Primary ovarian malignant lymphoma presenting as ovarian carcinomatosis: a case report and literature review

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Summary

Introduction: Primary ovarian lymphoma may present with a clinical scenario consistent with advanced epithelial ovarian carcinoma. Although ovarian lymphoma is a rare entity, accounting for 0.5% of all non-Hodgkin's lymphoma and 1.5% of all ovarian neoplasms, it should be included in the differential diagnosis of an ovarian mass. *Case:* We report a case of a 78-year-old woman who presented with an ovarian neoplasm suggestive of advanced ovarian carcinoma. During diagnostic laparoscopy, biopsies were obtained with frozen section analysis revealing malignant lymphoma. Further histopathologic analysis revealed a diffuse large B-cell lymphoma (DLBCL). The treatment plan was for six cycles of R–CHOP chemotherapy. A drammatic response was noted after only three cycles of R-CHOP. *Conclusion:* Primary ovarian lymphoma presenting as an ovarian tumor is exceedingly rare. Since the prognosis and treatment of lymphoma differs significantly from ovarian carcinoma, a representative tissue sample of the adnexal tumor should be obtained and sent for frozen section analysis to establish the diagnosis. Principal treatment for non-Hodgkin's lymphoma is chemotherapy without surgical cytoreductive efforts.

Key words: Ovarian carcinoma; Non-Hodgkin's lymphoma; Chemotherapy; Cytoreduction.

Introduction

Fewer than 1% of patients with malignant lymphoma present initially with ovarian enlargement [1, 2]. Malignant lymphoma involving the ovary may present as follows: I) a primary neoplasm arising in the ovary, II) as the initial clinical manifestation of occult nodal disease, and III) as a manifestation of widely disseminated systemic lymphoma [3]. Fox *et al*. [4] proposed the following criteria for diagnosis of primary ovarian lymphoma:

– At the time of diagnosis, the lymphoma is clinically confined to the ovary and a complete investigation fails to reveal evidence of lymphoma elsewhere. However, an ovarian lymphoma can still be considered as primary if it has spread to the immediate adjacent lymph nodes or directly spreads to infiltrate the immediate adjacent structures.

– The peripheral blood and bone marrow should not contain any 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 extraovarian lesions.

When these criteria are strictly applied, the diagnosis of primary ovarian lymphoma becomes extraordinarily rare [5]. We present a case of primary ovarian lymphoma in a patient referred to us with the presumable diagnosis of advanced epithelial ovarian carcinoma.

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Case Report

A 78-year-old nulligravid female presented to her local physician complaining of lower abdominal pain and urinary difficulty. The patient's surgical history was only significant for a prior laparotomy with an ovarian cystectomy secondary to endometriosis 50 years before.

Physical examination revealed a negative nodal survey with a large palpable mass noted in the left lower quadrant. Bimanual exam confirmed a pelvic mass extending posteriorly compressing the rectosigmoid colon. The patient reported a recent normal mammographic and colonoscopy examination. Computerized tomography (CT) scans of the abdomen and pelvis demonstrated a 6.8 cm left adnexal mass with an additional smaller mass in the right adnexa. There was no significant adenopathy or ascites. The liver showed three ill-defined lesions: one in the caudate lobe measuring 2.2 cm, another 3.4 cm lesion on the right inferior aspect of the liver and a 1.8 cm lesion in the right lobe. There were soft tissue densities in the intestinal mesentery and involving the omentum. The remainder of the solid organs and lymph nodes were normal. Preoperative CA-125 was 24 U/ml and LDH was 287. CBC was normal except for a mildly increased platelet count (406,000/l). Despite a normal CA-125, given findings on physical examination and radiologic imaging, the presumptive diagnosis of advanced stage ovarian carcinoma with carcinomatosis was suspected.

Management options were extensively discussed with the patient. Given her age and that she was the primary caregiver for her elderly husband, the patient was very concerned with quality of life issues. After discussion, the decision was made to proceed with diagnostic laparoscopy, assessment of intraperitoneal disease extent, and biopsy with probable neoadjuvant chemotherapy. If she had tolerated neoadjuvant chemotherapy, with acceptable disease response to therapy, the patient would then have considered interval cytoreduction followed by more systemic adjuvant chemotherapy.

At the time of assessment laparoscopy, bilateral fixed adnexal masses were noted. The tumor on the left adnexa was densely adherent to the peritoneum, just above the bladder. A large omental mass was present; however, peritoneal surfaces of the upper abdomen including that of the diaphragm appeared normal. Biopsies of the omentum and ovaries were obtained with frozen section analysis revealing a malignant lymphoma. Immunohistochemical staining studies showed large cells which were positive for CD20 and negative for CD3. There was a background infiltrate of small CD3-positive mature lymphocytes. The Mib-1 proliferation index was increased in malignant cells (estimated 50%). Cytokeratin AE1/AE3 was negative. Flow cytometric immunophenotyping was attempted, but was non-contributory (which could have been due to lack of viable cells). The final pathologic diagnosis was determined to be that of a diffuse large B cell lymphoma.

The patient was referred to Hemotology/Oncology and additional postoperative assessment included a bone marrow biopsy which was negative for lymphoma, normal CBC without lymphocytosis, normal creatinine, electrolytes and liver enzymes. Serum protein electrophoresis was unremarkable. Hepatitis B and C serology were negative. LDH was 287. A postoperative PET/CT scan was significant for multiple lesions in the abdomen and pelvis, predominantly in the omentum, mesentery and fat. A large confluent mass in the pelvis measuring 10.4 x 8.3 cm was noted. Other findings included lesions in the perirectal area, left diaphragm, spleen and multiple liver lesions. A decision was made to treat with six cycles of rituximab, cyclophosphamide, adriamycin, vincristin and prednisone (R-CHOP) chemotherapy. Follow-up CT scan performed after only three cycles of chemotherapy revealed a dramatic response to treatment. The pelvic mass decreased in size from 10.4 x 8.3 cm to 3 x 1.5 cm. Omental, mesenteric and splenic masses were no longer seen.

Discussion

Prognosis of ovarian lymphoma is based primarily on clinical stage, modality of onset, histological type and phenotype. Tumors are staged according to the FIGO system, as used for other ovarian neoplasms. Prognosis of primary ovarian lymphoma is not as good as for other primary sites. Five-year survival is estimated at approximately 40%.

The standard regimen for the treatment of non-Hodgkin's lymphoma is combination chemotherapy with cyclophosphamide, adriamycin, vincristin and prednisone (CHOP) [6]. Recently, CHOP, in combination with targeted immunotherapy, rituximab (R-CHOP), has resulted in significant survival improvement in this group of patients [7]. Importantly, there is evidence that an aggressive surgical cytoreductive effort is not necessary and is not associated with improvement in survival [8]. Most of the reported cases underwent surgery, but debulking of the tumor was not considered to be related to a better prognosis [9]. Dimopoulos *et al*. [1] and Yamada *et al*. [10] recommended that patients with ovarian lymphoma should be treated with curative intent with combination chemotherapy regimens appropriate for their histology. Therefore, in patients presenting with a pelvic mass with carcinomatosis, etiologies other than primary epithelial ovarian cancer must be considered [11]. Primary ovarian lymphoma should be considered in the differential diagnosis and surgical cytoreduction is not beneficial as the mainstay of treatment is systemic chemotherapy.

Furthermore, extra-nodal presentation of primary ovarian lymphoma is relatively frequent. Moreover, relapse in the central nervous system (CNS) is not uncommon. Therefore, in addition to systemic chemotherapy, consideration should also always be given for CNS prophylaxis with intrathecal methotrexate.

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