

CASE REPORT

Recurrent Non Hodgkin's Lymphoma in the uterine cervix: a case report and a review of the Literature.

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Abstract

Background: Lymphomas are a heterogeneous group of malignant lymphoproliferative diseases. As primary localization, the most common histological subtype of female genital lymphomas is a Non-Hodgkin Lymphoma (NHL), the diffuse large B-cell type. However cervical relapse of NHL is a very rare condition (0.3%).

Case: A 42-year-old Peruvian woman experienced relapse of NHL with uterine localization. She complained at first of abnormal vaginal bleeding and stranguria. The cervical biopsy performed showed a diffuse large B-cell lymphoma in the uterine cervix. The lack of clinical studies on this topic and its rarity make this type of recurrence very difficult to treat.

Conclusions: In case of a woman with vaginal bleeding and history of NHL, a disease relapse should always be considered and a biopsy should be performed to confirm the diagnosis.

Keywords: Lymphoma; Non Hodgkin Lymphoma; uterine cervix; recurrent; relapse

Introduction

Lymphomas are a heterogeneous group of malignant lymphoproliferative diseases and represent 3-4% of all neoplastic processes. [1]

Lymphoma can be divided into two types: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). NHL are further subdivided into nodal and extranodal. The extranodal form occurs in approximately 40% of all NHL, considering this, the extranodal lymphomas of the female genital tract account for only 0.5% to 1% of all NHL. [2]

The most common histological subtype of female genital lymphomas is diffuse large B-cell lymphoma.

Lymphomas of the female genital tract can be the primary manifestation of this disease or may occur as genital recurrences of lymphomas initially diagnosed elsewhere: considering this the ovary is the organ most often affected. [2]

We present a case of a patient with a recurrent NHL in the uterine cervix. Considering its rarity, the aim of this case report is to emphasize the possibility of a disease relapse in case of a woman with vaginal bleeding and history of NHL.

Case presentation

A 42-year-old Peruvian woman complaining of abnormal vaginal bleeding was admitted to our hospital. She had a history of NHL diagnosed in July 2018. She also reported hypothyroidism and a generalized anxiety syndrome. She did not take drugs, denied smoking, use of alcohol and any family history of cardiovascular diseases and neoplasia.

In July 2018, she presented with swelling of the right maxillary sinus: its biopsy diagnosed a diffuse large B-cell lymphoma (DLBCL) with double expressor (translocation of cMyc and Bcl-2, Bcl-6 negative).

Treatment consisted of chemotherapy with CODOX-M (cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate) and IVAC (ifosfamide, etoposide and cytarabine) for four cycles.

In March 2019, she underwent chemotherapy with FEAM (fotemustine, cytarabine, etoposide, melphalan) sequenced by infusion of autologous peripheral stem cells.

She had regular negative follow-up until July 2019 when she complained abnormal vaginal bleeding and stranguria. The patient was admitted to our department for a gynecological evaluation.

At the pelvic examination the cervix appeared hard, large and hyperemic without exophytic or erosive components. At the transvaginal ultrasound the uterine cervix appeared highly vascularized with no evidence of a tumor mass. Subsequently, a cervical biopsy was performed showing neoplastic cells with a positive test result for CD20, CD79a, Bcl2, CD10, cMyc, and negative test for CD3. These findings confirmed a recurrent DLBCL with cervical localization.

Moreover, a PET-CT scan was performed showing a skeleton relapse of the disease without clear image on relapse of the uterine cervix. The patient was referred to the hematology department and, in consideration of the disease recurrence, was started on P-VABEC (adriamycin, etoposide, cyclophosphamide, vincristine, bleomycin and prednisolone) for eight cycles and three doses of

Rituximab. Following this, the patient received therapy with Pixantrone, but only for three doses due to severe thrombocytopenia as collateral effect.

Finally, a body CT scan was performed confirming progression of the disease only interesting the maxillary sinus. Considering this and the poor general condition of the patient, she was discharged to continue with palliative care.

Differently from other cases reported in literature the diagnosis of the relapse in our case was diagnosed by vaginal biopsy without any finding of bulky mass at a diagnostic exam. Moreover, the biopsy was performed without evidence of exophytic mass of the cervix but considering the anamnesis and the vaginal bleeding complained by the patient.

Review of Literature

A PUBMED literature search was conducted from January 2000 to April 2021, using the key words "lymphoma", "cervix", "uterus", "Non Hodgkin lymphoma", identifying a total of 168 studies. Only the ones related to NHL recurrence of the uterine cervix were included for a total of 7 articles. [3-4] The other 161 cases were excluded because they were related to primary lymphomas of the cervix. The 7 articles included appeared to be all case reports.

