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How to Diagnose a Uterine Non-Hodgkin's Lymphoma?: A Case Report

Uterus Non-Hodgkin Lenfomasına Nasıl Tanı Koyalım?: Olgu Sunumu

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SUMMARY

Lymphoma of the female genital tract (FGT) is uncommon. This diagnosis, in such an unusual location, is very difficult to establish. Herein we report a case of FGT lymphoma and describe it's way to diagnosis. A 37 year-old-woman was referred to our institution due to undiagnosed cervical mass. Two consecutive biopsies had been taken from the mass, both of which yielded inflamation. An unusual-looking bulky cervical mass was seen and the upper part of vagina and parametrial tissues were deeply infiltrated. On magnetic resonance imaging a uterine mass measuring 7.0 cm x 8.8 cm x 2.3 cm was protruding into the vagina. A pathologic sized lymph node in the left iliac region was detected. The vaginal wall was thickened, 3.3 cm in diameter. Punch biopsy was reported as regenerative changes. After that a core biopsy was taken from a different area on the mass, from which biopsy was not taken before. Histopathological analysis retrieved a diffuse large cell non-Hodgkin's lymphoma according to REAL classification. Computed tomography (CT) and flourodeoxyglucose-18 positron emission tomography (FDG-PET) was used for staging. According to Ann Arbor staging system, stage was IIeb and after 6 courses of R-CHOP and additional 2 courses of rituximab therapy, patient is on complete remission. In case of pelvic masses with negative biopsy results, core biopsy should be preferred instead of using punch or excisional method. Uterine lymphomas may be easily masked by inflamation or misdiagnosed as inflamation unless it is not suspected. Probably using both CT and FDG-PET is the best for proper staging.

Key Words: *Core biopsy, diagnosis, lymphoma, uterus.*

ÖZET

Kadın genital sistem lenfoması oldukça nadir görülmektedir. Bu sıra dışı yerleşimde lenfoma tanısı koymak da oldukça zordur. Bu çalışmada bir kadın genital sistem lenfomasına nasıl tanı koyduğumuzu sunmaktayız. Otuz yedi yaşındaki bir kadın hasta, merkezimize tanımlanamayan servikal kitle nedeniyle sevk edildi. Ultrasonografide, sıra dışı görünen dev bir servikal kitlenin vajinanın üst kısmını ve parametriyal dokuları infiltre ettiği saptandı. Magnetik rezonans görüntülemede 7.0 cm x 8.8 cm x 2.3 cm boyutlarında uterustan kaynaklanan bir kitlenin vajinadan protruze olduğu saptandı. Kitleden alınan iki biyopsi inflamasyon olarak raporlandı. Sol iliyak bölgede patolojik boyutta bir lenf nodu saptandı. Vajina duvarı kalınlaşmıştı ve 3.3 cm çapa ulaşmıştı. "Punch" biyopsi sonucu rejenaratif değişiklikler olarak geldi. Daha sonra kitlenin daha önce biyopsi alınmamış bir bölgesinden alınan kor biyopsi sonucu REAL sınıflamasına göre difüz büyük hücreli non-Hodgkin lenfoma olarak çıktı. Çekilen florodeoksiglukoz-pozitron emisyon tomografi/bilgisayarlı tomografi (FDG-PET/BT) sonucuna göre Ann-Arbor evre IIeb uterin non-Hodgkin lenfoma olarak evrelenen hasta 6 kür R-CHOP + 2 kür rituksimab tedavisi sonucu tam remisyonda izlenmektedir. Biyopsi sonucu negatif olan pelvik kitlelerde eksizyoner ya da "punch" biyopsi yerine kor biyopsi tercih edilmelidir. Bu olguda ısrarlı biyopsilerle hasta total abdominal histerektomi gibi gereksiz organ kaybına yol açan cerrahilerden kaçınılmıştır. Eğer şüphe edilmezse uterus lenfomaları kolayca inflamasyon tarafından maskelenebilir veya inflamasyon olarak tanımlanabilir. FDG-PET/BT en iyi evreleme yöntemidir.

