

Malignant Lymphoma Involving Ovarian Brenner Tumor

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Abstract : Incidental finding in a 69-year-old woman of a diffuse large B-cell lymphoma involving the ovary with a benign Brenner tumor is presented. The benign Brenner tumor, which was composed of epithelial nests and fibrous stroma, was infiltrated by large cells with cleaved and noncleaved pleomorphic nuclei, showing B-cell phenotype. The patient was postoperatively found to have enlarged intraabdominal lymph nodes. To the best of our knowledge, this is the first reported case of Brenner tumor associated with malignant lymphoma.

Key Words : Brenner tumor, Lymphoma, Ovary

Introduction

Cases of primary ovarian lymphoma have been reported[1,2], but most reports of the ovarian lymphomas were actually limited in the initial presentation of the disease or a manifestation of disseminated malignancy. In an autopsy series[3] the ovarian involvement of lymphoma occurred with frequency as high as 26%.

We report a case of intraabdominal nodal non-Hodgkin's lymphoma, initially presenting as an infiltrating mass in a Brenner tumor of the ovary.

Case report

A 69-year-old multiparous woman was admitted to Keimyung University Dongsan Medical Center because of an incidentally discovered pelvic mass on a routine gynecologic examination. Because the mass showed same echo-density on ultrasonography as the myometrium that was adhered to it, the mass was initially diagnosed as a subserosal leiomyoma.

She had taken medicine to dilative cardiomyopathy for 8 years but had no other systemic diseases. All blood

chemistry parameters checked before operation were within normal ranges. In the operation field, the mass was found to be in the enlarged left ovary adhering to the left side of the uterus and small intestine.

Total hysterectomy with bilateral salpingo-oophorectomy was performed. The excised ovary was 11.0× 8.5×8.0 cm in dimensions, and its external surface was nodular and glistening (Fig. 1A). The cutting surface was homogeneously pale-yellowish and showed fibrous septation imparting vague lobulated or nodular appearance (Fig. 1B). There was no hemorrhage and necrosis. The uterus, right adnexa, and left salpinx were grossly unremarkable.

CT and MRI scans performed 1 month later showed multiple conglomerated lymph nodes in para-aortic, mesenteric and left common iliac areas. The lymph nodes had central necrosis. There was no recurrent lesion in the pelvic cavity. Peripheral blood smear and bone marrow biopsy showed no abnormal cells.

After 3 cycles of chemotherapy, the

enlarged nodes disappeared. The patient tolerated 6 cycles of chemotherapy without side effects. However the preexisting dilative cardiomyopathy worsened, and she died of congestive heart failure, pneumonia, and sepsis 7 months after the operation.

Materials and Methods

Sections of the enlarged ovary were fixed in 10% buffered neutral formalin, embedded in paraffin, and stained with hematoxylin and eosin. Additional sections were prepared for immunohistochemical staining, which was performed using the standard avidin-biotin preoxidase technique. The list of antibodies, dilutions, and sources is listed in Table 1.

