The Normal Female and the Male Breast Epithelium does not Express Prostate-Specific Antigen. Preliminary Immunohistochemical Observations of Autopsy Breast Tissues

ZAVIAČIČ M¹, ABLIN R J², RUŽIČKOVÁ M¹, ŠTVRTINA S¹, DANIHEL L¹, ZAVIAČIČ T³, POHLÍDEK K³, HOLOMÁN K³

¹ Department of Pathology, Comenius University, School of Medicine and Faculty Hospital, Sasinová 4, Bratislava, Slovak Republic
² Innapharma, Inc, Upper Saddle River, New Jersey, USA
³ Second Department of Obstetrics and Gynecology, Comenius University School of Medicine and Faculty Hospital, Bratislava, Slovak Republic

Abstract. In the normal female and male breast epithelial structures any prostate-specific antigen (PSA) immunohistochemical positivity was observed. Variable PSA expression, which often borders the positivity, was observed in membranes of adipocytes of fat tissue and in the endothelium of small vessels in a female and a male breast. Based on these initial observations, tissue of the normal breast, male or female, can not be considered to be the principal source of PSA.

Key words: Prostate-specific antigen (PSA) — Immunohistochemistry — Normal female breast — Normal male breast

Introduction

Some investigators consider the female breast to be the principal source of PSA. In female, not only the pathological breast tissue especially benign (hyperplastic) breast disease and cancer, but also the normal female breast tissue is assumed to be the principal source of...
PSA (Yu et al. 1996; Diamandis 1998) This assumption is based on the immunochemo-
ical quantification of PSA in the serum and breast fluids as well as extracts of women
with normal, benign and malignant breast disease (Mannello et al. 1996; Borchert et al.
1997; Diamandis 1998 and references therein). However, no immunohistochemical data
concerning the expression of PSA in the normal female and normal male breast have been
reported up to date. Since in healthy women serum PSA values cover the range from
nondetectable to high concentrations (up to 0.9 ng/ml), and a value approaching the
normal male reference ranges of PSA (1–2 ng/mL according to Borchert et al. 1997), it
appears to address the question: Which organ or tissue of the healthy female is actually
responsible for the production of this prostate marker? Therefore, aims of this preliminary
study were (1) Is the female breast the principal source of PSA in the healthy female and
(2) besides the male prostate, what role does the normal male breast tissue play in the
production of PSA?

Materials and Methods

Using immunohistochemical methods, PSA was examined in normal breast tissue obtained
by autopsy from 29 men and 23 women, of which 11 subjects were less than 50 years of
age and 41 subjects were above 50 years of age. Histological examination of normal female
breast revealed only age-dependent involutionary postmenopausal atrophic changes, char-
acteristic of female subjects over 50 years of age and resting female breast tissue seen in
younger female patients. Normal male breast histology revealed only ducts and no lactifer-
ous sinuses and lobule formation in the samples examined. Immunohistochemical staining
was carried out by the biotin–streptavidin–peroxidase technique with aminomethyl-
carbasole development, using the Universal Kit (Dako Corp., Carpinteria, CA, USA).
Primary antibodies—rabbit polyclonal and mouse monoclonal anti-prostate-specific an-
tigen antibody (Dako Corp., Carpinteria, CA, USA) were diluted 1:100–200. The study
invariably involved negative controls (slides processed without primary antibodies).

Results

PSA expression was not observed in any epithelial structures of the 29 normal male or 23
normal female breast tissues evaluated. Fig. 1 shows no positivity of PSA in normal post-
menopausal breast epithelial tissue of a 64-year-old female. Occasional borderline expression
of PSA was observed in membranes of adipocytes of fat tissue and in the endothelium of
small vessels of the female and male breast. Fig. 2 indicates PSA positivity in membranes
of adipocytes of fat tissue in resting normal female breast of a 44-year-old female.

Discussion

Results of our preliminary immunohistochemical study appear to provide a clear answer
concerning the role of normal female and normal male breast tissue in the production of
PSA. In contrary to the conclusion of Diamandis’s group (Yu et al. 1996; Diamandis 1998)
we have found that normal female breast epithelia do not produce PSA (Fig. 1). Differences
between the quantified immunohistochemical results of Diamandis and our findings may
be explained by the fact that despite the higher sensitivity of quantifiable immunohisto-
chemical compared to immunohistochemical methods, the former yield data on the heteroge-
neous homogenate, containing not only female breast glands, but also adipose tissue (Fig. 2)
and small vessels, in which positivity was observed on immunohistochemical examination. The
hypothesis of Diamandis's group suggesting PSA production in the normal female breast has not been confirmed by these preliminary studies and cannot be explain by the source of PSA in the normal healthy female. Therefore, pending further investigations, the tissue of the normal breast, male or female, can not be considered to be the producer of PSA.

Our studies of the female prostate (Zaviačič et al. 1985, Zaviačič 1987, Zaviačič and Whipple 1993, Zaviačič and Ablin 1998 a, b, c) suggest that in the male, the female prostate (Skene's gland) is the normal and the principal source of PSA. However, in consideration of recent reports of the anomalous expression of PSA in extraprostatic tissues, inclusive of the pathological female breast, one may envisage, as suggested by Ablin (1997), the existence of a regulatory gene network controlling its expression. Under such circumstances, a given tissue may, depending on the state of cellular differentiation, express repressed genes after neoplastic transformation. Additionally, somatic mutations may contribute to specific changes in PSA genes in cancer cell clones.

Acknowledgements. This study was supported by grant-in-aid from the Scientific Grant Agency of the Slovak Republic (Project No 1/5139/98)
References


Borchert G H , Giai M , Diamandis E P (1997) Elevated levels of prostate specific antigen in serum of women with fibroadenomas and breast cysts (correspondence) J Natl Cancer Inst 89, 587—588


Zaviačič M , Abhn R J (1998 c) The female prostate and prostate-specific antigen Immunohistochemical localization, implications of this prostate marker in women and reasons for using the term "prostate" in human female Histol Histopathol , submitted for publication


The Role of Adenylate Cyclase in Ischemic Preconditioning in the Rat Heart: A Cytochemical Study

Ľ OKRUHLICOVÁ, T RAVINGEROVÁ, D PANCZA, N TRIBULOVÁ AND R ŠTETKA

Institute for Heart Research, Slovak Academy of Sciences, Bratislava, Slovak Republic

Abstract. Using catalytic cytochemistry the AC activity was studied during ischemic preconditioning (IP) (5 min occlusion of LAD and 10 min reperfusion) followed by 30 min regional ischemia in isolated Langendorff-perfused rat heart In controls the specific precipitate of AC reaction was found on the sarcolemma (SL) and the junctional sarcoplasmic reticulum (JSR) of cardiomyocytes After prolonged ischemia the reaction product was absent, whereas IP followed by prolonged ischemia protected the AC activity on SL and JSR IP-induced enhancement of AC activity in this model was accompanied by significant reduction of ischemia/reperfusion fibrillation The results suggest involvement of AC system in mechanisms of IP

Correspondence address Ľ Okruhlicová, Institute for Heart Research, Slovak Academy of Sciences, Dúbravská cesta 9, 842 33 Bratislava, Slovakia E-mail usrdokru@savba.sk