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CASE REPORT

Primary Non-Hodgkins Lymphoma of Uterine Cervix: A Case Report of Two Patients

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About the Author

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Introduction

Primary lymphoma of the female genital tract (FGT) is a rare disease and accounts for less than 1 % of extra nodal lymphomas in females. In a series of 147 primary genital tract non-Hodgkins lymphoma, ovarian lymphoma (59 %) was the commonest followed by uterine corpus (15.5 %), uterine cervix (11.5 %), vulva, (7.5 %), and vagina (6 %) [1]. Role of surgery in this disease is questionable. Combined modality approach using chemoradiation has been used by various authors, which is associated with good prognosis. We report two cases of uterine lymphoma who presented to our clinic with pain in abdomen. Neither patient had any history of bleeding per vaginum.

Case History

Case 1

Thirty-four years old female presented with complains of abdominal pain since last 3 months. There was no history of fever, night sweats, weight loss, or bleeding per vaginum. Contrast-enhanced computed tomography (CECT) of abdomen and pelvis revealed a 5 × 6 × 3 cm sized mass in uterine cervix (Fig. 1a). Cervical biopsy was done twice: one of which was inconclusive and second biopsy showed diffuse infiltration of cervical stroma by atypical large lymphoid

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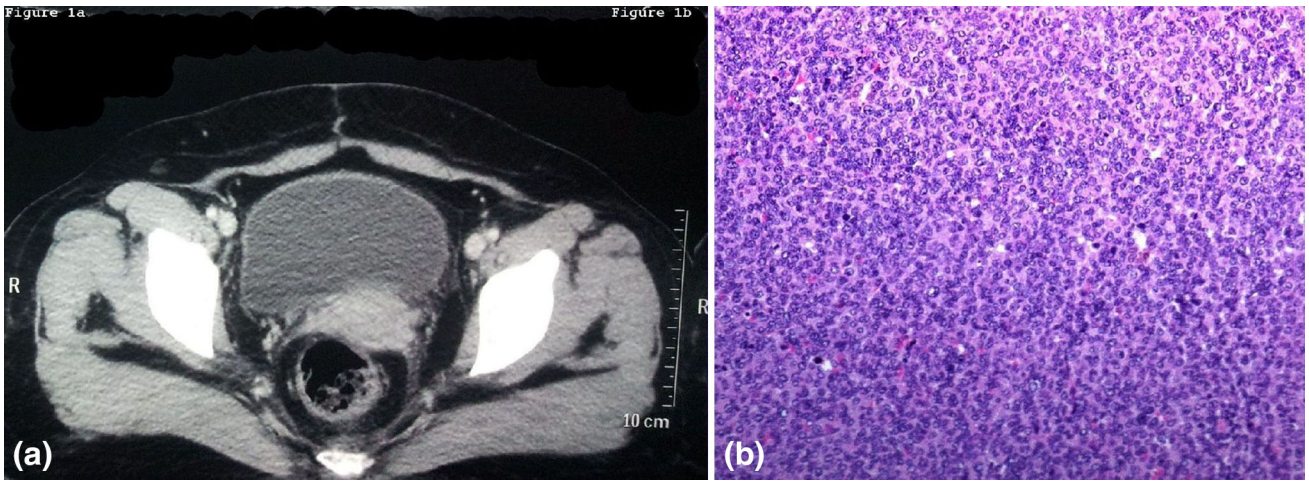

Fig. 1 **a** CECT showing heterogeneously enhancing mass with large necrotic component in cervix. **b** Diffuse infiltration of cervical stroma by atypical large lymphoid cells [H&E × 200]

cells. Immunohistochemistry (IHC) revealed the atypical lymphoid cells were positive for CD20 while negative for CD3, CD10, bcl-6, MUM-1, and CyclinD1 (Fig. 1b). Based on the IHC findings, diagnosis of diffuse large B cell lymphoma (DLBCL), post germinal center type was made. Metastatic workup was normal. She received 8 cycles of chemotherapy (Doxorubicin, Cyclophosphamide, Vincristine, and Prednisolone) with Rituximab (R-CHOP). There was partial response after 8 cycles of chemotherapy. Positron emission tomography (PET) scan after 8 cycles of chemotherapy revealed minimal residual disease involving the uterine cervix. She then received involved field radiotherapy (IFRT) 45 Gray in 25 fractions over a period of 5 weeks, by 3D conformal radiotherapy technique. A clinical examination and PET scan did not reveal any residual/recurrent disease after 3 months of radiotherapy. She does not have any evidence of disease after 5 years of treatment.