Results

1. Microscopic description

Microscopically, the ovarian mass showed

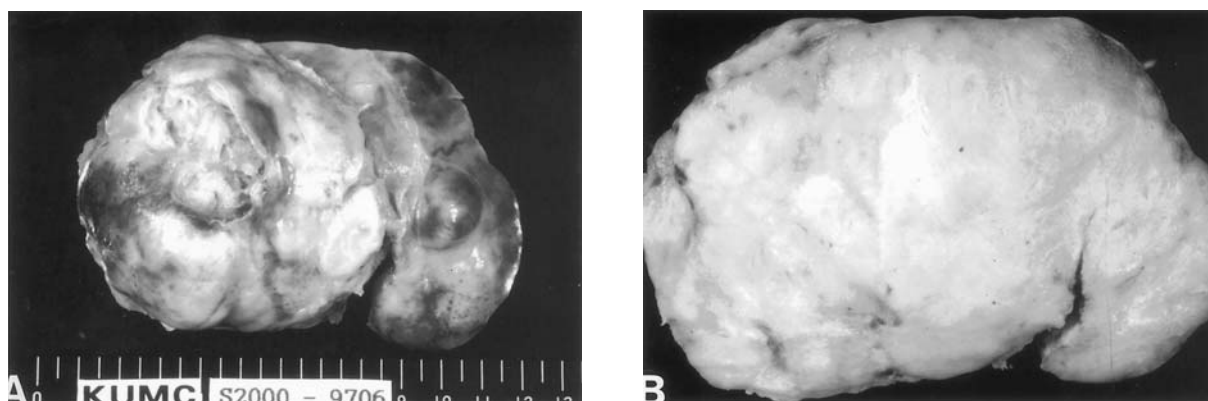


Fig. 1. Gross appearances of the tumor. (A) The external surface is nodular and glistening. (B) The cut surface is pale yellowish and shows lobulated or nodular appearance.

benign Brenner tumor characterized by round or oval nests, and was composed of cells with pale cytoplasm and oval nuclei often containing grooves, and fibrous stroma was definitely present in the mass. The remaining part of the mass was occupied with a diffuse dense infiltrate of large pleomorphic lymphoid cells with cleaved and noncleaved nuclei, several of which contained prominent nucleoli, small amount of cytoplasm, and exuberant mitoses.

At lower power field, vague nodular appearance imparted by fibrous tissue was focally noted and the malignant lymphoid cells were diffusely infiltrating the fibrous stroma and epithelial nests of Brenner tumor (Fig. 2A). Some preserved epithelial nests of Brenner tumor were floating in the lymphoid lesion, but the rest was totally or partially infiltrated (Fig. 2B). The tumor cells were arranged in small irregular shaped nests (Fig. 2C) and cords by delicate fibrous tissue. Some cells infiltrating the fibrous stroma were elongated and showed sweeping pattern. Focal areas showing starry-sky appearance (Fig. 2D) and vascular wall

infiltration were also noted.

Lymphatic channels contained aggregated similar cells with more uniform appearance. Small lymphocytes and eosinophils were scattered at the periphery of the tumor, but eosinophilic myelocytes were not noted. Overall, histologic findings were consistent with malignant lymphoma. Nevertheless metastatic or primary ovarian undifferentiated carcinomas, sarcomas and melanoma might also manifest similar appearance.

Dysgerminoma can grow in diffuse pattern but it should show mature lymphocytes and plasma cells in fine septa, and tumor cells are cytologically different from tumor cells of the present case. Diffuse, sarcomatous granulosa cell tumor and poorly differentiated Sertoli-Leydig cell tumor must be considered in differential diagnosis, but their specific growth pattern must also be present at least focally in order to make the diagnosis.

2. Immunohistochemistry

Cytokeratin, LCA, S-100 and Vimentin were applied as a screening immunohistochemical panel. LCA was positive in tumor cells and showed B-cell (CD20) phenotype (Fig. 3A). CD15 and CD30 were negative in tumor cells. Cytokeratin (Fig. 3B) and Vimentin were positive in Brenner tumor components.

Granulocytic sarcoma was excluded because the tumor cells showed negative immunoreactivity to lysozyme, CD30 and

Table 1. Panel of antibodies

Antibody	Dilution	Source
BM-1	Prediluted	Biogenex, USA
CD3	1:100	NCL, UK
CD15	1:10	NCL, UK
CD20	1:100	Dako, USA
CD30	1:40	Dako, USA
CK	1:100	Dako, USA
LCA	1:100	Dako, USA
Lysozyme	1:100	Dako, USA
S-100	1:80	Biogenex, USA
Vimentin	1:100	Biogenex, USA

BM-1, and no eosinophilic myelocytes in routine stain, and there were no any other systemic manifestations of the granulocytic sarcoma. The final diagnosis was diffuse large B-cell lymphoma, according to the REAL and WHO classification, infiltrating the benign brenner tumor.

