

# BÖLÜM 39

## Çocukluk Çağı Kanserlerinde Radyoterapinin Psikiyatrik Etkileri



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### GİRİŞ

Kanser, çocukluk çağında nadir görülmekle birlikte çocuk ve aileyi ruhsal ve psikososyal açıdan önemli derecede etkileyen bir sağlık sorunudur (1). Dünya'da her yıl yaklaşık 400,000 çocuk ve ergen kanser tanısı almakta ve kanser çocukluk çağının en önemli ölüm nedenleri arasında bulunmaktadır (2). Bununla birlikte çocukluk çağı kanserlerinin tedavisinde yıllar içerisinde büyük ilerlemeler sağlanmış, 1960'lı yıllarda %30'larda olan sağ kalım oranları son yıllarda birçok gelişmiş ülkede %80'lere kadar çıkmıştır (3, 4). Sağ kalım oranlarının artmasıyla birlikte kanser hayatı tehdit eden akut bir durum olmaktan çıkışip kronik bir sağlık durumu haline gelmiştir (5). Yapılan çalışmalarda kanser ve tedavilerinin sadece fiziksel sağlığı değil ruhsal sağlığı da etkileyebileceği gösterilmiştir, bu nedenle çocukluk çağı kanserinden kurtulanlarda kanser ve tedavilerinin sonraki yaşam dönemlerine psikiyatrik etkileri pediatrik onkolojinin ilgi alanlarından biri olmuştur (6).

Radyoterapi (RT), birçok çocukluk çağı tümörünün multimodal tedavisinde önemli bir unsurdur ve cerrahi tedavi sınırlılıklarında tedavide önemli rol oynamaktadır. Özellikle santral sinir sistemi (SSS)'nin veya kemik ve yumuşak doku solid tümörlerinin tedavisinde RT, multimodal tedavi stratejisinin çok önemli bir bileşeni olmaya devam etmektedir (7). RT malign dokuyu etkilemesinin yanı sıra normal dokuyu da etkilediği için bir dizi yan etkinin oluşumuna neden olmaktadır (7). RT tekniklerinin sürekli gelişimi günümüzde normal dokunun daha iyi korunmasını sağlamasına rağmen RT'ye bağlı yan etkiler halen önemli bir sorun olarak devam etmektedir (8). Araştırmalar, kanser hastalarının RT ile tedavi edildiklerinde psikolojik sorunlarla karşılaşabileceklerini göstermiştir ve 1970'lerin sonlarından bu yana, RT sırasında ve sonrasında görülen psikiyatrik sorunlara ilişkin çalışmaların sayısı hızla artmıştır (6). Çalışmalar çocuk ve ergenlerde RT'nin, anksiyete, depresyon, davranış problemleri gibi duygusal ve davranışsal sorunlara; dikkat, bellek, öğrenme gibi alanlarda

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- yol açabilmekte, hastalar zeka, dikkat, bellek, hafıza gibi nörobilişsel becerilerde ilerleyen dönemlerde zorluk yaşamaktadır. En tutarlı etkinleme zeka alanında bildirilmektedir.
- RT alan çocukların tedavi sırasında ve sonrasında nörobilişsel açıdan yakından takip edilmesi ve gerektiğinde bu becerilerinin desteklenmesi bu çocukların ilerde yaşayacağı sorunlar açısından hayatı önem taşımaktadır.
  - Bilişsel becerilerde gerilkite bireysel eğitim desteği, dikkat sorunlarında ise ilaç tedavisi olarak stimülün tedavisi ön plana çıkmaktadır.
  - RT alan hayatta kalanlarda duygusal, sosyal ve davranışsal işlevsellikle ilgili olarak umut verici sonuçlar olmasına karşın bazı çocuklar bu alanlarda zorluk yaşamabilmektedir. Bu nedenle çocukların tedavi sonrası bu alanlarda da değerlendirilmesi önemlidir.
  - Çocukların en kısa ve uygun zamanda okula dönüşlerinin sağlanması sosyal, davranışsal ve akademik alanlarda yaşanabilecek sorunların önlenmesi açısından önemlidir.
  - Sosyal ve davranışsal sorumlarda sosyal beceri eğitimlerinin etkili olabildiği gösterilmiştir.
  - Depresyon ve anksiyete belirtilerinin tedavisinde ise bilişsel davranışçı terapi ve SSGİ kullanımı öne plana çıkmaktadır.
  - Çocuk ve ergenlerde RT psikiyatrik etkileri rutin değerlendirmede yer almalı, sadece tedavi sürecinde değil, tedavi sonrasında da kanserli bir çocuğun uzun vadede psikiyatrik sorunlar yaşayabileceği akılda tutulmalıdır.