Case 2

A 77-year-old female presented with complaints of fever and pain abdomen. There was no history of night sweats, weight loss, or bleeding per vaginum. CECT abdomen and pelvis was suggestive of mass in uterine cervix, and a biopsy was performed. On histomorphology and immunohistochemistry, diagnosis of DLBCL was rendered. Her metastatic workup was normal. There was complete response after six cycles of R-CHOP. She then received IFRT 45 Gray in 25 fractions over a period of 5 weeks. There was no evidence of disease on clinical assessment and CT scan after a follow-up of 3 years.

Discussion

Primary lymphomas of uterine cervix are rare and occur generally in elderly females; however, the range of age may be wide (20–80 years). Ovaries are the most common site of the extranodal lymphoma in females (constituting <1 % of all extranodal lymphomas in females). If ovary is not taken into account, the FGT lymphomas form a meager 0.14 % of the extranodal lymphomas. The incidence of NHL, especially extra nodal lymphoma, has increased in recent decades. Chronic cervicitis has been implicated as one of the causative factors for primary cervical NHL [2].

The majority of the NHLs in uterine cervix are high-grade lymphomas with DLBCL being the commonest subtype. Other primary NHLs encountered are Burkitts lymphoma, marginal zone lymphoma, follicular lymphoma as well as primary T cell lymphomas [1].

The etiological factors for NHL have been hypothesized to include infectious agents such as the human immunodeficiency virus (HIV), immunosuppressive therapies, and environmental exposures to pesticides and pollutants. The commonest presentation of cervical lymphomas is polypoidal mass, and other complaints may include vaginal bleeding or discharge, dyspareunia, or pelvic pain.

One of the common reasons for delayed diagnosis in cervical lymphoma is frequent absence of bleeding per vagina and negative cytology due to subepithelial location of the tumor. The suggestive imaging findings are involvement of uterine corpus and cervix by homogenously enhancing lesion with intact epithelium and sparing of uterine junctional zone. Histopathology is mandatory in the diagnosis. The stromal invasion by monomorphic atypical lymphoid-like cells is the main histological features distinguishing lymphoma from chronic cervicitis. Immunohistochemical stains are pivotal in subcategorization of lymphoma. The histological differential diagnosis depends on the age of the patient and ranges from uterine stromal sarcoma, poorly differentiated carcinoma, neuroendocrine tumors, malignant melanoma, and pseudolymphoma. In

younger females, a possibility of rhabdomyosarcoma, Ewing's tumour, PNET, or metastasis from malignant round cell tumors is to be considered. An extended panel of immunohistochemistry for leucocyte common antigen (NHL), Cytokeratin (poorly differentiated carcinoma), CD 10 (uterine stromal sarcoma) HMB 45 (melanoma), CD 99, chromogranin, synaptophysin (ewings/PNET), desmin, and myogenin (rhabdomyosarcoma) is usually helpful.

The lymphoma of uterine cervix generally carries good prognosis and is primarily treated with chemotherapy. Radiotherapy is considered if there is bulky disease at presentation. For aggressive localized NHL, the addition of radiotherapy postchemotherapy does not seem to offer any benefit in progression free or overall survival [3].

Role of surgery seems to be limited. The management protocol of genital tract NHL is not standardized owing to its rarity. Combined modality treatment (CMT) protocols including chemoradiation have been found to be effective in management of NHL of uterine cervix by various authors. Combination chemotherapy including cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) with or without Rituximab (anti CD-20) followed by involved field radiotherapy (IFRT) is used as in case of nodal lymphoma [1].

Stroh et al. in their series of 16 cases of uterine NHL, achieved a 5-year disease-free survival of 90 % by the use of chemoradiation. Similar results were obtained by Heredia et al. in their case report of two cases. Management for the less common forms of aggressive NHL (MCL and PTCL) is less unified among experts, and cure rates are significantly lower. Autologous stem cell transplantation could be considered for recurrent or refractory DCBL with complete or partial remission, but its use as a first line treatment in aggressive NHL is not supported by a recent meta-analysis [4].

Till date, combined modality treatment with CHOP chemotherapy and radiation is considered favored treatment for cervical NHL.

Conclusion

Primary Non-Hodgkin's lymphoma of uterine cervix is rare. Cervical cytology may be non-contributory. In a female presenting with pelvic pain with or without abnormal vaginal bleeding and negative cytological smear examination, a diagnosis of primary lymphoma should be suspected. Further studies are needed to standardize the treatment protocols.

Compliance with ethical requirements and Conflict of interests As this is a case report, we have not applied for ethical clearance, and the authors declare that they have no conflict of interest.

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