Cervix An unusual site for extra nodal lymphoma a case report

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Abstract:
Primary lymphoma of the cervix is rare. We present a case of non-Hodgkin lymphoma involving the cervix, an extremely unusual presentation of non-Hodgkin lymphoma.

Keyword: Non-Hodgkin lymphoma, diffuse large B-cell lymphoma, cervix

INTRODUCTION
Non-Hodgkin Lymphoma of the cervix is an extremely rare disease, accounting for less than 1% of extra nodal lymphomas. (1,2) The incidence of extranodal non-Hodgkin lymphoma is rising. (3) Two types of non-Hodgkin lymphoma of cervix have been described, including primary lymphoma of cervix (uncommon) and secondary involvement of cervix in systemic non-Hodgkin lymphoma. The most common subtype is diffuse large B-cell lymphoma (DLBCL) with follicular lymphoma in second place. Patients with genital tract NHL can experience delay in diagnosis and misdiagnosis. Hence it is imperative for gynaecologists

CASE REPORT:
A 42 year old woman, presented to the medical outpatient department with complaints of fever for 2 months, loss of appetite and significant loss of weight of 4kgs in 2 months. She was apparently well prior to the illness with uneventful past medical and obstetric history. Physical examination revealed a moderately-nourished middle-aged woman with mild hepatosplenomegaly on systemic examination. There was no pallor, icterus, cyanosis, clubbing, generalised lymphadenopathy or pedal edema. There was no abdominal mass. Pelvic examination revealed a bulky, multinodular, exophytic, fleshy, white mass arising from the cervix. Her laboratory investigation showed increased erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and lactate dehydrogenase (LDH) values.

Cultures for mycobacteria, fungal microorganisms and tests for malarial parasites were negative. Serology confirmed she was negative for retrovirus as well as hepatitis B.
and C virus. CT abdomen and pelvis revealed a large mass arising from the cervix (10x 6.5x 10 cm), extending to the parametrium, indenting the bladder with loss of fat plane with anterior wall of rectum, multiple lesions in the liver and significant intra-abdominal lymphadenopathy, including iliac, peri-pancreatic and para-aortic lymphnodes. No evidence of involvement of the uterine body was seen. The spleen and kidneys were normal. [Figure 1]

Figure 1. CT image of the pelvis shows a bulky hypodense mass arising from cervix (*) which was confirmed to be non-Hodgkin lymphoma by punch biopsy.

Punch biopsy of the cervical mass was performed and histopathological examination confirmed a non-Hodgkin lymphoma of the uterine cervix. Bone marrow trephine biopsy revealed no evidence of involvement by non-Hodgkin’s lymphoma. In view of the histology and clinical presentation, a diagnosis of high grade non-Hodgkin lymphoma with predominant female genital tract involvement, consistent with diffuse large B-cell lymphoma, Ann Arbor stage IV was made. She had completed six courses of cytotoxic chemotherapy according to CVP regimen, which consisted of Cyclophosphamide, Vincristine and prednisone. Rituximab, an antiCD20 monoclonal antibody was added to regimen from the second cycle. After the completion of 6 cycles of chemotherapy, she will undergo assessment for consolidation radiation therapy.

**MICROSCOPIC FINDINGS:**
Punch biopsy from the cervical mass revealed diffuse infiltration of the cervical stroma by medium to large sized lymphoid cells with clumped chromatin, some with prominent nucleoli and scant amounts of eosinophilic cytoplasm. Occasional large cells with vesicular nuclei and distinct nucleoli were also present. There was increased mitotic and apoptotic activity. [Figure 2] Immunohistochemistry showed these tumour cells to be diffusely positive for CD20. The tumour cells were focally positive for Bcl2 and Bcl6 and negative for CD10. [Figure 3] MIB-1 proliferation index was about 80%. [Figure 4]
Figure 3. Immunohistochemistry for CD20 showing diffuse immunopositivity. [X20]

Figure 4. MIB-1 Proliferation index around 80%.[X20]

DISCUSSION:
Diffuse large B-cell lymphoma comprises 25%-30% of all adult non-Hodgkin lymphoma. Patients may present with nodal or extranodal disease with up to 40% being initially confined to extranodal sites.(4) Most common extranodal sites are stomach and ileo-caecal region. Other common sites are bone, testis, waldeyer’s ring, spleen, thyroid and salivary glands. Extranodal lymphomas present significant diagnostic challenge. Lymphoma is extremely uncommon at certain extranodal sites, hence, inflammatory and neoplastic lesions of those sites, which are much more common, are often considered in differential diagnosis, often leading to misdiagnosis or delayed diagnosis. Lymphoma very rarely presents with female genital tract involvement.

There is much debate as to what constitutes primary uterine lymphoma. The condition is called primary extranodal non-Hodgkin’s lymphoma when the extranodal site is the only site of disease or when the bulk of the disease is confined to the extranodal site.(5) Primary non-Hodgkin Lymphoma of the cervix accounts for less than 1% of extra nodal lymphomas. (1,2) Uterine involvement is relatively common in patients dying with lymphoid leukemias. In one autopsy study, 25% of patients with acute lymphoblastic leukemia and 14% with chronic lymphocytic leukemia had involvement of the uterus.(6)

Diffuse large B-cell lymphoma is the most common type of primary uterine lymphoma by far, in both the corpus and the cervix(7–13), accounting for about 70% of cases(13,14), with follicular lymphoma in second place. In a series of 147 isolated genital tract Non-Hodgkin lymphoma, the percentage breakdown was as follows: 59% ovarian, 15.5% uterine corpus, 11.5% uterine cervix, 7.5% vulval and 6% vaginal. The rest of the cases involved more than one organ.(15) In up to 80% of cases, uterine and cervical NHL appear to be the primary site of disease.(15) Uterine lymphoma affects adults over a broad age range, (16) with a mean and a median age in the fifth decade.(14,16–18)
The most common presenting symptom is abnormal vaginal bleeding (7–9,16,17,19,20). Less common complaints are dyspareunia, perineal, pelvic, or abdominal pain. A few patients have systemic symptoms such as fever or weight loss. (18) In a series of 118 cases of cervical lymphoma (21), the median age of presentation was 46 years (range 20-85 years), and most common histological subtype was DLBCL (37%). 5% cases were follicular lymphomas. The Ann Arbor stage at presentation was I (69%), II (22%) and III or more in 9% of the cases. Treatment included surgery in 42% cases, surgery only in 9.2% cases, chemotherapy only in 10.9% cases and rest case have multimodality treatment. 85% cases have no evidence of recurrence while 2% of the cases had recurrence. 8.6% patients died within 0-40 months of follow-up.

Due to rarity of genital tract isolated extranodal non-Hodgkin lymphoma management approach varies and seems to be individualized. Prognosis appears to be worse in advanced stage disease. The role of surgery appears to be limited, while that of immunotherapy and chemotherapy significant. The addition of Rituximab to chemotherapy, for treatment of aggressive non-Hodgkin lymphoma has improved overall survival for DCBL. (21)

This case could be 1) A primary cervical non-Hodgkin lymphoma which presented at a late stage OR 2) A non-Hodgkin lymphoma with predominant cervical involvement resulting in an unusual presentation.

REFERENCES:


