Bölüm
8

ORAL KAVİTE VE OROFARİNKS SKUAMÖZ HÜCRELİ KANSERLERİNDE RADYOTERAPİ

Ahmet KÜÇÜK[1]

GİRİŞ

Tüm dünyada her yıl yaklaşık 450.000 insan baş boyun kanseri (BBK) tanısı almaktadır. Oral kavite (OK) ve orofarinks (OF) squamöz hücreli karsinomları BBK'lar içinde önemli bir yer tutmaktadır[1]. BBK'li hastalarda servikal lenf nodu (LN) metastazlarının olması kötü prognostik faktör olup azalmış genel sağkalım ile ilişkilidir[2]. Bu sebeple servikal bölgenin etkin tedavisi hastalığa özgü genel sağkalımı iyileştirmektedir[3,4].

Anatomik olarak birbirleriyle yakın ilişkili bölgeler olmalarına rağmen biyolojik açıdan farklılık göstermektedirler. OK tümörleri daha çok sigara kullanımı ilişkilidir[5]. OF kanserlerinin ise; İnsan papilloma virüsünün (HPV) kronik gizli enfeksiyonunun sonucu olarak insidansi yıllar içinde artmakla birlikte orantısız olarak genç insanları etkilediği görülmektedir[6].

OF kanserli hastaların çoğunda tanı anında boyun metastazı (cN+) vardır. Tanı anında (cN+) olmayan her iki hasta grubunun %10-40'ında ise okkült servikal nodal metastaz riski mevcuttur[7,8].

Geçmişten bugüne hem OK hem de OF squamöz hücreli karsinomun servikal metastazlarının tedavisinde, boyun diseksiyonu ve radyoterapi temel dayanağı oluşturmaktadır[9].

ORAL KAVİTE KANSERLERİNDE RADYOTERAPİ

OK tümörleri; dudakların (en yaygın), dilin (dilin ön üçte ikisi) (en yaygın ikinci), sert damağın, bukkal mukozanın, retromolar trigonun, alveolar ridge ve ağız tabanının tümörleridir. Oral kavite kanserleri, ABD'deki tüm kanserlerin yaklaşık

1 Uz.Dr.Mersin Şehir Eğitim ve Araştırma Hastanesi, drakucuk@hotmail.com

kanserinin birincil ve ikincil önlenmesi, yaşam tarzıyla ilgili risk faktörleri hakkında daha iyi bir eğitim ve erken teşhis için gelişmiş farkındalık ve ek tetkikler gerektirmektedir.

Anahtar Kelimeler: Radyoterapi, kemoradyoterapi, oral kavite kanser, orofarinks kanser,tedavi.

KAYNAKLAR

1. Torre LA, Bray F, Siegel RL, et al: Global cancer statistics, 2012. CA Cancer J Clin 65:87-108, 2015
2. Schuller DE, McGuirt WF, McCabe BF, et al: The prognostic significance of metastatic cervical lymph nodes. Laryngoscope 90:557-570, 1980
3. D'Cruz AK, Vaish R, Kapre N, et al: Elective versus therapeutic neck dissection in node-negative oral cancer. N Engl J Med 373:521-529, 2015
4. O'Sullivan B, Huang SH, Su J, et al: Development and validation of a staging system for HPV-related oropharyngeal cancer by the International Collaboration on Oropharyngeal cancer Network for Staging (ICON-S): A multicentre cohort study. Lancet Oncol 17:440-451, 2016
5. Sturgis EM, Cinciripini PM: Trends in head and neck cancer incidence in relation to smoking prevalence: An emerging epidemic of human papillomavirusassociated cancers? Cancer 110:1429-1435, 2007
6. Hussein AA,Helder MN, de Visscher JG, et al: Global incidence of oral and oropharynx cancer in patients younger than 45 years versus older patients: A systematic review. Eur J Cancer 82:115-127, 2017
7. Amini A, Jasem J, Jones BL, et al: Predictors of overall survival in human papillomavirus-associated oropharyngeal cancer using the National Cancer Data Base. Oral Oncol 56:1-7, 2016
8. Kuo P,Mehra S, Sosa JA, et al: Proposing prognostic thresholds for lymph node yield in clinically lymph node-negative and lymph node-positive cancers of the oral cavity. Cancer 122:3624-3631, 2016
9. Helsen N, Van den Wyngaert T, Carp L, et al: FDG-PET/CT for treatment response assessment in head and neck squamous cell carcinoma: A systematic review and meta-analysis of diagnostic performance. Eur J Nucl Med Mol Imaging 45:1063-1071, 2018
10. Greenlee RT et al (2000) Cancer statistics, 2000.CA Cancer JClin. 50(1):7–33
11. Dobrossy L (2005) Epidemiology of head and neck cancer: magnitude of the problem. Cancer Metastasis Rev 24(1):9–17
12. Green FL et al (2002) AJCC cancer staging manual. Springer, New York
13. Winzenburg SM et al (1998) Basaloid squamous carcinoma: a clinical comparison of two histologic types with poorly differentiated squamous cell carcinoma. Otolaryngol Head Neck Surg 119(5):471–475
14. Chen AY, Myers JN (2001) Cancer of the oral cavity. Dis Mon 47(7):275–361
15. Oral cavity cancer. In: Amin MB, Edge SB, Greene FL, et al., eds.: AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer, 2017, pp. 79–94.
16. Harrison LB, Fass DE (1990) Radiation therapy for oral cavity cancer. Dent Clin North Am 34(2):205–222
17. Fu KK et al (1976) Time, dose and volume factors in interstitial Radium implants of carcinoma of the oral tongue. Radiology 119(1):209–213
18. Fu KK et al (1976) External and interstitial radiation therapy of carcinoma of the oral tongue. A review of 32 years' experience. AJR Am J Roentgenol 126(1):107–115
19. Dearnaley DP et al (1991) Interstitial irradiation for carcinoma of the tongue and fl oor of mouth: Royal Marsden Hospital Experience 1970–1986. Radiother Oncol 21(3):183–192
20. Pernot M et al (1995) Evaluation of the importance of systematic neck dissection in carcinoma

