



Focal neuroendocrine differentiation in prostatic gland carcinoma with basaloid pattern

Bazalnoćelijski karcinom prostate sa neuroendokrinom diferencijacijom

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Abstract

Introduction. Prostatic gland basal cell proliferations exhibit morphological continuum ranging from basal cell hyperplasia to basal cell carcinoma. In the following report, we described clinical features, morphological spectrum, neuroendocrine differentiation and histogenesis of prostatic gland basal cell carcinoma in our patient. **Case report.** Hematoxylin-eosin (HE), Alcian blue-periodic acid schiff (AB-PAS) at pH 2.5 stained sections and the avidin-biotin-peroxidase complex (ABC), were performed on prostate gland paraffin-embedded tissue. Monoclonal antibodies directed against cytokeratin (34βE12) which selectively stains basal cells, prostate specific antigen (PSA), chromogranin A, neuron-specific enolase (NSE), synaptophysin and CD56, were used. Basal cell proliferations exhibited a morphological continuum ranging from basal cell hyperplasia to prostatic gland carcinoma. In these prostatic lesions, positive reactivity was demonstrated for 34βE12 and CD56. These findings indicate that the basaloid cells of basal cell hyperplasia, florid basal cell hyperplasia, atypical basal cell hyperplasia and basal cell carcinoma are derived from basal cells of the normal prostate gland suggesting a continuum in the progression of hyperplasia to benign and then malignant neoplasia. The presence of CD56 protein in the discovered lesions may be related to their neuroendocrine differentiation. **Conclusion.** The fact, that our patient was well six years after the radical prostatectomy supports the belief of some authors that basal cell carcinoma represents a low grade carcinoma with an excellent prognosis.

Key words:

prostatic neoplasms; prostatic hyperplasia; antigens, differentiation; histological techniques; immunohistochemistry.

Apstrakt

Uvod. Proliferacija bazalnih ćelija žlezda prostate pokazuje morfološki kontinuum od hiperplazije do karcinoma bazalnih ćelija. Prikazali smo kliničke odlike, morfološki spektar, bazalnoćelijsku proliferaciju, neuroendokrinu diferencijaciju i histogenezu karcinoma bazalnih ćelija žlezda prostate. **Prikaz bolesnika.** Preseci parafinskih blokova tkiva prostate bojeni su metodom hematoksilin/eozin (HE), *alcian blue* (AB) – *Periodic acid Schiff* (PAS) pri pH 2,5 i *avidin-biotin complex* (ABC). Upotrebljena su monoklonska antitela usmerena prema citokeratinu (34βE12) koja selektivno boje bazalne ćelije, prostata specifični antigen (PSA), hromogranin A, neuron-specifična enolaza (NSE), sinaptofizin i CD56. Proliferacija bazalnih ćelija pokazala je morfološki kontinuum od hiperplazije bazalnih ćelija do karcinoma prostate. U identifikovanim lezijama prostate prikazana je pozitivna reakcija za 34βE12 i CD56. Ovi nalazi ukazuju na to da bazaloidne ćelije u hiperplaziji, floridnoj hiperplaziji bazalnih ćelija, atipičnoj hiperplaziji bazalnih ćelija i karcinomu bazalnih ćelija nastaju iz bazalnih ćelija normalnih žlezda prostate ukazujući na kontinuum u progresiji hiperplazije ka benignim i malignim neoplazmama. Prisustvo CD56 proteina u otkrivenim lezijama može biti posledica njihove neuroendokrine diferencijacije. **Zaključak.** Činjenica da je prikazani bolesnik u dobrom stanju šest godina posle radikalne prostatektomije u saglasnosti je sa mišljenjem nekih autora da karcinom bazalnih ćelija prostate predstavlja malignu neoplazmu niskog gradusa malignosti sa odličnom prognozom.

Ključne reči:

prostata, neoplazme; prostata, hiperplazija; antigeni, diferencijacija; histološke tehnike; imunohistohemija.

