

Böbrek ve mesane tümörlerinde aşı tedavileri

Vaccine therapy in kidney and bladder tumors

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Özet

Genel olarak aşı tedavisi çeşitli kanserlerin tedavisinde kullanılabilir. Ancak tüm araştırmalar rağmen henüz pek çok kanser türünde başarılı olunamamıştır. Aşı tedavisinin uygulanabilmesi için; kanserin immunojenik olması ve dokuya özgü proteinler içermesi, yavaş ilerlemesi, tedavilerin uygulanabilir olması gereklidir. Bu nedenle, ürolojik kanserler içinde çoğu faz 1/2 ve faz 3 olmak üzere çalışmalar böbrek ve prostat, daha az miktarda da mesane üzerine yoğunlaşmıştır (1,2). Testis kanserlerinde aşı çalışmalarının olmaması hızlı yayılma ve metastaz göstermesi, çeşitli olması ve genellikle mix tümörler halinde izlenmesi, kan-testis bariyerinin olması olarak açıklanabilir.

Aşı tedavisinin kullanımında amaç; tümörün tetiklediği toleransı yenerek, malign hücrelere karşı oluşan immun cevabı aktive etmektir. Bu tedaviler kansere karşı immun cevabı kullanarak etki göstermektedir. Literatürde yayınlanan ilk onkolojik aşı tedavisi 1893 yılında Coley tarafından yayınlanmıştır. Bu çalışmada inoperable yumuşak doku sarkomlarının streptokokal toksinler ile non-spesifikimmün cevap oluşturulurarak regrese olduğu gösterilmiştir (3). Üroonkolojide kullanılan aşılar; tümör hücreleri (otolog ve allojenik), dentritik hücre, DNA viral vektör, protein/peptid, immün düzenleyiciler olmak üzere ana başlıklar halinde sayılabilir (4). Böbrek ve mesane tümörlerinde aşı tedavilerinin uygulanmasına ait geçmiş çalışmalar olmasına rağmen özellikle araştırmalar son dönem de yoğunlaşmıştır.

Biz de bu derlemede üroloji hekimlerinin çok aşına olmadığı, güncel literatür eşliğinde böbrek ve mesane tümörlerinde kullanılan aşı tedavilerinden bahsedeceğiz.

Anahtar Kelimeler: böbrek tümörü, mesane kanseri, immunoterapi, aşı tedavisi

Abstract

Not every type of cancer is suitable for vaccine therapies. For a vaccine therapy to be implemented, the cancer should be immunogenic and contain tissue specific proteins, should have a slow progression, and treatments should be feasible. For that reason, studies regarding urological cancers, most of which are phase 1/2 and phase 3, are mostly focused on the kidneys and the prostate and less focused on the bladder (1,2). The reason for lack of vaccine studies in testicular cancer can be explained by the fact that it spreads and forms metastases very fast, it has various types and it is mostly seen as mixed tumors, and there is blood-testis barrier.

The aim of implementing vaccine therapy is to activate immune response against malignant cells by overcoming the tolerance triggered by the tumor. These treatments are effective using the immune response against cancer. The first oncological vaccine therapy ever published in the literature belongs to Coley dating back to 1893. In that study it is demonstrated that inoperable soft tissue sarcomas regressed by stimulating non-specific immune response with streptococcal toxins (3). Vaccine therapies used in uro-oncology can be categorized under the following titles; tumor cells (autologous and allogenic), dendritic cell, DNA viral vector, protein/peptide, immune regulators (4). Although there are old studies on the implementation of vaccine therapies in kidney and bladder tumors, researches have only been intensified recently. In this compilation, we will discuss vaccine therapies used in kidney and bladder tumors, which urologists are not so familiar with, in the light of the up-to-date literature.

