

## Bölüm 29

# VULVA KANSERİNDE RADYOTERAPİ VE BRAKİTERAPİ

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### GİRİŞ

Vulva kanseri tüm jinekolojik kanserlerin yaklaşık %4'ünü oluşturan ve son 40 yılda görülme sıklığı artan nadir tümörlerdir (1-4). Yılda yaklaşık 1-2/10000 kadını etkilemektedir (5). Vulva tümörlerinin %80-90'ı skuamöz hücreli kanserlerdir. Vestibular (Bartholin) bez tümörleri genellikle adenokarsinom veya adenokistik karsinomlardır fakat %20-50'sinde duktal epitel kaynaklı skuamöz histoloji saptanmaktadır. Daha nadir olarak melanom, bazal hücreli karsinom, merkel hücreli tümör, sarkom, karsinoid, apokrin bez kanseri, paget hastalığı histolojileri görülmektedir.

Tedavi kararını belirleyecek prognostik faktörler incelendiğinde inguinal lenf nodu metastazı varlığında tutulu lenf nodu sayısı, büyüklüğü ve ekstrakapsüler invazyon olup olmadığının prognoz üzerine etkisi gösterilmiştir (6). Cerrahi sınırın <8 mm olması durumunda lokal yineleme riskinin arttığı gözlenmiştir (7).

Vulva kanserinin nadir görülmesi, literatürdeki bilgilerin azlığı nedeniyle çoğu tedavi kılavuzu retrospektif serilere dayanmaktadır (8-13). Erken evre olan hastalarda sıklıkla tek başına cerrahi uygulanmaktadır. Yakın/ pozitif sınır ve nodal tutulum varsa lokorejyonel yineleme riskini azaltmak ve sağkalımı artırmak için adjuvan radyoterapi (RT) önerilmektedir (14). Lokal ileri hastalığın tedavisi daha karmaşık ve zorlayıcı olmaktadır. Cerrahi, RT veya kemoradyoterapi (KRT) kombinasyonları içeren tedaviler, oluşabilecek yan etkileri azaltmak için kişiselleştirilerek hastalara uygulanmaktadır (15). Primer tedavi olarak kabul edilen cerrahi tipi, tümörün yayılımına göre eksizyon veya parsiyel vulvektomiden radikal vulvektomiye kadar geniş bir spektruma sahiptir (16).

Vulvar kanserli hastaların %60'ı ileri evrede teşhis edilebildiğinden genellikle geniş cerrahi gerekmektedir. (1,3,17). Son 30 yılda bu nedenle vulva kanseri te-

## NADİR GÖRÜLEN VULVAR MALİNİTELER

### Vulvar melanom

Vulvar maliniteler arasında 2. En sık görülen tümör tipidir. Tedavisi cerrahidir (49). Cerrahi sınır yakınlığı veya nodal metastaz varlığında adjuvan RT eklenmelidir.

### Bartholin bezi kanseri

Nadir görülür. Çeşitli histolojik tipleri görülebilir. Tedavisi cerrahidir ancak yerleşimi nedeniyle genellikle yeterli cerrahi sınır sağlanamamakta ve lokal yinelemeyi azaltmak için adjuvan RT'ye ihtiyaç duyulmaktadır (50).

### Paget hastalığı

İki tipi vardır. Primer tip intraepitelyal lezyon olarak başlamaktadır. İkincil tip ise altta yatan adenokarsinomun invazyonuna bağlı oluşmaktadır. İntarepitelyal Paget hastalığının tedavisi cerrahidir. Yineleyen ve unrezektabl hastalıkta RT etkili bir tedavi olabilmektedir (51). Adenokarsinoma bağlı oluşan paget hastalığının tedavisi cerrahi ve skuamöz karsinomlarda uygulanan endikasyonlara göre adjuvan RT'dir (52).

### Sonuç

Vulva skuamöz hücreli kanserinde inguinofemoral makrometastaz ve yakın cerrahi sınır varlığında adjuvan RT uygulandığında genel sağkalım artmaktadır. Kemoterapinin eklenmesi sağkalıma katkı sağlayabilir. Definitif RT, cerrahi uygulanamadığı zaman yapılmalıdır.

