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Original contribution

Small cell–like change in prostatic intraepithelial neoplasia, intraductal carcinoma, and invasive prostatic carcinoma: a study of 7 cases

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Summary Small cell carcinoma of the prostate is associated with poor prognosis and different treatment from conventional acinar adenocarcinoma. Given the important clinicopathologic implications of a diagnosis of small cell carcinoma, we report 7 cases showing unusual, extensive small cell–like change in intraductal carcinoma and invasive carcinoma. Prostatic biopsies from 3 patients and radical prostatectomy specimens from 4 patients showed variably extensive small cell–like high-grade prostatic intraepithelial neoplasia and intraductal carcinoma. Five cases were associated with conventional acinar adenocarcinoma (2 cases with Gleason score 4 + 3 = 7; 3 cases with Gleason 3 + 4 = 7). No small cell carcinoma was seen. Small and large ducts with small cell–like change showed solid and cribriform proliferations of atypical cells with abrupt transition between centrally located populations of small cells and more typical large dysplastic cells at the duct periphery. Rosette-like formations were noted within some involved ducts. Small cell–like change was characterized by crowded cells with uniformly bland vesicular nuclei and minimal cytoplasm and no significant mitotic or apoptotic activity. In 3 cases, similar small cell–like morphology was noted focally in invasive carcinoma. The small cell–like areas were negative for synaptophysin and chromogranin, focally positive for TTF-1, and weakly positive for racemase. Ki-67 labeled less than 5% with predominant labeling of the larger atypical cells and minimal reactivity in the small cell–like population. In summary, small cell–like change in prostatic intraepithelial neoplasia, intraductal carcinoma, and invasive carcinoma is not associated with small cell carcinoma; shows no immunohistochemical evidence of neuroendocrine differentiation; and likely is not an adverse prognostic feature.

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1. Introduction

Small cell carcinoma of the prostate is an uncommon variant of prostatic carcinoma, which, similar to small cell carcinoma elsewhere in the body, carries a poor prognosis. The morphologic features are those of a high-grade malignant neoplasm with neuroendocrine differentiation characterized by small malignant cells with high nuclear-to-cytoplasm ratio, fine chromatin pattern, and prominent apoptosis, and mitotic activity [1].

Small cell neuroendocrine prostatic intraepithelial neoplasia (PIN) is an exceedingly rare PIN variant characterized by small cell morphology and neuroendocrine differentiation. Its prognostic significance and relationship to small cell carcinoma is currently not well defined, although the single documented case in the literature was associated with invasive mixed adenocarcinoma–small cell carcinoma [2]. However, approximately 50% of patients have de novo small cell carcinoma, with the remaining cases presenting with mixed conventional and small cell prostatic adenocarcinoma or as recurrent small cell carcinoma after hormonal therapy for conventional prostatic carcinoma [1]. As there are management implications in rendering a diagnosis of small cell carcinoma and possibly small cell neuroendocrine PIN, we herein describe extensive small cell–like change in PIN, intraductal carcinoma (IDC-P), and invasive carcinoma, which lacks immunohistochemical evidence of neuroendocrine differentiation.

2. Materials and methods

Seven cases were identified from the consult files of one of the authors (J. I. E.). Original hematoxylin and eosin (H&E)–stained sections in all cases were examined. Immunohistochemistry was performed in 7 cases at either Johns Hopkins Hospital (where blocks were available) or at the referring institution and included synaptophysin and chromogranin in 6 cases, PIN4 cocktail (high-molecular-weight cytokeratins/p63/AMACR) in 5, Ki-67 in 4, and TTF-1 in 4. PIN and IDC-P were defined using previously published diagnostic criteria [3-5]. Small cell–like change was characterized by crowded cells with uniformly bland vesicular nuclei and minimal cytoplasm.

3. Results

The Table summarizes the pathologic findings of 7 cases. Prostatic biopsies from 3 patients and radical prostatectomy specimens from 4 patients all showed variably extensive small cell–like change in IDC-P and high-grade PIN (HGPIN). Five cases were associated with conventional acinar adenocarcinoma (2 cases with Gleason score 4 + 3 = 7; 3 cases with Gleason 3 + 4 = 7). Of the remaining 2 cases without associated carcinoma, 1 was a set of core biopsies showing extensive IDC-P with small cell–like change, and the remaining case showed incidental focal HGPIN with small cell–like change in the prostate in a radical cystoprostatectomy specimen performed for invasive high-grade urothelial carcinoma. Small- and large-caliber ducts with small cell–like change typically showed solid and cribriform proliferations of atypical cells (Fig. 1A) with abrupt transition between mostly centrally located populations of small cells and large more typical PIN cells with enlarged nuclei and prominent nucleoli located at the duct periphery (Fig. 1B). Rosette-like formations were noted within some involved ducts in 3 cases (Fig. 1C). In 3 cases, similar small cell–like morphology was noted focally in the invasive component (Fig. 1D). No significant mitotic or apoptotic activity was identified in small cell–like areas (Fig. 1C). Of note, small cell–like change was not observed in nonneoplastic benign glands.

Table Clinicopathologic features

Case	Specimen	Small cell change	Coexisting carcinoma	Synaptophysin	Chromogranin	Racemase	TTF-1	Ki-67
1	RP	IDC-P, PIN, invasive carcinoma	4 + 3 = 7	Negative	Negative	Weak positive	Focally positive	<5%
2	RP	IDC-P, invasive carcinoma	3 + 4 = 7	Negative	Negative	–	Focally positive	–
3	RP	IDC-P	3 + 4 = 7	Negative	Negative	Weak positive	–	<5%
4	RCP	HGPIN	Bladder with invasive urothelial carcinoma	Negative	Negative	Weak positive	Negative	<5%
5	Bx	IDC-P, invasive carcinoma	4 + 3 = 7	–	–	Weak positive	Focally positive	–
6	Bx	IDC-P	None	Negative	Negative	–	–	–
7	Bx	IDC-P, invasive carcinoma	3 + 4 = 7	Negative	Negative	Negative	–	<5%

Abbreviations: RP, radical prostatectomy; RCP, radical cystoprostatectomy; Bx, biopsy; IDC-P, intraductal carcinoma; PIN, prostatic intraepithelial neoplasia; HGPIN, high-grade PIN.