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Original contribution

Variant of prostatic adenocarcinoma with Paneth cell–like neuroendocrine differentiation readily misdiagnosed as Gleason pattern 5☆

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Summary This study focused on 11 cases of prostatic adenocarcinoma with Paneth cell–like change, which had sparse to no Paneth cell–like granules; grading the tumor conventionally would have resulted in assigning a Gleason pattern 5 for the primary or secondary pattern. Ten cases were entirely composed of the Paneth cell–like component. Architectural patterns included the following: nest and cord-like architecture (n = 4; 36.4%), nests only (n = 6; 54.5%), and cords only (n = 1; 9.1%). All 11 cases had amphophilic cytoplasm. Among the 11 cases, 7 had rare granules, 1 had 10% of the cells with granules, and 3 had no granules. Within the Paneth cell–like feature component, rare nucleolar prominence was seen in only 4 (36.4%) of 11 cases. Eight cases were diffusely positive for chromogranin and synaptophysin, 2 for chromogranin only, and 1 for synaptophysin only. In the 3 cases where performed, Ki-67 showed a very low rate of less than 5%. The keys to recognizing these cases are as follows: (1) nests and cords in a small focus, (2) deeply amphophilic cytoplasm with careful search in most cases revealing rare Paneth cell–like eosinophilic granules, (3) indistinct nucleoli, and (4) immunohistochemical staining for neuroendocrine markers. Based on follow-up from prior studies and the current work, these tumors appear to have a favorable prognosis. The importance of recognizing this variant of adenocarcinoma with Paneth cell–like differentiation is that if these tumors were graded conventionally, 9 of the 11 cases would have been assigned a misleading Gleason score of 5 + 5 = 10 or 5 + 4 = 9.

1. Introduction

Neuroendocrine differentiation in prostatic adenocarcinoma has been well documented in various studies [1–4]. One of the types of neuroendocrine change that is commonly seen is Paneth cell–like change [5–7]. This change consists of cells with bright eosinophilic granules, which are chromogranin positive and contain neurosecretory granules by electron microscopy [8]. The current study is the first to systematically study a variant of adenocarcinoma of the prostate with Paneth cell–like change that is particularly difficult to diagnose and that has significant grading implications.

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2. Materials and methods

The Hopkins Pathology Database system was used to search for cases of prostatic adenocarcinoma with Paneth cell–like neuroendocrine differentiation from 2002 to 2014. Eighty-three cases were identified. Seventy-two cases had numerous Paneth cell–like granules (Fig. 1A) and were not further studied. The remaining 11 cases with sparse to no Paneth cell–like granules formed the basis of the current study. All 11 cases were obtained by transrectal ultrasound-guided needle biopsy specimens and had been sent to our institution for expert consultation.

The percentage of Paneth cell–like change present in the tumor was quantified. The presence of nests, cords, nucleolar prominence, and cytoplasmic granules along with staining pattern of the cytoplasm were also described. For the purpose of this study, cancers with Paneth cell–like change were Gleason graded as if they were the usual type of prostatic carcinoma. In addition, usual prostatic adenocarcinoma, if present, was also assigned a Gleason grade.

For cases with available unstained slides, immunoreactivity to chromogranin, synaptophysin, NKX3.1, and Ki-67 was performed. Immunohistochemical staining for synaptophysin (Leica; Buffalo Grove, IL), chromogranin (Ventana, Tucson, AZ), NKX 3.1 (Biocare, Concord, CA), and Ki-67 (Ventana) were done on 5-μm-thick formalin-fixed, paraffin-embedded sections using automated immunohistochemical stainers (Bond Leica [Leica Microsystems, Bannockburn, IL] or