**Anahtar Kelimeler:** Vulva kanseri, Radyoterapi, Brakiterapi

### KAYNAKÇA

1. Judson P.L., Habermann E.B., Baxter N.N., et al: Trends in the incidence of invasive and in situ vulvar carcinoma. *Obstet Gynecol* 2006; 107: pp. 1018-1022
2. Siegel R.L., Miller K.D., and Jemal A.: Cancer statistics, 2016. *CA Cancer J Clin* 2016; 66: pp. 7-30
3. Carter J.S., and Downs L.S.: Vulvar and vaginal cancer. *Obstet Gynecol Clin North Am* 2012; 39: pp. 213-231
4. Alkatout I., Schubert M., Garbrecht N., et al: Vulvar cancer: epidemiology, clinical presentation, and management options. *Int J Womens Health* 2015; 7: pp. 305-313
5. National Cancer Institute. Cancer Stat Facts: Vulvar Cancer. Bethesda, MD:National Cancer Institute. Available at:[https:// seer. cancer.gov/statfacts/html/vulva.html](https://seer.cancer.gov/statfacts/html/vulva.html). Accessed on August 3, 2018
6. Origoni M, Sideri M, Garsia S, et al.: Prognostic value of pathological patterns of lymph node positivity in squamous cell carcinoma of the vulva stage III and IVA FIGO. *Gynecol Oncol*. 45:313-316 1992
7. Heaps JM, Fu YS, Montz FJ, et al. Surgical-pathologic variables predictive of local recurrence in squamous cell carcinoma of the vulva. *Gynecol Oncol* 1990; 38:309-314

8. Pohar S., Hoffstetter S., Peiffert D., et al: Effectiveness of brachytherapy in treating carcinoma of the vulva. *Int J Radiat Oncol Biol Phys* 1995; 32: pp. 1455-1460
9. Tewari K., Cappuccini F., Syed A.M., et al: Interstitial brachytherapy in the treatment of advanced and recurrent vulvar cancer. *Am J Obstet Gynecol* 1999; 181: pp. 91-98
10. Perez C.A., Grigsby P.W., Chao K.C., et al: Irradiation in carcinoma of the vulva: factors affecting outcome. *Int J Radiat Oncol Biol Phys* 1998; 42: pp. 335-344
11. Copeland L.J., Sneige N., Gershenson D.M., et al: Bartholin gland carcinoma. *Obstet Gynecol* 1986; 67: pp. 794-801
12. Thibault I., Lavallée M.C., Aubin S., et al: Management of Bartholin's gland carcinoma using high-dose-rate interstitial brachytherapy boost. *Brachytherapy* 2013; 12: pp. 500-507
13. Kellas-Ślęzka S., Białas B., Fijałkowski M., et al: Interstitial high-dose-rate brachytherapy in locally advanced and recurrent vulvar cancer. *J Contemp Brachytherapy* 2016; 8: pp. 32-40
14. Montana GS, Kang SK. Carcinoma of the vulva. In: Halperin EC, Perez CA, Brady LW editors. *Perez and Brady's principles and practice of radiation oncology*. 5th Edition. Philadelphia: Lippincott Williams & Wilkins; 2008. pp. 1692 – 1707.
15. Jhingran A. Potential advantages of intensity-modulated radiation therapy in gynecologic malignancies. *Semin Radiat Oncol* 2006; 16:144 – 151