## KAYNAKLAR

1. Kurtz BP, Abrams AN. Psychiatric aspects of pediatric cancer. *Child and Adolescent Psychiatric Clinics*. 2010; 19(2):401-421.
2. WHO (2021). Childhood Cancer. (18/12/2021 tarihinde <https://www.who.int/news-room/fact-sheets/detail/cancer-in-children> adresinden ulaşılmıştır).
3. Gatta G, Botta L, Rossi S, et al. EUROCARE Working Group. Childhood cancer survival in Europe 1999–2007: results of EUROCARE-5—a population-based study. *The Lancet Oncology*. 2014; 15(1): 35-47.
4. Steliarova-Foucher E, Colombet M, Ries LA, et al. International incidence of childhood cancer, 2001–10: a population-based registry study. *The Lancet Oncology*. 2017; 18(6):719-731.
5. Apter A, Farbstein I, Yaniv I. Psychiatric aspects of pediatric cancer. *Child and Adolescent Psychiatric Clinics*. 2003; 12(3):473-492.
6. Stieglis HE, Ranchor AV, Sanderman R. Psychological functioning in cancer patients treated with radiotherapy. *Patient Education and Counseling*. 2004; 52(2):131-141.
7. Steinmeier T, Schleithoff SS, Timmermann B. Evolving radiotherapy techniques in paediatric oncology. *Clinical Oncology*. 2019; 31(3): 142-150.
8. Ajithkumar T, Price S, Horan G, et al. Prevention of radiotherapy-induced neurocognitive dysfunction in survivors of paediatric brain tumours: the potential role of modern imaging and radiotherapy techniques. *The Lancet Oncology*. 2017; 18(2), e91-e100.
9. Kreitler S, Krivoy E, Toren A. Psychosocial aspects of radiotherapy in pediatric cancer patients. In Kreitler S, Ben-Arush MW, Martin A. (Eds), *Pediatric Psycho-Oncology: Psychosocial Aspects and Clinical Interventions*. 2012; (2<sup>nd</sup> ed., pp. 62-70). John Wiley & Sons.
10. Kreitler S, Ben-Arush MW, Krivoy E, et al. Psychosocial aspects of radiotherapy for the child and family with cancer. In Constine, L.S., Tarbell, N.J., & Halperin, E.C (Eds.), *Pediatric radiation oncology*. 2010; (6<sup>th</sup> ed., pp. 447-456). Philadelphia: Lippincott, Williams & Wilkins.
11. Lew CC. Special needs of children. In Dow KH, Hilderly LJ (Eds.), *Nursing care in radiation oncology*. 1992; (pp. 177–202). Philadelphia: Saunders.
12. Tyc VL, Klosky JL, Kronenberg M, et al. Children's distress in anticipation of radiation therapy procedures. *Children's Health Care*. 2002; 31(1), 11-27.
13. Klosky JL, Tyc VL, Tong X, et al. Predicting pediatric distress during radiation therapy procedures: the role of medical, psychosocial, and demographic factors. *Pediatrics*. 2007; 119(5), e1159-e1166.
14. Lansky SB, Cairns NU. Poor school attendance in children with malignancies. Proceedings of the American Association for Cancer Research. 1979; 20:390.
15. Soanes L, Hargrave D, Smith L, et al. What are the experiences of the child with a brain tumour and their parents?. *European Journal of Oncology Nursing*. 2009; 13(4), 255-261.
16. Tadmor CS, Rosenkranz R, Ben-Arush MW. Education in Pediatric Oncology: Learning and Reintegration into School. In Kreitler S, Ben-Arush MW, Martin A. (Eds), *Pediatric Psycho-Oncology: Psychosocial Aspects and Clinical Interventions*. 2012; (2<sup>nd</sup> ed., pp. 104-117). John Wiley & Sons.
17. Evan EE, Kaufman M, Cook AB, et al. Sexual he-



