25

PROSTATIC CANCER: PROGNOSTIC VALUE OF THE HISTOPATHOLOGICAL PATTERN ACCORDING TO DIFFERENT CATEGORIES (GAETA, GLEASON GRADE AND UICC)

J.J. de la Pena, J. Cisneros, M. Mora, J. Machuca, L. Martinez-Pineiro, M.L. Picazo, J.A. Martinez-Pineiro
U. Autonoma de Madrid. F. de Medicina, S. de Urologia y Dpto de A. Patologica. H. La Paz, P de la Castellana 261, 28046 Madrid, Spain

From 1970 to 1986 we reviewed the histologic sections of 469 patients with prostatic carcinoma. All of them were reclassified according to Gleason grade, Gaeta nuclear pattern and UICC criteria, and survival curves were generated as a function of each classification. All cases were evaluated according to the clinical stage, and the relationship with the different histologic classifications was established.

26

EFFECT OF DIHYDROTESTOSTERONE (dHT)+ ESTRADIOL (E_2+), dHT + PROLACTIN (PRL) COMBINATIONS ON THE CELL PROLIFERATION OF HUMAN PROSTATIC ADENOMAS.

Y.de Launoit (1), R.Kiss (1), G.Lenglet (1), E.De Backer (2), R.Peridoens (3)
1) Lab.Histologie, Fac.Med., ULB; Serv.Urologie, Clin.Ste Elisabeth, 3) Serv.Med., Inst.Bordet, Brussels, Belgium

Explants (5 x 1mm^3)/tumor/experimental condition of 10 human prostatic adenomas were maintained in serum free minimum essential medium (MEM) either alone (control) or supplemented with dHT (10^{-9}M) and E_2 (10^{-9}M), or dHT and PRL (1µg/ml), or E_2 and PRL for 12, 24, 36, 48 and 72 hrs. Two hrs before the end of incubation, 2 µCi of tritiated thymidine/ml were added; thereafter samples were fixed and processed for autoradiography. Nuclear labeling indices (TLI) were systematically assessed. The results showed that the combinations of dHT + E_2, dHT + PRL or E_2 + PRL always significantly increase the TLI in the glandular part of the tumor, as compared to a single pulse of dHT, E_2 or PRL. In conclusion, dHT, E_2 and PRL might possess synergistic properties on the cell proliferation of prostatic adenomas.

Supported by CBER and FRSM, Belgium.

27

ESTABLISHMENT OF MONOCLONAL ANTIBODY TO HUMAN ANDROGEN RECEPTOR AND ITS CLINICAL APPLICATION FOR PROSTATIC CANCERS

T.Demura[1], N.Kuzumaki[2], A.Oda[2], Y.Asano[1], N.Takayama[1] and T.Koyanagi[1]
[1]Dpt. of Urology and [2]Lab.of Molecular Genetics Cancer Institute, Hokkaido University School of Medicine, Sapporo, Hokkaido, Japan.

Prostate is one of the target organs of androgen. This fact is the foundation of the anti-androgen therapy to the prostatic cancer. But there are not a few prostatic cancers without response to the hormone therapy. In this study, we describe the establishment of monoclonal antibody to androgen receptor (AR) and the trials to predict the responsiveness of the hormone therapy to prostatic cancers.
Materials and Methods: AR was partially purified from 500g of human prostates (BPH) by sequential chromatography on DEAE-cellulose, testosterone-Sepharose and Blue-Sepharose CL-6B. Two-month old BALB/c mice were immunized with purified AR. Immune splenocytes were fused with NS-1 cells by using polyethylene glycol. To screen antibody production by hybridoma cells, ELISA was used at first. As the second screening, ELISA positive wells were determined for production of antibodies against AR by immunoprecipitation assay (IPA) described by Greene et al. with some modifications. BPH tissues and 13 prostatic cancer (PC) tissues were analyzed for immunohistochemical localization of AR by using avidin-biotin-peroxidase complex (ABC) procedure.
Results: Nine hybridomas were proved to produce antibodies against AR by IPA. The specific binding of androgen in the supernatant after precipitation by the antibodies decreased to be 20-60%, suggesting that the antibodies absorbed 40-80% of AR of prostatic cytosol. One of the clones, 5F4, was chosen for analysis of immunohistochemical localization of AR. In BPH tissues, nuclei and cytoplasms of glandular epithelial cells were predominantly stained. Of 13 PC tissues, two were composed of AR positive cancer cells exclusively (AR positive type), five were of AR negative cells (AR negative type) and six contained both AR positive cells and negative cells (mixed type). Of 8 cases which were AR positive type or mixed type, 6 cases responded to the hormone therapy, and two were impossible to be determined for the responsiveness because the patients were dead of other diseases at early stages. Of five cases of AR negative type, all but one unestimable case had no response to the hormone therapy.
Conclusions: Immunohistochemical analysis of AR by using the monoclonal antibody, 5F4, was a very useful tool for determining androgen dependency of prostatic cancers.

28

CELLULAR DNA CONTENT AND PROLIFERATIVE INDEX AS MARKERS IN HUMAN PROSTATE CANCER

R. De Vita[1], D. Forte[1], F. Maggi[1], R.Tenaglia[2] and F. Di Silverio[2]
1) Div. of Physics and Biomedical Sc., ENEA Casaccia, 00060 Rome. 2) Urologic Pathology, University "La Sapienza", 00100 Rome, Italy.

In human prostatic tumors, it is possible to correlate flow cytometric cellular DNA content and specific proliferative index, on the basis of the percent of S phase cells, with histopathological and biochemical parameters in the attempt to obtain new informations of clinical relevance. Bioptic samples from 71 prostatic tumors (65 carcinomas and 6 adenomas) have been analysed. Monocellular suspensions were obtained by mechanical and enzymatic (0.5% pepsin) treatments, stained with combined ethidium bromide and mithramycin, and measured by arc lamp flow cytometer. All adenoma samples resultes cytometrically diploid; 51% carcinomas resulted aneuploid (9% multiclonal) and 49% diploid. The frequency of cytometric aneuploidy increases in relation to histopathological grading, G1 (17%), G2 (37%), G3 (79%). The percent of S phase cells showed a significant increase ($p<0.001$) from adenomas (4.1) to diploid carcinomas (9.3) to aneuploid carcinomas (14.6), while a significant decrease of the cellular Diidrotestosterone values was found from diploid (2.1) to monoclonal aneuploid (1.6) ($p<0.01$) to multiclonal aneuploid malignant tumors (1.4) ($p<0.001$).