BÖLÜM 6

JİNEKOLOJİK KANSERLERDE TANI VE SINIFLANDIRMA

Çetin ÇELİK[1]
Mete Can ATEŞ[2]

VAJEN KANSERİ

Vajen, serviksten vulvaya uzanan farklı doku tipleri ve planları olan 7-10 cm uzunluğunda tüp şeklinde fibromusküler bir organdır. Vajen kanseri nadir olarak görülen jinekolojik malignitedir. Vajen kanserleri daha çok metastatik olup primer vajen kanseri oldukça nadirdir. Vajene metastazların çoğu diğer reprodüktif organlardan (serviks, endometrium veya over) kaynaklanabildiği gibi kolon, meme veya pankreas gibi organlardan da kaynaklanabilir. Vajinal metastazlar direk yayılım veya lenfatik / hematojen yayılım şeklinde oluşabilir. Primer vajen kanseri tüm genital kanserlerin yaklaşık %1-2'sini oluşturur [(1)].

Epidemiyoloji

Vajen kanseri klinik olarak heterojen bir hastalıktır. İnsan papilloma virüsü (HPV) vajen kanseri için bilinen bir kanserojendir; ancak HPV dışı faktörler de kanser gelişiminde rol alabilir [(2)]. Eskiden hamilelerde kullanılan sentetik bir östrojen olan dietilstilbestrol (DES), kız çocuklarında vajinal berrak hücreli adenokarsinom ile ilişkilendirilmiş olup dietilstilbestrolün rutin kullanımı 1970'lerde durdurulduğundan bu yana bu kanserin görülme sıklığı azalmıştır [(3)]. Yaklaşık 100.000 kadından 1'ine in situ veya invaziv vajinal kanser (tipik ola-

[1] Prof. Dr, Selçuk Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum AD, celikcet@hotmail.com
[2] Op. Dr., Selçuk Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum AD, metecanates@gmail.com

Klinik

SKST'lü hastalar genellikle epitelyal veya germ hücreli over neoplazileri olan hastalarla benzer klinikle; kitlenin abdominal veya pelvik semptomlar oluşturması nedeniyle başvurur ya da muayene/görüntüleme sırasında adneksiyal kitle tesadüfi olarak tespit edilir. Bazı tümörler steroid hormon sentezine bağlı bulgu verirler. Östrojen fazlalığı anormal uterin kanama, endometrial neoplaziye neden olurken çocuklarda prekoks puberteye neden olur. Eğer tümör androjen sekrete eden bir tümörse hirsutizm, akne, alopesi, menstruel anormallikler (oligomenore, amenore), kliteromegali, seste kalınlaşma gibi hastada virilizasyon bulguları ortaya çıkar [71]. Bazı hastalarda SKST'ün tipine bağlı olarak batında ani distansiyon, asit, sklerozan peritonit ya da barsak obstrüksiyonu gelişebilir. Adneksiyal kitle ve anormal uterin kanaması olan premenopozal hastalarda ve postmenopozal kanaması olan hastalarda endometriyal örnekleme yapılmalıdır.

Tanı

Overin SKST'lerinin tanısı histopatoloji ile konulur. Adneksiyal kitle varlığı ile östrojen veya androjen salınımında artış ya da serum tümör belirteç düzeylerinin artışı ile preoperatif tanıdan şüphelenildiğinde, cerrahi spesmenin incelenmesi ile kitlenin spesifik histolojik tipi ve malignite riski ortaya konulur.

KAYNAKLAR

1. Adams TS, Cuello MA. Cancer of the vagina. *Int J Gynaecol Obstet*. 2018;143 Suppl 2:14-21.
2. Smith JS, Backes DM, Hoots BE, Kurman RJ, Pimenta JM. Human papillomavirus type-distribution in vulvar and vaginal cancers and their associated precursors. *Obstet Gynecol*. 2009;113(4):917-924.
3. Conlon JL. Diethylstilbestrol: Potential health risks for women exposed in utero and their offspring. *JAAPA*. 2017;30(2):49-52.
4. Daling JR, Madeleine MM, Schwartz SM, et al. A population-based study of squamous cell vaginal cancer: HPV and cofactors. *Gynecol Oncol*. 2002;84(2):263-270.
5. Hacker NF, Eifel PJ, van der Velden J. Cancer of the vagina. *Int J Gynaecol Obstet*. 2015;131 Suppl 2:S84-S87.
6. Lee CK, Lin H, Su CF, Kok VC. Primary Vaginal Melanoma With Rhabdoid Features: A Case Report and Literature Review. *Int J Gynecol Pathol*. 2017;36(5):499-504.
7. Berek JS, Hacker NF. Berek & Hacker's Gynecologic Oncology, 6th edition, Wolters Kluwer, Philadelphia 2015.

8. Matsuo K, Blake EA, Machida H, Mandelbaum RS, Roman LD, Wright JD. Incidences and risk factors of metachronous vulvar, vaginal, and anal cancers after cervical cancer diagnosis. *Gynecol Oncol*. 2018;150(3):501-508.
9. Rajaram S, Maheshwari A, Srivastava A. Staging for vaginal cancer. *Best Pract Res Clin Obstet Gynaecol*. 2015;29(6):822-832.
10. Moore KL, Dalley AF, Agur AMR. Clinically oriented anatomy. Baltimore (MD): Lip- pincott Williams & Wilkins; 2013. p. 1171.
11. DSÖ (2020). Dünya Sağlık Örgütü Küresel Kanser Gözlemevi 2020. (30.04.2021 tarihinde https://gco.iarc.fr adresinden ulaşılmıştır).
12. Amerika Birleşik Devletleri Ulusal Kanser Enstitüsü. (30.04.2021 tarihinde https://seer.cancer.gov/statfacts/html/vulva.html adresinden ulaşılmıştır).
13. Brinton LA, Thistle JE, Liao LM, Trabert B. Epidemiology of vulvar neoplasia in the NIH-AARP Study. Gynecol Oncol. 2017;145(2):298-304.
14. Kurman RJ, Carcangiu ML, Herrington CS, et al. World Health Organization classification of tumours of the female reproductive organs, International Agency for Research on Cancer. Tumours Vulva 2014;6:230.
15. Faber MT, Sand FL, Albieri V, Norrild B, Kjaer SK, Verdoodt F. Prevalence and type distribution of human papillomavirus in squamous cell carcinoma and intraepithelial neoplasia of the vulva. Int J Cancer. 2017;141(6):1161-1169.
16. Huh WK, Joura EA, Giuliano AR, et al. Final efficacy, immunogenicity, and safety analyses of a nine-valent human papillomavirus vaccine in women aged 16-26 years: a randomised, double-blind trial. Lancet. 2017;390(10108):2143-2159.
17. Bleeker MC, Visser PJ, Overbeek LI, van Beurden M, Berkhof J. Lichen Sclerosus: Incidence and Risk of Vulvar Squamous Cell Carcinoma. Cancer Epidemiol Biomarkers Prev. 2016;25(8):1224-1230.
18. Sugiyama VE, Chan JK, Shin JY, Berek JS, Osann K, Kapp DS. Vulvar melanoma: a multivariable analysis of 644 patients. Obstet Gynecol. 2007;110(2 Pt 1):296-301.
19. Collins CG, Lee FY, Roman-Lopez JJ. Invasive carcinoma of the vulva with lymph node metastasis. Am J Obstet Gynecol. 1971;109(3):446-452.
20. Walboomers, J. M., Jacobs, M. V., Manos, M. M., Bosch, F. X., Kummer, J. A., Shah, K. V., Snijders, P. J., Peto, J., Meijer, C. J., & Muñoz, N. (1999). Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *The Journal of pathology*, *189*(1), 12–19.
21. Quinn M, Babb P, Jones J, Allen E. Effect of screening on incidence of and mortality from cancer of cervix in England: evaluation based on routinely collected statistics. *BMJ*. 1999;318(7188):904-908.
22. International Collaboration of Epidemiological Studies of Cervical Cancer. Comparison of risk factors for invasive squamous cell carcinoma and adenocarcinoma of the cervix: collaborative reanalysis of individual data on 8,097 women with squamous cell carcinoma and 1,374 women with adenocarcinoma from 12 epidemiological studies [published correction appears in Int J Cancer. 2007 Jun 1;120(11):2525. Berrington de González, Amy [removed]; Green, Jane [removed]]. *Int J Cancer*. 2007;120(4):885-891.