- alth and self-esteem in adolescents and young adults with cancer. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2006;107(Suppl 7):1672-9.
18. Patenaude AF, Kupst MJ. Psychosocial functioning in pediatric cancer. *Journal of pediatric psychology*. 2005; 30(1), 9-27.
19. Yildirim NS, Demirkaya M, Sevinir BB, et al. A prospective follow-up of quality of life, depression, and anxiety in children with lymphoma and solid tumors. *Turkish Journal of Medical Sciences*. 2017; 47(4), 1078-1088.
20. Last BF, Grootenhuis MA. Psychosocial Interventions: a Cognitive Behavioral Approach. In Kreitler S, Ben-Arush, MW, Martin A. (Eds), *Pediatric Psycho-Oncology: Psychosocial Aspects and Clinical Interventions*. 2012 ; (2<sup>nd</sup> ed., pp. 62-70). John Wiley & Sons.
21. O'Connor M, Halkett GK. A systematic review of interventions to reduce psychological distress in pediatric patients receiving radiation therapy. *Patient Education and Counseling*. 2019; 102(2), 275-283.
22. Rummel-Kluge C, Pitschel-Walz G, Bäuml J, et al. Psychoeducation in schizophrenia—results of a survey of all psychiatric institutions in Germany, Austria, and Switzerland. *Schizophrenia bulletin*. 2006; 32(4), 765-775.
23. Sengun F, Ustun B, Altıok Hö. Kanita Dayalı Uygulama: Psikoeğitim. *Ege Üniversitesi Hemşirelik Fakültesi Dergisi*. 2011; 27(3), 66-74.
24. Haeberli S, Grotzer MA, Niggli FK, et al. A psychoeducational intervention reduces the need for anesthesia during radiotherapy for young childhood cancer patients. *Radiation Oncology*. 2008; 3(1), 1-6.
25. Scott MT, Todd KE, Oakley H, et al. Reducing anesthesia and health care cost through utilization of child life specialists in pediatric radiation oncology. *International Journal of Radiation Oncology Biology Physics*. 2016; 96(2), 401-405.
26. Klosky JL, Tyc VL, Srivastava DK, et al. Brief report: Evaluation of an interactive intervention designed to reduce pediatric distress during radiation therapy procedures. *Journal of Pediatric Psychology*. 2004; 29(8), 621-626.
27. Holt DE, Hiniker SM, Kalapurakal JA, et al. Improving the pediatric patient experience during radiation therapy-a children's oncology group study. *International Journal of Radiation Oncology\* Biology\* Physics*. 2021; 109(2), 505-514.
28. Engvall G, Lindh V, Mullaney T, et al. Children's experiences and responses towards an intervention for psychological preparation for radiotherapy. *Radiation Oncology*. 2018; 13(1), 1-12.
29. Filin A, Treisman S, Peles Bortz A. Radiation therapy preparation by a multidisciplinary team for childhood cancer patients aged 3½ to 6 years. *Journal of pediatric oncology nursing*. 2009; 26(2), 81-85.