Anahtar Kelimeler: *Kor biyopsi, tanı, lenfoma, uterus.*

INTRODUCTION

Malignant lymphoma of the female genital tract (FGT) is a very rare disease. The incidence of uterine lymphoma is estimated to be less than 0.5% of all non-Hodgkin's lymphomas (NHL) (1). Review of the literature would suggest that one in 175 female extranodal lymphomas is likely to originate in FGT (2). FGT lymphoma is very difficult to diagnose, it can easily be misdiagnosed as usual type cervical cancer and due to it's systemic nature, it's management and treatment approach is quite different than usual type cervical cancer. Herein we report a complicated case of FGT lymphoma and describe it's long and bothersome diagnostic way.

CASE REPORT

A 37 year-old-woman was referred to our institution due to undiagnosed cervical mass. The outside pap smear cytology was normal. We learnt that two consecutive biopsies had been taken from the mass. The first was an excisional biopsy and yielded acute inflamation and the second was a punch biopsy which was reported as active chronic inflamation. She was complaining about menstrual irregularity, dysuria, pelvic pain, difficulty with urination, fever, nausea and vomiting. Her past medical history was completely uneventful. The initial physical examination revealed a suprapubic mass extending near umblicus level. Since urinary globe was suspected, the bladder was catheterized and 3500 ml urine was drained. An unusual-looking bulky cervical mass was seen and the upper part of vagina and parametrial tissues were deeply infiltrated on bi-manual examination. Sonography revealed a hypoechoic heterogeneous pelvic mass measuring 12 cm in diameter and mild pelvicaliceal dilatation. Laboratory tests indicated mild anemia and seriously impaired kidney functions. Thereby the case was consulted with nephrology department and subsequently she underwent hemodialysis.

On magnetic resonance imaging (MRI) a uterine mass measuring 7.0 cm × 8.8 cm × 2.3 cm was protruding into the vagina. The bladder was anteriorly and the rectum was posteriorly pushed by the mass (Figure 1A,1B). A patologic size lymph node in the left iliac region was detected. There was no evidence of parametrial involvement. The vaginal wall was thickened, 3.3 cm in diameter. Punch biopsy was repeated and the result was of no value, it was reported as regenerative changes. After that a core biopsy was taken from a different area on the mass, from which

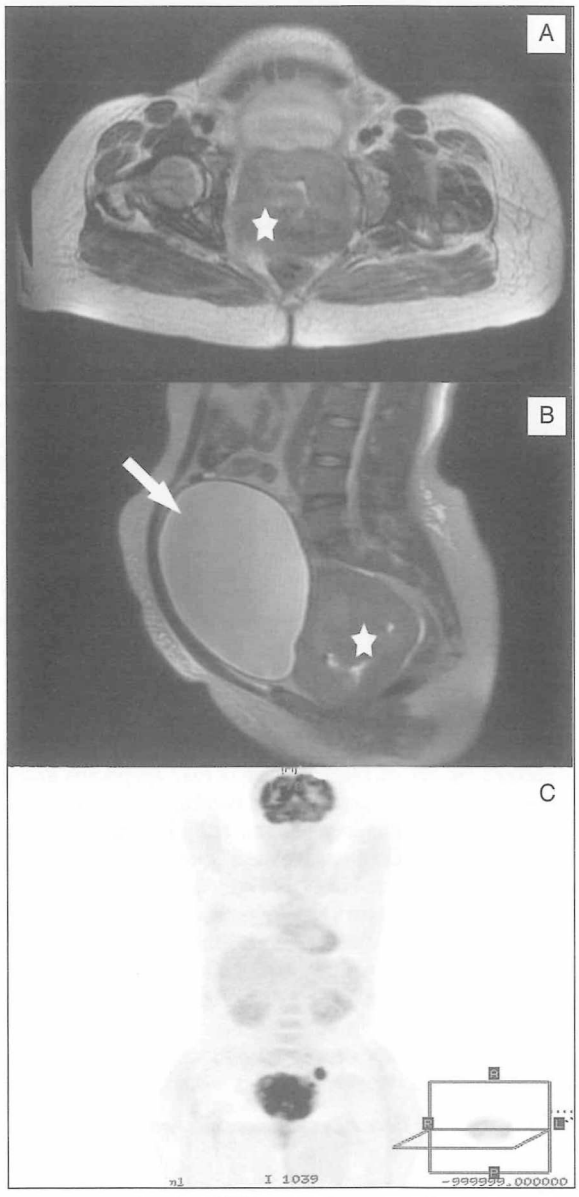

Figure 1. (A) Axial MRI and (B) sagital MRI show the mass (*) and globe of urinary bladder (arrow). (C) Coronal FDG-PET image demonstrating high tracer activity in the midpelvis and left iliac region.