Discussion

Ovarian involvement by malignant lymphomas is generally categorized in three forms. The first and the most

common is ovarian involvement developing in known cases of disseminated lymphoma, where the ovaries are involved as a secondary phenomenon. Secondly, the initial presentation of a malignant lymphoma can be an ovarian mass, as in endemic Burkitt's lymphoma. Thirdly, malignant lymphoma may arise in the ovaries as a primary extranodal lymphoma.

Primary ovarian lymphoma is a disease of poor prognosis[4]. However, many reported cases actually represent ovarian involvement by diffuse lymphomatous process or misdiagnosis of granulosa cell

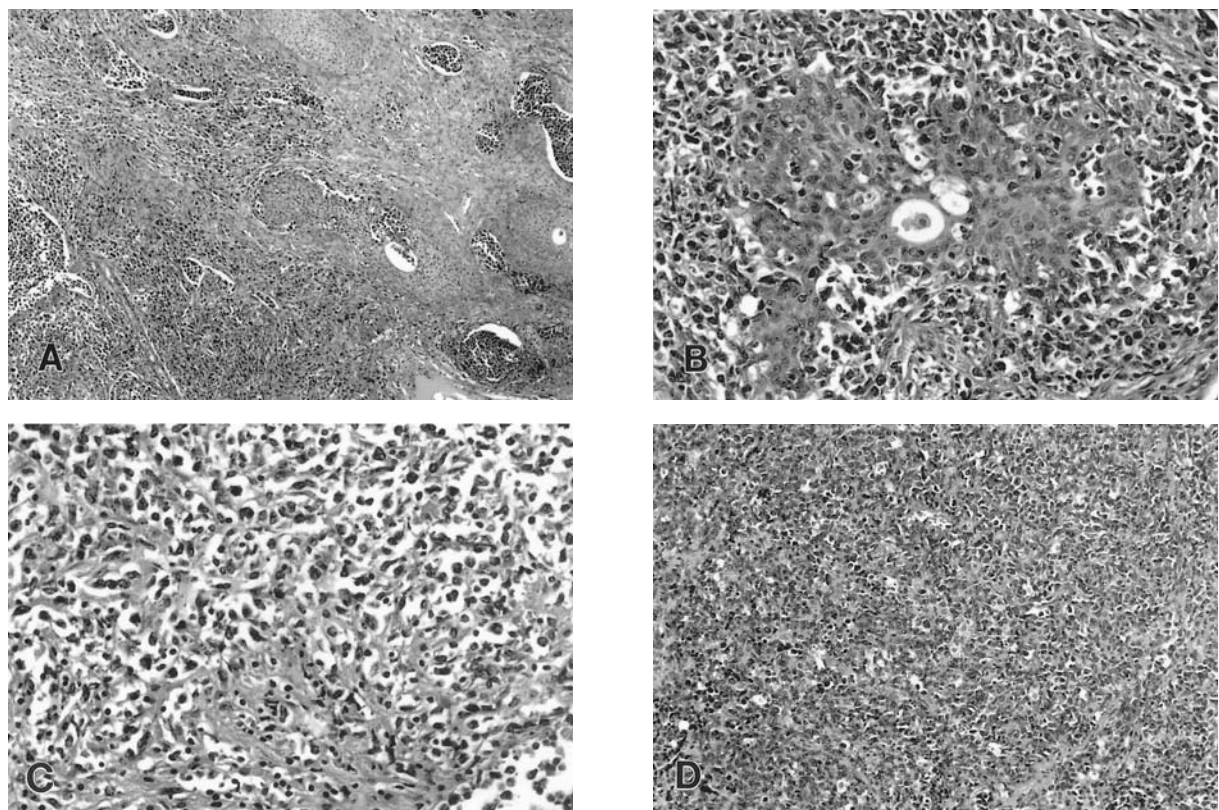


Fig. 2. Microscopic appearances of the tumor. (A) Malignant cells are diffusely infiltrating the fibrous and epithelial nests of Brenner tumor. (B) Some preserved epithelial nests of Brenner tumor are floating in the higher-grade lesion. (C) The tumor cells are arranged in small irregular shaped nests by delicate fibrous tissue. (D) Focal stary-sky appearance is noted.

tumors, dysgerminoma, and metastatic cancer[5,6].

