CASE REPORT

Primary Non-Hodgkin's Lymphoma of Diffuse Large B-Cell Phenotype [DLBCL] of Uterine Corpus: A Rare Case Report with Brief Review of the Literature

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Abbreviation

AFP	Alpha fetoprotein
CD	Cluster of differentiation
CEA	Carcino-embryonic antigen

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CHOP	Cyclophosphamide, hydroxydaunorubicin (also called doxorubicin or Adriamycin), Oncovin (vincristine), prednisone
CT	Contrast tomography
DLBCL	Diffuse large B-cell lymphoma
NHL	Non-Hodgkin lymphoma
IHC	Immunohistochemistry
MPO	Myeloperoxidase
LCA	Leucocyte common antigen
PV	Per vagina
PAP	Papanicolaou test

Introduction

Primary extra-nodal NHL commonly involves gastrointestinal tract followed by bone, testis, salivary gland, thyroid, liver, kidney and adrenal gland [1]. Involvement of

Fig. 1 Ultrasonography image showing diffusely thickened myometrium (a), gross photograph depicting a bisected enlarged uterus with diffusely thickened “fish-flesh” appearance of myometrium (b),

photomicrographs showing diffuse infiltration of tumor cells, areas with infiltration into myometrium (arrow) and in between benign endocervical glands (star) (c, d) (H&E, $\times 400$)

the female genital tract is uncommon and still uncommon is the involvement of uterine corpus as compared to cervix and ovaries [2]. The incidence of primary NHL of uterine corpus ranges from 0.54 to 0.64 % of all extra-nodal NHL [3]. DLBCL subtype is the most common variant of lymphoma encountered among the documented cases. The treatment modalities of this disease are also not well defined.

We report a case of primary NHL of uterine corpus of DLBCL immuno-phenotype in a 62-year-old lady clinically presented with postmenopausal bleeding. The classical B symptoms of lymphoma were absent in the case. Clinical and radiological findings were in favor of uterine mass lesion possibly leiomyoma/sarcoma.

Case Report

A 62-year-old lady presented with postmenopausal irregular bleeding per vagina of 15 days duration with a sensation of heaviness of lower abdomen. She attained menopause 12 years back. There are no significant past

history and family history. Her general examination findings were mild pallor, no icterus, no lymphadenopathy, no cyanosis and no edema. Her pulse was 78 per min, regular. Her CVS and respiratory system examinations were unremarkable. Per abdomen there was no organomegaly. Bimanual per vaginal examination revealed a normal cervix and a 16-week-size uterus, mobile with fornices free. Clinical diagnosis was bulky uterus with DUB possibly leiomyoma/endometrial carcinoma/uterine sarcoma.

Routine laboratory hematology findings were all normal except mild microcytic hypochromic anemia in peripheral smear with a hemoglobin value of 9.8 g/dL. Routine serum chemistry values were all within normal limits. PAP test result was negative for intraepithelial lesion or malignancy.

Chest X-ray was unremarkable. Transvaginal ultrasonography revealed an enlarged uterus of 16 weeks gravid size, diffuse thickening of the walls, no endometrial thickening and a normal cervix (Fig. 1a). Abdomino-pelvic CECT showed a diffusely involving uterine mass. No lymphadenopathy was noticed. Radiological impression was possibly sarcoma/leiomyoma with degeneration.

Significant intraoperative findings were diffuse enlargement of uterus, soft and friable mass replacing the entire myometrial wall. Cervix appeared as if taken up, ovaries were unremarkable and no abdomino-pelvic lymphadenopathy.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Grossly we received an intact oriented specimen of uterus, cervix and bilateral appendages measuring $13.5 \times 10 \times 8$ cm, weighing 400 g (Fig. 1b). Bilateral appendages were grossly unremarkable. Cervix appeared as partly taken up which on cut opening showed a normal canal with thickened walls. Endometrium and its cavity were normal. Myometrium was diffusely thickened, greyish white, homogeneous and friable fish-flesh-like appearance.

Microscopy revealed a tumor in the myometrium completely replacing the myometrial musculature and an atrophic endometrium. Tumor is composed of sheets of monotonous population of round to oval cells with scanty to moderate amount of eosinophilic cytoplasm with round nuclei with clumped chromatin and indistinct nucleoli. Foci of necrosis were seen. Similar tumor cells infiltrating the cervical stroma were noted (Fig. 1c, d). On immunohistochemical evaluation, tumor cells were found to be immuno-positive for LCA and CD 20 and were immuno-negative for CD 3, MPO, CD 5, CD 10 and CD 23. The p53 showed positive reaction and 80 % of tumor cells were positive for Ki-67(MIB-1) labeling index (Fig. 2). A diagnosis of diffuse large B-cell lymphoma, primary in

uterine myometrium with involvement of cervical stroma, was rendered. Patient then received six cycles of CHOP regimen along with radiation, and on follow-up, she was fine for last 18 months.

Discussion

NHL arising primarily in sites other than lymph nodes and other lymphoid tissues like spleen and bone marrow is categorized as extra-nodal NHL. Extra-nodal NHL is uncommon compared to its nodal counterpart with a ratio of 30:70 [4]. Bone, testis, salivary gland, thyroid, liver, kidney and adrenal gland are common primary sites of extra-nodal NHL. Female genital tract as the primary site is rare ~2 % of all extra-nodal lymphomas [2]. In the female genital tract, uterine corpus is rarely involved in comparison with cervix and ovaries [5]. DLBCL subtype is the most prevalent [6].

The criteria for diagnosing a primary uterine corpus extra-nodal NHL as proposed by Fox and More [7] are (a) clinically confined to the uterus, (b) no evidence of leukemia and (c) a fairly long interval between the appearance of primary uterine lymphoma and the secondary tumor. The present case confirms to the criteria just proposed.

The median age onset for uterine corpus lymphoma is 54.5 years, older than that of cervical lymphoma's median age of 44 years [6, 8]. The predominant presenting

Fig. 2 Tumor cells showing immuno-positive for LCA and CD 20 and immuno-negative for CD 3, CD 5. Inset 80 % of tumor cells were positive for Ki-67 (IHC, $\times 400$)

manifestation of primary NHL of uterine corpus is usually asymptomatic in early stages and dysfunctional uterine bleeding; “B” symptoms of lymphoma are uncommon [9]. The microscopic differential diagnoses include granulocytic sarcomas, small cell carcinomas and endometrial stromal sarcomas. Immuno-positivity for LCA and CD 20 and immuno-negativity for CD 3, MPO, CD 5, CD 10 and CD 23 in the present case confirmed the diagnosis of NHL DLBCL type.

Primary uterine NHL carries a relatively good prognosis and the single most important prognostic marker is the Ann Arbor staging [10]. Stage lower than IIE carries a better prognosis as documented in the study of Harris and Scully involving 25 cases of primary uterine and vaginal lymphomas.

There is no well-established therapeutic protocol because of the low incidence of the tumor. Combination therapy, i.e., CHOP regimen chemotherapy with radiation for 3–6 cycles yielded 60–70 % cure rate [11]. Rituximab a monoclonal antibody against CD20 antigen is now available and is found to have a synergistic effect [12].

Conclusion

Primary NHL of uterus though very rare its incidence is on the rise. Delayed diagnosis is common because it is commonly mistaken for much more common benign lesions like leiomyoma as the presenting symptoms are non-specific. Even if the incidence is very rare, gynecologists must keep in their minds primary NHL of uterus as a differential diagnosis to uterine mass lesions. This will help in early diagnosis and better prognosis.

Compliance with Ethical Standards

Conflict of interest None.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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