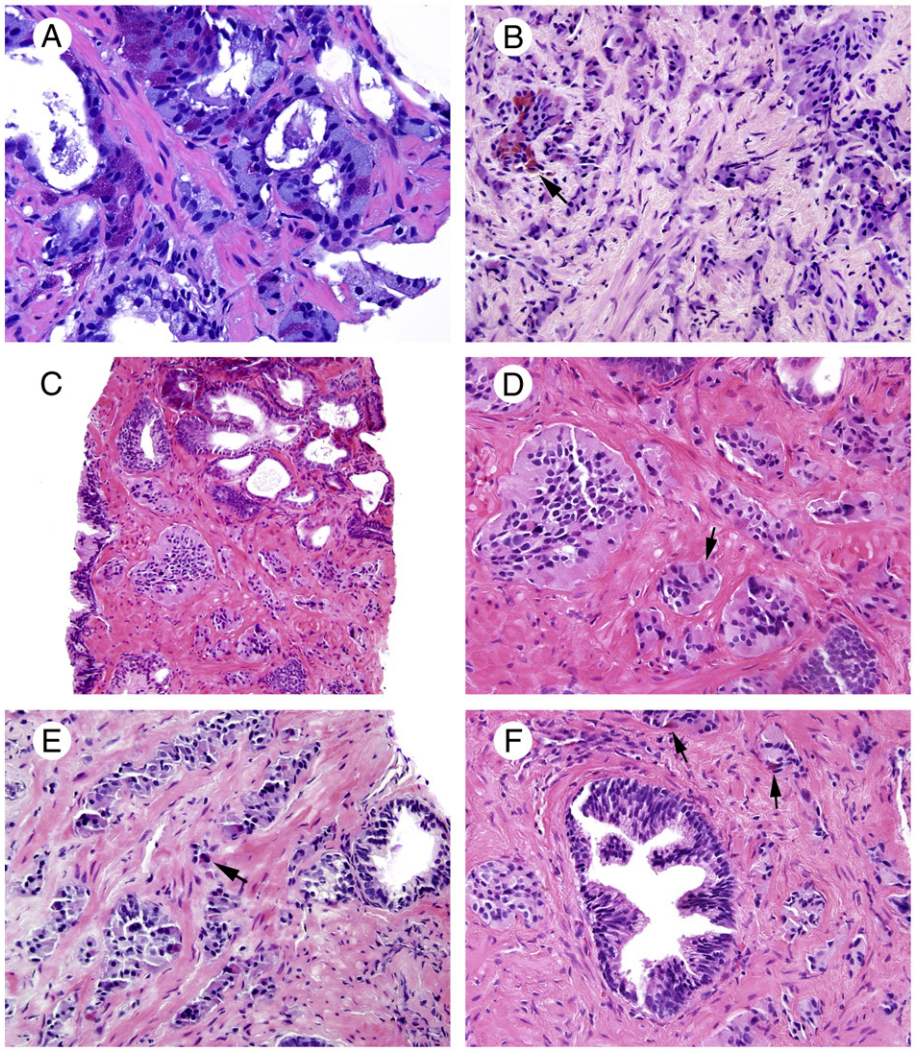

Fig. 1 A, Adenocarcinoma of the prostate with numerous Paneth cell–like granules. Note densely amphophilic cytoplasm of cells lacking eosinophilic granules (hematoxylin and eosin [H&E], ×20). B, Adenocarcinoma with Paneth cell–like change composed of nests and cords with focal cells displaying cytoplasmic eosinophilic granules (arrow) and others dense amphophilic cytoplasm (H&E, ×10). C, Adenocarcinoma with Paneth cell–like change. Areas of tumor are composed of well-formed glands with eosinophilic granules (top) and others nests of cells (bottom), lacking granules (H&E, ×4). D, Higher magnification of panel C showing nests of cells with bland nuclei and amphophilic cytoplasm. Rare cells with Paneth cell–like granules are noted (arrow) (H&E, ×20). E, Cords of adenocarcinoma of the prostate with amphophilic cytoplasm and scattered cells with eosinophilic granules (arrow; H&E, ×20). F, Nests of adenocarcinoma of the prostate with amphophilic cytoplasm and rare cells with eosinophilic granules (arrows; H&E, ×20).