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.


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 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. 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). 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. 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 such as thyroid, salivary, gastrointestinal and pleural lymphoma has been suggested. 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
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 curetage 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. Her past 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 $12 \times 7 \times 4$ 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...
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.

**DISCUSSION**

Lymphomas presenting with initial manifestations of female genital tract disease are extremely uncommon. Those involving primarily the uterus favor the cervix rather than the body of this organ. In 1965 Fox and More proposed strict criteria for diagnosing a primary uterine lymphoma. 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. 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. was stage I. 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. 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. The current study comprised three cases with corporeal and four with cervical lymphoma. This preponderance of cervix to corpus lymphoma was in agreement with previous studies from North America and Japan.

Vaginal bleeding was the most common symptom in the current and previously reported cases of uterine lymphoma, 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. Fox and More reported a case of corpus lymphoma presenting with abdominal pain and vaginal bleeding. Generally, patients with cervical lymphoma were younger (median age 44 years) at onset of disease than those with corpus lymphoma (median age 52 years). In the series reported by Harris et al. by colposcopy, cervical lymphoma showed diffuse enlargement of the cervix with or without erosion or polypoid mass. 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{4,8,15} All six of the current cases with preserved reactivities to antibodies were B-cell in nature,\textsuperscript{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.\textsuperscript{22,26,28} Uterine lymphomas have responded to surgery,\textsuperscript{28} combination chemotherapy and radiotherapy\textsuperscript{25,26} and chemotherapy alone\textsuperscript{27,28} with variable response to radiation treatment.\textsuperscript{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**


