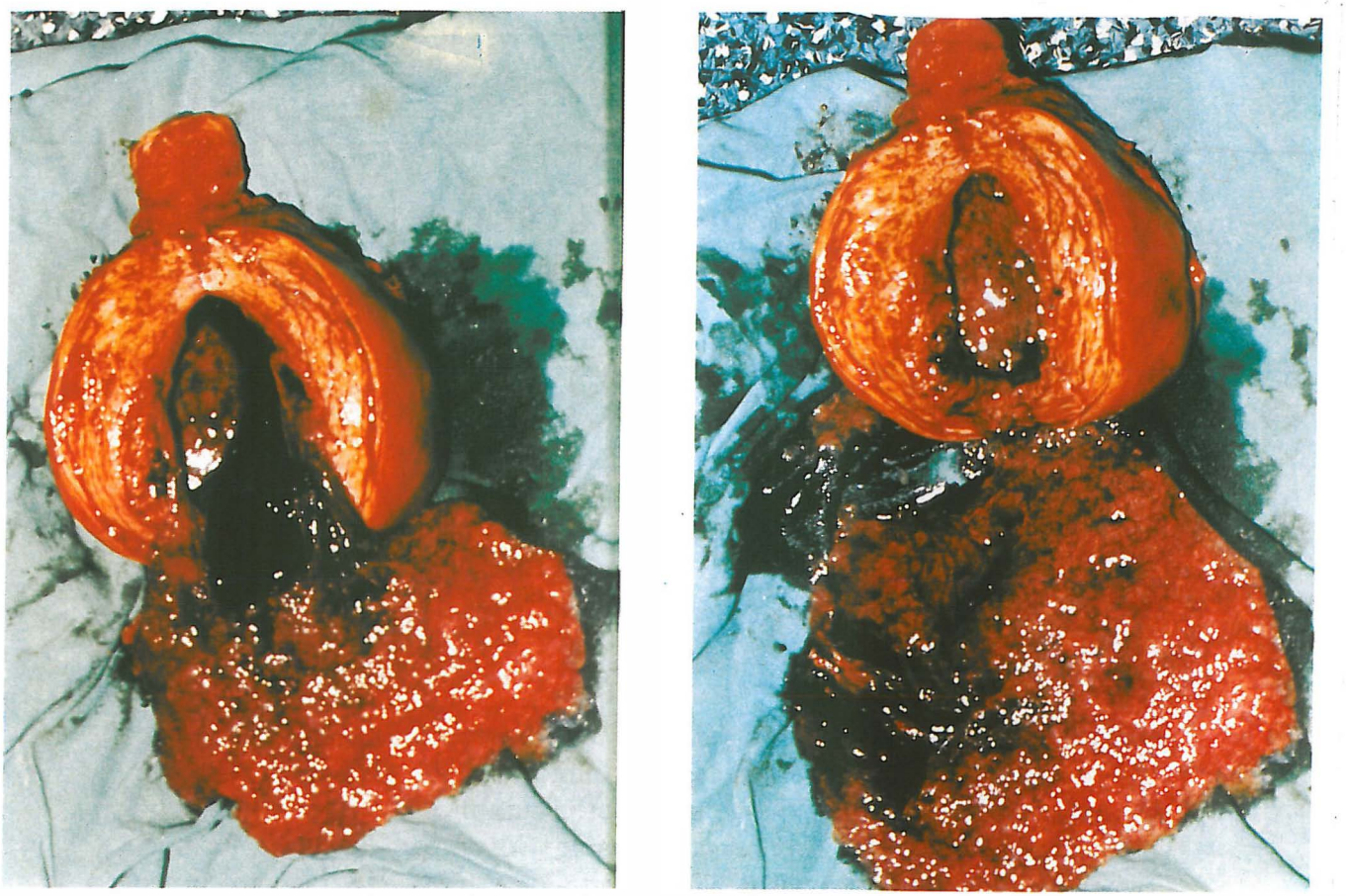

Fig. 1. Uterus infiltrated with malignant lymphoma and a huge mass.

three children who complained of occasional vaginal bleeding in the past four months. Because of severe vaginal bleeding she was admitted to the emergency room at midnight. Subsequently, dilatation and curretage were carried out and endometrial biopsy was obtained. Because she was severely anemic she received two units of whole blood. On the following day the pathologist reported suspicion of a lympho-proliferative process. She then underwent investigation for possible malignant lymphoma. She had no weight loss, no fever, chills, or night sweats; but she had a persistent foul-odored purulent vaginal discharge of four months' duration which was unresponsive to antibiotics.

