

Bölüm 17

RENAL TRANSPLANTASYON HASTALARINDA RENAL HÜCRELİ KARSİNOM GELİŞİMİ VE TEDAVİSİ

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GİRİŞ

Organ transplantasyonu sonrası malignite riski genel popülasyona göre 3-4 kat artmaktadır (1, 2) ve organ transplantasyon ilişkili malignite gelişim insidansı yaklaşık olarak % 2.3-3.1 oranında bildirilmiştir. (3, 4)

Renal transplantasyon, solid organ transplantasyonları içinde en sık yapılan transplantasyonların başında gelmektedir. Renal transplantasyon hastalarında malignite sıklığı normal popülasyona göre 3-5 kat daha fazla bulunmuştur. (5,6) Transplantasyona giden hastalarda cilt kanserleri, hematolojik maligniteler ve kaposi sarkom gelişme ihtimalinin daha yüksek olduğu saptanmıştır. (7) Bunlar içinde en sık malignitelerin yaklaşık % 40-50 oranı ile skuamöz hücreli karsinom ve bazal hücreli cilt kanserleri olduğu belirtilmiştir. (8) Üriner sistem maligniteleri böbrek transplantasyonundan sonra en sık gelişen 3. Solid tümörlerdir. (9) Allojenik transplant hastalarında en sık görülen ürolojik kanser renal hücreli karsinom (RHK) olup, doğal böbrek veya transplant böbreğin her ikisinden de gelişebilir. (10, 11) RHK patogenezi tam olarak aydınlatılamamıştır, fakat sıklıkla son dönem böbrek yetmezliği hastalarında geliştiği iyi bilinmektedir. (9) Yine bulgular RHK'un transplant olan hastalarda henüz transplant olmamış, sırada bekleyen hastalara göre daha sık olduğunu desteklemektedir. (12)

Predominant RHK formu clear cell karsinomdur. (13) Başka bir çalışmada ise en sık papiller tip RHK görüldüğü bildirilmiştir. Böbrek nakil hastalarında papiller RHK gelişme riskinin 16 kat arttığı belirtilmiştir. Genel popülasyonda clear cell RHK ve papiller RHK oranları, % 70'e karşın % 10-15'dir. Aynı çalışmada RHK riskinin transplant öncesi uzun süreli hemodiyaliz uygulananlarda daha yüksek olma eğiliminde olduğu belirtilmiştir. Yine çoğunluk RHK vakaları doğal böbrekten gelişirken sadece % 11'inin donör böbrekten geliştiği saptanmıştır. (14)

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KAYNAKLAR

1. Sheil AG. Development of malignancy following renal transplantation in Australia and New Zealand. *Transplant Proc.* 1992;24(4):1275-9.
2. Gutierrez-Dalmau A, Campistol JM. Immunosuppressive therapy and malignancy in organ transplant recipients: a systematic review. *Drugs.* 2007;67(8):1167-98.
3. Penn I. Incidence and treatment of neoplasia after transplantation. *J Heart Lung Transplant.* 1993;12(6 Pt 2):S328-36.
4. Penn I. Depressed immunity and the development of cancer. *Cancer Detect Prev.* 1994;18(4):241-52.
5. Birkeland SA, Lokkegaard H, Storm HH. Cancer risk in patients on dialysis and after renal transplantation. *Lancet.* 2000;355(9218):1886-7.
6. Buell JF, Gross TG, Woodle ES. Malignancy after transplantation. *Transplantation.* 2005;80(2 Suppl):S254-64.
7. Hevia V, Gómez V, Nicolás VD, Alvarez S, Del Canizo CG, Galeano C, et al., editors. Development of urologic de novo malignancies after renal transplantation. *Transplantation proceedings*; 2014: Elsevier.
8. Bieryło A, Brzosko S, Laudanska E, Naumnik B. [Skin cancers in kidney transplant recipients]. *Wiad Lek.* 2017;70(1):68-73.
9. Stewart JH, Buccianti G, Agodoa L, Gellert R, McCredie MR, Lowenfels AB, et al. Cancers of the kidney and urinary tract in patients on dialysis for end-stage renal disease: analysis of data from the United States, Europe, and Australia and New Zealand. *Journal of the American Society of Nephrology.* 2003;14(1):197-207.
10. Penn I. Occurrence of cancers in immunosuppressed organ transplant recipients. *Clinical transplants.* 1998:147-58.
11. Melchior S, Franzaring L, Shardan A, Schwenke C, Plümpe A, Schnell R, et al. Urological de novo malignancy after kidney transplantation: a case for the urologist. *The Journal of urology.* 2011;185(2):428-32.
12. Kasiske BL, Snyder JJ, Gilbertson DT, Wang C. Cancer after kidney transplantation in the United States. *American Journal of Transplantation.* 2004;4(6):905-13.
13. Redova M, Svoboda M, Slaby O. MicroRNAs and their target gene networks in renal cell carcinoma. *Biochemical and biophysical research communications.* 2011;405(2):153-6.
14. Karami S, Yanik E, Moore L, Pfeiffer R, Copeland G, Gonsalves L, et al. Risk of renal cell carcinoma among kidney transplant recipients in the United States. *American Journal of Transplantation.* 2016;16(12):3479-89.
15. Bieniasz M, Chmura A, Kwapisz M, Czerwińska M, Kieszek R, Domagała P, et al., editors. Renal Tumor in Allogeneic Kidney Transplant Recipient. *Transplantation proceedings*; 2016: Elsevier.
16. Wetmore JB, Calvet JP, Alan S, Lynch CF, Wang CJ, Kasiske BL, et al. Polycystic kidney disease and cancer after renal transplantation. *Journal of the American Society of Nephrology.* 2014;25(10):2335-41.
17. Imao T, Ichimaru N, Takahara S, Kokado Y, Okumi M, Imamura R, et al. Risk factors for malignancy in Japanese renal transplant recipients. *Cancer.* 2007;109(10):2109-15.
18. Guba M, Graeb C, Jauch K-W, Geissler EK. Pro-and anti-cancer effects of immunosuppressive agents used in organ transplantation. *Transplantation.* 2004;77(12):1777-82.