of the oral cavity treated by brachytherapy alone for the primary lesion (apropos of a series of 346 patients). Bull Cancer Radiother 82(3):311–317
21. Decroix Y, Ghossein NA (1981) Experience of the Curie Institute in treatment of cancer of the mobile tongue: II. Management of the neck nodes. Cancer 47(3):503–508
22. Pernot M et al (1995) Epidermoid carcinomas of the fl oor of mouth treated by exclusive irradiation: statistical study of a series of 207 cases. Radiother Oncol 35(3):177–185
23. Robertson AG et al (1998) Early closure of a randomized trial: surgery and postoperative radiotherapy versus radiotherapy in the management of intra-oral tumours. Clin Oncol (R Coll Radiol) 10(3):155–160
24. Sh JP, Lydiatt W (1995) Treatment of cancer of the head and neck. CA Cancer J Clin 45(6):352–368
25. Vikram B et al (1980) Elective postoperative radiation therapy in stages III and IV epidermoid carcinoma of the head and neck. Am J Surg 140(4):580–584
26. Licitr L et al (2003) Primary chemotherapy in resectable oral cavity squamous cell cancer: a randomized controlled trial. J Clin Oncol 21(2):327–333
27. Vollin P et al (1999) Results of a prospective randomized trial with induction chemotherapy for cancer of the oral cavity and tonsils. HNO 47(10):899–906
28. Mohr C et al (1994) Preoperative radiochemotherapy and radical surgery in comparison with radical surgery alone. A prospective, multicentric, randomized DOSAK study of advanced squamous cell carcinoma of the oral cavity and the oropharynx (a 3-year follow-up). Int J Oral Maxillofac Surg 23(3):140–148
29. Bernier J et al (2004) Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 350(19):1945–1952
30. Cooper JS et al (2004) Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. N Engl J Med 350(19):1937–1944
31. BrownJS, Shaw RJ, Bekiroglu F, Rogers SN. Systematic review of the current evidence in the use of postoperative radiotherapy for oral squamous cell carcinoma. Br J Oral Maxillofac Surg. 2012;50:481–489.
32. Huang TY, Hsu LP, Wen YH, Huang TT, Chou YF, Lee CF. Predictors of locoregional recurrence in early stage oral cavity cancer with free surgical margins. Oral Oncol. 2010;46:49–55.
33. Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C, Lee LY. Does adjuvant radiation therapy improve outcomes in pT1-3N0 oral cavity cancer with tumor-free margins and perineural invasion. Int J Radiat Oncol Biol Phys. 2008;71:371–6.
34. Huang SH, Hwang D, Lockwood G, Goldstein DP, O'Sullivan B. Predictive value of tumor thickness for cervical lymph-node involvement in squamous cell carcinoma of the oral cavity: a meta-analysis of reported studies. Cancer. 2009;115:1489–1497
35. Liao CT,Lin CY,Fan KH,Wang HM,Ng SH, Lee LY.Identification of a high-risk group among patients with oral cavity squamous cell carcinoma and pT1-2N0disease. Int J Radiat Oncol Biol Phys. 2012;82:284–90.
36. Huang SF, Cheng SD, Chien HT, Liao CT, Chen IH, Wang HM. Relationship between epidermal growth factor receptor gene copy number and protein expression in oral cavity squamous cell carcinoma. Oral Oncol. 2012;48:67–72.
37. Chen IH, Chang JT, Liao CT, Wang HM, Hsieh LL, Cheng AJ. Prognostic significance of EGFR and Her-2 in oral cavity cancer in betel quid prevalent area cancer prognosis. Br J Cancer. 2003;89:681–6.
38. Wheeler S, Siwak DR, Chai R, LaValle C, Seethala RR, Wang L. Tumor epidermal growth factor receptor and EGFR PY1068 are independent prognostic indicators for head and neck squamous cell carcinoma. Clin Cancer Res. 2012;18:2278–89.
39. Bonner JA, Harari PM, Giralt J, Azarnia N, Shin DM, Cohen RB. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. N Engl J Med. 2006;354:567–78.
40. Adelstein DJ, Ridge JA, Brizel DM, Holsinger FC, Haughey BH, O'Sullivan B, Genden EM, Beitler JJ, Weinstein GS, Quon H et al (2012) Transoral resection of pharyngeal cancer: sum-

