

THE DIAGNOSTIC CHALLENGE OF AN UTERINE MASS: UTERINE LYMPHOMA

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SUMMARY

Background: Lymphoma of primary genital tract is uncommon. The similarity of its symptoms (vaginal bleeding, pelvic pain, etc..) with other genital system diseases, presence of nonspecific symptoms on histologic and imaging examinations may make the diagnosis delayed and may cause overtreatment.

Case report: A-62 years old woman presented with postmenopausal bleeding. All the imaging studies [transvaginal ultrasonography (USG), Doppler USG, magnetic resonance imaging (MRI)] showed only enlarged uterus with a mass lesion originated from uterine wall. The histopathologic analysis of fractionated cervical and uterine curettage were not diagnostic for postmenopausal bleeding and uterine mass lesion. To clarify the diagnosis, total abdominal hysterectomy (TAH), bilateral salpingooferectomy (BSO), peritoneal cytology sampling and frozen were carried out. While the frozen was reported in favour of malign pathology, the operation was continued with bilateral pelvic and paraaortic lymph node dissection (BPPLND) and omentectomy.

Routine pathology demonstrated diffuse large B cell lymphoma infiltrating myometrial wall. Bone marrow examination was normal. Flourodeoxyglucose positron emission tomography / computered tomography (FDG-PET/CT) showed no FDG-avid area in favour of lymphoma on whole body scan. She was considered as primary uterine lymphoma and received rituximab, cyclophosphamide, ,adriamycin, vincristine ve prednisolone (R-CHOP) chemotherapy by hematology clinical follow up. She remains in complete clinical and radiological remission 6 months after the treatment.

Conclusion: Lymphoma of genital tract should be kept in mind in the case of difficulty to clarify the differential diagnosis of uterine bleeding or mass. Especially if uterine lymphoma infiltrated to the uterine wall deeply, preoperative histological analysis could not reveal the real pathology

Key words: diffuse large B cell lymphoma, primary malign lymphoma, uterus

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PREOPERATİF TANI GÜÇLÜĞÜ YARATAN UTERİN KİTLE: PRİMER UTERİN LENFOMA

ÖZET

Giriş: Kadın genital sisteminin primer lenfoması oldukça nadirdir. Primer uterin lenfoma, genital sistemin diğer hastalıklarıyla benzer bulgular (vajinal kanama, pelvik ağrı vs) vermesi, doku örneklemeleri ve görüntüleme tetkiklerinde de spesifik bulgular vermemesi ayırıcı tanıda yer alamamasına ve tanıda gecikmelere, ayrıca lüzumsuz cerrahi yaklaşımlara neden olabilmektedir.

Olgu: 62 yaşındaki hasta postmenopozal vajinal kanama şikayetiyle başvurdu. Uygulanan laboratuvar ve görüntüleme yöntemlerinde [transvajinal ultrasonografi (USG), Doppler USG, manyetik rezonans görüntüleme (MRG)] uterus boyutunda artış ve uterin duvar kaynaklı kitle dışında bulgu tespit edilemedi. Uygulanan endoservikal küretaj ve endometrial örneklemenin histopatolojik inceleme sonucunun postmenopozal kanama ve uterin kitleyi açıklayıcı olmaması nedeni ile hastaya total abdominal histerektomi (TAH), bilateral salpingooferektomi (BSO), batın yıkama sıvısı alınması uygulandı, operasyon sırasında frozen sonucunun malign olarak bildirilmesi üzerine operasyona bilateral pelvik ve paraaortik lenfadenektomi (BPPLND) ve omentektomi eklendi.

Nihai patolojinin diffüz büyük B hücreli lenfoma olarak raporlanması üzerine hastaya kemik iliği biyopsisi yapılmış, sonucu da lenfoma infiltrasyonu saptanmayan normoselüler kemik iliği olarak raporlanmıştır. Florodeoksiglukoz pozitron emisyon tomografi/ bilgisayarlı tomografi (FDG-PET/BT) 'sinde tüm vücutta lenfoma lehine herhangi bir tutulum saptanmaması üzerine primer uterin lenfoma tanısı konulan hasta hematoloji takibinde rituximab, siklofosamid, adriamisin, vinkristin ve prednison (R-CHOP) kemoterapisi almıştır. Kemoterapi sonrası 6 aylık takibinde tam bir klinik ve radyolojik cevap saptandı.

Sonuç: Preoperatif dönemde tanısı konulamayan uterin kanamaların veya kitlelerin ayırıcı tanısında primer genital lenfomalar akılda tutulmalıdır. Uterus kaynaklı lenfomada kitle uterin duvar içinde yerleşimli ise preoperatif histolojik tanıda güçlüklerle karşılaşılabilir.

