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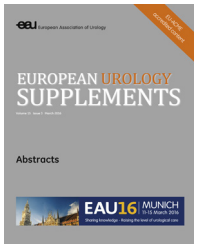

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Morphologic Variants of Epithelial and Neuroendocrine Tumors of the Prostate. The Pathologist's Point of View

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Abstract

More than 95% of all carcinomas of the prostate are referred to as acinar, microacinar, usual, or conventional type. A minority have been classified as variants. Variants can vary in histologic appearance and divergent differentiation compared with usual acinar adenocarcinoma. Some variants constitute different types of carcinoma and are not adenocarcinomas. Variants that represent a challenge to diagnose include the deceptively benign-looking atrophic, pseudohyperplastic, microcystic, and foamy gland variants. The signet ring-like, pleomorphic giant cell, and sarcomatoid variants have worse prognosis than usual acinar adenocarcinoma. Some variants can occur after therapy, such endocrine and radiation therapy: squamous neoplasms, neuroendocrine tumors, sarcomatoid carcinoma (ie, carcinosarcoma), and pleomorphic giant cell variant. Neuroendocrine prostate cancer is an aggressive variant of prostate cancer that often arises in later stages of castration-resistant prostate cancer.

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1. Introduction

The 2016 World Health Organization (WHO) classification of epithelial and neuroendocrine (NE) tumors of the prostate is summarized in Tables 1 and 2 [1]. More than 95% of all carcinomas of the prostate (CaPs) are referred to as acinar, conventional, or usual type [1,2]. Acinar adenocarcinoma is an invasive CaP consisting of malignant prostatic epithelial cells with secretory/luminal differentiation arranged in a variety of architectural patterns, such as glands, sheets, cords, and single cells. By definition, basal cells are absent.

A minority of CaPs have been classified as variants [1]. The term *variant* is used to describe a distinctively different morphotype of a certain neoplasm. CaP variants can vary in histomorphological appearance and divergent differentiation compared with acinar adenocarcinoma. Some variants constitute different morphotypes of CaPs and are not adenocarcinomas.

The aim of this contribution is to review some of the main morphologic features of the variants in the current 2016 WHO classification of epithelial and NE tumors of the prostate. For a more comprehensive report on all possible

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Table 1 – Classification of epithelial tumors of the prostate

Glandular neoplasms
Acinar adenocarcinoma
Atrophic
Pseudohyperplastic
Microcystic
Foamy gland
Mucinous (colloid)
Signet ring-like cell
Pleomorphic giant-cell
Sarcomatoid
Prostatic intraepithelial neoplasia, high grade
Intraductal carcinoma
Ductal adenocarcinoma
Cribriform
Papillary
Solid
Urothelial carcinoma
Squamous neoplasms
Adenosquamous carcinoma
Squamous cell carcinoma
Basal cell carcinoma

Table 2 – Classification of neuroendocrine tumors of the prostate

Adenocarcinoma with neuroendocrine differentiation
Well-differentiated neuroendocrine tumor
Small-cell neuroendocrine carcinoma
Large-cell neuroendocrine carcinoma

CaP variants and variations, readers should consult the WHO blue book [1], upon which this current contribution was based, and recent comprehensive reviews [2].

2. Histological variants of acinar adenocarcinoma

Morphological variants of acinar adenocarcinoma can be of importance because of difficulties in making a diagnosis and differences in prognosis compared with acinar adenocarcinoma [1,2]. In particular "Variants that can be a challenge to diagnose include the deceptively benign-looking atrophic, pseudohyperplastic, microcystic, and foamy gland variants. The signet ring-like, pleomorphic giant cell, and sarcomatoid variants have a worse prognosis than does usual acinar adenocarcinoma" [1].

2.1. Deceptively benign-looking variants

2.1.1. Atrophic variant

Compared to simple atrophy and postatrophic hyperplasia, atrophic acinar adenocarcinoma has one or more of the following features: a more infiltrative appearance, with the cancer glands infiltrating as isolated glands in between benign glands, associated with nonatrophic cancer, and prominent cytological atypia (Fig. 1A) beyond what can be seen with benign atrophy [1,3,4].

In simple atrophy and postatrophic hyperplasia there is lobular configuration (Fig. 1B), basophilia from the lack of cytoplasm both apically and laterally in comparison to normal epithelium, with the nuclei appearing crowded and a nuclear outline of the glands visible at low power. The stroma is altered by a pale fibrosis, with periacinar collagen deposition [3,4].

A focus of atrophic cancer should be supported by negative immunohistochemistry (IHC) for basal cell markers. IHC for basal cell markers shows uniform staining of the basal cells in simple atrophy and postatrophic hyperplasia, ruling out CaP. α-Methylacyl CoA racemase (AMACR; P504S), a marker preferentially expressed in CaP, is generally negative in simple atrophy and very uncommonly expressed in postatrophic hyperplasia [5].

2.1.2. Pseudohyperplastic variant

Pseudohyperplastic acinar adenocarcinoma is a variant that mimics medium- to large-sized hyperplastic glands (Fig. 2A–D) [1,6]. The differential diagnosis is based on the following morphologic and immunohistochemical features present in hyperplastic glands: lack of crowding; lack of association with usual acinar CaP; benign-appearing nuclei; presence of a basal cell layer according to hematoxylin and eosin staining; and the absence of IHC AMACR staining. However, approximately a quarter of pseudohyperplastic CaPs are negative for AMACR [7].

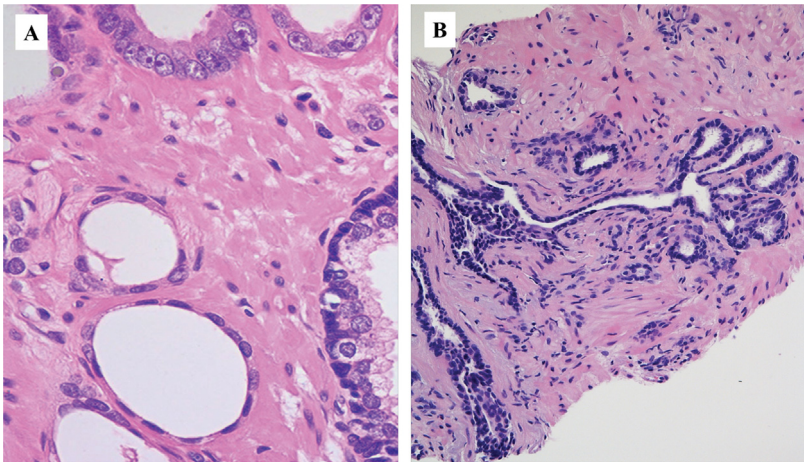

Fig. 1 – (A) Atrophic variant of acinar adenocarcinoma and (B) simple atrophy with the lobular configuration retained.

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