Key Words: kidney cancer, bladder cancer, immunotherapy, vaccine therapy

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24. Frankenberger B, Regn S, Geiger C, et al. Cell-based vaccines for renal cell carcinoma: genetically-engineered tumor cells and monocyte-derived dendritic cells. *World J Urol* 2005;23:166-74.
25. Gouttefangeas C, Stenzl A, Stevanovic S, Rammensee HG. Immunotherapy of renal cell carcinoma. *Cancer Immunol Immunother* 2007;56: 117-28.
26. Uemura H, Fujimoto K, Tanaka M, et al. A Phase I trial of vaccination of CA9-derived peptides for HLA-A24-positive patients with cytokine-refractory metastatic renal cell carcinoma. *Clin Cancer Res* 2006;12:1768-75.
27. Bleumer I, Tiemessen DM, Oosterwijk-Wakka JC, et al. Preliminary analysis of patients with progressive renal cell carcinoma vaccinated with CA9-peptide pulsed mature dendritic cells. *J Immunother* 2007;30:116-22.
28. Liyama T, Udaka K, Takeda S, et al. WT1 (Wilms' tumor 1) peptide immunotherapy for renal cell carcinoma. *Microbiol Immunol* 2007;51:519-30.
29. Patel PM, Sim S, O'Donnell DO, et al. An evaluation of a preparation of *Mycobacterium vaccae* (SRL172) as an immunotherapeutic agent in renal cancer. *Eur J Cancer* 2008;44:216-23.
30. Rahma OE, Ashtar E, Ibrahim R, et al. A pilot clinical trial testing mutant von Hippel-Lindau peptide as a novel immune therapy in metastatic renal cell carcinoma. *J Transl Med* 2010;8:8-16.
31. Kim DW, Krishnamurthy V, Bines SD, Kaufman HL. Trovax, a recombinant modified vaccinia Ankara virus encoding 5T4. Lessons learned and future development. *Hum Vaccin* 2010;10:1-8.
32. Amato RJ, Hawkins RE, Kaufman HL, et al. Vaccination of metastatic renal cancer patients with MVA-5T4: a randomized, double-blind, placebo-controlled Phase III study. *Clin Cancer Res* 2010;22:5539-47.
33. Walter S, Weinschenk T, Stenzl A, et al. Multipeptide immune response to cancer vaccine IMA901 after single-dose cyclophosphamide associates with longer patient survival. *Nat Med* 2012;18:1254-61.
34. Wood C, Srivastava P, Bukowski R, et al. An adjuvant autologous therapeutic vaccine (HSPCC-96; vitespen) versus observation alone for patients at high-risk of recurrence after nephrectomy for renal cell carcinoma: a multicentre, open-label, randomized Phase III trial. *Lancet* 2008;372:145-54.
35. Sharma P, Shen Y, Wen S, et al. CD8 tumor-infiltrating lymphocytes are predictive of survival in muscle-invasive urothelial carcinoma. *Proc Natl Acad Sci USA* 2007;104:3967-72.
36. Sharma P, Shen Y, Wen S, et al. Cancer-testis antigens: expression and correlation with survival in human urothelial carcinoma. *Clin Cancer Res* 2006;12:5442-7.
37. Nishiyama T, Tachibana M, Horiguchi K, et al. Immunotherapy of bladder cancer using autologous dendritic cells pulsed with human lymphocyte antigen-A24-specific MAGE-3 peptide. *Clin Cancer Res* 2001;7:23-31.
38. Sharma P, Bajorin DF, Jungbluth AA, et al. Immune responses detected in urothelial carcinoma patients after vaccination with NY-ESO-1 protein plus BCG and GM-CSF. *J Immunother* 2008;31:849-57.
39. Obara W, Ohsawa R, Kanehira M, et al. Cancer peptide vaccine therapy developed from oncoantigens identified through genome-wide expression profile analysis for bladder cancer. *Jpn J Clin Oncol* 2012;42:591-600.
40. Honma I, Kitamura H, Torigoe T, et al. Phase I clinical study of anti-apoptosis protein survivin-derived peptide vaccination for patients with advanced or recurrent urothelial cancer. *Cancer Immunol Immunother* 2009;58:1801-7.
41. Zhang P, Wang J, Wang D, et al. Dendritic cell vaccine modified by Ag85A gene enhances anti-tumor immunity against bladder cancer. *Int Immunopharmacol* 2012;14:252-60.
42. Sandoval F, Terme M, Nizard M, et al. Mucosal imprinting of vaccine-induced CD8 T cells is crucial to inhibit the growth of mucosal tumors. *Sci Transl Med* 2013;5:172.
43. Domingos-Pereira S, Derré L, Warpelin-Decrausaz L, et al. Intravaginal and subcutaneous immunization induced vaccine specific CD8 T cells and tumor regression in the bladder. *J Urol* 2014;191:814-22.
44. Domingos-Pereira S, Decrausaz L, Derré L, et al. Intravaginal TLR agonists increase local vaccine-specific CD8 T cells and human papillomavirus-associated genital-tumor regression in mice. *Mucosal Immunol* 2013;6:393-404.