Fox and Langley[7] suggested the criteria of the primary ovarian lymphoma as follows: (i) At the time of diagnosis the disease process is clinically confined to the ovary, and full investigation fails to reveal any evidence of lymphoma elsewhere in the body. However, a tumor can be accepted as probably primary in the ovary, if spread has occurred to immediately adjacent lymph nodes or if there has been direct spread to infiltrate immediately neighboring structures. (ii) The peripheral blood and the bone marrow should not contain any abnormal cells. (iii) If further lymphomatous deposits occur at sites remote from the ovary, then at least several months should have elapsed between the appearance of primary and secondary tumors. If these stringent criteria are applied, primary ovarian lymphoma becomes very rare disease and carries a favorable prognosis[1].

Reactive lymphocytes can secondarily

populate the ovary in response to various ovarian lesions[8], and benign lymphoid aggregates have been found in approximately half of normal ovaries [9,10]. These probably can give rise to primary ovarian lymphoma in a manner similar to MALT lymphoma.

Because of the lack of preoperative radiologic studies and staging study, we do not know whether the malignant lymphoma in this case actually arose in the ovary or rather an initial manifestation of generalized lymphoma. We had previously thought that the lesion was probably primary in the ovary, because of the unilateral, no definite mass, no pelvic lymphadenopathy at surgery, normal peripheral blood and bone marrow findings, and no systemic manifestations of the disease, and that the cause of patient's death was not directly related to the lymphoma. However, because the enlarged lymph nodes found 1 month after the surgery were too large and could not be considered to be local nodes, it must then be designated as an intra-abdominal

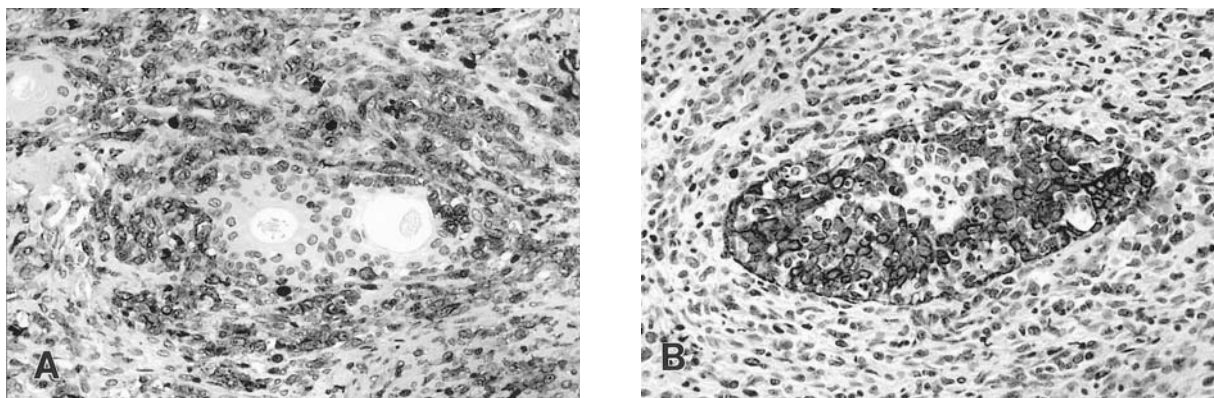


Fig. 3. Malignant cells are positive for CD20 immunostaining (A). Cytokeratin is positive in epithelial nests of Brenner tumor (B).

nodal lymphoma presenting as a ovarian mass.

A case combined of lymphoma and serous carcinoma[9], a lymphoma arising in thyroid tissue of mature cystic teratoma[11], and a squamous cell carcinoma metastatic to an ovarian Brenner tumor[12] have been reported in literature. Our present case is another unusual tumor composed of benign Brenner tumor and diffuse large B cell lymphoma, however, whether the latter is primary in the ovary or not is not established.

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