

CASE REPORT

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Prostatic adenocarcinoma with a peculiar morphology – a rare case of pseudohyperplastic variant with inverted polarity

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Abstract

Background: The inverted (hobnail) variant of high-grade prostatic intraepithelial neoplasia (HGPIN) has been reported in two previous series and one case of inverted polarity in invasive adenocarcinoma has been reported. We reported an additional case of invasive carcinoma with this peculiar morphology.

Case presentation: We reported an additional case of invasive carcinoma with this peculiar morphology. A prostatectomy specimen of a 64-year-old patient showed a GG2 adenocarcinoma with extensive intraprostatic perineural infiltration and extraprostatic extension. Half of the entire tumor showed a distinctive inverted morphology.

Conclusion: Although pseudohyperplastic adenocarcinoma is believed to be a low-grade tumor to be graded as Gleason pattern 3, awareness of this morphology is important to collect more information on its biologic behavior and clinical implication.

Keywords: Prostate, Adenocarcinoma, Prostatic Intraepithelial Neoplasia

Background

The inverted (hobnail) variant of high-grade prostatic intraepithelial neoplasia (HGPIN) has been reported in two series (Argani and Epstein 2001; Öznur et al. 2015). Only one case of inverted polarity in invasive adenocarcinoma has been described (Öznur et al. 2015). We reported an additional case of invasive carcinoma with this peculiar morphology. Since these tumors are currently diagnosed as (low grade) pseudohyperplastic variant of prostatic adenocarcinoma, awareness of this morphology (or maybe sub-variant) is important to collect more data on the clinical implications of this distinctive morphology.

Case presentation

A 64-year-old patient sought urologic assistance due to an elevated serum Prostate Specific Antigen (PSA) level (7.2 ng/mL). His previous medical history was unremarkable. A biopsy was performed (and evaluated by other Pathology Laboratory) with diagnosis of GG1 adenocarcinoma. The treatment option was for a radical prostatectomy without lymphadenectomy. The specimen (41 g, 5.5 × 4.0 × 2.5 cm) revealed a GG2 adenocarcinoma with extensive intraprostatic perineural infiltration and extraprostatic extension (at left posterior base and left posterior mid-gland). Surgical margins were negative. The multifocal tumor involved 20% of the whole gland with 2% of gland involvement by Gleason pattern 4. Gleason pattern 4 consisted predominantly of poorly formed glands, with minor coexistent cribriform morphology. PSA was undetectable in serum collected 45 days after surgery.

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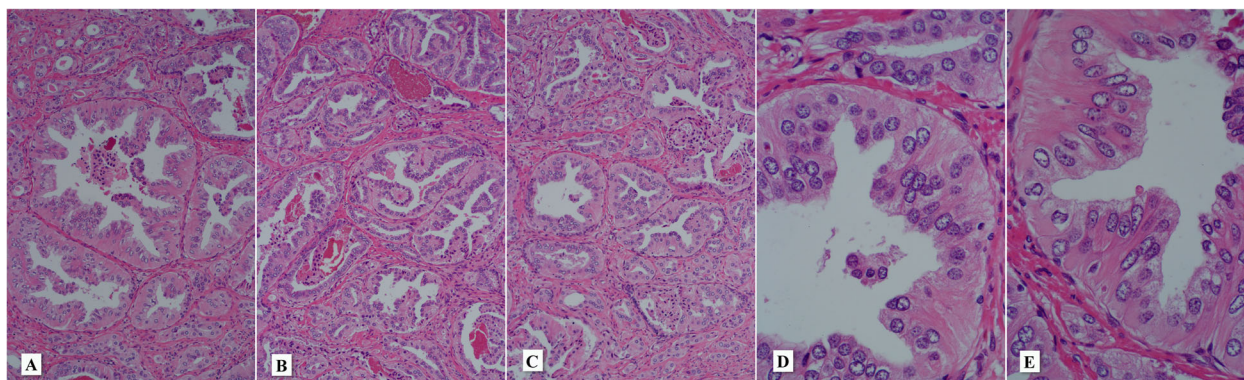


