

Primary Ovarian Burkitt's Lymphoma: A Rare Type at a Rare Site

Gore Charusheela R, Sawaimul Komal D, Karia Kunjal M*, Koshy Ashily, Paranjape Sourabh P, Harsh Kumar
Department of Pathology, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Dr. D.Y. Patil Vidyapeeth, Pimpri, Pune-411018

***Corresponding author**

Karia Kunjal M

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Abstract: The lymphomatous processes involving ovary is extremely rare. Lymphomas presenting as an initial manifestation in ovary is rarer. The clinical outcome and patient survival in cases of ovarian lymphoma depends on characterization of the variety of non-Hodgkin's lymphoma. We report an extremely rare case of 33 year old female with ovarian Burkitt lymphoma, clinico-radiologically mimicking acute abdomen with left twisted ovarian cyst. The routine laboratory evaluation was unremarkable. The diagnosis of malignant ovarian lymphoma was made on histopathology and immunohistochemistry of the excised tissue.

Keywords: Acute abdomen, Burkitt, Non-Hodgkin's lymphoma, ovarian lymphoma.

INTRODUCTION

Non-Hodgkin's lymphoma (NHL) arising primarily in ovary is a rare variant of extranodal lymphoma [1]. It accounts for 0.5% to 1 % of all NHL [2,3]. Burkitt lymphoma (BL) is a highly aggressive subtype of NHL that usually occurs as a manifestation of systemic disease [4]. Primary ovarian Burkitt lymphoma is extremely rare and seen usually in children and immunocompromised hosts [5]. As per the literature review, ovarian Burkitt lymphomas are frequently bilateral [4].

Pathologically, majority of cases of malignant ovarian lymphomas are diffuse large B-cell type [6]. Prognosis of malignant ovarian lymphoma is poor. Treatment of ovarian lymphoma is similar to that of other non-Hodgkin's lymphoma which includes surgery, combination chemotherapy and or radiotherapy [7,8]. The case is presented due to its rarity and uncommon presentation.

CASE REPORT

A 33 year old tubetomised female patient with previous history of tuberculosis presented to the emergency department with acute abdominal pain of 2 days duration. The frequency of urination was also decreased. There was no history of any other medical illness. There was no palpable lymphadenopathy. The routine haematological and biochemical investigations were within normal reference range. The patient was immune-competent.

USG abdomen revealed a large well defined cystic lesion of size 10.5 cm x 8.8 cm x 7.4 cm involving the left sided ovary. The emergency exploratory laparotomy was performed in view of twisted ovarian cyst and excision of left ovarian tissue was done. The excised specimen in multiple tissue pieces and fragments received for histopathological

examination measured approximately 10.2 cm x 7.0 cm x 4.0 cm. The specimen was irregular having solid, cystic as well as hemorrhagic areas.

Microscopic examination unveiled monomorphic population of lymphoid cells in diffuse sheets and trabeculae. The cells were uniform in size and had round nuclei with prominent 3-4 nucleoli and scant cytoplasm. Numerous mitotic figures, apoptotic cells were noted along with tingible body macrophages giving a "starry sky" appearance. On immunohistochemistry the lymphoid cells were positive for LCA, CD20 and LMP1 (latent membrane protein). The tumour cells were negative for CD3, CD30, EMA, and CD117. Ki67 proliferative index was 97% to 98%. The patient was thus diagnosed as Burkitt lymphoma of left sided ovary.

The peripheral smear, bone marrow aspiration and biopsy showed no involvement by lymphoma cells. Serum LDH level was 152 IU/L which was in the normal reference range. F18-FDG (fluorodeoxyglucose) whole body PET CT scan unmasked weakly metabolic bilateral pelvic nodes. The patient is presently on cyclophosphamide, adriamycin, vincristine, cytarabine, methotrexate, ifosomide, mesna, etoposide based chemotherapy.