16. Prempre T., and Amornmarn R.: Radiation treatment of recurrent carcinoma of the vulva. *Cancer* 1984; 54: pp. 1943-1949
17. Beller U., Quinn M.A., Benedet J.L., et al: Carcinoma of the vulva. *Int J Gynecol Obstet* 2006; 95: pp. S7-S27
18. Ellis F. Cancer of the vulva treated by radiation; an analysis of 127 cases *Br J Radiol* 1949; 22: 513–520.
19. Slevin NJ, Pointon RC. Radical radiotherapy for carcinoma of the vulva. *Br J Radiol* 1989;62: 145–147.
20. S.A.Sullivan, N.Desravines, A.Liberty, K.Allman, M.Gornet, K.K.Zorn, J.Acuna, R.L.Stone, V.L. Bae-Jump, L.Van Le. Surgical management vs primary radiotherapy for vulvar cancer. *Gynecol Oncol* Volume 145, Supplement 1, June 2017, Pages 216-217
21. Landrum LM, Skaggs V, Gould N, Walker JL, McMeekin DS. Comparison of outcome measures in patients with advanced squamous cell carcinoma of the vulva treated with surgery or primary chemoradiation. *Gynecol Oncol*. 2008 Mar;108(3):584-90. Epub 2007 Dec 26.
22. Natesan D, Hong JC, Foote J, Sosa JA, Havrilesky L, Chino J. Primary Versus Preoperative Radiation for Locally Advanced Vulvar Cancer. *Int J Gynecol Cancer*. 2017 May;27(4):794-804.
23. Corney RH<sup>1</sup>, Crowther ME, Everett H, Howells A, Shepherd JH. Psychosexual dysfunction in women with gynaecological cancer following radical pelvic surgery. *Br J Obstet Gynaecol*. 1993 Jan;100(1):73-8.
24. Boronow RC. Combined therapy as an alternative to exenteration for locally advanced vulvovaginal cancer; rationale and results. *Cancer*. 1982;49: 1085–91.
25. Hacker NF, Berek JS, Juillard JF, Lagasse LD. Preoperative radiation therapy for locally advanced vulvar cancer. *Cancer*.1984;54:2056–61.
26. Moore DH, Thomas GM, Montana GS, Saxer A, Gallup DG, Olt G. Preoperative chemoradiation for advanced vulvar cancer: a phase II study of the Gynecologic Oncology Group. *Int J Radiat Oncol Biol Phys*. 1998 Aug 1;42(1):79-85.
27. Moore, D. H., Ali, S., Koh, W.-J., Michael, H., Barnes, M. N., McCourt, C. K., ... Walker, J. L. (2012). A phase II trial of radiation therapy and weekly cisplatin chemotherapy for the treatment of locally-advanced squamous cell carcinoma of the vulva: A gynecologic oncology group study. *Gynecologic Oncology*, 124(3), 529–533.
28. Eifel PJ<sup>1</sup>, Morris M, Burke TW, Levenback C, Gershenson DM. Prolonged continuous infusion cisplatin and 5-fluorouracil with radiation for locally advanced carcinoma of the vulva. *Gynecol Oncol*. 1995 Oct;59(1):51-6.
29. Gerszten K, Selvaraj RN, Kelley J, Faul C. Preoperative chemoradiation for locally advanced carcinoma of the vulva. *Gynecol Oncol*. 2005 Dec;99(3):640-4. Epub 2005 Sep 19.

