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Uterine Lymphoma - A case report

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Abstract : Extra nodal type of Non Hodgkins lymphoma occurring in female genital tract is rare. The diagnosis is challenging. We report a case of primary extra nodal NHL of stage IIAE according to Ann Arbor staging. A sixty three year postmenopausal unmarried lady, presented with pressure symptoms of the bladder . On evaluation, she was found to have a large cervical mass extending into the uterine cavity. Imaging, cervical biopsy and immuno histochemistry of the cervical lesion was suggestive of Double hit high grade diffuse large B cell lymphoma (DHL-DLBCL). Double hit lymphomas do not have a favourable prognosis. She was treated with five cycles of R-CHOP regimen (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone). She was in good condition but expired after five cycles of chemotherapy, probably due to myocardial infarction.

Keyword : Extranodal non hodgkin's lymphoma, Double hit lymphoma

Introduction

Non Hodgkins lymphoma occurs rarely in the extra nodal site. Extra nodal lymphomas, particularly in female genital tract constitutes about 1% (1). They are known for their rarity and difficulty in diagnosing the disease. The diagnosis is usually made using immunohistochemical markers. There is no established treatment regimen. Double hit lymphoma is a type of large B cell lymphoma which involves mutations of multiple oncogenes. The median survival time is 0.2 to 1.5yrs (2). R-CHOP regimen is considered as the treatment for DHL-DLBCL. However, standard treatment is not yet established.

Case report

A 63 year unmarried postmenopausal, sexually inactive lady, presented with history of increased frequency of micturition, straining to void, incomplete emptying of bladder and constipation for 2months. She had to void 5 to 6 times in the day and 5 times in the night. She was evaluated elsewhere. Ultrasonogram was reported as bulky uterus with pyometra and an ill defined lesion in the cervix. A CT scan done elsewhere was reported as bulky cervix with enlargement of paraaortic nodes. The pap smear showed atypical glandular cells of unknown significance, for which a biopsy was done. The biopsy was reported as moderately differentiated adenocarcinoma. The patient came to our hospital for further management. On examination the cervix was ballooned out with right parametrial involvement, short of pelvic side walls. Hence clinically she was suspected to have cancer cervix stage IIB. Fractional curettage was done and the biopsy was reported as poorly differentiated carcinoma, probably squamous cell type. MRI done at this stage to further categorise this mass revealed a large mass replacing the uterus and cervix with bilateral parametrial involvement and involvement of common iliac and inguinal lymph nodes.

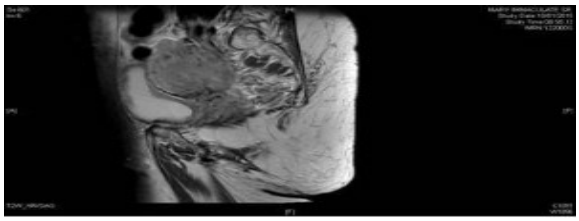

Figure1: Sagittal section of pelvis(T2W) - Diffusely enlarged uterus and the cervix which is replaced by heterogeneous T2 hyperintense soft tissue(6x4x7cm) showing restricted diffusion.

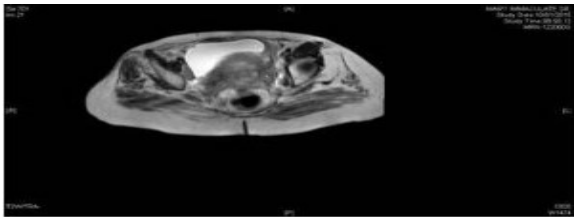

Figure 2:Coronal section of pelvis(T2W)- Complete loss of endocervical stromal ring with bilateral parametrial infiltration.

As on MRI, it was suspected to be lymphoma, immunohistochemical markers for lymphoma was done. The cells were positive for CD20, Bcl-2, C-myc(>50% cells) and MIB-1 of more than 90%. They were negative for Pan CK, CD10 and CD3. Hence she was diagnosed to have “High grade B-Non Hodgkins Lymphoma consistent with diffuse large B cell lymphoma – suggestive of Double hit lymphoma”.

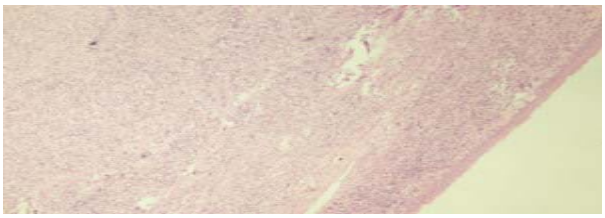

Figure 3: Cervix with Non Hodgkin’s Lymphoma, H&E 40x

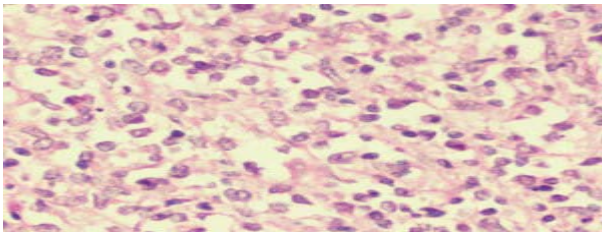

Figure4: Cervix with NHL (H&Ex400) showing atypical neoplastic lymphocytes

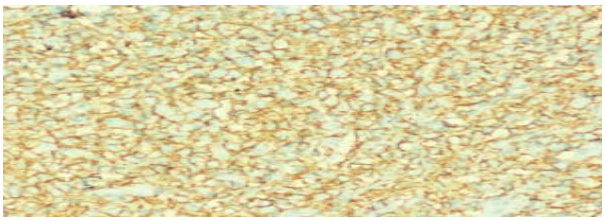

Figure5: T cells positive for CD20(H&Ex200)