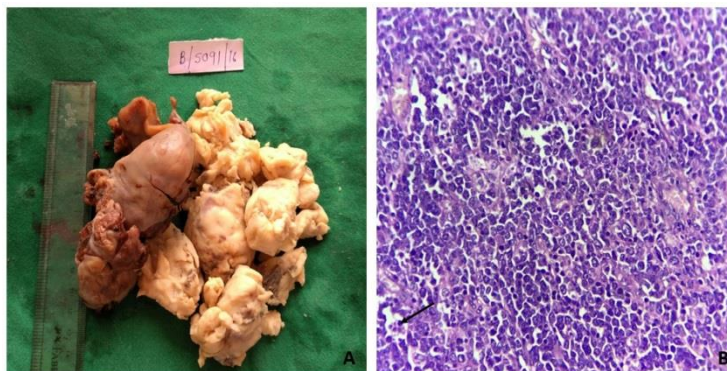


Fig-1: A: Grossly irregular greyish white specimen in multiple friable tissue pieces and fragments measuring approximately 10.2 cm x 7.0 cm x 4.0 cm. B: Diffusely arranged non-cohesive monomorphic population of round tumor cells having non-cleaved nuclei with basophilic cytoplasm. Occasional tangible body macrophages noted (Arrow), (H & E x 400)

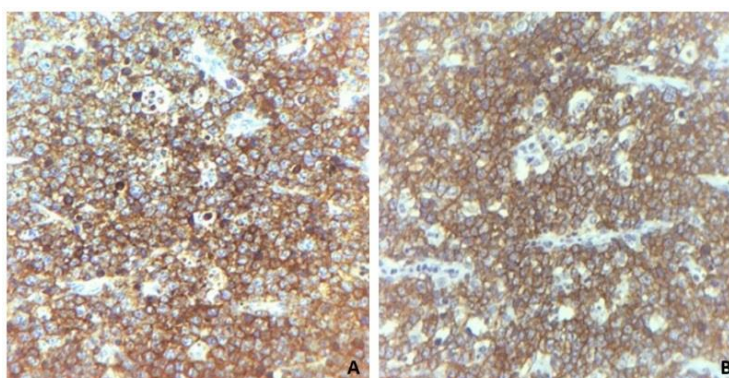


Fig-2: Immunohistochemical study; A. Tumor cells are positive for LCA; B. Tumor cells are positive for CD20

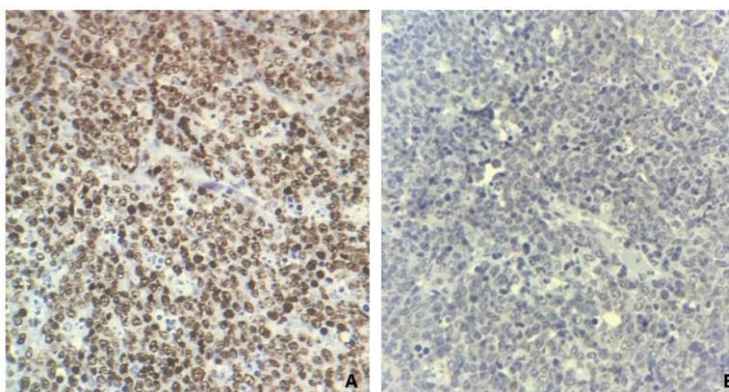


Fig-3: Immunohistochemical study; A: Ki 67 showing proliferative index 97% to 98%; B: Tumor cells are negative for EMA

DISCUSSION

Malignant lymphoid tumours uncommonly involve the female genital tract [1, 7]. The ovaries are the most frequent sites to be affected, with death rate of 25% [9, 10]. The incidence of ovarian non-Hodgkin's Lymphoma (NHL) is 1.5% among all ovarian neoplasm [3, 11]. Involvement of the ovary by lymphomatous processes is usually secondary; however 10% of cases have their onset in ovary [11]. The distinction between primary and secondary lymphomas is of importance as both have different course.

Fox and Langley in 1976 proposed the criterias for the diagnosis of primary ovarian lymphomas as:

- Clinical confinement of lymphoma to the ovary at the time of diagnosis with investigations supporting no evidence of lymphoma elsewhere. An ovarian lymphoma can be considered as primary if it is spread to adjacent lymph nodes or it has directly infiltrated adjacent structures immediately.
- Absence of lymphoma cells in peripheral blood smear and bone marrow.

- Presence of lymphomatous lesions at sites remote from ovary, having elapsed time of several months between appearance of ovarian and extra ovarian lesions [1,12].