Anahtar kelimeler: diffüz büyük B hücreli lenfoma, primer malign lenfoma, uterus

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INTRODUCTION

Approximately 1/4 of malignant lymphomas originate from extranodal areas, mostly gastrointestinal system and skin^(1,2). Female genitalia is seen rarely in extranodal lymphoma involvement, even involvement secondary to disseminated disease is more common. Primary genital system lymphomas constitute approximately %1,5 of extranodal lymphomas⁽¹⁾. Most commonly seen primary genital system lymphoma is diffuse large B cell non-hodgkin lymphoma (NHL)^(4,5). Average age at diagnosis is 55(35-67y)^(6,7). Vaginal bleeding is the most common symptom of those seen in cervix and vagina; but symptoms related to obstructive effect of the mass can be seen (pelvic pain, urinary obstruction, etc)^(6,8).

So we want to discuss this case having prediagnosis of uterine intramural mass, which we could not diagnose properly preoperatively, and focus on symptoms of primary genital lymphomas during diagnosis.

CASE

62 year old postmenopausal woman presented with complaining about postmenopausal bleeding ongoing for a month. In pelvic examination of the patient, who defined last menstrual period as 10 years ago, cervix was intact, uterus was of 12 weeks pregnancy in size and there was no palpable mass in bilateral adnexial area.

With transvaginal doppler ultrasonography, uterine size was measured as 127 x 87 x 56 mm and in corpus uteri, hypoechogenic, centrally hypervascular solid multiple mass, of which largest was 64 x 50 mm in size was found. Histopathological correlation of these structures was advised.

Also endometrial lining thickness was 5,7 mm and in uterine cavity ovoidal in shape, echogenic, polipoidal, 13 mm in diameter lesion was seen, bilateral ovarias were noted as intact.

Tumor markers were found in normal ranges as follows:

CA-125 (cancer antigen-125): 12 U/ml, CEA (carcinoembryonic antigen): 1,5 ng/ml, CA 19-9 (cancer antigen 19-9): 21U/ml, CA 15-3 (cancer antigen 15-3): 6U/ml. In magnetic resonance imaging, myometrial layer diffuse signal intensity discrimination was not clear and myometrial contour had lobulations which was 66 x 48mm in largest diameter and it was reported that sarcoma or lymphoma should be considered in differential diagnosis (Figure 1).

The pathology results of endometrial sampling which was performed following postmenopausal bleeding was reported as endometrial polyp and endocervical results yield endocervical epithelium fragments. Conventional pap smear results were defined as negative for intraepithelial lesion or malignancy according to Bethesda system⁽⁹⁾.

In light of this data to clarify the diagnosis, total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), peritoneal cytology sampling and frozen were carried out. During operation, while the frozen was reported in favour of malign pathology, the operation was continued with bilateral pelvic and paraaortic lymph node dissection (BPPLND) and omentectomy

In macroscopic pathological investigation, surgical margins were intact in cervix and in cervical and myometrial cross sectional samples, locally united separately placed yellow colored nodules were found (Figure 2a).

In cross sectional sampling of yellow colored tumoral nodules, endometrial and cervical surface epithelium was regular, diffuse atypical lymphoid cellular proliferation was seen which had main mass on myometrial and cervical wall, infiltrating myometrium in full thickness without expanding surgical borders and infiltrating endometrial stroma locally (Figure 2b) With immunohistochemical study, these cells were shown as positive for CD 45 cytoplasmic dye and for CD 20, bcl -2, bcl -6, Ki-67 and negative for CD 3.

With Real/WHO classification depending on histopathological and immunohistochemical investigation it was defined as NHL diffuse large B cell type⁽¹⁰⁾.

It was shown that bilateral tuba uterina and ovaries were intact and in lymph node dissection 4 out of 32, which were in left pelvic area, lymphoma infiltration was seen and no atypical cell defined in abdominal wash fluid.

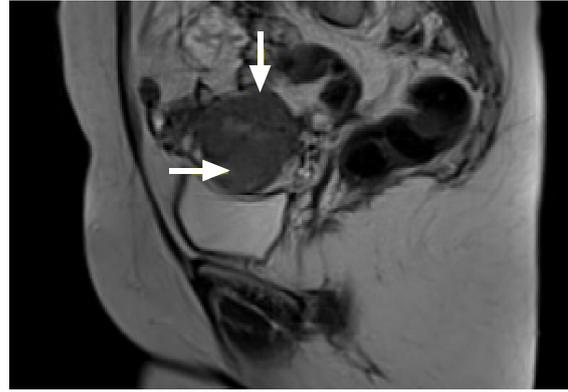


Figure 1: Lobulations in myometrium are shown by arrows.