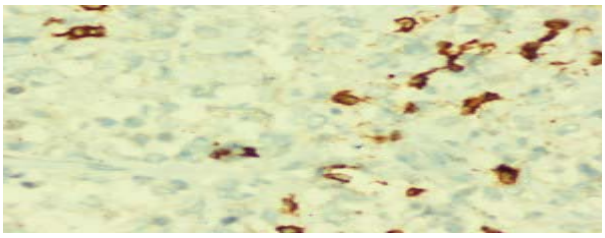

Figure6:CD3 positive in background T cells

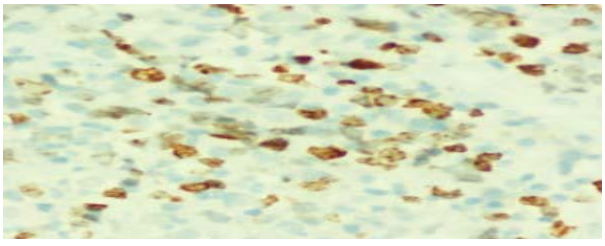

Figure7: Cervix with NHL showing high MIB(>60%) (H&Ex100)

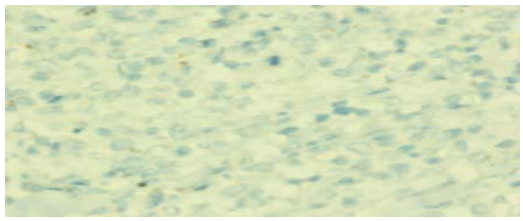

Figure8:Cervix with NHL, cells are CK negative(H&Ex400)

She was referred to hematology department where she underwent a bone marrow biopsy, which was reported to be normal. She was diagnosed as stage IIAE according to Ann Arbor staging . She received 3 cycles of R-CHOP regimen following which her MRI showed features of regression. She was planned for another 3 cycles, but patient expired after the 5th cycle of chemotherapy due to myocardial infarction.

Discussion

Lymphomas are lympho proliferative malignancies that account for 3-4% of all neoplasms. They are of two types- Hodgkin’s(15%) and Non hodgkin’s lymphoma (85%)(3). Non Hodgkins lymphoma occurring in extragonadal sites are rare. They are commonly in gastrointestinal tract and skin. They occur in one third of patients. Extragonadal NHL in female genital tract constitutes about 1%(1) .The challenging issue in NHL is the workup leading to diagnosis. Diffuse Large B cell Lymphoma is one of the common type of NHL occurring in female genital tract(4). The median age of the patient with cervical lymphoma is 44 years, ranging from 27 to 80 years(5). The symptoms are usually non specific. The most common presenting symptom is abnormal uterine bleeding. They can also present as any other pelvic mass with abdominal pain, dyspareunia and pressure symptoms (5). The classical symptoms of fever and night sweats associated with lymphomas are usually absent. Diagnosis is challenging even after a detailed work up. Histolopathological picture shows a solid sheet of cells with round nuclei and mitotic figures. The cells are positive for CD20, CD10, HLA-DR, bcl-2, CD5(6). The grade and stage of the disease in cervical lymphoma is considered as the prognostic factors (1). Chronic lymphocytic cervicitis and lymphoma like lesions can be considered as differential diagnosis . Fox et al. described primary uterine lymphoma as (i) During the time of diagnosis, the disease has to be confined to uterus (ii) No evidence of disease elsewhere in the body (iii) No evidence of leukemia and (iv) There should be interval of several months’ between the primary and secondary disease(7). Our patient presented with pressure symptoms which is a very unusual presentation for an uterine lymphoma. She was initially diagnosed to have a cervical malignancy which considering the fact she was sexually inactive and nulliparous was a rare diagnosis. However, MRI imaging was suggestive of lymphoma with extensive nodal involvement. CT and MRI helps in the diagnosis of lymphomas. CT also helps in planning the therapeutic regimen and follow up after treatment (5). In MRI, T1 weighted sections appear as low intense images and T2 weighted sections appear hyperintense (9) .Immunohistochemistry markers helped us clinch the diagnosis . Double hit lymphoma is the presence of bcl-2 and MYC mutations. bcl-2 gene expression results in anti-apoptotic activity and MYC causes proliferation. Her bone marrow biopsy and her counts were found to be

normal. Hence she was considered as primary uterine lymphoma stage IIAE according to Ann Arbor classification. This kind of lymphomas are difficult to treat (ASCO post). Advanced stage, central nervous system involvement, leucocytosis and elevated lactate dehydrogenase (LDH) is associated with poor prognosis. The median survival time was found to be 22months and progression free survival was 11months. It was also reported that less than 50% of patients with DHL were alive at 2 years (8). Hysterectomy is not the treatment of choice and it does not prognosticate the survival. It also results in large amount of bleeding during hysterectomy(10) .The standard treatment for uterine lymphoma has not been established yet; however, chemotherapy is administered in many cases of systemic disease. R-CHOP therapy, the combination of CHOP therapy, which until now has been the standard treatment, and rituximab, a chimeric anti-CD20 monoclonal immunoglobulin G antibody, has been successfully used to treat CD20-positive B-cell non-Hodgkin's lymphoma(11,12). In conclusion, primary uterine lymphoma is known for its rarity and challenges in diagnosis. Double hit lymphomas have poor prognosis. R-CHOP or CHOP regimen has been proven to be effective in the treatment of these tumours. Other modalities like radiation can be considered as palliative therapy.

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