Primary Ovarian Non- Hodgkin's Lymphoma: A Rare Case Scenario

Sarder Md.Abu Horaira[a], Shah Md. Badruddoza[a], M Manzurul Haque[b], Hasina Akhter[c] Dipak Kumar Mahanta[d]

Abstract

One of the very rare types of the ovarian tumor is lymphoma. 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 with others, much more frequent primary ovarian tumors. To report an uncommon case of primary ovarian Non- Hodgkin's lymphoma in a peri- menarche girl with an attempt to delineate the clinical features and characteristics of this tumor with respect to histological findings. A 13-year of aged young girl was admitted with signs and symptoms suggestive of an ovarian tumor. Histopathology of the ovarian mass was done after an exploratory laparotomy. After surgery, Computed tomography (CT) of the chest, abdomen and pelvis, serum CA-125 and a bone marrow study were also done. Computed tomography revealed a heterogeneous mass, measuring 6.5×5.5 cm in diameter. Diagnosis of Non-Hodgkin's lymphoma was made on histopathology. Tumor was classified as a diffuse large B cell lymphoma. The patient was treated with surgery followed by chemostherapy using standard CHOP regimen using cyclophosphamide, doxorubicin, vincristine and prednisolone. She has now been without disease for 9 months after the surgery and chemotherapy. According to previous reports the treatment principles and prognosis of primary ovarian lymphoma is the same as that of other nodal lymphomas.

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[a]Department of Pathology, Rajshahi Medical College, Rajshahi, Bangladesh.

[b]Department of Surgery, Barind Medical College, Rajshahi, Bangladesh.

[c]Department of Gynaecology and Obstetrics, Barind Medical College, Rajshahi, Bangladesh.

[d]Department of Pathology, Shaheed M Monsur Ali Medical College, Sirajganj, Bangladesh.

Correspondence to : SMA Horaira horaira14@gmail.com

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INTRODUCTION

Involvement of the ovary by malignant lymphoma is a well-known late manifestation of disseminated nodal disease. But primary ovarian lymphoma is rare. Primary ovarian Non-Hodgkin's lymphoma accounts for 0.5% of all Non-Hodgkin's lymphomas and 1.5% of all ovarian neoplasm, with diffuse large B cell lymphoma being the commonest type.[1]The origin of these rare tumors is controversial. There has been debated 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. The malignant transformation of benign lymphoid infiltrates seen in up to 50% of normal ovaries, as suggested by Monterroso *et al.* may partly explain their pathogenesis.[2] The symptoms are nonspecific, but presence of constitutional symptoms and the rapid progression in a young patient should raise the suspicion of a lymphoma. The probability of tumor lysis syndrome is very high in this setting. Fox *et al.* suggested diagnostic criteria for primary ovarian lymphoma, which needs (a) the disease to be confined to the ovary, (b) absence of disease in the blood and bone marrow and (c) the extraovarian deposits, if any, should appear at least after few months.[3]

Lymphomas are diagnosed based on histopathological findings, immunophenotyping, and cytogenetic tests. Diagnostic staging is established by means of clinical picture, laboratory analysis, biopsy ,X rays, CT, MRI, contrast scan, various endoscopies and scintigraphy of certain organ or if necessary of the whole body.[4]

The prognosis of ovarian lymphomas is excellent.[5] B cell lymphomas far better than T cell histologies. The treatment is mainly combination chemotherapy and the protocol depends on the primary histology. The role of surgery is debatable with present day chemotherapy regimes. We hereby report an uncommon case of primary ovarian Non- Hodgkin's lymphoma in a peri- menarche girl with an attempt to delineate the clinical features and characteristics of this tumor with respect to histological findings.

CASE REPORT

A young peri- menarche young girl, aged 13 years was admitted to Gyne & obstetric department of our hospital with the complaints of fever for one month, weight loss, pain and heaviness in the lower abdomen. Physical examination revealed a mobile abdominal mass, mobile with regard to the deep and superficial plains; ascites positive on percussion. Computed tomography (CT) showed a heterogeneous mass, measuring 6.5×5.5 cm in diameter, in the area of the left uterine adnexa ; there were no enlarged lymph nodes. The serum tumor

markers were positive, with CA-125 being 252 U/ml (normal < 25 U/ml). The erythrocyte sedimentation rate was increased, being 85 mm in the first hour.

An exploratory laparotomy was done through a abdominal vertical midline incision so as to establish the diagnosis. Removal of tumor with left salpingo-oophorectomy was performed; there were no peritoneal implants, hepatic metastases, or adenomegaly. On gross examination the left ovary was enlarged showing a solid nodule measuring approximately 6.3x 5.6x 5.1 cm with a grey white cut-surface (Figure 1).

Figure1: A well circumscribed solid mass with a grey white cut-surface.