30. Montana GS, Thomas GM, Moore DH, Saxer A, Mangan CE, Lentz SS, Averette HE. Preoperative chemo-radiation for carcinoma of the vulva with N2/N3 nodes: a gynecologic oncology group study. *Int J Radiat Oncol Biol Phys*. 2000 Nov 1;48(4):1007-13.
31. Beriwal S, Shukla G, Shinde A, Heron DE, Kelley JL, Edwards RP, Sukumvanich P, Richards S, Olawaiye AB, Krivak TC. Preoperative intensity modulated radiation therapy and chemotherapy for locally advanced vulvar carcinoma: analysis of pattern of relapse. *Int J Radiat Oncol Biol Phys*. 2013 Apr 1;85(5):1269-74.
32. Maneo A, Landoni F, Colombo A, Villa A, Caspani G. Randomised study between neoadjuvant chemoradiotherapy and primary surgery for the treatment of advanced vulval cancer. *International Journal of Gynecological Cancer*. 2003; Vol. 13 (Suppl 1):6, Abstract PL 19.
33. van Doorn HC, Ansink A, Verhaar-Langereis M, Stalpers L. Neoadjuvant chemoradiation for advanced primary vulvar cancer. *Cochrane Database Syst Rev*. 2006 Jul 19;(3):CD003752. Review. Update in: *Cochrane Database Syst Rev*. 2011;(4):CD003752.
34. Scheistroen M, Trope C. Combined bleomycin and irradiation in preoperative treatment of advanced squamouscell carcinoma of the vulva. *Acta Oncologica* 1993;32(6): 657-61.
35. Landoni F, Maneo A, Zanetta G, Colombo A, Nava S, Placa F, et al. Concurrent preoperative chemotherapy with 5-fluorouracil and mitomycin C and radiotherapy (FUMIR) followed by limited surgery in locally advanced and recurrent vulvar carcinoma. *Gynecologic Oncology* 1996;61(3):321-7.
36. Lupi G, Raspagliesi F, Zucali R, Fontanelli R, Paladini D, Kenda R, di Re F. Combined preoperative chemoradiotherapy followed by radical surgery in locally advanced vulvar carcinoma. A pilot study. *Cancer*. 1996 Apr 15;77(8):1472-8.
37. Faul CM, Mirmow D, Huang Q, et al. Adjuvant radiation for vulvar carcinoma: improved local control. *Int J Radiat Oncol Biol Phys* 1997; 38:381 - 389.
38. Kunos C, Simpkins F, Gibbons H, Tian C, Homesley H. Radiation therapy compared with pelvic node resection for node-positive vulvar cancer: a randomized controlled trial. *Obstet Gynecol*. 2009 Sep;114(3):537-46.
39. Fons G, Groenen SMA, Oonk MHM, Ansink AC, van der Zee AGJ, Burger MPM, et al. Adjuvant radiotherapy in patients with vulvar cancer and one intra capsular lymph node metastasis is not beneficial. *Gynecol Oncol*. 2009;114(2):343-5.
40. Ansink AC, van Tinteren H, Aartsen EJ, et al.: Outcome, complications and follow-up in surgically treated squamous cell carcinoma of the vulva 1956-1982. *Eur J Obstet Gynecol Reprod Biol*. 42:137-143 1991
41. Parthasarathy A, Cheung MK, Osann K, Husain A, Teng NN, Berek JS, et al. The benefit of adjuvant radiation therapy in single-node-positive squamous cell vulvar carcinoma. *Gynecol Oncol*. 2006;103(3):1095-9.
42. Dusenbery KE, Carlson JW, LaPorte RM, et al.: Radical vulvectomy with postoperative irradiation for vulvar cancer. Therapeutic implications of a central block. *Int J Radiat Oncol Biol Phys*. 29:989-998 1994 8083101
43. Perez CA, Grigsby PW, Chao C, et al. Irradiation in carcinoma of the vulva: factors affecting outcome. *Int J Radiat Oncol Biol Phys* 1998; 42:335 -344.
44. Gaffney DK, King B, Viswanathan AN, Barkati M, Beriwal S, Eifel P, et al. Consensus recommendations for radiation therapy contouring and treatment of vulvar carcinoma. *Int J Radiat Oncol Biol Phys*. 2016;95(4):1191-200.
45. Hoffman M., Greenberg S., Greenberg H., et al: Interstitial radiotherapy for the treatment of advanced or recurrent vulvar and distal vaginal malignancy. *Am J Obstet Gynecol* 1990; 162: pp. 1278-1282
46. Mahantshetty U, et al. Clinical outcome of high-dose-rate interstitial brachytherapy in vulvar cancer: a single institutional experience. *Brachytherapy*. 2017;16(1):153-60.
47. Castelnau-Marchand P, et al. Brachytherapy as part of the conservative treatment for primary and recurrent vulvar carcinoma. *Brachytherapy*. 2017;16(3):518-25.

48. Kevin Albuquerque, Sushil Beriwal, Akila N. Viswanathan, Beth Erickson. Radiation Therapy Techniques for Gynecological Cancers. A Comprehensive Practical Guide
49. Linda J. Rogers, Mauricio A. Cuello. Cancer of the vulva. *Int J Gynaecol Obstet.* 2018 Oct;143 Suppl 2:4-13.
50. Di Donato V, Casorelli A, Bardhi E, Vena F, Marchetti C, Muzii L, Benedetti Panici P. Crit Bartholin gland cancer. *Rev Oncol Hematol.* 2017 Sep;117: 1-11.
51. Tolia M, Tsoukalas N, Sofoudis C, et al. Primary extramammary invasive Paget's vulvar disease: what is the standard, what are the challenges and what is the future for radiotherapy? *BMC Cancer* 2016;16: 563.
52. Karam A, Dorigo O. Treatment outcomes in a large cohort of patients with invasive Extramammary Paget's disease. *Gynecol Oncol.* 2012 May;125(2):346-51.