Case Report

Non-Hodgkin's lymphoma presenting as an ovarian mass

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ABSTRACT

Involvement of the ovary by malignant lymphoma is a well-known late manifestation of disseminated nodal disease. Lymphoma presenting with ovarian mass as an initial manifestation is a rare entity and may cause confusion for the clinician since its presentation might resemble other, much more frequent primary ovarian tumors. We present a case of non-Hodgkin's lymphoma where the initial presentation was an ovarian tumor. The patient underwent surgery and was receiving chemotherapy when she developed generalized lymphadenopathy. She did not respond well to the therapy, had a progressive disease and expired after 5 months.

Key words: Non-Hodgkin's lymphoma, ovarian tumor, lymphadenopathy

INTRODUCTION

Whereas leukemic and lymphomatous involvement of the ovary is frequent at autopsy (25%) in patients with these diseases, ovarian enlargement as the initial manifestation is rare (0.3%). Although a few individuals have prolonged survival after surgery only, it is generally accepted that most patients probably have nodal lymphoma, which has not been detected by available clinical methods, but which has presented in an unusual fashion.[1]

We report here a case of secondary involvement of the ovary in non-Hodgkin's lymphoma (NHL) with occult extra-ovarian nodal disease at the time of presentation. We also discuss the histogenesis of ovarian lymphomas with criteria for diagnosis and differential diagnosis.

CASE REPORT

The present case report is about a 35-year-old woman who presented with the complaints of post-meal bloating and associated pain in the lower abdomen of 2 months' duration. A physical examination revealed mild pallor and on abdominal examination, a tender mass was felt in the right iliac fossa, which appeared to be arising from the pelvis. Vaginal examination revealed a mass in the right fornix pushing the uterus to the left side. Liver and spleen were not palpable. The hematological profile of the patient was found to be normal except for mild anemia with hemoglobin level of 9 g%. Red blood cell (RBC) morphology was microcytic hypochromic. CA-125 levels were raised to 113.5 IU/ml. An abdomino-pelvic ultrasound showed a heterogeneous, mainly solid, space-occupying lesion with few cystic areas and irregular margins in right adnexal region, measuring 8 cm × 6 cm × 3.5 cm. Computed tomography (CT) scan of the abdomen showed a large enhancing mass lesion with hypodense areas in the right tubo-ovarian region along with multiple enlarged para-aortic lymph nodes. There were no peritoneal implants, hepatic metastases or organomegaly.

An exploratory laparotomy was performed, which revealed an encapsulated right ovarian mass and fluid in the pouch of Douglas. Total abdominal hysterectomy with bilateral salpingo-oopherectomy, omentectomy along with fluid drainage was done. The abdomen was closed after peritoneal toileting. The entire operated specimen was submitted for histopathological examination.

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PATHOLOGICAL FINDINGS

Gross findings

The right ovary was converted into an 8 cm × 6 cm × 4 cm sized encapsulated solid mass having a bosselated outer surface. The cut surface showed compressed normal ovarian tissue on one side and the mass was grey-white in color, homogeneous and fleshy. The uterus and cervix along with the other side ovary and fallopian tube were unremarkable [Figure 1].

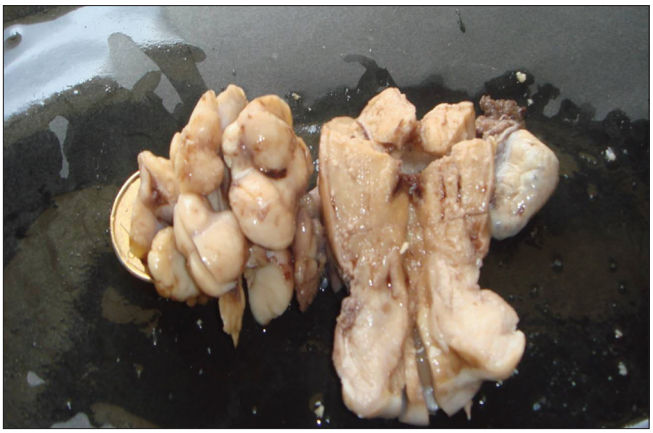

Figure 1: Gross photograph showing utero-cervix, normal looking left fallopian tube and ovary along with right ovary converted into a solid mass with bosselated outer surface

Microscopic findings

The myometrium and the right side fallopian tube showed lymphoid aggregates. Sections from the ovarian mass showed normal ovarian tissue pushed to the periphery by intersecting cords of tumor cells, focally forming vague nodules comprised of uniform population of small round to irregular nuclei and inconspicuous to prominent nucleoli admixed with histiocytic cells, scattered plasma cells and eosinophils. There was increased mitotic activity with many atypical mitoses [Figure 2]. Sections from omentum revealed focal collections of cells with above described morphology and acute inflammatory infiltrate. On the basis of microscopic findings supported by immunohistochemistry (positive for leukocyte common antigen [LCA] and negative for cytokeratin), a diagnosis of NHL involving the ovary was rendered.

