26.
BÖLÜM

GASTROİNTESTİNAL KANSERLERDE BRAKİTERAPİ KOMPLİKASYONLARI

Özgür ALTMIŞDÖRTOĞLU[1]

GİRİŞ

Brakiterapi uygulamaları, etkili ve güvenli bir tedavi biçimi olup, eksternal radyoterapide olduğu gibi akut ve geç yan etkileri de mevcuttur. Uygulamadaki komplikasyonlar genel olarak bazı organlarda uygulamanın girişimsel olmasından dolayı cerrahiye ya da kullanılan kaynağın neden olduğu radyasyona sekonder gelişir. Bu bölümde uygulamadaki zorluklar, akut ve geç komplikasyonlar ve risk faktörleri belirtilecektir.

ÖZOFAGUS KANSERİNDE BRAKİTERAPİ KOMPLİKASYONLARI

Özofagus kanserlerine yönelik olarak yapılan brakiterapi uygulamalarında akut dönemde en sık mukozit ve özofajit gözlenirken, geç dönemde ise kronik ülser, striktür ve fistül gibi komplikasyonlar sık görülmektedir.

Amerikan Brakiterapi Derneği'nin (ABS) Özofagus Kanseri için Brakiterapi adlı rehberinde uygulamalar için önerilerde bulunmuştur. Gerçek anlamda özofagus kanserine yönelik brakiterapi için optimal doz-fraksiyon şeması bilinmemektedir. ABS'nin standart tedavi önerisi; 45-50 Gy lik dozun günlük 1.8-2 Gy fraksiyonla 5 hafta süreyle uygulanması ve daha sonra brakiterapi uygulamasına geçilmesidir. Burada önemli olan nokta brakiterapi zamanlamasıdır ve yan etkilerin azaltılması için mutlaka eksternal ışınlamaya (EBRT) bitiminden sonra 2-3 hafta beklenip brakiterapi uygulamalarına geçilmelidir (1).

Kemoradyoterapi sonrası brakiterapi uygulamalarında fistül riski nedeniyle eşzamanlı kemoterapi rejimleri önerilmemektedir. Servikal özofagusdaki tü-

[1] Uzm. Dr., Yakın Doğu Üniversitesi, drozgur64oglu@hotmail.com

Doyen ve ark. 105 hasta içeren retrospektif bir çalışmalarında, akut ve geç yan etkiler için süre olarak 2 ay süresini referans almışlar. Ciddi akut toksisite % 31.4 ve ciddi geç toksisite % 17.1 olarak bildirilmiştir. Grade 3-4 akut cilt toksisitesi % 27.6 oranında iken, geç dönemde %14.2 oranında bulunmuş. Proktit için grade 3-4 proktit % 8.5 ve geç dönemde %4.7 oranında tespit edilmiştir. Cilt ve GİS toksisiteleri için bazı prediktif fatörler bulunmuştur. Tek değişkenli analizde klinik evre, boostun uygulanma şekli (BT vs EBRT şeklindedir ve BT de % 11.8 oranındayken EBRT ile yapılanlarda %40.7 oranına çıkmaktadır) ve kemoterapi kullanımıdır. Çok değişkenli analizde ise sadece boostun uygulanma şekli anlamlı olrak çıkmıştır (54).

Saarilahti ve ark. IMRT ve HDRBT boost uygulanan hastalarda BT ile boost öncesi IMRT tekniği ile ışınlama yapılmasının akut radyasyonla ilişkili yan etkilerde azalma sağlandığını bildirdiler (55). Cagetti ve ark. HDR ve LDR IBT ile boost yapılan hastaları kullanılan BT uygulaması tipi ile toksisite açısından karşılaştırdıklarında HDR IBT nin toksisite açısından daha üstün olduğunu bildirdiler (56).

SONSÖZ

Gastrointestinal sistem kanserlerinde brakiterapi uygulamaları, cerrahiye uygun olmayan hastalarda, küratif veya palyatif amaçlı olarak ya da incebarsak ve diğer riskli organlar nedeniyle doz kıstlaması olan ve eksternal boost uygulanamayan durumlarda eksternal tedaviye ek olarak uygulanmaktadır. Bu durumlarda lokal kontrol ve kür şansını arttırmak amacıyla toksisiteyi daha fazla arttırmadan doz artımına yardımcı yöntem olan brakiterapi uygun bir seçenektir. Klinik deneyim ile birlikte daha çok hastada brakiterapi tedavinin önemli bir parçası olarak yerini alacaktır.

