

Pelvic Lymphomas in the Differential Diagnosis of Gynecological Diseases: 10 Years of Experience of the Tertiary Center

Jinekolojik Hastalıkların Ayırıcı Tanısında Pelvik Lenfomalar: Üçüncü Basamak Merkezin 10 Yıllık Deneyimi

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Abstract

It was aimed to raise awareness about pelvic lymphoma among gynecologists by evaluating and sharing the clinical features of 12 patients diagnosed with pelvic lymphoma in the obstetrics and gynecology clinic of Eskişehir Osmangazi university. The clinicopathological data of 12 patients who were presented to our clinics with gynecological complaints and diagnosed with lymphoma between 2010 and 2020 were analyzed retrospectively from their files. In our study, extranodal primary pelvic lymphoma was detected in ten patients, while nodal lymphoma was diagnosed in two patients. The most common histological lymphoma type detected in patients was diffuse large B-cell lymphoma seen in ten patients (83.3%). It was the cervical involvement that was most commonly observed in four patients (33.3%) with primary pelvic lymphoma. Total abdominal hysterectomy was performed as a gynecological surgical procedure in two patients, while a staging surgical procedure was performed in addition to total abdominal hysterectomy in five patients. Frozen pathology method was used in only four of the patients who underwent surgical procedure. While the diagnosis of lymphoma was made by minimally invasive tissue biopsy in five patients (41.6%), it could be made after surgery in seven patients (58.3%). Keeping pelvic lymphomas in mind in the differential diagnosis of patients who are evaluated with non-specific gynecological complaints and a preliminary diagnosis of pelvic mass may prevent some unnecessary extensive oncological surgeries. Increasing awareness of pelvic lymphoma among gynecologists can help prevent delays in diagnosis and treatment

Keywords: Pelvic lymphomas, atypical diagnosis, pelvic mass

Özet

Üniversitemiz kadın doğum polikliniğinde pelvik lenfoma tanısı konulan 12 hastanın klinik özelliklerinin değerlendirilip paylaşarak jinekologlar arasında pelvik lenfoma konusunda farkındalık yaratılması amaçlanmıştır. 2010-2020 yılları arasında jinekolojik şikayetlerle Eskişehir Osmangazi Üniversitesi kadın doğum bölümüne başvuran ve lenfoma tanısı alan 12 hastanın klinikopatolojik verileri dosyalarından retrospektif olarak incelendi. Çalışmamızda 10 hastada ektranodal primer pelvik lenfoma saptanırken, iki hastada nodal lenfoma tanısı konuldu. Hastalarda en sık saptanan histolojik lenfoma tipi, on hastada (%83.3) görülen diffüz büyük B hücreli lenfoma idi. Primer pelvik lenfomalı dört hastada (%33.3) en sık görülen servikal tutulumdu. İki hastaya jinekolojik cerrahi olarak total abdominal histerektomi, beş hastaya total abdominal histerektomiye ek olarak evreleme cerrahisi uygulandı. Cerrahi işlem uygulanan hastaların sadece dördünde frozen patoloji yöntemi kullanıldı. Lenfoma tanısı beş hastada (%41.6) minimal invaziv doku biyopsisi ile konulurken, yedi hastada (%58.3) cerrahi sonrası konulabildi. Non-spesifik jinekolojik şikayetleri olup pelvik kitle ön tanısı alan hastaların ayırıcı tanısında pelvik lenfomaların akılda tutulması gereksiz yere yapılacak onkolojik ameliyatların önüne geçebilir. Jinekologlar arasında pelvik lenfoma farkındalığının artması, tanı ve tedavide gecikmelerin önlenmesine yardımcı olabilir.

Anahtar Kelimeler: Pelvik lenfomalar, atipik tanı, pelvik kitle

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Received 06.04.2022 Accepted 05.05.2022 Online published 16.05.2022