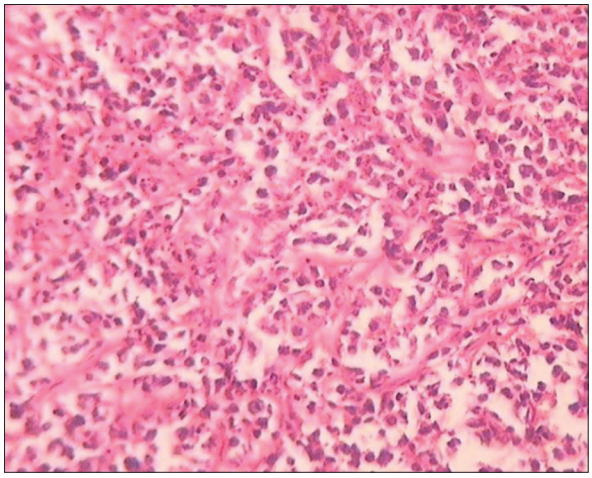

Figure 2: Histopathology section from the ovarian mass comprised of uniform population of small round to irregular nuclei admixed with histiocytic cells, scattered plasma cells and eosinophils (H and E, ×400)

The patient was reviewed after receiving the histopathology report for any lymphadenopathy and was found to have none. Bone marrow aspirate and biopsy ruled out any marrow involvement. A diagnosis of primary NHL of the ovary was given. A chemotherapy protocol comprising of six cycles of CHOP regime was started, but the patient did not respond well to therapy and had a progressive disease. When the patient visited the hospital for the second cycle, she was found to have mild bilateral pleural effusion and two tiny superficial lymph nodes, one each in the right anterior axillary and right cervical region. Fine needle aspiration cytology from both the lymph nodes was done and it revealed cellular smears comprised of monotonous population of intermediate lymphoid cells having round nuclei with 1-3 nucleoli and scant basophilic cytoplasm admixed with the population of centrocyte-like cells with cleaved nuclei. The background showed abundant lymphoglandular bodies admixed with RBCs [Figure 3]. A cytological diagnosis of follicular center cell lymphoma (centroblastic/centrocytic) was made. Pleural fluid also showed the presence of numerous lymphoid cells. A final diagnosis of Stage IV (Ann Arbor staging) NHL with secondary ovarian involvement with an initial clinical presentation of occult extra-ovarian disease was made. The patient was shifted to some other oncology center but expired after 5 months.

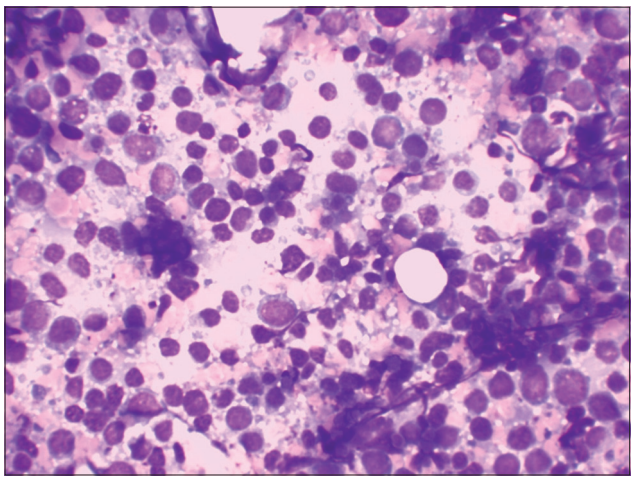

Figure 3: Aspiration smear from the right cervical lymph node comprising of a monotonous population of intermediate lymphoid cells having round nuclei and scant basophilic cytoplasm admixed with the population of centrocyte-like cells with cleaved nuclei. The background shows abundant lymphoglandular bodies admixed with Red blood cells (Giemsa, ×400)