23. Amerika Birleşik Devletleri Hastalık Kontrol ve Önleme Merkezi. Ulusal Kanser Enstitüsü Bilgi Notu. İnsan papilloma virüsü ve kanser: Sorular ve Cevaplar. (30.04.2021 tarihinde https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-and-cancer adresinden ulaşılmıştır).
24. Smith JS, Herrero R, Bosetti C, et al. Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. *J Natl Cancer Inst*. 2002;94(21):1604-1613.
25. Kurman RJ, Norris HJ, Wilkinson EJ. Atlas of tumor pathology: Tumors of the cervix, vagina, and vulva, 3rd, Armed Forces Institute of Pathology, Washington, DC 1992.
26. Dursun P, Gultekin M, Bozdag G, et al. Primary cervical lymphoma: report of two cases and review of the literature. *Gynecol Oncol*. 2005;98(3):484-489.
27. DiSaia PJ, Creasman WT. Invasive cervical cancer. In: Clinical Gynecologic Oncology, 7th ed., Mosby Elsevier, Philadelphia 2007. p.55.
28. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü. Serviks Kanseri Tarama Programı Ulusal Standartları. (30.04.2021 tarihinde https://hsgm.saglik.gov.tr/tr/kanser-tarama-standartlari/listesi/serviks-kanseri-tarama-programı-ulusal-standartları.html adresinden ulaşılmıştır).
29. Tropé CG, Abeler VM, Kristensen GB. Diagnosis and treatment of sarcoma of the uterus. A review. Acta Oncol. 2012;51(6):694-705.
30. Clarke MA, Devesa SS, Harvey SV, Wentzensen N. Hysterectomy-Corrected Uterine Corpus Cancer Incidence Trends and Differences in Relative Survival Reveal Racial Disparities and Rising Rates of Nonendometrioid Cancers. J Clin Oncol. 2019;37(22):1895-1908.
31. Ricci S, Stone RL, Fader AN. Uterine leiomyosarcoma: Epidemiology, contemporary treatment strategies and the impact of uterine morcellation. Gynecol Oncol. 2017;145(1):208-216.
32. Wysowski DK, Honig SF, Beitz J. Uterine sarcoma associated with tamoxifen use. N Engl J Med. 2002;346(23):1832-1833.
33. Toro JR, Nickerson ML, Wei MH, et al. Mutations in the fumarate hydratase gene cause hereditary leiomyomatosis and renal cell cancer in families in North America. Am J Hum Genet. 2003;73(1):95-106.
34. WHO Classification of Tumours Editorial Board. WHO Classification of Tumours: Female Genital Tumours, 5th edition, volume 4, 2020.
35. Nordal RR, Thoresen SO. Uterine sarcomas in Norway 1956-1992: incidence, survival and mortality. Eur J Cancer. 1997;33(6):907-911.
36. Goto A, Takeuchi S, Sugimura K, Maruo T. Usefulness of Gd-DTPA contrast-enhanced dynamic MRI and serum determination of LDH and its isozymes in the differential diagnosis of leiomyosarcoma from degenerated leiomyoma of the uterus. *Int J Gynecol Cancer*. 2002;12(4):354-361.
37. Huang GS, Chiu LG, Gebb JS, et al. Serum CA125 predicts extrauterine disease and survival in uterine carcinosarcoma. *Gynecol Oncol*. 2007;107(3):513-517.
38. Quade BJ, Wang TY, Sornberger K, Dal Cin P, Mutter GL, Morton CC. Molecular pathogenesis of uterine smooth muscle tumors from transcriptional profiling. *Genes Chromosomes Cancer*. 2004;40(2):97-108.