biopsy was not taken before. Histopathological and further immunohistochemical study delineated a diffuse large B-cell NHL (Figure 2). Histologic examination of the biopsy material revealed a diffuse proliferation of atypical lymphoid cells beneath the ectocervical squamous epithelium besides the mixed type inflamatory cells. The lymphoid cells showed mild nuclear enlargement and slight irregularities of the nuclear contour. Atypical lymphoid cells infiltrated the fatty tissue. Immunohistochemical study demonstrated cytoplasmic staining with leukocyte common antigen (LCA), a B-cell phenotype of the lymphoid cells

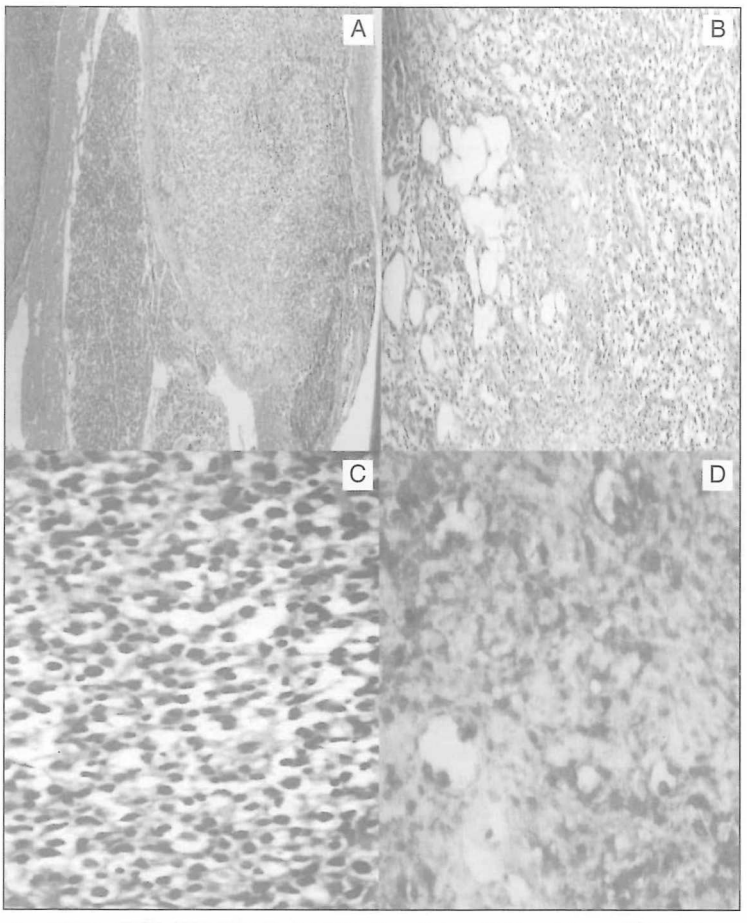

Figure 2. (A) Hematoxylen-Eosin (HE), 40x. Tumoral infiltration beneath the ectocervical squamous epithelium. (B) HE, 100x. Tumor infiltrates the fatty tissue. (C) HE, 400x. Lymphoma cells and intervening normal lymphocytes. (D) 400x. Immunohistochemical study shows cytoplasmic staining with leukocyte common antigen (LCA), the tumor cells were positive for CD 20, bcl-2, bcl-6, Ki-67 and negative for CD3.

are positive for (CD 20), bcl-2, bcl-6, Ki-67 and negative for CD 3.