mary of a National Cancer Institute Head and Neck Cancer Steering Committee Clinical Trials Planning Meeting, November 6–7, 2011, Arlington, Virginia. Head Neck 34(12):1681–1703
41. Li RJ, Richmon JD (2012) Transoral endoscopic surgery: new surgical techniques for oropharyngeal cancer. Otolaryngol Clin North Am 45(4):823–844
42. Selek U, Garden AS, Morrison WH, El-Naggar AK, Rosenthal DI, Ang KK (2004) Radiation therapy for early-stage carcinoma of the oropharynx. Int J Radiat Oncol Biol Phys 59(3):743–751
43. DenisF,Garaud P, Bardet E, Alfonsi M, Sire C, Germain T, Bergerot P, Rhein B, Tortochaux J, Calais G (2004) Final results of the 94–01 French Head and Neck Oncology and Radiotherapy Group randomized trial comparing radiotherapy alone with concomitant radiochemotherapy in advanced-stage oropharynx carcinoma. J Clin Oncol 22(1):69–76
44. Hitt R,Grau JJ,Lopez-Pousa A, Berrocal A,Garcia-GironC, Irigoyen A, Sastre J, Martinez- Trufero J, Brandariz Castelo JA, Verger E et al (2014) A randomized phase III trial comparing induction chemotherapy followed by chemoradiotherapy versus chemoradiotherapy alone as treatment of unresectable head and neck cancer. Ann Oncol 25(1):216–225
45. Pignon JP, Bourhis J, Domenge C, Designe L (2000) Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-Analysis of Chemotherapy on Head and Neck Cancer. Lancet 355(9208):949–955
46. Pignon JP, le Maitre A, Maillard E, Bourhis J (2009) Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. Radiother Oncol 92(1):4–14
47. Huguenin P, Beer KT, Allal A, Rufi bach K, Friedli C, Davis JB, Pestalozzi B, Schmid S, Thoni A, Ozsahin M et al (2004) Concomitant cisplatin signifi cantly improves locoregional control in advanced head and neck cancers treated with hyperfractionated radiotherapy. J Clin Oncol 22(23):4665–4673
48. Budach V, Stuschke M, Budach W, Baumann M, Geismar D, Grabenbauer G, Lammert I, Jahnke K, Stueben G, Herrmann T et al (2005) Hyperfractionated accelerated chemoradiation with concurrent fl uorouracil-mitomycin is more effective than dose-escalated hyperfractionated accelerated radiation therapy alone in locally advanced head and neck cancer: fi nal results of the radiotherapy cooperative clinical trials group of the German Cancer Society 95–06 Prospective Randomized Trial. J Clin Oncol 23(6):1125–1135
49. Bensadoun RJ, Benezery K, Dassonville O, Magne N, Poissonnet G, Ramaioli A, Lemanski C, Bourdin S, Tortochaux J, Peyrade F et al (2006) French multicenter phase III randomized study testing concurrent twice-a-day radiotherapy and cisplatin/5-fl uorouracil chemotherapy (BiRCF) in unresectable pharyngeal carcinoma: results at 2 years (FNCLCC-GORTEC). Int J Radiat Oncol Biol Phys 64(4):983–994
50. Ang K, Zhang Q, Wheeler RH, Rosenthal DI, Nguyen-Tan F, Kim H, Lu C, Axelrod RS, Silverman CI, Weber RS (2010) A phase III trial (RTOG 0129) of two radiation-cisplatin regimens for head and neck carcinomas (HNC): impact of radiation and cisplatin intensity on outcome. J Clin Oncol 28(15s):abstr 5507
51. Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefebvre JL, Greiner RH, Giralt J, Maingon P, Rolland F, Bolla M et al (2004) Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 350(19):1945–1952
52. Bernier J,Cooper JS,Pajak TF,van Glabbeke M,Bourhis J, Forastiere A, Ozsahin EM, Jacobs JR, Jassem J, Ang KK et al (2005) Defi ning risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and RTOG (# 9501). Head Neck 27(10):843–850
53. Cooper JS, Pajak TF,Forastiere AA, Jacobs J,Campbell BH, Saxman SB, Kish JA, Kim HE, Cmelak AJ, Rotman M et al (2004) Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. N Engl J Med 350(19):1937–1944
54. Cooper JS, Zhang Q, Pajak TF, Forastiere AA, Jacobs J, Saxman SB, Kish JA, Kim HE, Cmelak