1. Introduction

Lymphomas are hematological malignancies arising from mature and precursors of T and B lymphocyte cells and plasma cells. Lymphomas can be divided into two main groups as Hodgkin and non-Hodgkin and can be seen in all age groups. Non-Hodgkin lymphomas constitute 90% of lymphomas^[1,2]. While the incidence of non-Hodgkin lymphomas in the United States is 19.6/100,000, it is predicted that 4.3% of all new cancer cases will be non-Hodgkin lymphoma for 2021^[3]. Less than one-third of non-Hodgkin lymphomas involve the extranodal area. The most common extranodal involvement sites are the gastrointestinal tract, skin, bone, central nervous system, and testis, while more rarely kidney, bladder, prostate, and genital system organs^[4-7]. Although primary lymphoma in the female genital tract is extremely rare, it constitutes approximately 0.2-1.5% of all extranodal lymphomas^[7-10]. Lymphomas with nodal involvement present itself with bone marrow and peripheral blood involvement together with a mass in lymphoid or visceral organs^[11]. While most patients have B symptoms (fever, weight loss, malaise, and sweating), lymphadenopathy and laboratory changes, the definitive diagnosis is made by histological tissue biopsy. Patients with primary pelvic lymphomas apply to gynecology clinics with different clinical findings than lymphomas with nodal involvement. While few patients have B symptoms, most patients complain of irregular vaginal bleeding, vaginal discharge, and pelvic pain. After their initial evaluation in gynecology clinics, a preliminary diagnosis of pelvic mass, gynecological malignancy or uterine leiomyoma is made and surgery is planned. This causes delays in the diagnosis and treatment of the disease. Biopsy and immunochemotherapy are primarily used instead of surgery in the diagnosis and treatment of lymphomas.

The majority of literature studies on pelvic lymphomas consist of case reports. Case series are very few. Considering pelvic lymphomas in the differential diagnosis of gynecological diseases is a distant possibility for gynecologists. Therefore, in our study, it was aimed to raise awareness about pelvic

lymphoma among gynecologists by evaluating and sharing the clinical features of 12 patients diagnosed with pelvic lymphoma in the obstetrics clinic of our university.

2. Material and Method

The medical data of 12 patients who presented to the gynecology clinic of Eskisehir Osmangazi University, which was a tertiary center, with various gynecological complaints and were diagnosed with pelvic lymphoma as a result of the evaluations between 2010 and 2020, were retrospectively analyzed from their files. Ethics committee approval was obtained before starting the study. Etic committee approval number is 2020/13

Demographic data such as age, gravida, parity, and menopause status were examined from the files of the patients. The complaints of the patients at the time of admission to the gynecology clinic, and the histopathological findings after clinical examination and diagnostic procedures were reviewed from their files. The histopathological type, sites of involvement, and surgical procedures of lymphomas were examined retrospectively from their files. Staging information was made according to the Ann Arbor Staging System^[11,12]. In addition, the general survival information of the patients was reviewed.

Statistical analyzes were performed by using the statistical software package SPSS version 22.0 (SPSS, Inc. Chicago, IL). The data were expressed as median and range for continuous variables. Binary variables were reported as counts and percentages.

3. Result

In our study, extranodal primary pelvic lymphoma was detected in ten patients, while nodal lymphoma was diagnosed in two patients. While the mean age of the patients was 50.41 ± 14.58 , the mean gravida was 3.41 ± 2.6 . While seven of the patients (58.3%) were in the premenopausal period, five of them (41.6%) were found to be postmenopausal. Demographic data of the patients were shown in Table 1.

The patients mostly applied to the gynecology service with complaints of pelvic pain, irregular menstrual bleeding, and vaginal

discharge. Other clinical complaints of the patients were shown in Table 2.

Table 1. Clinical characteristics of the patients

| | |
|-------------------------------|---------------------|
| Age | 50.41 ±14.58 |
| Gravida | 3.41 ±2.6 |
| Parity | 2.75 ±2.56 |
| Ca125 | 29.75 ±29.05 |
| Diabetes Mellitus (n%) | 6 (50%) |
| Hypertension (n%) | 4 (33.3%) |
| Menopause Status | |
| Pre-menopausal (n%) | 7 (58.3%) |
| Post-menopausal (n%) | 5 (41.6%) |

Table 2. Complaints of patients applying to the clinic

| | |
|--------------------------------|-----------|
| Complaints | |
| Pelvic pain | 5 (41.6%) |
| Postmenopausal bleeding | 2 (16.6%) |
| Irregular bleeding | 7 (58.3%) |
| Vaginal discharge | 5 (41.6%) |
| Difficulty urinating | 2 (16.6%) |
| Post coital bleeding | 4 (33.3%) |
| Symptoms of B | 3 (25%) |
| No complaints | 1 (8.3%) |

The most common histological lymphoma type detected in patients was diffuse large B-cell lymphoma seen in ten patients (83.3%). According to the Ann Arbor Classification, six patients (50%) were in Stage 1, while three patients (25%) were detected in Stage 2, and the remaining three patients had advanced stage tumors. In our study, it was the cervical involvement that was most commonly observed in four patients (33.3%) with primary pelvic lymphoma. Total abdominal hysterectomy was performed as a gynecological surgical procedure in two patients, while a staging surgical procedure

was performed in addition to total abdominal hysterectomy in five patients. Frozen pathology method was used in only four of the patients who underwent surgical procedure. While the diagnosis of lymphoma was made by minimally invasive tissue biopsy in five patients (41.6%), it could be made after surgery in seven patients (58.3%). The clinical features of lymphomas are shown in Table 3. While four patients died due to lymphoma, eight patients are still alive. The overall survival of the patients was found to be 48.08±47.17 months.