19. Euvrard S, Morelon E, Rostaing L, Goffin E, Brocard A, Tromme I, et al. Sirolimus and secondary skin-cancer prevention in kidney transplantation. *New England Journal of Medicine*. 2012;367(4):329-39.
20. Boratyńska M, Wątopek E, Smolska D, Patrzalek D, Klinger M, editors. Anticancer effect of sirolimus in renal allograft recipients with de novo malignancies. *Transplantation proceedings*; 2007: Elsevier.
21. Motzer RJ, Bacik J, Murphy BA, Russo P, Mazumdar M. Interferon-alfa as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. *Journal of clinical oncology*. 2002;20(1):289-96.
22. Leibovich BC, Blute ML, Cheville JC, Lohse CM, Frank I, Kwon ED, et al. Prediction of progression after radical nephrectomy for patients with clear cell renal cell carcinoma. *Cancer*. 2003;97(7):1663-71.
23. Javaid MM, Chowdhury S, Henderson A, Olsburgh J. Advanced native kidney renal cell carcinoma in renal transplant recipients: role of sirolimus as dual anti-cancer and anti-rejection agent. *Clinical nephrology*. 2013;79(2):154-60.
24. Tillou X, Doerfler A, Collon S, Kleinclauss F, Patard JJ, Badet L, et al. De novo kidney graft tumors: results from a multicentric retrospective national study. *Am J Transplant*. 2012;12(12):3308-15.
25. Klatte T, Seitz C, Waldert M, De Martino M, Kikic Ž, Böhmig GA, et al. Features and outcomes of renal cell carcinoma of native kidneys in renal transplant recipients. *BJU international*. 2010;105(9):1260-5.
26. Hasegawa Y, Mita K, Matsubara A, Ohdan H. Multidisciplinary treatment including sorafenib stabilized the bone metastases of renal cell carcinoma in an immunosuppressed renal transplant recipient. *International journal of clinical oncology*. 2009;14(5):465-7.
27. Hongo F, Oishi M, Ueda T, Naitoh Y, Nakamura T, Naya Y, et al. Complete response of sunitinib therapy for renal cell cancer recurrence in the native kidney after renal transplantation: a case report. *BMC research notes*. 2014;7(1):526.
28. Hanafusa T, Ichikawa Y, Kishikawa H, Kyo M, Fukunishi T, Kokado Y, et al. Retrospective study on the impact of hepatitis C virus infection on kidney transplant patients over 20 years. *Transplantation*. 1998;66(4):471-6.
29. Nakamoto T, Igawa M, Mitani S, Ueda M, Usui A, Usui T. Metastatic renal cell carcinoma arising in a native kidney of a renal transplant recipient. *The Journal of urology*. 1994;152(3):943-5.
30. Tang S, Cheng IK, Leung VK, Kuok UI, Tang AW, Ho YW, et al. Successful treatment of hepatitis C after kidney transplantation with combined interferon alpha-2b and ribavirin. *Journal of hepatology*. 2003;39(5):875-8.
31. Strumberg D, Clark JW, Awada A, Moore MJ, Richly H, Hendlisz A, et al. Safety, pharmacokinetics, and preliminary antitumor activity of sorafenib: a review of four phase I trials in patients with advanced refractory solid tumors. *The oncologist*. 2007;12(4):426-37.
32. Postow MA, Chesney J, Pavlick AC, Robert C, Grossmann K, McDermott D, et al. Nivolumab and ipilimumab versus ipilimumab in untreated melanoma. *New England Journal of Medicine*. 2015;372(21):2006-17.
33. Borghaei H, Paz-Ares L, Horn L, Spigel DR, Steins M, Ready NE, et al. Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *New England Journal of Medicine*. 2015;373(17):1627-39.
34. Ansell SM, Lesokhin AM, Borrello I, Halwani A, Scott EC, Gutierrez M, et al. PD-1

- blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. *New England Journal of Medicine*. 2015;372(4):311-9.
35. Lesouhaitier M, Dudreuilh C, Tamain M, Kanaan N, Bailly E, Legoupil D, et al. Checkpoint blockade after kidney transplantation. *European Journal of Cancer*. 2018;96:111-4.
 36. Kittai AS, Oldham H, Cetnar J, Taylor M. Immune checkpoint inhibitors in organ transplant patients. *Journal of Immunotherapy*. 2017;40(7):277-81.
 37. Stallone G, Infante B, Grandaliano G. Management and prevention of post-transplant malignancies in kidney transplant recipients. *Clinical kidney journal*. 2015;8(5):637-44.
 38. Watorek E, Boratynska M, Smolska D, Patrzalek D, Klinger M. Malignancy after renal transplantation in the new era of immunosuppression. *Annals of transplantation*. 2011;16(2):14-8.
 39. Molina AM, Feldman DR, Voss MH, Ginsberg MS, Baum MS, Brocks DR, et al. Phase 1 trial of everolimus plus sunitinib in patients with metastatic renal cell carcinoma. *Cancer*. 2012;118(7):1868-76.