Contrast-enhanced axial computed tomography (CT) of the neck, thorax, abdomen and pelvis was ordered for proper clinical staging. On CT; a mass of 7.2 cm × 8.7 cm × 3.0 cm size, occupying the region of uterus and containing necrotic hypodens areas, was seen. It was pushing the adjacent organs and it's borders with bladder and rectum were not clear and possibly infiltrating the pelvic floor. There were suspicious nodullary lessions within the lungs and liver. The spleen and kidneys were normal. No pathologic lymphadenopathy, by size criteria, was noted. Due to suspicion of lung and liver involvement. Flourodeoxyglucose-18 positron emission tomography (FDG-PET) images were obtained. Such an involvement was not confirmed by FDG-PET (Figure 1C). Bone marrow biopsy was negative for lymphoma cells. The patient had "B" symptoms. The lactate dehydrogenase level was 381 U/L (normal level, < 480 U/L). The final diagnosis was uterine NHL, diffuse large B cell type, Ann Arbor stage 2B. Serology showed that she was negative for retrovirus as well as hepatitis B and C virus. Surgical treatment was not offered and R-CHOP chemotherapy protocol (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) was initiated. Patient is currently on remission after 6 courses of R-CHOP and 2 additional courses of rituximab therapy.

DISCUSSION

Lymphoma of FGT has non-spesific symptoms such as abnormal vaginal bleeding, vaginal discharge, dyspareunia, or pelvic pain. Even "B" symptoms are usually not encountered (3). Because of these common symptoms, it may mimic other entities, such as cervical or endometrial carcinoma, uterine fibroids, adenomyosis, endometriosis and etc. That's why differential diagnosis is critically important and

histopathological examination is necessary to reach the definitive diagnosis because non of the imaging modalities is reliable by this means. Unfortunately due to the fact that most lymphomas are subepithelial unless there is ulceration; the cervical smear is mostly negative and it's very hard to obtain adequate tissue sample by conventional biopsy techniques such as punch and excisional biopsy (4). Such an experience was also reported by Van Renterghem et al. (1). In the present case; the cervical smear was normal and the first three biopsies revealed no malignancy. The first two biopsies were performed at outside and the third biopsy was performed by us. After yielding the regenerative changes result on the third biopsy, we understood that we had taken it from the previous biopsy areas. So we decided to take the next biopsy from a different area from which any biopsies were not taken before and a core biopsy was necessary to penetrate the thickened vaginal wall, which was seen on the MRI. Thereby we diagnosed the nature of mass. That's way we recommend that in case of pelvic masses with negative biopsy results, core biopsy should be preferred instead of using punch or excisional method again. In our opinion this inference is the main learning of the present case.

As known lymphoma is the malignant transformation of lymphocytes. These cells are the predominant elements of inflamation, principally in chronic conditions. In the cervix inflamatory processes are very common especially due to infections and foreign bodies like intrauterine device, condoms, lubricants and etc. Hence in such localizations, atypical lenfoid proliferations like lymphoma may be easily masked by inflamation or misdiagnosed as inflamation unless it is not suspected. For sure, this probability is not strong but in case of pelvic masses, biopsies of which repetitively reported as inflamation; then attention must be orientated to the morphology of lymphocytes to seek for atypical features and when such features are encountered then immunohistochemical markers should be used. From this point of view, we concluded that in such unusual locations like FGT lymphoma diagnosis needs strong suspicion.

CT is commonly used for the staging of NHL (5). CT enables accurate measurement of both tumour size and extent, and provides information that can be used to plan an appropriate therapeutic regimen as well as follow response to treatment. Somehow in the present case, CT did not show the left iliac lymphadenopathy which was detected by MRI and verified to be malignant tissue by FDG-PET. Actually in this case FDG-PET was ordered to investigate liver and lung involvement, it helped us to see that mentioned lymphadenopathy was involved by the disease. So we don't know which one of the two areas, the uterus or the left iliac lymph node, is the primary source and if we only relied on CT then our staging would be Ann Arbor Stage 1B which was more advanced in fact. This result let us to think the superiority of FDG-PET over the CT, in fact Delbeke has postulated that these two modalities have comparable sensitivities (6). We believe that probably using these two modalities together is the best for proper staging.

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