Table 3. Clinicopathological characteristics of the patients

| | |
|---|------------|
| Histology | |
| Diffuse large B cell lymphoma (n%) | 10 (83.3%) |
| Follicular lymphoma (n%) | 1 (8.3%) |
| Hodgkin mixed celluler (n%) | 1 (8.3%) |
| stage | |
| 1 (n%) | 6(50%) |
| 2 (n%) | 3(25%) |
| 3 (n%) | 1(8.3%) |
| 4 (n%) | 2(16.6%) |
| Site of involvement | |
| Ovary(n%) | 2 (16.6%) |
| Uterus(n%) | 1 (8.3%) |
| Cervics(n%) | 4 (33.3%) |

| | |
|--|-------------|
| Mixed involvement(n%) | 3 (25%) |
| Pelvic lymph node (nodal involvement) (n%) | 2 (16.6%) |
| Surgery treatment | |
| Total hysterectomy + bilateral salpingooferectomy (n%) | 2 (16.6%) |
| Total hysterectomy + bilateral salpingooferectomy +omentectomy+ pelvic paraaortic lymph node dissection (n%) | 5 (41.6%) |
| Frozen | |
| Diagnostic for lymphoma (n%) | 1 (25%) |
| Diagnostic for malignite (n%) | 3 (75%) |
| Diagnostic method | |
| Biospy | 5 (41.6%) |
| Surgery | 7 (58.3%) |
| Overall survival (mean±std) | 48.08±47.17 |

Preliminary diagnoses of pelvic mass, cervical cancer, and leiomyoma were considered primarily in the clinical examination and ultrasonographic evaluation of the patients. While myomas prolapsing the vagina were observed in two of the gynecological examinations, hydronephrosis, which is an oncological emergency of lymphomas, was observed as a clinical finding in two patients. One of our patients was diagnosed with lymphoma concurrent with endometrial cancer. The clinical features of the patients were shown in Table 4.

4. Discussion

In patients with pelvic pain, irregular menstrual bleeding, vaginal discharge, and pelvic mass findings on ultrasonography, gynecological diseases, especially gynecological malignancies, are considered in the foreground and extensive abdominopelvic surgical procedures are performed. The inclusion of pelvic lymphomas will prevent delays in the diagnosis and treatment of lymphoma and contribute to the prognosis in a good way, despite the fact that they are very rare in the differential diagnosis of pelvic mass and gynecological diseases.

In lymphomas with nodal involvement, involvement of gynecological organs is seen in approximately 30-40% of patients with advanced disease. Primary pelvic lymphoma involving gynecological organs constitutes only 1.5% of all extranodal lymphomas [13,14]. In advanced state nodal-involvement lymphomas, classical clinical B symptoms, fever, weight loss, sweating and malaise, as well as multiple lymph node involvement facilitate the diagnosis, while non-specific symptoms are seen in primary pelvic lymphoma. This causes the diagnosis to be

made after complex surgical procedures. Due to its rarity, failure to provide standardization in treatment and delays in clinical diagnosis cause poor prognosis [10,14-17]

In our study, extranodal non-Hodgkin primary pelvic lymphoma was detected in ten of our patients. The most common complaints were irregular bleeding (58%), pelvic pain (41%), and vaginal discharge (41%). These rates were followed in accordance with the literature data [10, 13, 18].

In rare case reports in the literature, it has been stated that Cancer antigen 125 (Ca125) value can be used in the diagnosis, treatment, and follow-up of advanced lymphoma cases [16]. A moderate increase in Ca125 value was observed in our two postmenopausal patients. This not very high increase in Ca125 is of limited use in differential diagnosis because it increases in many gynecological and non-gynecological diseases.

Diffuse large B-cell lymphoma was detected histologically in 83.3% of our primary pelvic lymphomas. Diffuse large B-cell type is the most common type in the literature [19,20]. Although different rates are given in many studies, the most common site of involvement is expressed as the ovary [10,19]. In our study, cervix involvement was most frequently followed by involvement of more than one focus.