The secondary ovarian lymphoma occurs either as manifestation of disseminated disease or as an initial presentation of occult extra- ovarian disease [1].

Burkitt's lymphoma (BL) is a highly aggressive and rapidly growing mature B-cell neoplasm that usually presents at extranodal sites or as an acute leukaemia[5,11]. Burkitt lymphoma accounts for approximately 19% of adnexal lymphomas [1]. It is usually bilateral and associated with ascites [11]. However in our case it showed unilateral involvement of the ovary without ascitis. Clinically these patients present with abdominal pain, distension, nausea, vomiting, bowel obstruction, amenorrhoea, irregular menses and osteoarticular aches [8]. Majority of the patients (70%) with burkitt lymphoma present in advanced stage. WHO 2016 classification describes three forms of BL endemic, sporadic and immunodeficiency associated [10, 11]. The intra-abdominal BL diagnosis is difficult due to nonspecific presentation [5].

The bone marrow infiltration can be seen in 30% to 38% of cases and central nervous system involvement is encountered in 13% to 17 % of the cases. There is tendency of partial torsion and intermittent lower abdomen pain in patients of BL due to hyper vascularity and increased ovarian weight [8]. The acute abdominal pain was the presenting symptom in our patient.

The lymphomas that involve ovary are diffuse large B-cell lymphoma (DLBCL), Burkitt's lymphoma (BL), follicular lymphomas, lymphoblastic lymphoma or anaplastic large cell lymphoma [5,11,13]. Lymphocytes surrounding the blood vessels at the hilum and those related to the corpus luteum are thought to be the cell of origin of the ovarian lymphomas [2]. The interaction of reactive cells with lymphoma cells is mediated through cytokines. In BL, the expression of multiple cytokines like IL-8, IL-10, tumor necrosis factor (TNF) alpha and beta is promoted by EBV [12]. Burkitts lymphoma is classified based on presentation as low risk group and high risk group. The low risk group includes non-bulky disease (<10 cm), early stage (I or II) disease, good performance status, and a normal lactate dehydrogenase (LDH) level. The high risk group includes huge tumour masses greater than 10 cm (stage III and IV), bone marrow infiltration, cerebral manifestation, elevated LDH level [10].

The differential diagnosis includes granulosa cell tumour (juvenile type), germ cell tumour, dysgerminoma, sex cord stromal tumour, granulocytic

sarcomas [2, 14]. The monomorphic proliferation of medium-sized lymphoma cells with several small nucleoli and a starry-sky appearance are the histologic hallmark of Burkitt's lymphoma. Immunohistochemically the neoplastic cells express CD19, CD20, and CD10. Burkitt's lymphoma is differentiated from DLBCL and other lymphomas based on identification of c-myc rearrangement and Ki-67 fraction close to 100% [12]. In our case the Ki 67 index was >95% and LMP1 were positive thus indicating the probable etiology of EBV infection.

The standard treatment modality for Burkitt lymphoma includes intensive chemotherapy [4]. Other modes of treatment include surgery, radiotherapy or combination [7, 8]. The recommended treatment by National Comprehensive Cancer Network panel for low risk patient of BL is use of CODOX-M or HyperCVAD. The treatment of choice for high risk patients of BL is CODOX-M/IVAC with or without rituximab, or HyperCVAD alternating with methotrexate plus cytarabine, with or without rituximab [2, 10]. This patient is on CODOX-M/IVAC. The PET CT scan performed post three chemotherapy cycles showed regression of the pelvic nodes. BL is a potentially curable malignancy with cure rate of approximately 90% in cases of localized disease and 30% in cases of disseminated disease [4, 6]. The clinical tool used to assess the prognosis of patients with aggressive NHL is the International Prognostic Index (IPI) that includes Ann Arbor staging, age, elevated serum lactate dehydrogenase (LDH), performance status, and number of extranodal sites of disease for scoring [11]. The prognosis of aggressive BL is poor with 5 year survival rate of 33% [1, 13].

CONCLUSION

Malignant primary ovarian lymphoma is an extremely rare entity. The prognosis and treatment is different for primary and secondary lymphomatous processes in ovary. It is thus essential to distinguish them. Early and prompt diagnosis of non- Hodgkin lymphoma of the ovary yields better survival.

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