Her vital signs showed a blood pressure of 90/65 and pulse rate of 140. Respiratory rate was 28 per minute, and temperature was 38°C. Herpast history revealed no medical problems. She was taking no medication except iron pills and vitamins. Abdominal examination revealed severe tenderness, with some distension of the mid lower abdomen. No organomegaly and no lymphadenopathy were present. Her bone marrow aspiration showed only hypercellularity of bone marrow with no abnormal cells. Peripheral blood smear showed hypochromic, microcytic cells. The hematocrit was 22 percent. The white cell count was 12,500 with 77% neutrophils and 23% lymphocytes. The platelet count was 125,000 per cubic millimeter. The chest x-ray was reported as normal. A total abdominal hysterectomy/salpingo-oophorectomy and lymph node biopsy were performed (Fig. 1).

Pathological findings were: the uterus weighed 310 grams and measured 12×7×4 cm. The shape of the organ was distorted by a diffusely infiltrative process involving predominantly the corpus and to a lesser degree the lower uterine segment. The uterine cervix and bilateral adnexa were not grossly involved by tumor. Sectioning of the uterus revealed a distorted uterine wall measuring up to 3 cm in maximum thickness with a homogenous white tan fleshy cut surface. The fallopian tubes and ovaries were grossly unremarkable. Hematoxylin and eosin-stained sections of the uterus demonstrated replacement of the endometrium and myometrium by a cellular infiltrate constituted by sparse scattered large cells with large, irregular sometimes multilobulated nuclei and numerous small lymphocytes and histiocytes. The sum of the two latter types of cells constituted more than 85% of the total cells present (Fig. 2). The tumor consisted of darkly stained lymphoid cells with a prominent starry-sky scattering of large, pole histiocytes. The neoplastic cells have rounded

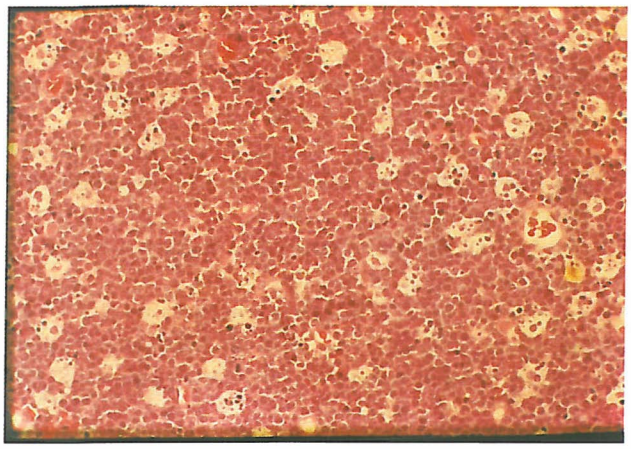

Fig. 2. Tumor consists of darkly stained lymphoid tissue with a prominent "starry sky" scattering of large pale histiocytes.

to oval nuclei, reticulated chromatin and darkly stained small nucleoli. In another view there were numerous cytoplasmic clear vacuoles that contain neutral fat by Sudan stain (Figs. 3, 4). Immunopathology study revealed strongly positive staining with anti-CD 10, CD 19, CD 20, CD 22 and LCA.

According to the Ann-Arbor system she was a case of stage II uterine malignant non-Hodgkin B-cell lymphoma, small non-cleaved cell type or Burkitt's lymphoma. A week later she was started on CHOP (cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², vincristine 1.4 mg/m² and prednisone 75 mg/m². Up to the typing of this article she has received two courses of chemotherapy with no response.

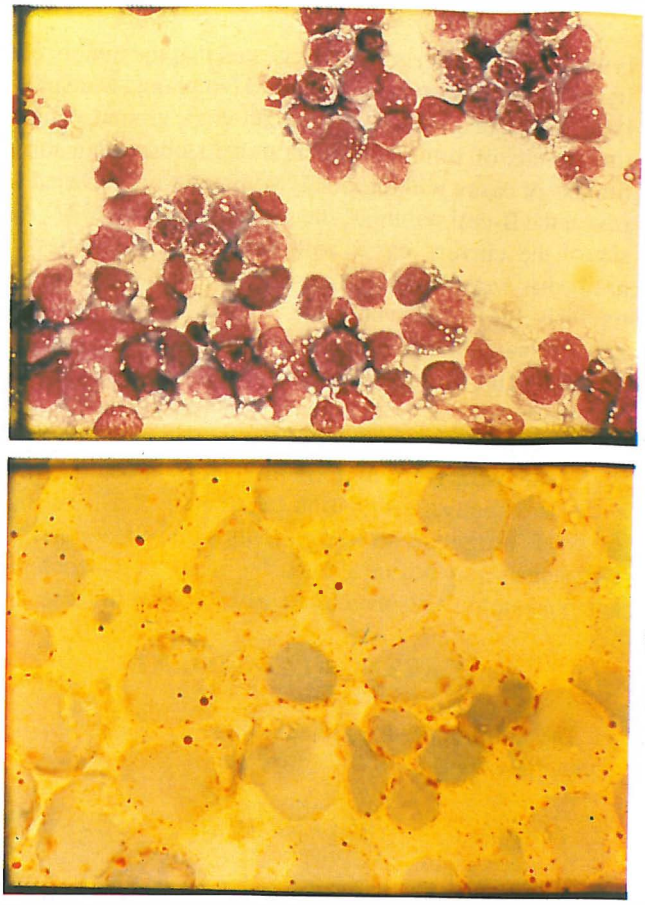

Fig. 3. The neoplastic cells have numerous cytoplasmic clear vacuoles that contain neutral fat by Sudan stain.