Table 4. All characteristics of the patients (Ct: chemotherapy, Dbcl:Diffuse b large cell lymphoma)

| Patient | Pre-diagnosis | Ultrasound finding | Places of involvement | Diagnostic method | Treatment | Clinic finding | Histological diagnosis | Stage | Alive | Overall survival |
|---------|----------------|---|---------------------------------------|-------------------|--------------------------------|--|-----------------------------|-----------------------|-------|------------------|
| 1 | Pelvic mass | 6 * 4 cm right adnexial solid mass | ovary | surgery | Tah+bso+Ct | - | Dbcl | 1 | yes | 135 |
| 2 | Pelvic mass | 7 * 5 cm semisolid mass in the left adnex | ovary | surgery | Tah+bso+bpplnd +omentectomy+Ct | - | Dbcl | 2 | yes | 48 |
| 3 | leiomyoma | 4 cm degenerated myoma | Uterus Ovary Cervics | surgery | Tah+bso+Ct | - | Dbcl | 1 | yes | 60 |
| 4 | Endometrium ca | 7 * 5 cm uterine myoma | Cervics | surgery | Tah+bso+bpplnd +omentectomy+Ct | - | Endometrioid ca+Dbcl | Endo as3a+ lenfo masl | yes | 108 |
| 5 | Cervics ca | cervical enlargement | Cervics | biopsy | Ct | hydronephrosis | Dbcl | 1 | yes | 24 |
| 6 | Cervics ca | cervical enlargement | Cervics | biopsy | Ct | - | Follicular+Dbcl | 4 | ex | 8 |
| 7 | vaginal myoma | 9 * 9 cm fibroids in the vagina | Cervics | biopsy | Ct | mass with vaginal bleeding | Dbcl | 3 | ex | 10 |
| 8 | leiomyoma | enlarged uterus and cervix | Uterus | biopsy | Ct+Rt | Hydronephrosis+ kidney failure | Dbcl | 2 | ex | 10 |
| 9 | Pelvic mass | 10*6 cm right adnexial solid mass | Right obturatory lymph node | surgery | Tah+bso+bpplnd +omentectomy+Ct | Endometrial hyperplazi | Dbcl (Nodal) | 1 | yes | 24 |
| 10 | leiomyoma | 10*7 cm left adnexial solid mass | Left external lymph node | surgery | Tah+bso+bpplnd +omentectomy+Ct | - | hodgkin mixed cellular type | 2 | yes | 120 |
| 11 | Pelvic mass | 7*4 cm right adnexial solid mass | Ovary+fallo pian tuba+retroperitoneal | surgery | Tah+bso+bpplnd +omentectomy+Ct | extensive involvement of the lungs and abdomen | Dbcl | 4 | ex | 6 |
| 12 | Vaginal myoma | 5*5 cm fibroids in the vagina | Cervics+uterus | biopsy | surgical excision+Ct | mass with vaginal bleeding | Dbcl | 1 | yes | 24 |

While lymphoma was diagnosed in the final pathology after abdominal hysterectomy operation in seven of our patients, this rate was found to be 62% in the study of Dimitros *et al.* [19]. Of the patients who underwent abdominal hysterectomy, surgery was performed due to the diagnosis of pelvic mass in 4, leiomyoma in 2, and endometrial ca in one patient. It is seen that the diagnosis of our patients applying to the clinic is mostly in the form of pelvic mass, cervical mass, uterine and vaginal leiomyoma, as in the literature [10].

Imaging methods do not have sufficient sensitivity in diagnosing pelvic lymphoma [19-21]. On ultrasonographic imaging, a non-specific pelvic mass image of solid consistency is seen in the majority of our patients. The diagnosis of lymphoma can be made mainly by pathological examination of tissue samples and immunohistochemical staining. For this purpose, ultrasound-guided biopsy may be useful [22-24].

In patients with a preliminary diagnosis of myomas prolapsing the vagina, cervical mass, and uterine leiomyoma, it is possible to diagnose with biopsy before complex surgery. In our study, lymphoma was diagnosed by biopsy in five patients.

Although ultrasonography, biochemical tumor markers, and clinical examination findings provide important information in the diagnosis of malignant ovarian diseases, the diagnosis of lymphoma can mostly be made after complex surgery. Frozen method during abdominal surgery can be helpful in the diagnosis of lymphoma, although it is not definitive. In our study, frozen was applied to four patients and lymphoma diagnosis was made in only one patient. In case of suspected lymphoma diagnosis, hemato-pathologist support will increase the diagnosis rate.

The addition of surgery to immunochemotherapy in the treatment of pelvic lymphomas has not been shown to contribute positively to the survey of the disease [19]. Complex abdominal surgery causes delay in diagnosis and treatment [6-8,10,15,16,25-26]. In many studies, immunochemotherapy [Cyclophosphamide, Doxorubicin, Vincristine, Prednisone (CHOP) + rituximab] is recommended as primary therapy.

In conclusion, keeping pelvic lymphomas in mind in the differential diagnosis of patients who

are evaluated with non-specific gynecological complaints and a preliminary diagnosis of pelvic mass may prevent some unnecessary extensive oncological surgeries. Increasing awareness of pelvic lymphoma among gynecologists can help prevent delays in diagnosis and treatment.

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