39. Malpica A, Euscher ED, Hecht JL, et al. Endometrial Carcinoma, Grossing and Processing Issues: Recommendations of the International Society of Gynecologic Pathologists. Int J Gynecol Pathol. 2019;38 Suppl 1(Iss 1 Suppl 1):S9-S24.
40. American Cancer Society. Cancer Facts & Figures 2019. Atlanta: American Cancer Society; 2019 Available from: http://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf
41. Henderson BE. The cancer question: an overview of recent epidemiologic and retrospective data. Am J Obstet Gynecol. 1989;161(6 Pt 2):1859-1864.
42. The NAMS 2017 Hormone Therapy Position Statement Advisory Panel. The 2017 hormone therapy position statement of The North American Menopause Society. Menopause. 2017;24(7):728-753.
43. Mourits MJ, De Vries EG, Willemse PH, Ten Hoor KA, Hollema H, Van der Zee AG. Tamoxifen treatment and gynecologic side effects: a review. Obstet Gynecol. 2001;97(5 Pt 2):855-866.
44. Althuis MD, Moghissi KS, Westhoff CL, et al. Uterine cancer after use of clomiphene citrate to induce ovulation. Am J Epidemiol. 2005;161(7):607-615.
45. Cao Z, Zheng X, Yang H, et al. Association of obesity status and metabolic syndrome with site-specific cancers: a population-based cohort study. Br J Cancer. 2020;123(8):1336-1344.
46. Berek JS, Hacker NF. Berek & Hacker's Gynecologic Oncology, 6th edition, Wolters Kluwer, Philadelphia 2015.
47. NCCN. Cancer risks in Lynch syndrome by gene compared to the general population. version 3.2019
48. Shu CA, Pike MC, Jotwani AR, et al. Uterine Cancer After Risk-Reducing Salpingo-oophorectomy Without Hysterectomy in Women With BRCA Mutations. JAMA Oncol. 2016;2(11):1434-1440.
49. Iversen L, Sivasubramaniam S, Lee AJ, Fielding S, Hannaford PC. Lifetime cancer risk and combined oral contraceptives: the Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol. 2017;216(6):580.e1-580.e9.
50. Brinton LA, Felix AS, McMeekin DS, et al. Etiologic heterogeneity in endometrial cancer: evidence from a Gynecologic Oncology Group trial. *Gynecol Oncol*. 2013;129(2):277-284.
51. WHO Classification of Tumours Editorial Board. WHO Classification of Tumours: Female Genital Tumours, 5th edition, volume 4, 2020.
52. Raffone A, Travaglino A, Mascolo M, et al. TCGA molecular groups of endometrial cancer: Pooled data about prognosis. *Gynecol Oncol*. 2019;155(2):374-383.
53. Stasenko M, Tunnage I, Ashley CW, et al. Clinical outcomes of patients with POLE mutated endometrioid endometrial cancer. *Gynecol Oncol*. 2020;156(1):194-202.
54. McConechy MK, Talhouk A, Li-Chang HH, et al. Detection of DNA mismatch repair (MMR) deficiencies by immunohistochemistry can effectively diagnose the microsatellite instability (MSI) phenotype in endometrial carcinomas. *Gynecol Oncol*. 2015;137(2):306-310.