AJ, Rotman M et al (2012) Long-term follow-up of the RTOG 9501/intergroup phase III trial: postoperative concurrent radiation therapy and chemotherapy in high-risk squamous cell carcinoma of the head and neck. Int J Radiat Oncol Biol Phys 84(5):1198–1205

55. Ko EC,Genden EM, Misiukiewicz K,Som PM, Kostakoglu L,Chen CT, Packer S, Kao J (2012) Toxicity profi le and clinical outcomes in locally advanced head and neck cancer patients treated with induction chemotherapy prior to concurrent chemoradiation. Oncol Rep 27(2):467–474
56. Vokes EE, Stenson K, Rosen FR, Kies MS, Rademaker AW, Witt ME, Brockstein BE, List MA, Fung BB, Portugal L et al (2003) Weekly carboplatin and paclitaxel followed by concomitant paclitaxel, fl uorouracil, and hydroxyurea chemoradiotherapy: curative and organ- preserving therapy for advanced head and neck cancer. J Clin Oncol 21(2):320–326
57. Posner MR, Hershock DM, Blajman CR, Mickiewicz E, Winquist E, Gorbounova V, Tjulandin S, Shin DM, Cullen K, Ervin TJ et al (2007) Cisplatin and fl uorouracil alone or with docetaxel in head and neck cancer. N Engl J Med 357(17):1705–1715
58. Cohen EEW, Karrison T, Kocherginsky M, Huang CH, Agulnik M, Mittal BB, Yunus F, Samant S, Brockstein B, Raez LE et al (2012) DeCIDE: a phase III randomized trial of docetaxel (D), cisplatin (P), 5-fl uorouracil (F) (TPF) induction chemotherapy (IC) in patients with N2/N3 locally advanced squamous cell carcinoma of the head and neck (SCCHN). J Clin Oncol 30(15s):abstr 5500
59 Ang K, Zhang Q, Rosenthal DI, Nguyen-Tan F, Wheeler RH, Sherman EJ, Weber RS, Galvin JM, Schwartz DL, El-Naggar AK et al (2011) A randomized phase III trial (RTOG 0522) of concurrent accelerated radiation plus cisplatin with or without cetuximab for stage III-IV head and neck squamous cell carcinomas (HNC). J Clin Oncol 29(15s):abstr 5500
60. Urban D, Corry J, Rischin D (2014) What is the best treatment for patients with human papillomavirus- positive and -negative oropharyngeal cancer? Cancer 120(10):1462–1470
61. Hafkamp HC, Manni JJ,Haesevoets A,Voogd AC, Schepers M, Bot FJ, Hopman AH, Ramaekers FC, Speel EJ (2008) Marked differences in survival rate between smokers and nonsmokers with HPV 16-associated tonsillar carcinomas. Int J Cancer 122(12):2656–2664
62. Goldenberg D, Begum S, Westra WH, Khan Z, Sciubba J, Pai SI, Califano JA, Tufano RP, Koch WM (2008) Cystic lymph node metastasis in patients with head and neck cancer: an HPV-associated phenomenon. Head Neck 30(7):898–903
63. Huang SH,O'Sullivan B, Xu W,Zhao H,Chen DD, Ringash J, Hope A, Razak A, Gilbert R, Irish J et al (2013) Temporal nodal regression and regional control after primary radiation therapy for N2-N3 head-and-neck cancer stratifi ed by HPV status. Int J Radiat Oncol Biol Phys 87(5):1078–1085
64. Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI,Nguyen-Tan PF, Westra WH, Chung CH, Jordan RC, Lu C et al (2010) Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 363(1):24–35
65. O'Sullivan B,Huang SH,Siu LL,Waldron JZhao H,Perez-Ordonez B, Weinreb I, Kim J, Ringash J, Bayley A et al (2013) Deintensifi cation cand idate subgroups in human papillomavirus-related oropharyngeal cancer according to minimal risk of distant metastasis. J Clin Oncol 31(5):543–550