30. Shrimpton BJ, Willis DJ, Tongs CD, et al. Movie making as a cognitive distraction for paediatric patients receiving radiotherapy treatment: qualitative interview study. *BMJ open*. 2013; 3(1), e001666.
31. Barry P, O'Callaghan C, Wheeler G, et al. Music therapy CD creation for initial pediatric radiation therapy: a mixed methods analysis. *Journal of music therapy*. 2010; 47(3), 233-263.
32. Scott L, Langton F, O'Donoghue J. Minimising the use of sedation/anaesthesia in young children receiving radiotherapy through an effective play preparation programme. *European Journal of Oncology Nursing*. 2002; 6(1), 15-22.
33. Robbins M, Greene-Schloesser D, Peiffer AM, et al. Radiation-induced brain injury: a review. *Frontiers in oncology*. 2012; 2, 73.
34. Perry A. Therapy-associated neuropathology. In Perry, A.,& Brat, D.J. (EDS), *Practical Surgical Neuropathology: A Diagnostic Approach*. 2010; (pp.417-425). Philadelphia: Churchill Livingstone Elsevier.
35. Makale MT, McDonald CR, Hattangadi-Gluth JA, et al. Mechanisms of radiotherapy-associated cognitive disability in patients with brain tumours. *Nature Reviews Neurology*. 2017; 13(1), 52-64.
36. Krull KR, Gioia G, Ness KK, et al. Reliability and validity of the childhood cancer survivor study neurocognitive questionnaire. *Cancer*. 2008; 113(8), 2188-2197.
37. Mulhern RK, Merchant TE, Gajjar A, et al. Late neurocognitive sequelae in survivors of brain tumours in childhood. *The lancet oncology*. 2004; 5(7), 399-408.
38. Dowell Jr RE, Copeland DR, Francis DJ, et al. Absence of synergistic effects of CNS treatments on neuropsychologic test performance among children. *Journal of clinical oncology*. 1991; 9(6), 1029-1036.
39. Mulhern RK, Hancock J, Fairclough D, et al. Neuropsychological status of children treated for brain tumors: a critical review and integrative analysis. *Medical and pediatric oncology*. 1992; 20(3), 181-191.
40. Kolotas C, Daniel M, Demetriou L, et al. Long-term effects on the intelligence of children treated for acute lymphoblastic leukemia. *Cancer investigation*. 2001; 19(6), 581-587.
41. Reinhardt D, Thiele C, Creutzig U. Neuropsychological sequelae in children with AML treated with or without prophylactic CNS-irradiation. *Klinische Padiatrie*. 2002; 214(1), 22-29.
42. Kahalley LS, Peterson R, Ris MD, et al. Superior intellectual outcomes after proton radiotherapy compared with photon radiotherapy for pediatric medulloblastoma. *Journal of Clinical Oncology*. 2020; 38(5), 454.
43. Wolfe KR, Madan-Swain A, Kana RK. Executive dysfunction in pediatric posterior fossa tumor survivors: a systematic literature review of neurocog-



