

BÖLÜM 19

ANAL KANSERLER

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GENEL BİLGİLER

Epidemiyolojik Veriler

Anal kanserler nadir olup, tüm gastrointestinal malignitelerin yaklaşık %3'ünü oluştururlar. Amerika Bileşik Devletleri (ABD)'nde 2021 yılında 9090 (3020 erkek, 6070 kadın) yeni anal kanseri vakası tespit edilmiştir. Yine 2021 yılında ABD'de anal kansere bağlı yaklaşık 1430 ölümün gerçekleştiği tahmin edilmektedir (1). Genel popülasyonda anal kanser insidansı hem ABD'de hem de tüm dünyada son 30 yıl içinde artış göstermiştir. Skuamöz hücreli anal kanser insidansı 2001-2015 yılları arasında yıllık %2.7'lük bir artış göstermiş olup en büyük artış 50 ve üzeri yaş grubunda izlenmiştir (2).

Anal kanserli hastalarda 1 yıllık sağ kalım oranı yaklaşık %81 iken; 5 yıllık sağ kalım oranı yaklaşık %56'dır. Anal kanser ölüm oranlarında da 2001-2016 yılları arasında yılda ortalama %3.1'lük artış görüldü. Bu artış; 50 ve üzeri yaş grubundaki kadın hastalarda daha belirgindi (2).

Risk Faktörleri

Anal kanserinin risk faktörleri arasında, insan papilloma virüsü (HPV) enfeksiyonu, insan bağılıklık yetmezliği virüsü (HIV), anal ilişki, cinsel yolla bulaşan hastalık öyküsü, servikal, vulvar veya vajinal kanser öyküsü, solid organ transplantasyon sonrası immunsüpresyon, otoimmun hastalık, sigara yer almaktadır (3).

Danimarka ve İsveç'te yapılan çalışmada anal kanserli hastaların yaklaşık %80'inde HPV tespit edilmiş olup; bunların yaklaşık % 70'inde HPV tip 16 bulunmuştur. HPV tip 18 de anal karsinom için yüksek riskli formdur (4). Servikal intraepitelial neoplazide olduğu gibi, HPV'nin düşük dereceli displaziden yüksek dereceli displaziye ve nihayetinde invaziv kansere ilerleyebilen anal intraepitelial neoplaziye neden olduğu gösterilmiştir. Kondom kullanımı HPV enfeksiyonundan korunmada iyi bir seçenektır.

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Anal melanom tedavisi geniş eksizyondur. APR ile geniş eksizyon arasında sağıkalım farkı görülmemiştir. Adjuvan kemoterapi ve radyoterapi, hastanın evre-sine göre önerilir (49).

BAZAL HÜCRELİ KARSİNOM

Anal kanalın bazal hücreli karsinomu (BCC), tüm anal kanserlerin %0,2'sini oluşturur. Bazal hücreli karsinom tipik olarak cildin ultraviyole ışığına maruz kalan bölgelerinde bulunur. Risk faktörleri arasında bazal hücreli nevüs sendromu veya kseroderma pigmentosum, kronik inflamasyon, radyasyon öyküsü, travma veya yanık öyküsü bulunur (50).

Cildin diğer bölgelerinde bulunan BCC'ye benzer şekilde, bu lezyonlar tipik olarak merkezi bir ülserasyon ve kabarık bir inci gibi kenar ile kendini gösterir. Genellikle hemoroid veya anal fissür olarak yanlış teşhis edilirler. Nadiren invazyon veya metastaz yaparlar. Tedavisi sağlam cerrahi sınırlarla geniş eksizyondur (50).