DISCUSSION

Lymphoma is a rare tumor of the ovary and its presence most commonly represents involvement in overt systemic disease, almost always of the non-Hodgkin's type. There has been debate as to whether lymphoma can arise de novo in the ovary; lymphoid aggregates do exist in normal ovarian tissue, which could give rise to such lesions. Although ovarian lymphoma is a rare entity, accounting for 0.5% of all NHL and 1.5% of all ovarian neoplasms, it should be included in the differential diagnosis of an ovarian mass.[2] NHL involving the ovaries may cause confusion for the clinician since its presentation might resemble other, much more frequent tumors. Lymphomas of the ovary may occur at any age, but mostly women in their 40 s are affected.[3] The most common presenting signs or symptoms of malignant lymphomas involving the ovaries are abdominal or pelvic pain or mass.[1] Some cases present with ascites and elevated serum CA-125.[2] Our patient presented with a pelvic mass, omental involvement and elevated serum CA-125 at the time of surgery. The presence of positive staining for LCA in the histological specimen distinguishes malignant lymphoma from non-lymphoid neoplasm.[2] These cells are negative for cytokeratin.

The ovarian involvement in malignant lymphoma may be primary or secondary. Fox *et al*.[4] suggested the following criteria for the diagnosis of primary ovarian lymphoma:

- At the time of diagnosis, the lymphoma is clinically confined to the ovary and a full investigation fails to reveal evidence of lymphoma elsewhere. A lymphoma can still, however, be considered as primary if spread has occurred to immediately adjacent lymph nodes or if there has been direct spread to infiltrate immediately adjacent structures
- The peripheral blood and bone marrow should not contain abnormal cells
- If further lymphomatous lesions occur at sites remote from the ovary then at least several months should have elapsed between the appearance of the ovarian and extra-ovarian lesions.

The secondary involvement may be of two types: (1) As an initial clinical presentation of occult extra-ovarian disease or (2) as a manifestation of widely disseminated disease. The distinction is of considerable importance because primary extra-nodal lymphomas run a less aggressive course and have a 5 years survival rate of 80% as compared to the malignant lymphomas affecting the lymph nodes, which have a 5 years survival rate of only 33%.[3]

As our patient had presented with no evidence of generalized lymphadenopathy pre-operatively, a diagnosis of primary ovarian lymphoma was considered. However, on subsequent axillary and cervical lymph node involvement along with pleural effusion, a diagnosis of secondary ovarian lymphoma with an initial presentation of occult extra-ovarian disease was considered and the patient was treated accordingly.

CT is the mainstay of lymphoma staging in the chest, abdomen and pelvis as well as in other nodal lymphomas. Bone marrow biopsy is also mandatory for staging. Positron emission tomography with ^{18}F-fluorodeoxyglucose has been reported as being a useful method for staging and for assessment of therapeutic response.[5]

The histological appearances of lymphoma in the ovary are generally similar to those seen in the extra-ovarian sites. In the ovary, however, there is a great tendency for the tumor cells to grow in cords and nests, appearing to cling to the reticulin, forming pseudoacini. The most common types of lymphomas encountered in the ovary are diffuse large-cell, Burkitt and follicular lymphomas. Rarely precursor B-cell lymphoblastic lymphomas are also encountered. However, these need to be distinguished from other round-cell tumors such as metastatic poorly-differentiated carcinoma, especially of mammary origin; primary small-cell carcinoma; adult granulosa cell tumor; and dysgerminoma. Immunohistochemical studies will help to distinguish between these tumors.[3] It should be noted that diffuse infiltration of the adjacent fallopian tube and/or broad ligament is much more common in lymphomas than in most of the tumors in the differential diagnosis. Dysgerminomas may be indistinguishable on gross examination from malignant lymphomas. However, only 10% of dysgerminomas are bilateral in contrast to 50% of lymphomas. Moreover, on microscopic examination, the nuclei and immunohistochemical features are strikingly different. Granulocytic sarcomas should be considered when one is evaluating cases of suspected ovarian lymphoma. They can be distinguished with chloracetate esterase staining or more accurately by immunostaining for myeloperoxidase. On routine stains, granulocytic sarcoma is often composed of cells with more finely dispersed nuclear chromatin and more abundant cytoplasm, which may be deeply eosinophilic, compared with lymphoma cells with nuclei of the same size.[6]

CONCLUSION

The treatment of choice of ovarian NHL is chemotherapy without surgical cyto-reductive efforts. In the presence of an ovarian tumor, the possibility of ovarian NHL must be considered and its clinical, biological and/or radiological signs must be actively sought. Since the prognosis and treatment of lymphoma differs significantly from ovarian carcinoma, a representative tissue sample should be

obtained and sent for frozen section analysis to establish the diagnosis and to avoid mutilating surgery.

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