- nitive deficits and interventions. *Developmental neuropsychology*. 2012; 37(2), 153-175.
44. Kiehna EN, Mulhern RK, Li C, et al. Changes in attentional performance of children and young adults with localized primary brain tumors after conformal radiation therapy. *Journal of clinical oncology*. 2006; 24(33), 5283-5290.
45. Mabbott DJ, Snyder JJ, Penkman L, et al. The effects of treatment for posterior fossa brain tumors on selective attention. *Journal of the international neuropsychological society*. 2009; 15(2), 205-216.
46. Baron IS. *Neuropsychological evaluation of the child: Domains, methods, & case studies*. 2018. Oxford University Press.
47. Spiegler BJ, Bouffet E, Greenberg ML, et al. Change in neurocognitive functioning after treatment with cranial radiation in childhood. *Journal of Clinical Oncology*. 2004; 22(4), 706-713.
48. Ribi K, Relly C, Landolt MA, et al. Outcome of medulloblastoma in children: long-term complications and quality of life. *Neuropediatrics*. 2005; 36(06), 357-365.
49. Children's Oncology Group. (2008). Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. (22/02/2022 tarihinde www.survivorshipguidelines.org. adresinden ulaşılmıştır).
50. Castellino SM, Ullrich NJ, Whelen MJ, et al. Developing interventions for cancer-related cognitive dysfunction in childhood cancer survivors. *Journal of the National Cancer Institute*. 2014; 106(8), dju186.
51. Palmese CA, Raskin SA. The rehabilitation of attention in individuals with mild traumatic brain injury, using the APT-II programme. *Brain Injury*. 2000; 14(6), 535-548.
52. Gormez V. Dikkat Eksikliği ve Hiperaktivite Bozukluğunun Psikofarmakolojik Tedavisi. In Pekcanlar Akay, A. & Ercan, E.S. (eds) *Çocuk ve Ergen Ruh Sağlığı ve Hastalıkları*. 2016; (pp: 56-63). Ankara: Türkiye Çocuk ve Genç Psikiyatrisi Derneği Yayıncıları.
53. Conklin HM, Helton S, Ashford J, et al. Predicting methylphenidate response in long-term survivors of childhood cancer: a randomized, double-blind, placebo-controlled, crossover trial. *Journal of Pediatric Psychology*. 2010; 35(2), 144-155.
54. Conklin HM, Reddick WE, Ashford J, et al. Long-term efficacy of methylphenidate in enhancing attention regulation, social skills, and academic abilities of childhood cancer survivors. *Journal of Clinical Oncology*. 2010; 28(29), 4465.
55. Winterstein AG, Gerhard T, Shuster J, et al. Cardiac safety of central nervous system stimulants in children and adolescents with attention-deficit/hyperactivity disorder. *Pediatrics*. 2007; 120(6), e1494-e1501.
56. Knight M. Stimulant-drug therapy for attention-de-
- ficit disorder (with or without hyperactivity) and sudden cardiac death. *Pediatrics*. 2007; 119(1), 154-155.
57. Pinsky EG, Abrams AN. Psychopharmacology in Pediatric Oncology. In Kreitler S, Ben-Arush MW, Martin A. (Eds), *Pediatric Psycho-Oncology: Psychosocial Aspects and Clinical Interventions*. 2012; (2<sup>nd</sup> ed., pp. 118-134). John Wiley & Sons.
58. Gehring K, Patwardhan SY, Collins R, et al. A randomized trial on the efficacy of methylphenidate and modafinil for improving cognitive functioning and symptoms in patients with a primary brain tumor. *Journal of neuro-oncology*. 2012; 107(1), 165-174.
59. Castellino SM, Tooze JA, Flowers L, et al. Toxicity and efficacy of the acetylcholinesterase (AChE) inhibitor donepezil in childhood brain tumor survivors: a pilot study. *Pediatric blood & cancer*. 2012; 59(3), 540-547.
60. Huisman J, Aukema EJ, Deijen JB, et al. The usefulness of growth hormone treatment for psychological status in young adult survivors of childhood leukaemia: an open-label study. *BMC pediatrics*. 2008; 8(1), 1-8.
61. Michel G, Brinkman TM, Wakefield CE, et al. Psychological outcomes, health-related quality of life, and neurocognitive functioning in survivors of childhood cancer and their parents. *Pediatric Clinics*. 2020; 67(6), 1103-1134.
62. Kaye EC, Brinkman TM, Baker JN. Development of depression in survivors of childhood and adolescent cancer: a multi-level life course conceptual framework. *Supportive Care in Cancer*. 2017; 25(6), 2009-2017.
63. Rola R, Raber J, Rizk A, et al. Radiation-induced impairment of hippocampal neurogenesis is associated with cognitive deficits in young mice. *Experimental neurology*. 2004; 188(2), 316-330.
64. Belleau EL, Treadway MT, Pizzagalli DA. The impact of stress and major depressive disorder on hippocampal and medial prefrontal cortex morphology. *Biological psychiatry*. 2019; 85(6), 443-453.
65. Klineberg E, Clark C, Bhui KS, et al. Social support, ethnicity and mental health in adolescents. *Social psychiatry and psychiatric epidemiology*. 2006; 41(9), 755-760.
66. Vannatta K, Gerhardt CA, Wells RJ, et al. Intensity of CNS treatment for pediatric cancer: Prediction of social outcomes in survivors. *Pediatric Blood & Cancer*. 2007; 49(5), 716-722.
67. Lemerise EA, Arsenio WF. An integrated model of emotion processes and cognition in social information processing. *Child development*. 2000; 71(1), 107-118.
68. Mabbott DJ, Spiegler BJ, Greenberg ML, et al. Serial evaluation of academic and behavioral outcome after treatment with cranial radiation in childho-



