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INVESTIGATIVE UROLOGY

Androgen receptor expression is inversely correlated with pathologic tumor stage in bladder cancer

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Urology. 2004; 64: 383-8

Objectives: To evaluate the expression of the androgen receptor (AR) in transitional cell carcinoma (TCC) of the bladder, and to assess whether its expression correlated with pathologic tumor stage. TCC of the bladder is three times more common in males than in females. The origin of this sex difference in incidence is unknown.

Methods: We evaluated tumor specimens from 49 consecutive patients treated for TCC of the bladder at our institution between July 2002 and June 2003. Immunohistochemistry was performed using a monoclonal mouse anti-AR antibody on paraffin-embedded tissue sections of tumors obtained from transurethral resection, radical cystectomy, or resection of metastases. Specimens were assessed for AR expression, and, in tumors that demonstrated AR staining, the percentage of nuclei that stained positive was recorded.

Results: Of the 49 tumors, 26 (53.1%) expressed the AR. The percentage of tumors that expressed the AR decreased with increasing pathologic stage, from 88.9% of pTa lesions to 0% of pT3 tumors. Overall, 75% of superficial tumors (pTa + pT1 + carcinoma in situ) expressed the AR compared with 21.4% of invasive tumors (pT2 + pT3; P = 0.002). In addition, among AR-expressing tumors, the mean percentage of nuclei that stained positive for the AR was significantly greater in pTa tumors (62.5%) than in pT1 (31%) or pT2 (20%) tumors (P = 0.005).

Conclusions: We found a decrease in AR protein expression in tumors with increased pathologic stage. Our data suggest that the loss of AR expression is associated with invasive bladder cancer.

Editorial Comment

A previous study that considered smoking and occupational risks showed that the sex-related risk of bladder cancer for men persists independently of other risks (1). Some experimental studies in rats showed that the bladder tumors development is significantly grater in males than in females (2,3), although studies in humans are still scarce. A functional role for the AR in human bladder cancer has been suggested by a recent study that demonstrated that androgen treatment inhibited bacille Calmette-Guérin-induced interleukin-6 expression in bladder cancer cell lines that expressed the AR. The study also demonstrated that pharmacologic androgen deprivation restored bacille Calmette-Guérin-induced interleukin-6 expression (4).

In this present important contribution, Boorjian et al., after evaluating 49 tumor specimens, found a decrease in androgen receptors correspondent to increased pathologic stage. The authors suggest that as a

potential therapeutic application, given the high percentage of superficial (particularly Ta) tumors that expressed the AR in the present study, together with the results of androgen deprivation therapy in animal studies, the potential exists to investigate the impact of androgen deprivation therapy in superficial bladder cancer.

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Dendritic cell immunotherapy for urological cancers using cryopreserved allogeneic tumour lysate-pulsed cells: a phase I/II study

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Objective: To assess the feasibility, toxicity and immunogenicity of dendritic cell (DC)-based immunotherapy in patients with advanced urological cancers.

Patients and Methods: Patients with hormone-refractory prostate cancer (11) and metastatic renal cell carcinoma (five) received 1-3 x 10(6) intradermal allogeneic tumour lystate-pulsed DCs fortnightly for six vaccinations then monthly until disease progression. Intradermal keyhole limpet haemocyanin was injected near the DCs as the adjuvant. DC vaccine was prepared from buffy coats, then lysate-pulsed, cryopreserved in aliquots, and tested for phenotypic expression and activity in an allogeneic mixed lymphocyte reaction before clinical use.

Results: There was no evidence of significant toxicity from vaccine or adjuvant. Delayed-type hypersensitivity skin testing and biopsy revealed a cellular infiltrate to intradermal re-challenge to tumour lysate and adjuvant in almost all patients. In addition, there was increased expression of T helper type 1 cytokines, interferon-gamma-expressing T cell by ELISPOT analysis, but also interleukin-10 in a few patients. Vaccination resulted in a reduction in the level of prostate-specific antigen (PSA) in one patient, a reduction in PSA velocity in a further man and an increased PSA doubling time in six. Two of five patients with renal cell carcinoma had stabilization of disease.

Conclusion: The cryopreservation and repeated administration of DC vaccine was feasible and not toxic. There was evidence of induction of both humoral and cellular immunity to vaccine and adjuvant in most patients. The use of sequential aliquots of identical cryopreserved vaccine will ensure quality control and

greatly facilitate future clinical studies in terms of consistency of vaccine administered and the provision of primed DCs for in vitro assessment of response.

Editorial Comment

This is a very well done scientific research with immediate potential clinical implications. As the authors stated, one of the most significant limitation to current dendritic cell-based immunotherapy is the need to prepare fresh vaccine repeatedly. The ability to culture and cryopreserve numerous aliquots of identical dendritic cells from a single venesection would reduce hospital intervention for patients, and greatly facilitate clinical trials by allowing the manipulation of dendritic cells before or after freezing, and their subsequent use as sequential vaccines.

The authors demonstrated the feasibility of a potentially generic approach to cellular immunotherapy, and the preparation of identical aliquots of dendritic cell vaccine that were readily tested for safety and immunoreactivity before injecting into patients. Dendritic cell therapy resulted in significant in vitro immunological responses in patients even with very advanced disease. Also, in this study, dendritic cell vaccine showed to be safe and non-toxic

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RECONSTRUCTIVE UROLOGY

Vaginal and penile reconstruction

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Purpose of Review: Reconstructive surgery for patients with genital abnormalities or for patients who require reconstructive efforts is challenging. This review highlights those articles, which are outstanding among all those important papers, which have been published during the last year (2002-2003).

Recent Findings: A greater understanding of embryonal development improves the success of reconstructive surgery. Other factors, such as the patient's sex, influence the surgical technique used and the degree of invasiveness or complexity. In the adult the pressure to shorten hospital stays has played a big part in the continual modification and enhancement of surgical techniques. In addition to modified techniques, new off-the-shelf materials are introduced to the clinic, which seem to have the potential to improve the surgical outcome and shorten hospital stays.

Summary: With the continued successful basic anatomy and basic research, reconstructive surgery brings higher success rates. Long-term results are still required to validate the reliability of these new surgical techniques and materials.

Editorial Comment

This paper nicely outlines the current status of reconstruction of male and female genitalia for a successful reconstruction in genital abnormalities a greater understanding of the embryonal development is advantages. Flap technology and prefabrication are the currently preferred methods for surgical success in transsexual