KAYNAKLAR

1. Gaspar et al.The Clinical Research Committee, (1997). American Brachytherapy Society (ABS) consensus guidelines for brachytherapy of esophageal cancerInternational Journal of Radiation OncologyBiologyPhysics, 38(1), 127–132.
2. Sur R, Timotin E, Doerwald-Munoz L, et al. Fungal infection is a significant cause of odynophagia in esophageal cancer patients after brachytherapy. Radiother Oncol 2009;90:
3. Gava et al. High-dose-rate brachytherapy in esophageal carcinoma: the Italian experience-Radiol Med. Jan-Feb 1996;91(1-2):118-21.
4. Hu et al. Risk Factors Associated with Esophageal Fistula after Radiotherapy for Esophageal Squamous Cell Carcinoma. J Cancer. 2020; 11(12): 3693–3700.
5. Dawes CM, Dean ME. Combined external beam and intracavitary radiotherapy for carcinoma of the esophagus. In: RF M, editor. Brachytherapy 2: Proceedings of the 5th International Selectron Users' Meeting, 1988. Nucletron International B.V: The Hague, The Netherlands; 1989.

6. Sur RK, Donde B, Krawitz HE, et al. What influences the incidence of complications in esophageal cancer treated with telebrachytherapy? Response to Kumar et al., IJROBP 27:1069-1072; 1993. Int J Radiat Oncol Biol Phys 1995;32:277.
7. Gaspar LE, Qian C, Kocha WI, Coia LR, Herskovic A, Graham M.A. Phase I/II Study of External Beam Radiation, Brachytherapy and Concurrent Chemotherapy in Lokalized Cancer of the Esophagus (RTOG 92-07): Preliminary Toxicity Report, Int. Radiation Oncology Biol. Phys., Vol. 37, No. 3, pp. 593-599, 1997.
8. Bergquist H, Wenger U, Johnsson E, et al. Stent insertion or endoluminal brachytherapy as palliation of patients with advanced cancer of the esophagus and gastroesophageal junction. Results of a randomized, controlled clinical trial. Dis Esophagus 2005;18: 131-139.
9. Fuccio L, Mandolesi D, Farioli A, et al. Brachytherapy for the palliation of dysphagia owing to esophageal cancer: a systematic review and meta- analysis of prospective studies. Radiother Oncol 2017; 122:332e339
10. Sur RK, Singh SC, et al. DP, Sharma Radiation therapy of esophageal cancer: role of high dose rate brachytherapy. Int J Radiat Oncol Biol Phys 1992;22:1043e1046.
11. Leung J, Guiney M, Das R. Intraluminal brachtherapy in bile duct carcinomas. Aust. N Z J Surg. 1996 Feb; 66(2):74-7
12. Skowronek J, Sowier A, Skrzywanek P. Intraluminal pulsed dose rate (PDR) brachytherapy and trans-hepatic technique in treatment of locally advanced bile duct cancer – preliminary assessment. Rep Pract Oncol Radiother 2007;12(2):125–133
13. Rosa Autorino , Silvia Bisiello , et al. Intraluminal Brachytherapy in Unresectable Extrahepatic Biliary Duct Cancer: An Italian Pooled Analysis. Anticancer Res . 2020 Jun;40(6):3417-3421.
14. M L Foo, L L Gunderson, C E Bender, S J Buskirk. External radiation therapy and transcatheter iridium in the treatment of extrahepatic bile duct carcinoma Int. J. Radiation Oncology BioI. Phys., Vol. 39, No.4,
15. Francesco Deodato 1, Gennaro Clemente et al. Chemoradiation and brachytherapy in biliary tract carcinoma: long-term results. Int J Radiat Oncol Biol Phys. 2006 Feb 1;64(2):483-8.
16. Fritz E, Brambs H-J, Schraube E et al. Combined external beam on bile duct carcinomas. Int J Radiat O radiotherapy and intraluminal high dose rate brachytherapy 855-861. Oncol Biol Phys 1994; 29:
17. Janusz Skowronek and Grzegorz Zwierzchowski, Braythcherapy in the treatment of bile duct cancer – a tough challenge. J Contemp Brachytherapy 2017; 9, 2: 187–195
18. Saurabh Mukewar et al. Endoscopically inserted nasobiliary catheters for high dose-rate brachytherapy as part of neoadjuvanttherapy for perihilar cholangiocarcinoma, Endoscopy 2015; 47: 878.
19. Dechao Jiao · Gang Wu · Jianzhuang Ren · Xinwei Han . Study of self-expandable metallic stent placement intraluminal 125I seed strands brachytherapy of malignant biliary obstruction. Surg Endosc .
20. Sandeep Jain, Tejinder Kataria et al.Malignant obstructive jaundice – brachytherapy as a tool for palliation , Jain at all, J Contemp Brachytherapy 2013; 5, 2: 83-88.
21. Jens Ricke, Peter Wust Computed Tomography–Guided Brachytherapy for Liver Cancer, Seminars in Radiation Oncology1016/j.semradonc, pp: 287-293 doi:10..2011.05.005
22. Brinkhaus et al. CT-Guided High-Dose-Rate Brachytherapy of Liver Tumours Does Not Impair Hepatic Function and Shows High Overall Safety and Favourable Survival Rates. Ann Surg Oncol (2014) 21:4284–4292
23. Powerski et al. Biliary duct stenosis after image-guided high-dose-rate interstitial brachytherapy of central and hilar liver tumors, Powerski et al,Strahlenther Onkol (2019) 195:265–273
24. Federico Collettini · Nadja Schreiber · Dirk Schnapauff et al.CT-guided high-dose-rate brachytherapy of unresectable hepatocellular carcinoma. Strahlenther Onkol (2015) 191:405–412