All cases included were B-cell lymphomas and the most common histologies were: Chronic Lymphocytic Leukemia (3 cases- 43%) [5,6,4], Blastic B-cell lymphoma- Acute Lymphoblastic Leukemia (3 cases- 43%) [7,8,9] and Mantle Cell Lymphoma (1 case -14%) [3].

Surgery, radiotherapy and chemotherapy as well as combinations of these treatment modalities have been used. In particular, chemotherapy was used in almost all cases (7 cases – 87-5%).

There is only little data regarding the prognosis of these patients, however the main prognostic factor seems to be the initial stage of the disease: as later is the diagnosis as worse is the prognosis. Due to the rarity of extranodal cervical NHL, there is no consensus in the literature concerning the optimal management of cervical extranodal NHL [10].

Discussion

The lymphoma involving the uterine cervix is very rare, and it accounts for only 0.3% of cervical malignancies. [2,11, 12]. Non-Hodgkin's lymphoma (NHL) can involve extranodal sites. Common extranodal locations include the gastrointestinal tract and the skin. Female genital tract involvement can represent a site of origin. [2]

Cancers involving the genital tract represents tumors with high psychological impact for a woman, especially during the reproductive age. Diagnosis alone represents a very stressful experience for a women and its treatment often lead to physical and sexual changes that severely compromise the female identity. [13]

For these reasons, fertility preservation options have greatly improved in recent years, including embryo and oocyte cryopreservation and fertility-sparing surgery [14]. These techniques aim to reduce as much as possible the impact of a tumor of the genital tract on the sexual and physiological functioning of the affected patient. [15] Great results are described in the literature, in fact, despite its aggressiveness, several cases of preservation of fertility after treatment for a lymphoma of the cervix, show the possibility to conceiving and giving birth vaginally even after treatments. [16]

Looking in the literature, in addition to pregnancies obtained after surgery for cervical cancer, cases of diagnosis of this tumor in pregnancy are also described: it is clear that this condition also finds problems in the diagnosis, as well as in the timing of treatment. [17]

Even more rare is the NHL relapse of uterine cervix. The majority of relapses in NHL occur two years after the end of the treatment, they are frequently asymptomatic and hard to identify by the only imaging surveillance. Standard therapeutic regimen has not been established. According to the current literature, treatment options for non-Hodgkin's lymphoma of the cervix include chemotherapy, radiation, or radiation combined with either chemotherapy or surgery.

Conclusion

Cervical relapse of NHL is a very rare condition and has a variable and nonspecific presentation. Nevertheless, in case of vaginal bleeding in women with NHL history, relapse of NHL should always be considered, helping for an early diagnosis of the relapse, obtained by biopsy or surgical resection.

The best treatment hasn't been found yet, leaving a poor prognosis for these patients.

Declarations

Availability of data and materials Not applicable.

Conflicts of Interest The authors declare that they have no conflicts of interests.

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Authors' contributions MGP conceived, designed, and coordinated the project. IF and MD collected and assembled data. VP, AM and GP drafted the manuscript. VP, AM and GP edited the manuscript. GP and MGP critically revised the manuscript. MGP gave final approval of the manuscript. The author(s) read and approved the final manuscript.

Ethics approval and consent to participate Non applicable.

Consent for publication Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Table I. Clinical studies describing cases of recurrent malignant lymphoma of the uterine

AUTHORS	YEAR	NUMBER CASES	HISTOLOGY	STAGE	TREATMENT
Santangelo et al [3]	2020	1	Mantle Cell Lymphoma	IIIA	R-CHOP, R-DHAP, FEAM
Korivi et al [4]	2014	1	Blastic B-cell lymphoma	-	EPOCH; IMRT
Kazi et al [5]	2013	1	Acute Lymphoblastic Leukemia	-	CHXT
Udupa et al [6]	2012	1	Chronic Lymphocytic Leukemia	-	CHXT
Magley et al [7]	2010	1	Chronic Lymphocytic Leukemia	IV	-
Ikuta et al [8]	2006	1	Blastic B-cell lymphoma- Acute Lymphoblastic Leukemia	-	HE, CHXT
Mikami et al [9]	2004	1	Chronic Lymphatic Leukemia	IE	Surgery+RXT+CHXT

cervix.

Rchop: Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone; R-Dhap: Rituximab, Cisplatin, Cytarabine, Dexamethasone; Feam: Fotemustine, Cytarabine, Etoposide, Melphalan; Epoch: Etoposide, Prednisone, Vincristine, Cyclophosphamide, And Doxorubicin; Imrt: Intensity Modulated Radiation Therapy; CHXT: Chemotherapy; He: Hysterectomy; Rxt: Radiotherapy