Introduction

Prostatic basal cell carcinoma is an uncommon neoplasm accounting for less than 0.01% of all prostatic gland carcinomas, composed of prostatic basal cells¹⁻¹⁴. In addition, the gross patterns have been reported for fewer than 10 cases¹⁵. It is believed that a subset of basal cells are prostatic epithelial stem cells, which can give rise to a spectrum of proliferative lesions ranging from basal cell hyperplasia (BCH) to basal cell carcinoma (BCC)¹⁻⁴. The distinction between these forms of BCH (including the variant with florid BCH) and BCC depends on morphological, immunohistochemical criteria and on the degree of cell proliferation²⁻⁸. Prostatic BCC is characterised by proliferation of cells arranged in various architectural patterns. Two morphological variants of BCC can be recognised in the prostate^{8,9}. Islands and cords of epithelial cells with peripheral palisading characterise the first type, morphologically similar to BCC of the skin. The second type, also called adenoid cystic carcinoma, is composed of nests of infiltrating tumor cells with an adenoid cystic pattern, morphologically similar to adenoid cystic carcinoma of the salivary glands^{8,9}. Neuroendocrine differentiation has been reported only in typical and small cell prostatic carcinoma. It takes several forms. Pure neuroendocrine carcinoma is rare and includes carcinoid tumor¹⁰⁻¹³. Immunohistochemistry clearly indicates that basal cell proliferations have the same immunophenotype as the basal cells present in normal ducts and acini. The cells are positively and strongly stained for high-molecular weight cytokeratin (34 β E12) and p63, consolidated markers for basal cells in the prostate^{4,7}. We reported a case with prostatic BCC, pointing out its neuroendocrine differentiation and an excellent prognosis.

Case report

A 58-year-old man presented in April 2001 with a 16-month history of increasing urinary obstructive symptoms. Diffuse enlargement of the prostate was documented by

transrectal ultrasound and digital rectal examination. The preoperative total serum prostate-specific antigen (PSA) concentration was 2.5 μ g/mL. The patient had radical prostatectomy. After diagnosing basal cell carcinoma of the prostate, a metastatic workup for tumor had normal results. The patient was alive without evidence of disease six years after the prostatectomy. Twelve blocks of prostate from a prostatectomy specimen were examined. Formalin-fixed, paraffin-embedded sections, 5 μ m in thickness, were classically processed and stained with hematoxylin-eosin (HE) slides, also were stained with Alcian blu (AB) –periodic acid schiff (PAS) at pH 2.5. For immunoperoxidase studies on the formalin fixed, paraffin wax embedded tissues, antibodies to the following antigens were used: 34 β E12 to highlight the basal cells (Dako Cytomation), rabbit anti PSA to mark prostatic secretory cells and, rabbit anti-chromogranin A, synaptophysin, and CD56 (to discover neuroendocrine differentiation of the prostatic gland BCPs). Selected sections of the prostate were stained by means of the labeled streptavidin – biotin method (Dako Cytomation; 1 : 100). The immunohistochemical staining of cells was recorded as either positive or negative one. At least 500 cells were counted on each slide.

Gross and microscopical pathology

The surgical specimen weighted 120 g and measured 4 \times 3.5 cm. The cut surface was white and nodular. At one end of the specimen an ovoid area was identified. The parenchyma was otherwise gray-white with occasional small cysts (Figure 1a). The surrounding prostate tissue was grossly and histologically unremarkable.

Microscopically, basal cell proliferations (BCPs) exhibit a morphological continuum ranging from ordinary BCH to prostatic gland BCC (Figures 1b–2d). The nests were composed of small, ovoid, basaloid cells having scanty cytoplasm and uniform nuclei with finely dispersed chromatin. Nucleoli were absent (Figures 1b and 1c). These cells stained

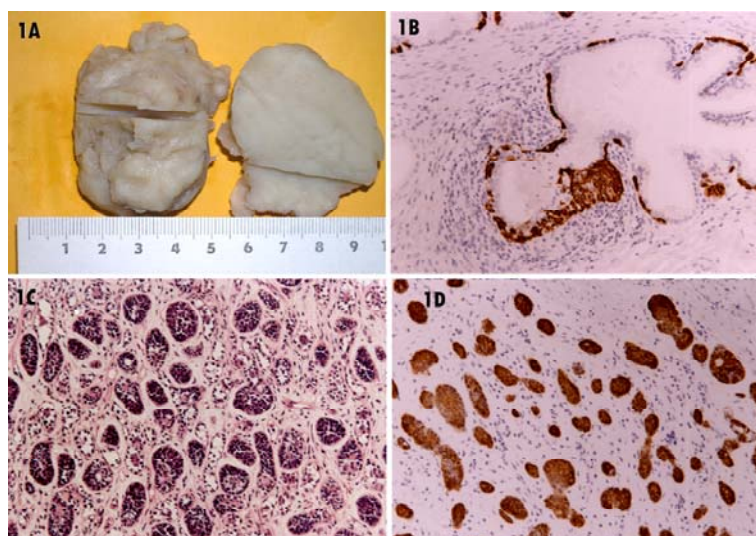


Fig. 1: A – macroscopic pattern; B – origin of solid nest from normal basal cells (immunostain for 34 β E12, \times 300); C – BCH (solid clusters of basaloid cells, HE \times 200); D – immunostain for 34 β E12 cytokeratin demonstrating strong positive reactivity (ABC \times 200).