DISCUSSION

Lymphomas presenting with initial manifestations of female genital tract disease are extremely uncommon.[1,2,8,9] Those involving primarily the uterus favor the cervix rather than the body of this organ.[10] In 1965 Fox and More proposed strict criteria for diagnosing a primary uterine lymphoma.[14] Among these criteria they stipulated that the disease should be present only in the uterus or stage I disease. The study by Harris et al.[6] was outstanding in its higher frequency (78%) of stage I disease; meanwhile only 1 of 10 cases with uterine lymphoma reported by Castaldo et al.[11] was stage 1. Four of the current cases were collected through review of Annual of Pathologic Autopsy cases in Japan which resulted in a high frequency of cases with advanced disease resulting in the poor survival rate. Among the cases selected for the current study, the pathology registry cases were older and had more advanced disease than other cases. The prognosis of uterine lymphoma was reported to be relatively favorable when the disease was in early stage and treated properly.[5-6] Several studies reported a poor prognosis of cervical lymphoma. Two of five cases reported by Castaldo et al. died within one year, and four of six patients reviewed by Komaki et al. died of disease in less than one year.[7] The current study comprised three cases with corporeal and four with cervical lymphoma.[13] This preponderance of cervix to corpus lymphoma was in agreement with previous studies from North America[6] and Japan.[4]

Vaginal bleeding was the most common symptom in the current and previously reported cases of uterine lymphoma,[6,7,11] although abdominal pain or backache were the main symptoms in two of four cases of corpus lymphoma. Abdominal or pelvic masses with or without perineal discomfort were the presenting symptoms in three patients with corpus lymphoma reported by Chorlton et al.[5] Fox and More reported a case of corpus lymphoma presenting with abdominal pain and vaginal bleeding.[14] Generally, patients with cervical lymphoma were younger (median age 44 years) at onset of disease than those with corpus lymphoma (median age 52 years).[7, 11, 14, 21] In the series reported by Harris et al.[6] by colposcopy, cervical lymphoma showed diffuse enlargement of the cervix with or without erosion or polypoid mass.[6, 11, 12]

Histologically, all cases in the current series were NHL of the diffuse type, mainly of the large cell morphology, which was similar to the previous studies of uterine

lymphoma.[3,6,7] Harris et al. suggested that the tumor cells in their cases of uterine and vaginal lymphoma were of B-lymphocytic origin on purely morphologic grounds.[6] Since then results of immunohistochemical studies on a small number of cases with uterine lymphoma were reported to reveal the B-cell nature of the proliferating cells.[4,8,15] All six of the current cases with preserved reactivities to antibodies were B-cell in nature,[29] further confirming the exclusively B-cell nature of the uterine lymphoma. Lymphoma confined to the uterus or with limited spread beyond the uterus has been described as having an overall favorable response to treatment.[22,26,28] Uterine lymphomas have responded to surgery,[28] combination chemotherapy and radiotherapy[25,26] and chemotherapy alone[27,28] with variable response to radiation treatment.[27,28] The overall favorable prognosis seen in patients with primary uterine lymphomas may be due to the prominence of gynecologic symptomatology displayed in early stages of the disease.