55. Reijnen C, Küsters-Vandevelde HVN, Prinsen CF, et al. Mismatch repair deficiency as a predictive marker for response to adjuvant radiotherapy in endometrial cancer. *Gynecol Oncol*. 2019;154(1):124-130.
56. León-Castillo A, de Boer SM, Powell ME, et al. Molecular Classification of the PORTEC-3 Trial for High-Risk Endometrial Cancer: Impact on Prognosis and Benefit From Adjuvant Therapy. *J Clin Oncol*. 2020;38(29):3388-3397.
57. Ronghe R, Gaudoin M. Women with recurrent postmenopausal bleeding should be re-investigated but are not more likely to have endometrial cancer. *Menopause Int*. 2010;16(1):9-11.
58. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65(2):87-108.
59. Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018;68(4):284-296.
60. Wentzensen N, Poole EM, Trabert B, et al. Ovarian Cancer Risk Factors by Histologic Subtype: An Analysis From the Ovarian Cancer Cohort Consortium. J Clin Oncol. 2016;34(24):2888-2898.
61. Scheuer L, Kauff N, Robson M, et al. Outcome of preventive surgery and screening for breast and ovarian cancer in BRCA mutation carriers. *J Clin Oncol*. 2002;20(5):1260-1268. doi:10.1200/JCO.2002.20.5.1260
62. Banks E. The epidemiology of ovarian cancer. Methods Mol Med. 2001;39:3-11.
63. Reproduced with permission from: Kurman RJ, Carcangiu ML, Herrington S, Young RH. World Health Organization Classification of Tumours of the Female Reproductive Organs. IARC, Lyon, 2014.
64. Friedrich M, Villena-Heinsen C, Schweizer J, Holländer M, Stieber M, Schmidt W. Primary tubal carcinoma: a retrospective analysis of four cases with a literature review. *Eur J Gynaecol Oncol*. 1998;19(2):138-143.
65. Shanbhogue AK, Shanbhogue DK, Prasad SR, Surabhi VR, Fasih N, Menias CO. Clinical syndromes associated with ovarian neoplasms: a comprehensive review. *Radiographics*. 2010;30(4):903-919.
66. Moore RG, McMeekin DS, Brown AK, et al. A novel multiple marker bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass. *Gynecol Oncol*. 2009;112(1):40-46.
67. Geomini P, Kruitwagen R, Bremer GL, Cnossen J, Mol BW. The accuracy of risk scores in predicting ovarian malignancy: a systematic review. *Obstet Gynecol*. 2009;113(2 Pt 1):384-394.
68. Zalel Y, Piura B, Elchalal U, Czernobilsky B, Antebi S, Dgani R. Diagnosis and management of malignant germ cell ovarian tumors in young females. *Int J Gynaecol Obstet*. 1996;55(1):1-10.
69. Tewari K, Cappuccini F, Disaia PJ, Berman ML, Manetta A, Kohler MF. Malignant germ cell tumors of the ovary. *Obstet Gynecol*. 2000;95(1):128-133.
70. Imai A, Furui T, Tamaya T. Gynecologic tumors and symptoms in childhood and adolescence; 10-years' experience. *Int J Gynaecol Obstet*. 1994;45(3):227-234.
71. Varras M, Vasilakaki T, Skafida E, Akrivis C. Clinical, ultrasonographic, computed tomography and histopathological manifestations of ovarian steroid cell tumour,

not otherwise specified: our experience of a rare case with female virilisation and review of the literature. *Gynecol Endocrinol*. 2011;27(6):412-418.
72. Quirk JT, Natarajan N. Ovarian cancer incidence in the United States, 1992-1999. *Gynecol Oncol*. 2005;97(2):519-523.
73. Sköld C, Bjørge T, Ekbom A, et al. Pregnancy-related risk factors for sex cord-stromal tumours and germ cell tumours in parous women: a registry-based study. *Br J Cancer*. 2020;123(1):161-166.
74. Boyce EA, Costaggini I, Vitonis A, et al. The epidemiology of ovarian granulosa cell tumors: a case-control study. *Gynecol Oncol*. 2009;115(2):221-225.