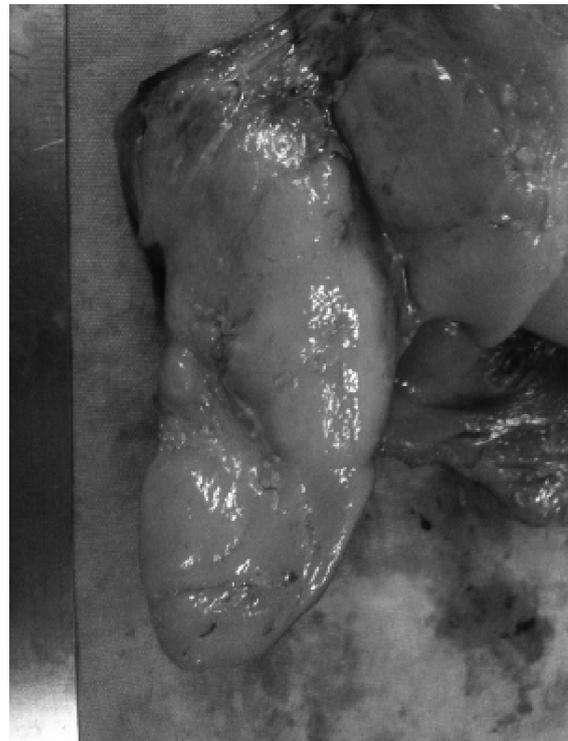


Figure 2a: Diffuse yellow colored tumoral nodules infiltrating full thickness of endometrium and myometrium.



Figure 2b: (HE, X200) Atypical lymphoid cell infiltration, invading endometrium and stroma.

In order to differentiate nodal/extranodal lymphoma, flourodeoxyglucose positron emission tomography / computered tomography (FDG-PET/CT) was performed and showed FDG-avid area in favour of lymphoma on whole body scan, in pelvis around operation area, fluid collection which is 120 x 92 mm in size, deplasing bladder superolaterally, resembling lymphocele and having no metabolic activity was seen. Bone marrow biopsy results were as normocellular bone marrow without lymphoma infiltration. With the help of this data, as there is only one extralymphatic organ involvement and no B symptoms (night sweating, fever, weight loss) seen in %40 of lymphomas she was considered as primary uterine lymphoma, grade 1E according to Ann Arbour classification and received 3 times rituximab, cyclophosphamide, adriamycin, vincristine ve prednisolone (R-CHOP) chemotherapy by hematology clinical follow up^(11,12). After 6 months follow up of chemotherapy full clinical and radyological cure was seen. Before publishing this case report informed concent was done.

DISCUSSION

According to literature, vaginal bleeding is generally the presenting sign of most of cases diagnosed as primary uterine lymphoma. Despite the fact that diagnosis generally depends on biopsy, small pieces of sampling may not be adequate to define the lesion⁽¹³⁾. In uterine lymphomas with cervical involvement, the diagnosis could be possible by punch biopsy, endocervical sampling or conization⁽¹⁴⁾.

In this case presenting sign was vaginal bleeding. However preoperative biopsy sampling was not adequate for diagnosis because tumour was deep in myometrium⁽¹³⁾.

According to MRI examination of 4 cases in literature, common properties of uterine lymphomas were being large masses having homogenous signal intensity and multinodular enlargement pattern⁽¹⁵⁾. In our case masses causing dissapperance of boundary between myometrium and endometrium and showing lobulation was seen and thought as sarcoma radiologically for the initial diagnosis. For our case and similar cases (intramurally located masses), the most powerful preoperative diagnostic tool would be MRI.

According to USG and MRI examinations showing

mass in myometrium, tissue sampling figuring out malignancy, frozen section results concerning malignancy during operation, this case is defined as primary uterine malignancy anf staging laparatomy is carried out. As seen in this case also, in lymphomas unrelated to endometrium, having no cervical involvement biopsy results would be unclusive, in such cases staging performed would not change survival rate and even may worsen life quality by increasing morbidity.

According to limited literature primary uterine lymphomas could be managed by TAH BSO, chemotherapy, radiation treatment or combination of both⁽⁴⁾. Depending on published litareture, 3 diagnostic criteria are defined for primary uterine lymphomas, 1) tumour is clinically limited to uterus, 2) no atypical cells in periferal vasculature and bone marrow, 3) presence of at least a few months between genital system lymphomas and secondary involvements^(16,17). Considering all these criteria mentioned above support that this case could be diagnosed as primary uterine lymphoma due to tumour limited to uterus in imaging examinations, bone marrow biopsy incompatible with lymphoma, no secondary focus after 6 months of chemotherapy .

Retrospectively it could be concluded that, about 15,4% of lymphocyst appearance after gynecological staging surgery and morbidity due to operation would be a cause of more radical approach⁽¹⁸⁾. In future, it would be possible to apply more conservative approach in similar cases as frozen techniques.

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