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REFERENCES

1. Carr I, Hill AS, Hancock B, Neal FE: Malignant lymphoma of the cervix uteri: histology and ultrastructure. J Clin Pathol 29: 680-6, 1976.
2. Freeman C, Berg JW, Cutler S: Occurrence and prognosis of extranodal lymphomas. Cancer 29: 252-60, 1972.
3. Aozasa K, Tsujimoto M, Sakurai M, Honda M, Yamashita K, Hanada M, et al: Non-Hodgkin's lymphomas in Osaka, Japan. Eur J Cancer Clin Oncol 21: 487- 92, 1985.
4. Murotsuki A, Yazaki A, Hayakawa S, Yamashita T, Takahashi K: A case of primary malignant lymphoma of the cervix uteri. Cancer Clin 335: 1716-20, 1989. (in Japanese)
5. Chorlton I, Karnei RF Jr, King FM, Norris HJ: Primary malignant reticuloendothelial disease involving the vagina, cervix, and corpus uteri. Obstet Gynecol 44: 735-48, 1974.
6. Harris NL, Scully RE: Malignant lymphoma and granulocytic sarcoma of the uterus and vagina: a clinicopathologic analysis of 27 cases. Cancer 53: 2530-45, 1984.
7. Komaki R, Cox JD, Hansen RM, Gunn WG, Greenberg M: Malignant lymphoma of the uterine cervix. Cancer 54: 1699-704, 1984.
8. Matsuyama T, Tsukamoto N, Kaku T, Matsukawa K, Hirakawa T: Primary malignant lymphoma of the uterine corpus and cervix. Report of a case with immunohistochemical analysis. Acta Cytol 23: 228-32, 1989.
9. Maeda T, Kumagai H, Mori H: Malignant lymphoma presenting as initial symptom in the uterus: case report. Br J Obstet Gynecol 95: 1195-7, 1988.
10. Cunningham D, Gilchrist NL, Lee FD, Haxton M, Heppleston A, Forrest GJ, et al: T-cell lymphoblastic lymphoma of the uterus complicated by *Chlamydia trachomatis* pneumonia. Post Grad Med J 62: 55-7, 1986.
11. Castaldo TW, Ballon SC, Lagasse LD, Petrilli ES: Reticuloendothelial neoplasia of the female genital tract. Obstet Gynecol 54: 167-70, 1979.
12. Retikas DG: Hodgkin's sarcoma of the cervix: report of a case. Obstet Gynecol 80: 1104-7, 1960.
13. Johnson CE, Soule EH: Malignant lymphoma as a gynecologic problem: report of five cases including one primary lymphosarcoma of the cervix uteri. Obstet Gynecol 9: 149-57, 1957.
14. Fox H, More JRS: Primary malignant lymphoma of the uterus. J Clin Pathol 18: 723-8, 1965.
15. Nishikawa T, Kasajima T, Takeo Y, Ando A, Masuda A, Kawakami M: Two cases of primary lymphoma of uterus-an inmmunohistochemical study. Jpn J Reticuloendothel Soc 31: 87-94, 1991.
16. Holm FM, Blomgren H, Lowhagen H: Cancer risks in patients with chronic lymphocytic thyroiditis. N Engl J Med 312: 601-4, 1985.
17. Aozasak UEDA, et al: Prognostic value of histology and clinical factors in fifty-six patients with gastrointestinal lymphomas. Cancer 61: 309-15, 1988.
18. Aozasa K, Ohsawa M, Saeki K, Horiuchi K, Kawano K, Taguchi T: Malignant lymphoma of the breast: its immunologic type and association with lymphocytic mastopathy. Am J Clin Pathol 97: 699-704, 1992.
19. The Non-Hodgkin's Lymphoma Pathologic Classification Project. National Cancer Institute sponsored study of classification of non-Hodgkin's lymphomas; summary and description of a working formulation for clinical usage. Cancer 49: 2112-35, 1982.
20. Anderson GG: Hodgkin's disease of the uterine cervix: report of a case. Obstet Gynecol 29: 170-2, 1967.
21. Retikas DG: Hodgkin's sarcoma of the cervix: report of a case. Obstet Gynecol 80: 1104-7, 1960.
22. Wright CJ: Solitary malignant lymphoma of the uterus. Am J Obstet Gynecol 117: 114-120, 1973.
23. Kuo HC, Chou Cy, Chang CH, Liu MT, Tzeng CC, Huang KE: Primary malignant lymphoma of the uterine cervix shows favorable response to neoadjuvant chemotherapy. Gynecol Oncol 52: 408-410, 1994.
24. Kazadi Buanga J, Alcazar Zambrano JL, Villamizar N: Primary cervical non-Hodgkin's lymphoma. Case report and review of the literature. Rev Fr Gynecol Obstet 88: 318-320, 1993.
25. Johnston C, Senekjian EK, Ratain MJ, Talerman A: Conservative management of primary cervical lymphoma using combination chemotherapy; a case report. Gynecol Oncol 35: 391-394, 1989.
26. Brockmans FJ, Swartjes JM, Van der Valk P, Schutter EM: Primary malignant lymphoma of the uterus: localization in a cervical polyp. Eur J Obstet Gynecol Reprod Biol 48: 215-

219, 1993.

27. Awwad JT, Khalil AM, Shamseddine AI, Mufarrij AA: Primary malignant lymphoma of the uterine cervix; is radiotherapy the best therapeutic choice for stage IE? Gynecol Oncol 52: 91-93, 1994.
28. Muntz HG, Ferry JA, Flynn D, Fuller AF, Tarraza HM: Stage IE primary malignant lymphomas of the uterine cervix. Cancer 68: 2023-2032, 1991.
29. Ballesteros E, Osborne BM: CD5+ low-grade marginal zone B-cell lymphomas with localized presentation. Am J Surg Pathol 22(2): 210-7, 1998.