BCH – basal cell hyperplasia; HE – hematoxylin-eosin; ABC – avian-biotin complex

positively for 34 β E12 and negatively for PSA (Figures 1d, 2a). Neuroendocrine markers-chromogranin, neuron-specific enolase (NSE) and synaptophysin could not mark neuroendocrine cells. The only marker that was able to detect these cells was CD56 (Figure 2b). The basal cells of the florid BCH contained minimal cytoplasm, moderate nuclear pleomorphism, prominent nucleoli and mitosis. The prostatic gland BCC was characterized by infiltrative growth and large irregular nests punctuated by cribriform spaces filled with small globules of dense eosinophilic material surrounded by basal cells. This material was AB-positive mucin in some areas and intensive PAS-positive hyaline material in others; peripheral palisading pattern also was evident, as well as myxoid stroma (Figure 2c). Some dense cords and islands of basaloid cells showed a significant nuclear hyperchromasia and higher mitotic activity (Figure 2d).

BCC from florid/atypical BCH is also very important, including extensive infiltration between normal prostatic gland, extension out of the prostate gland, perineural invasion or necrosis, as well as rare distant metastasis²⁻¹¹.

Prostatic neuroendocrine cells most likely derive from local stem cells and represent terminal differentiation in benign prostate tissue. A frequent occurrence of neuroendocrine (NE) differentiation in prostatic adenocarcinoma (author's experience) obviously reflects the differentiation repertoire of its stem cells^{12,13}. Pure neuroendocrine differentiation is rare and includes carcinoid tumor¹². However, to the best of the authors knowledge, the neuroendocrine differentiation has not been described in prostatic BCC, by using chromogranin, neuron-specific enolase and synaptophysin, that we also have confirmed. But, by using CD56 (neural cell adhesion molecule), neuroendocrine marker for

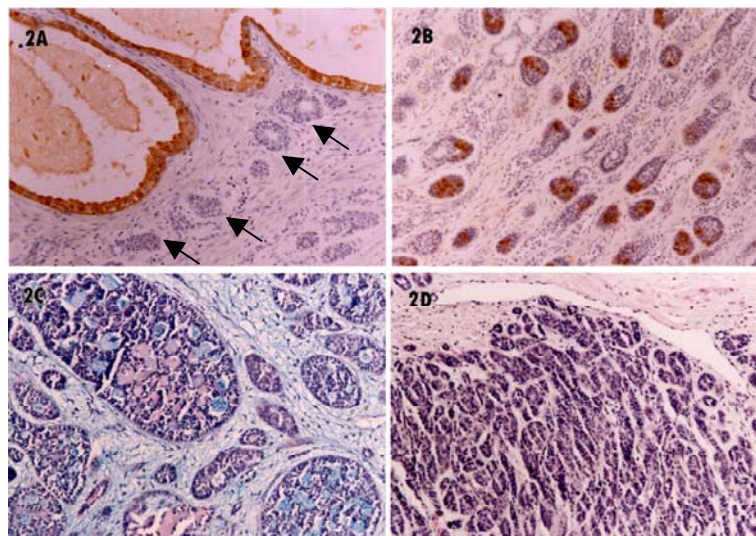


Fig. 2: A – BSH (positive PSA activity in normal ductal epithelium and negative in basaloid nests arrows, ABC \times 200); B – positive CD54 activity in hyperplastic basaloid nests (ABC \times 200); C – ACC (classic pattern of ACC; note nests having multiple lumina with mixoid stroma containing both AB and PAS positive material, AB-PAS \times 300); D – BCC (atypical basal cells infiltrate prostatic surrounding stromal tissue, HE \times 200).

PSA – prostate-specific antigen; ABC – avidin-biotin complex; ACC – adenoid cystic carcinoma; AB – Alcian blu; PAS – periodic acid schiff; BCC – basal cell carcinoma; HE – hematoxylin-eosin

Discussion

Prostatic gland BCH is an uncommon proliferative lesion whose major importance is possible confusion with prostatic intraepithelial neoplasia (PIN) and poorly differentiated (mostly Glisson's 5) adenocarcinoma^{2, 9, 13}. The distinction between these two carcinomas depends on the following morphological and immunohistochemical features: small nests of basaloid cells have scanty cytoplasm, uniform nuclei, finely dispersed chromatin and occasional small nucleoli, with multilayered positively staining of the basal cells for 34 β E12 and, negatively for PSA¹²⁻¹⁴. The distinction of

both lung and prostatic small cell carcinomas and natural killer cells¹⁴, we found a strong expression of CD56 inside BCHs.

Conclusion

Prostatic gland basal cell proliferations range from ordinary BCH, to florid BCH and to BCC. Diagnosis of these lesions depends on morphological and immunohistochemical criteria. CD56 is an excellent marker for detection of neuroendocrine differentiation of BCHs.

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