25. Nikolaos Tselis , Georgios Chatzikonstantinou, et al. Computed tomography-guided interstitial high dose rate brachytherapy for centrally located liver tumours: a single institution study, Eur Radiol (2013) 23:2264–2270
26. Robert Damm, Shahen El-Sanosy, et al. Ultrasound Interventional Radiology (2018). Ultrasound assisted catheter placement in CT-guided HDR brachytherapy for the local ablation of abdominal malignancies: Initial experience
27. Denecke et al. CT-guided Interstitial Brachytherapy of Hepatocellular Carcinoma before Liver Transplantation: an Equivalent Alternative to Transarterial Chemoembolization. Eur Radiol (2015) 25:2608–2616
28. Ricke et al. LiverMalignancies: CT-Guided Interstitial Brachytherapy in Patients with Unfavorable Lesions for Thermal Ablation. J Vasc Interv Radiol 2004; 15:1279–1286
29. Ricke et al. CT-guided interstitial brachytherapy of liver malignancies alone or in combination with thermal ablation: phase I-II results of a novel technique. Int J Radiat Onc. Biol Phy. 2004 Apr 1;58(5):1496-505.
30. Collettini et al,Computed-tomography-guided high-dose-rate brachytherapy (CT-HDRBT) ablation of metastases adjacent to the liver hilum.,European Journal of Radiology ,pp 509-514
31. Collettini et al. Percutaneous Computed Tomography–guided High-Dose-Rate Brachytherapy Ablation of Breast Cancer Liver Metastases: Initial Experience with 80 Lesions . J Vasc Interv Radiol 2012; 23:618–626.
32. Collettini et al. Unresectable Colorectal Liver Metastases: PercutaneousAblation Using CT-Guided High-Dose-Rate Brachytherapy(CT-HDBRT) Interventional Radiology; 606-612.
33. Bhutani et al. An open-label, single-arm pilot study of EUS-guided brachytherapy with phosphorus-32 microparticlesin combination with gemcitabine +/- nab-paclitaxel in unresectable locally advanced pancreaticcancer (OncoPaC-1): Technical details and study protocol: Endosc Ultrasound. Jan-Feb 2020;9(1):24-30.
34. Zhao YP. Emphasis on prevention and treatment of postoperative pancreatic fistula. Chin J Pract Surg 2015;35:805-7
35. Shrikhande SV, Barreto SG, Shetty G, Suradkar K, Bodhankar YD, Shah SB, et al. Post-operative abdominal drainage following majorupper gastrointestinal surgery: Single drain versus two drains.J Cancer Res Ther 2013;9:267-71.
36. Qingchun Li, Yun Liang, Ye Zhao, Baodong Gai Interpretation of adverse reactions and complications in Chinese expert consensus of Iodine-125 brachytherapy for pancreatic cancer. Journal of Cancer Research and Therapeutics - Volume 15 - Issue 4 – 2019 pp 751-754.
37. Wei-Fu Lv et al. The side effects and complications of percutaneous iodine-125 seeds implantation under CT-guide for patients with advanced pancreatic cancer, Wei-Fu Lv at all, Medicine (2017) 96:52
38. Slobodan Devic, Hamed Bekerat, Aurelie Garant, Te Vuong, Optimization of HDRBT boost dose delivery for patients with rectal cancer . Brachytherapy - (2019)
39. Chiang et al. Toxicity outcome of endorectal brachytherapy boost in medically inoperable patients. Strahlenther Onkol (2020) 196:993–997
40. Garant et al. Image-Guided Adaptive Endorectal Brachytherapy in the Non-Operative Managementof Patients with Rectal Cancer, Int. Journal of Radiation Oncology • Biology
41. Jakobsen et al. Dose-Effect Relationship in Chemoradiotherapy forLocally Advanced Rectal Cancer: A Randomized TrialComparing Two Radiation Doses, Int J Radiation Oncol Biol Phys, Vol. 84, No. 4, pp. 949e954, 2012
42. T. Vuong, S. Devicy, E. Podgorsak High Dose Rate Endorectal Brachytherapy as a Neoadjuvant Treatment for Patients with Resectable Rectal Cancer, Clinical Oncology (2007) 19:
43. Voung and at all.High Dose Rate Endorectal Brachytherapy for Patients With Curable Rectal Cancer , Seminars in Colon & Rectal Surgery (2010), pp 115-119.
44. Myint and at all. Dose Escalation Using Contact X-rayBrachytherapy After External Beam