KAYNAKLAR

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA: a cancer journal for clinicians. 2021;71(1):7-33.
2. Deshmukh AA, Suk R, Shiels MS, Sonawane K, Nyitray AG, Liu Y, et al. Recent Trends in Squamous Cell Carcinoma of the Anus Incidence and Mortality in the United States, 2001-2015. Journal of the National Cancer Institute. 2020;112(8):829-38.
3. Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, et al. Human papillomavirus, smoking, and sexual practices in the etiology of anal cancer. Cancer. 2004;101(2):270-80.
4. Frisch M, Glimelius B, van den Brule AJ, Wohlfahrt J, Meijer CJ, Walboomers JM, et al. Sexually transmitted infection as a cause of anal cancer. The New England journal of medicine. 1997;337(19):1350-8.
5. Chaturvedi AK, Madeleine MM, Biggar RJ, Engels EA. Risk of human papillomavirus-associated cancers among persons with AIDS. Journal of the National Cancer Institute. 2009;101(16):1120-30.
6. Clark MA, Hartley A, Geh JI. Cancer of the anal canal. The Lancet Oncology. 2004;5(3):149-57.
7. Frisch M. On the etiology of anal squamous carcinoma. Danish medical bulletin. 2002;49(3):194-209.
8. Young AN, Jacob E, Willauer P, Smucker L, Monzon R, Oceguera L. Anal Cancer. The Surgical clinics of North America. 2020;100(3):629-34.
9. Valvo F, Ciurlia E, Avuzzi B, Doci R, Ducreux M, Roelofsen F, et al. Cancer of the anal region. Critical reviews in oncology/hematology. 2019;135:115-27.
10. Hoff PM, Coudry R, Moniz CM. Pathology of Anal Cancer. Surgical oncology clinics of North America. 2017;26(1):57-71.
11. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. Jama. 2002;287(16):2114-9.
12. Darragh TM, Colgan TJ, Thomas Cox J, Heller DS, Henry MR, Luff RD, et al. The Lower Anogenital Squamous Terminology Standardization project for HPV-associated lesions: background and consensus recommendations from the College of American Pathologists and the American

- Society for Colposcopy and Cervical Pathology. International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists. 2013;32(1):76-115.
- 13. Berry JM, Palefsky JM, Welton ML. Anal cancer and its precursors in HIV-positive patients: perspectives and management. *Surgical oncology clinics of North America*. 2004;13(2):355-73.
 - 14. Arens Y, Gaisa M, Goldstone SE, Liu Y, Wisnivesky J, Sigel CS, et al. Risk of Invasive Anal Cancer in HIV-Infected Patients With High-Grade Anal Dysplasia: A Population-Based Cohort Study. *Diseases of the colon and rectum*. 2019;62(8):934-40.
 - 15. Wieland U, Oellig F, Kreuter A. Anal dysplasia and anal cancer. English version. *Der Hautarzt; Zeitschrift für Dermatologie, Venerologie, und verwandte Gebiete*. 2020;71(Suppl 2):74-81.
 - 16. Klas JV, Rothenberger DA, Wong WD, Madoff RD. Malignant tumors of the anal canal: the spectrum of disease, treatment, and outcomes. *Cancer*. 1999;85(8):1686-93.
 - 17. Shida D, Kanemitsu Y, Hamaguchi T, Shimada Y. Introducing the eighth edition of the tumor-node-metastasis classification as relevant to colorectal cancer, anal cancer and appendiceal cancer: a comparison study with the seventh edition of the tumor-node-metastasis and the Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma. *Japanese journal of clinical oncology*. 2019;49(4):321-8.
 - 18. Touboul E, Schlienger M, Buffat L, Lefkopoulos D, Pène F, Parc R, et al. Epidermoid carcinoma of the anal canal. Results of curative-intent radiation therapy in a series of 270 patients. *Cancer*. 1994;73(6):1569-79.
 - 19. Gunderson LL, Moughan J, Ajani JA, Pedersen JE, Winter KA, Benson AB, 3rd, et al. Anal carcinoma: impact of TN category of disease on survival, disease relapse, and colostomy failure in US Gastrointestinal Intergroup RTOG 98-11 phase 3 trial. *International journal of radiation oncology, biology, physics*. 2013;87(4):638-45.
 - 20. Ajani JA, Winter KA, Gunderson LL, Pedersen J, Benson AB, 3rd, Thomas CR, Jr, et al. US intergroup anal carcinoma trial: tumor diameter predicts for colostomy. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2009;27(7):1116-21.
 - 21. Bartelink H, Roelofsen F, Eschwege F, Rougier P, Bosset JF, Gonzalez DG, et al. Concomitant radiotherapy and chemotherapy is superior to radiotherapy alone in the treatment of locally advanced anal cancer: results of a phase III randomized trial of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 1997;15(5):2040-9.
 - 22. Glynne-Jones R, Sebag-Montefiore D, Adams R, Gollins S, Harrison M, Meadows HM, et al. Prognostic factors for recurrence and survival in anal cancer: generating hypotheses from the mature outcomes of the first United Kingdom Coordinating Committee on Cancer Research Anal Cancer Trial (ACT I). *Cancer*. 2013;119(4):748-55.
 - 23. Serup-Hansen E, Linnemann D, Skovrider-Ruminski W, Høgdall E, Geertsen PF, Havsteen H. Human papillomavirus genotyping and p16 expression as prognostic factors for patients with American Joint Committee on Cancer stages I to III carcinoma of the anal canal. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2014;32(17):1812-7.
 - 24. Giuliano AR, Palefsky JM, Goldstone S, Moreira ED, Jr, Penny ME, Aranda C, et al. Efficacy of quadrivalent HPV vaccine against HPV Infection and disease in males. *The New England journal of medicine*. 2011;364(5):401-11.
 - 25. Richel O, de Vries HJ, van Noesel CJ, Dijkgraaf MG, Prins JM. Comparison of imiquimod, topical fluorouracil, and electrocautery for the treatment of anal intraepithelial neoplasia in HIV-positive men who have sex with men: an open-label, randomised controlled trial. *The Lancet Oncology*. 2013;14(4):346-53.
 - 26. Ryan DP, Compton CC, Mayer RJ. Carcinoma of the anal canal. *The New England journal of medicine*. 2000;342(11):792-800.
 - 27. Nigro ND, Vaitkevicius VK, Considine B, Jr. Combined therapy for cancer of the anal canal: a