Histopathology of the left ovarian mass was reported to be consistent with diffuse large B-cell lymphoma, Non-Hodgkin's lymphoma (2008 WHO Classification) based on morphological and immunohistochemical features (Figure-2). Most of the neoplastic cells were positive for CD-20 and for leucocyte common antigen (LCA) antibody. After surgery, CT of the chest, abdomen, and pelvis was normal and serum CA-125 was also normal. A bone marrow study showed no abnormalities. The patient was prescribed eight cycles of the standard CHOP regimen using cyclophosphamide, doxorubicin, vincristine and prednisolone. She has completed eight cycles and, 9 months after surgery, she remains disease free.

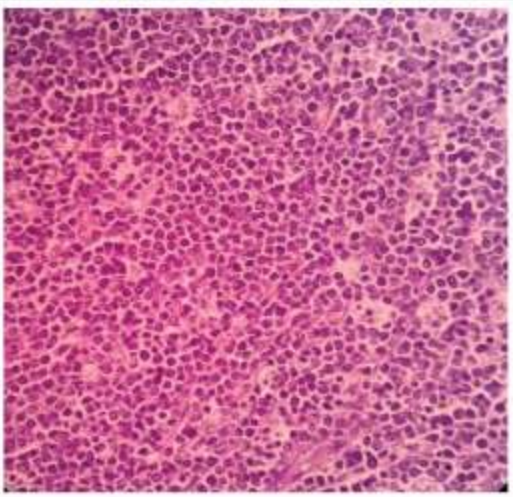

Figure 2 Histopathology showing diffuse large B-cell Non-Hodgkin's lymphoma.
(Haematoxylin and eosin, × 40)

DISCUSSION

Genital tract involvement in Non-Hodgkin's lymphoma is uncommon. However, when involved, the ovary seems to be one of the more common anatomic sites (25%).[6] Ovarian involvement is usually secondary, occurring as part of a systemic disease. Localized primary lymphoma of the ovary is unusual and rare, with few reported cases. The distinction is important because primary extra nodal lymphoma runs a less aggressive course with 5 year survival rate of 80% as compared to secondary malignant lymphoma, which has a 5 year survival rate of only 33%.[7] But diagnosis of primary lymphoma may still be considered if the spread has occurred to the adjacent lymph nodes or to the immediately adjacent structures. In our case there was no obvious lymphadenopathy and blood, bone marrow, spleen or hepatic involvement. All these findings favour the diagnosis of primary ovarian lymphoma.

Lymphomas of the ovary may occur at any age, but mostly women in their 40s are affected.[6,7] In our case this lymphoma was diagnosed in a very young age of 13 years. Whether primary or secondary, ovarian lymphomas may have varied presentation, most of them being discovered

incidentally during the work up for pelvic or abdominal complaints.[6] Patients presenting with rapid onset abdominal pain and distension had worse prognosis.[3] Our patient also presented with rapid onset of abdominal pain and distension which proved fatal. The majority of primary ovarian lymphomas present with pelvic complaints; some cases present with ascites and elevated serum CA-125.[8] Our patient presented with a pelvic mass and elevated serum CA- 125.

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; granulocytic sarcomas and dysgerminoma. Immunohistochemical studies will help to distinguish between these tumors.[9] 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, on microscopic examination, the nuclei and immunohistochemical features are strikingly different. Microscopically the cells of dysgerminoma are uniform with PAS+ve, diastase sensitive, clear cytoplasm whereas in lymphoma cytoplasm is scanty and PAS negative.[6] Granulocytic sarcomas should be considered when one is evaluating cases of suspected ovarian lymphoma. Granulocytic sarcoma on routine stains is often composed of cells with more finely dispersed chromatin and abundant deeply eosinophilic cytoplasm compared to lymphoma cells which have nuclei of same size with coarse chromatin and scanty cytoplasm. The findings of granulated myelocytes are diagnostic of granulocytic sarcoma.[6,10]

The single file arrangement of lymphoma cells may simulate metastatic carcinoma particularly one of breast origin.[3,10] However in such cases history of primary mammary carcinoma is present. Morphologically cells in breast carcinoma have irregular margins, they retain their intercellular attachments, form cohesive sheets and at times produce small amount of intracytoplasmic mucin[10]. Granulosa cell tumours are distinguished from lymphoma by grooved nuclei, formation of Call- Exner bodies and tendency to merge with thecomatous areas.[10]

Immunohistochemistry in our case showed positivity of tumor cells for B lineage markers (CD20 and LCA) and negativity for T lineage markers (CD3 and CD43). On the basis of microscopic findings supported by immunohistochemistry, diagnosis of primary diffuse large B-cell Non-Hodgkin's lymphoma of the ovary was made.

The protocol of chemotherapy used in diffuse, large B-cell Non-Hodgkin's lymphoma is the standard CHOP regimen. Our patient was treated with left salpingo-oophorectomy and appendectomy followed by eight cycles of CHOP. The outcome of these patients, treated with appropriate chemotherapy, appears to be similar to that of patients with other nodal Non-Hodgkin's lymphomas.

Conclusion

Primary lymphoma of the ovary is a rare entity. It needs to be differentiated from other ovarian malignancies, as its management differs from other primary and metastatic ovarian tumors.

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