- od. *Journal of Clinical Oncology*. 2005; 23(10), 2256-2263.
69. Mulhern RK, Carpentieri S, Shema S, et al. Factors associated with social and behavioral problems among children recently diagnosed with brain tumor. *Journal of Pediatric Psychology*. 1993; 18(3), 339-350.
70. Mulhern RK, Wasserman AL, Friedman AG, et al. Social competence and behavioral adjustment of children who are long-term survivors of cancer. *Pediatrics*. 1989; 83(1), 18-25.
71. Vannatta K, Zeller M, Noll RB, et al. Social functioning of children surviving bone marrow transplantation. *Journal of Pediatric Psychology*. 1998; 23(3), 169-178.
72. Maurice-Stam H, Grootenhuis MA, Caron HN, et al. Course of life of survivors of childhood cancer is related to quality of life in young adulthood. *Journal of psychosocial oncology*. 2007; 25(3), 43-58.
73. Fossen A, Abrahamsen TC, Storm-Mathisen I. Psychological outcome in children treated for brain tumor. *Pediatric Hematology and Oncology*. 1998; 15(6), 479-488.
74. Radcliffe J, Bennett D, Kazak AE, et al. Adjustment in childhood brain tumor survival: Child, mother, and teacher report. *Journal of Pediatric Psychology*. 1996; 21(4), 529-539.
75. Schultz KAP, Ness KK, Whitton J, et al. Behavioral and social outcomes in adolescent survivors of childhood cancer: a report from the childhood cancer survivor study. *Journal of clinical oncology*. 2007; 25(24), 3649-3656.
76. Van der Geest IM, van Dorp W, Hop WC, et al. Emotional distress in 652 Dutch very long-term survivors of childhood cancer, using the hospital anxiety and depression scale (HADS). *Journal of Pediatric Hematology/Oncology*. 2013; 35(7), 525-529.
77. Zebrack BJ, Gurney JG, Oeffinger K, et al. Psychological outcomes in long-term survivors of childhood brain cancer: a report from the childhood cancer survivor study. *Journal of Clinical Oncology*. 2004; 22(6), 999-1006.
78. Elçigil A. Kanserli çocuk okula gidebilir mi. *Cumhuriyet Üniversitesi Hemşirelik Yüksekokulu Dergisi*. 2007; 11(2), 40-46.
79. Varni JW, Katz ER, Colegrove Jr R, et al. The impact of social skills training on the adjustment of children with newly diagnosed cancer. *Journal of Pediatric Psychology*. 1993; 18(6), 751-767.
80. Barakat LP, Hetzke JD, Foley B, et al. Evaluation of a social-skills training group intervention with children treated for brain tumors: A pilot study. *Journal of pediatric psychology*. 2003; 28(5), 299-307.
81. Birmaher B, Brent D, AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with depressive disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2007; 46(11), 1503-1526.
82. Connolly SD, Bernstein GA. Practice parameter for the assessment and treatment of children and adolescents with anxiety disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2007; 46(2), 267-283.
83. Gothelf D, Rubinstein M, Shemesh E, et al. Pilot study: fluvoxamine treatment for depression and anxiety disorders in children and adolescents with cancer. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2005; 44(12), 1258-1262.
84. Kersun LS, Kazak AE. Prescribing practices of selective serotonin reuptake inhibitors (SSRIs) among pediatric oncologists: a single institution experience. *Pediatric blood & cancer*. 2006; 47(3), 339-342.