- preliminary report. Diseases of the colon and rectum. 1974;17(3):354-6.
- 28. Epidermoid anal cancer: results from the UKCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil, and mitomycin. UKCCR Anal Cancer Trial Working Party. UK Co-ordinating Committee on Cancer Research. Lancet (London, England). 1996;348(9034):1049-54.
 - 29. Flam M, John M, Pajak TF, Petrelli N, Myerson R, Doggett S, et al. Role of mitomycin in combination with fluorouracil and radiotherapy, and of salvage chemoradiation in the definitive nonsurgical treatment of epidermoid carcinoma of the anal canal: results of a phase III randomized intergroup study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 1996;14(9):2527-39.
 - 30. James RD, Glynne-Jones R, Meadows HM, Cunningham D, Myint AS, Saunders MP, et al. Mitomycin or cisplatin chemoradiation with or without maintenance chemotherapy for treatment of squamous-cell carcinoma of the anus (ACT II): a randomised, phase 3, open-label, 2 × 2 factorial trial. The Lancet Oncology. 2013;14(6):516-24.
 - 31. Peiffert D, Tournier-Rageard L, Gérard JP, Lemanski C, François E, Giovannini M, et al. Induction chemotherapy and dose intensification of the radiation boost in locally advanced anal canal carcinoma: final analysis of the randomized UNICANCER ACCORD 03 trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2012;30(16):1941-8.
 - 32. Rao S, Guren MG, Khan K, Brown G, Renéhan AG, Steigen SE, et al. Anal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up(☆). Annals of oncology : official journal of the European Society for Medical Oncology. 2021;32(9):1087-100.
 - 33. Meulendijks D, Dewit L, Tomasa NB, van Tinteren H, Beijnen JH, Schellens JH, et al. Chemoradiotherapy with capecitabine for locally advanced anal carcinoma: an alternative treatment option. British journal of cancer. 2014;111(9):1726-33.
 - 34. Dee EC, Byrne JD, Wo JY. Evolution of the Role of Radiotherapy for Anal Cancer. Cancers. 2021;13(6).
 - 35. Ortholan C, Ramaioli A, Peiffert D, Lusinchi A, Romestaing P, Chauveinc L, et al. Anal canal carcinoma: early-stage tumors < or =10 mm (T1 or Tis): therapeutic options and original pattern of local failure after radiotherapy. International journal of radiation oncology, biology, physics. 2005;62(2):479-85.
 - 36. Constantinou EC, Daly W, Fung CY, Willett CG, Kaufman DS, DeLaney TF. Time-dose considerations in the treatment of anal cancer. International journal of radiation oncology, biology, physics. 1997;39(3):651-7.
 - 37. Salama JK, Mell LK, Schomas DA, Miller RC, Devissetty K, Jani AB, et al. Concurrent chemotherapy and intensity-modulated radiation therapy for anal canal cancer patients: a multicenter experience. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2007;25(29):4581-6.
 - 38. Darragh TM, Colgan TJ, Cox JT, Heller DS, Henry MR, Luff RD, et al. The Lower Anogenital Squamous Terminology Standardization Project for HPV-Associated Lesions: background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. Archives of pathology & laboratory medicine. 2012;136(10):1266-97.
 - 39. Bryant AK, Huynh-Le MP, Simpson DR, Gupta S, Sharabi AB, Murphy JD. Association of HIV Status With Outcomes of Anal Squamous Cell Carcinoma in the Era of Highly Active Antiretroviral Therapy. JAMA oncology. 2018;4(1):120-2.
 - 40. Oehler-Jänne C, Huguet F, Provencher S, Seifert B, Negretti L, Riener MO, et al. HIV-specific differences in outcome of squamous cell carcinoma of the anal canal: a multicentric cohort study of HIV-positive patients receiving highly active antiretroviral therapy. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2008;26(15):2550-7.
 - 41. Glynne-Jones R, Meadows HM, Lopes A, Muirhead R, Sebag-Montefiore D, Adams R. Impact of compliance to chemoradiation on long-term outcomes in squamous cell carcinoma of the

