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EUO Collaborative Review – Prostate Cancer

Features and Prognostic Significance of Intraductal Carcinoma of the Prostate

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Abstract

Context: Intraductal carcinoma of the prostate (IDC-P) is an intraglandular/ductal neoplastic growth of glandular epithelial cells characterized by marked abnormality of the glandular architecture and/or cytological atypia that exceeds what is typically seen in high-grade prostatic intraepithelial neoplasia (HPGIN). It has been shown that IDC-P is a strong independent indicator of poor prognosis for prostate carcinoma (PCa).

Objective: To review the pathological and genetic features, diagnostic criteria and differential diagnosis, and clinical significance of IDC-P.

Evidence acquisition: PubMed was searched using keywords including prostate carcinoma, intraductal carcinoma, IDC, histology, diagnostic criteria, and prognosis. The references in relevant articles were also reviewed.

Evidence synthesis: IDC-P is a distinct entity with characteristic morphological and genetic features. It is strongly associated with aggressive PCa with high Gleason score/grade groups and large tumor volume, and portends unfavorable clinical outcomes. Morphological diagnostic criteria have been established to distinguish it from other lesions with similar histological features. IDC-P is an uncommon finding in prostate biopsies, and is even rarer as an isolated finding without concomitant PCa. However, patients with isolated IDC-P in biopsy specimens are recommended to have either definitive treatment or immediate repeat biopsy.

Conclusions: It is critical to recognize and report IDC-P, especially in prostate biopsies, where the clinical impact of such a diagnosis is greatest.

Patient summary: Intraductal carcinoma is a unique form of aggressive prostate cancer. In this report, we review its pathological and genetic features and poor prognostic significance. It is critical for pathologists to recognize and report this lesion in prostate specimens, especially in prostate biopsies for patient management.

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1. Introduction

Intraductal carcinoma of the prostate (IDC-P) is now considered a unique type of prostatic glandular neoplasia with a propensity to grow within and expand benign prostatic ducts and acini [1]. IDC-P is strongly associated with aggressive, high-grade, typically Gleason patterns 4/5, and high-volume invasive prostate carcinoma (PCa). It is therefore critical to report and distinguish IDC-P from other lesions with similar histological appearance, especially in prostate biopsies. Patients with a diagnosis of IDC-P in a biopsy are counseled to either undergo an immediate repeat biopsy or, as recommended by some experts, definitive therapy even in the absence of documented invasive PCa. Here we review the historical perspective, morphological features, diagnostic criteria and differential diagnosis, and genetics of IDC-P. The clinical significance of IDC-P in both radical prostatectomy and prostate biopsy specimens is emphasized. Reporting of IDC-P in prostate biopsies is also discussed.

2. Evidence acquisition

A comprehensive PubMed search was performed up to January 2018 using keywords including prostate carcinoma, intraductal carcinoma, IDC, IDC-P, intraductal spread, histology, diagnostic criteria, prognosis, and therapy. The search was restricted to articles published in the English language. The references in relevant articles were also reviewed.

3. Evidence synthesis

3.1. Historical perspective

In the earlier literature, "intraductal carcinoma" was used variably to describe the extension into prostatic ducts and acini of prostatic acinar and ductal carcinoma and urothelial and squamous carcinoma [2]. At present, the term IDC-P refers specifically to the proliferation of prostate adenocarcinoma cells within pre-existing prostatic glandular structures.

Kovi et al. [3] were the first to perform a detailed analysis of this phenomenon. They described PCa cells invading adjacent benign prostatic ducts and supplanting the normal epithelial component while preserving the general architectural framework of the affected ducts and acini. In a later study, McNeal et al. [4] found that PCa with cribriform morphology was predominantly located within prostatic ducts and acini, with cancer cells following the normal duct contour and retaining basal cells. The majority of cribriform PCa with intraductal location was prognostically equivalent to Gleason patterns 4/5 PCa. The authors coined the term "intraductal carcinoma of the prostate" to emphasize the unique histological and clinical features of this lesion. Subsequently, McNeal and Yemoto [5] proved that IDC-P was a unique form of PCa with a peculiar propensity for intraductal spread and growth, as IDC-P was almost never seen in the absence of invasive carcinoma, and the concomitant invasive component was usually of high grade.

The concept of "intraductal carcinoma" has evolved significantly since then. The current concept is that the vast majority of IDC-P represents intraductal extension of advanced-stage invasive PCa. Very rarely, IDC-P can be found without a concomitant invasive prostate PCa [6] and therefore may represent a stage of prostate carcinogenesis beyond high-grade prostatic intraepithelial neoplasia (HGPIN) but before invasive PCa develops. IDC-P is accepted as a distinct entity in the 2016 World Health Organization (WHO) classification of tumors of the urinary system and male genital organs [1].

3.2. Morphological features of IDC-P

Almost all cases of IDC-P have two morphological hallmarks, including expansile growth of atypical cells that forms a dense cribriform and/or solid architecture and at least partial preservation of basal cells around these glands. Architecturally, IDC-P can exhibit a plethora of patterns (Table 1), including a dense cribriform pattern (Fig. 1A–C), solid tumor (Fig. 1D), and comedonecrosis (Fig. 1E), representing progressively increasing proliferation of cancer cells. It is not uncommon that IDC-P partially involves benign glands (Fig. 1F). Cytologically, neoplastic cells may exhibit either the typical cytology of PCa or, in a minority of cases, marked variation in nuclear size and pleomorphic nuclei that are six or more times the size of adjacent nuclei (Fig. 1G). In some cases with marked cytological atypia, the IDC-P cells line ducts/acini in a single layer or piled up cells without a cribriform and/or solid architecture.

There are also lesions that may represent a lower-grade form of IDC-P, with a small and smooth glandular contour and uniform nuclei that are morphologically difficult to distinguish from HGPIN glands (Fig. 2; see the discussion below) [7].

3.3. Diagnostic criteria for IDC-P

The diagnosis of IDC-P is based on morphology. Several diagnostic criteria have been proposed. Cohen et al. [8] proposed a set of five major and three minor criteria. The first four major criteria are always present in IDC-P and are: (1) large-caliber glands that are more than twice the diameter of normal peripheral-zone glands; (2) preserved basal cells, as confirmed by basal cell markers; (3) cytologically malignant cells; and (4) an expansile cell mass that spans the glandular lumen. The fifth major criterion, central comedonecrosis, is diagnostic of IDC-P but is not always present. Minor criteria include glands with (1) right-angle branching or (2) smooth, rounded outlines, and (3) a two-cell population with an outer perimeter cell group composed of tall, pleomorphic, and mitotically active cells that stain poorly for prostate-specific antigen (PSA), and a central group that is cuboidal, monomorphic, and quiescent, with abundant cytoplasm containing abundant PSA and occasional extracellular mucin.