Radiotherapyas Nonsurgical Treatment Option for RectalCancer: Outcomes From a Single-centerExperience. Int J Radiat Oncol Biol Phys. 2018 Mar 1;100(3):565-573.
45. Omidvari et al. Efficacy and Safety of Low-Dose-Rate Endorectal Brachytherapy as a Boost to Neoadjuvant Chemoradiation in the Treatment of Locally Advanced Distal Rectal Cancer: A Phase-II Clinical Trial. Ann Coloproctol 2015;31(4):123-130
46. Hesselager C, Vuong T, Pahlman L, et al. Short-term outcome after neoadjuvant high-dose-rate endorectal brachytherapy or short-course external beam radiotherapy in resectable rectal cancer. Colorectal Dis. 2013;15:662–666.
47. Corner C, Bryant L, Chapman C, et al. High-dose-rate afterloadingintraluminal brachytherapy for advanced inoperable rectal carcinoma Brachytherapy. 2010; 9:66–70.
48. Laval Grimard, Hartley Stern, Johanna N Spaans Brachytherapy and local excision for sphincter preservation in T1 and T2 rectal cancer. Int J Radiat Oncol Biol Phys. 2009 Jul 1;74(3):803-9.
49. Guerra et al. Twenty-year experience in the management of squamous cell anal canal carcinoma with interstitial brachytherapy Clin Transl Oncol (2011) 13:472-479,
50. Cordoba et al. Low-dose-rate interstitial brachytherapy boost for the treatment of anal canal cancers, Brachytherapy-2016 1-6.
51. Tagliaferri et al MITHRA – multiparametric MR/CT image adapted brachytherapy (MR/CT-IABT) in anal canal cancer:a feasibility study. Journal of Contemporary Brachytherapy (2015/volume 7/number 5)
52. Frakulli et al. Brachytherapy boost after chemoradiation in anal cancer: a systematic review, J Contemp Brachytherapy. 2018 Jun; 10(3): 246–253. Published online 2018 Jun 29. doi: 10.5114/jcb.2018.76884
53. Lestrade et al. Role of brachytherapy in the treatment of cancers of the anal canal Long-term follow-up and multivariate analysis of a large monocentric retrospective series. Strahlenther Onkol 2014 · 190:546–554
54. Doyen et al. Predictive Factors for Early and Late Local Toxicitiesin Anal Cancer Treated by Radiotherapy inCombination With or Without Chemotherapy, Dis Colon Rectum. 2013 Oct;56(10):1125-33.
55. Saarilahti et al. The effect of intensity-modulated radiotherapy and high doserate brachytherapy on acute and late radiotherapy-relatedadverse events following chemoradiotherapy of anal cancer. Radiotherapy and Oncology 87 (2008) 383–390
56. Cagetti et al. High-dose-rate vs. low-dose-rate interstitial brachytherapy boost for anal canal cancers, Brachytherapy (2019)