- anus: results of a post hoc analysis from the randomised phase III ACT II trial. *Annals of oncology : official journal of the European Society for Medical Oncology.* 2020;31(10):1376-85.
- 42. Eson G, Foo M, Harrow S, McGregor G, Hay J. Outcomes of salvage surgery for epidermoid carcinoma of the anus following failed combined modality treatment. *American journal of surgery.* 2011;201(5):628-33.
 - 43. Greenall MJ, Quan SH, Stearns MW, Urmacher C, DeCosse JJ. Epidermoid cancer of the anal margin. Pathologic features, treatment, and clinical results. *American journal of surgery.* 1985;149(1):95-101.
 - 44. Rao S, Sclafani F, Eng C, Adams RA, Guren MG, Sebag-Montefiore D, et al. International Rare Cancers Initiative Multicenter Randomized Phase II Trial of Cisplatin and Fluorouracil Versus Carboplatin and Paclitaxel in Advanced Anal Cancer: InterAACT. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2020;38(22):2510-8.
 - 45. Morris VK, Salem ME, Nimeiri H, Iqbal S, Singh P, Ciombor K, et al. Nivolumab for previously treated unresectable metastatic anal cancer (NCI9673): a multicentre, single-arm, phase 2 study. *The Lancet Oncology.* 2017;18(4):446-53.
 - 46. Ott PA, Piha-Paul SA, Munster P, Pishvaian MJ, van Brummelen EMJ, Cohen RB, et al. Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with recurrent carcinoma of the anal canal. *Annals of oncology : official journal of the European Society for Medical Oncology.* 2017;28(5):1036-41.
 - 47. Anwar S, Welbourn H, Hill J, Sebag-Montefiore D. Adenocarcinoma of the anal canal - a systematic review. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland.* 2013;15(12):1481-8.
 - 48. McCarter MD, Quan SH, Busam K, Paty PP, Wong D, Guillem JG. Long-term outcome of perianal Paget's disease. *Diseases of the colon and rectum.* 2003;46(5):612-6.
 - 49. Malik A, Hull TL, Floruta C. What is the best surgical treatment for anorectal melanoma? *International journal of colorectal disease.* 2004;19(2):121-3.
 - 50. Graham RP, Arnold CA, Naini BV, Lam-Himlin DM. Basaloid Squamous Cell Carcinoma of the Anus Revisited. *The American journal of surgical pathology.* 2016;40(3):354-60.