Fig. 1 Invasive prostatic adenocarcinoma with pseudohyperplastic morphology and inverse polarity. See nuclei arranged towards the lumen. Microscopic architecture is very reminiscent of high-grade prostatic neoplasia with inverted polarity. Hematoxylin and eosin stain: A,B and C (40x) and D and E (400x)

Despite the presence usual acinar adenocarcinoma of both Gleason pattern 3 and Gleason pattern 4 morphologies, 50% of the entire tumor was composed of a pseudohyperplastic component with peculiar, inverted polarity (Figs. 1 and 2). In these areas, almost all nuclei were arranged away from the basement membrane and located close to glandular lumina. This component showed extensive association with intraprostatic perineural infiltration and extraprostatic extension (Figs. 3 and 4). Immunohistochemical antibody cocktail staining (P63, high molecular weight cytokeratins and alpha-methylacyl-CoA racemase, AMACR) showed that most of pseudohyperplastic / inverted component was devoid of basal cells and showed weak AMAC staining (Fig. 5). Minor areas with this morphology showed preserved basal cells which was consistent with the diagnosis of inverted HGPI (see discussion).

Discussion

Twenty years ago, Argani and Epstein described the inverted (hobnail) variant of high-grade prostatic intraepithelial neoplasia (Argani and Epstein 2001). These lesions were characterized by the arrangement of nuclei polarized towards the lumen. Among 15 cases reported, seven were associated with invasive acinar adenocarcinoma (usual type). In 2015, Öznur and colleagues described additional 13 cases of inverted variant of HGPI N, seven associated with invasive adenocarcinoma – and one of them with inverted polarity also in the invasive component (Öznur et al. 2015). To the best of our knowledge, this is the second reported case of pseudohyperplastic (HGPI-like) invasive adenocarcinoma with inverted polarity.

In current practice, an invasive prostatic adenocarcinoma that resembles high-grade prostatic intraepithelial neoplasia is better designated pseudohyperplastic variant

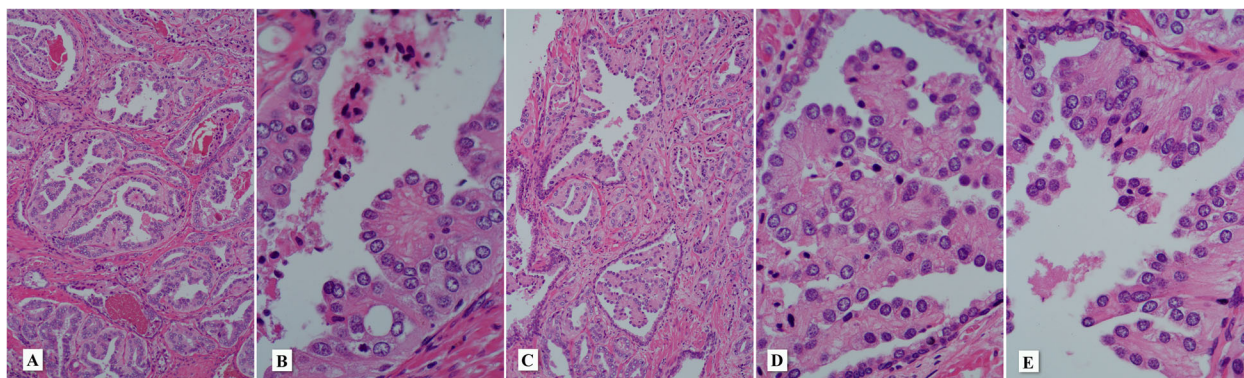


Fig. 2 Small micropapillary projections in invasive prostatic adenocarcinoma with pseudohyperplastic morphology and inverse polarity (A–D). This proliferation can be seen within preexistent ducts with bland double epithelial layer suggesting colonization of benign glands (C–E). Hematoxylin and eosin stain: A (100x), B (400x), C (100x), D (400x) and E (400x)

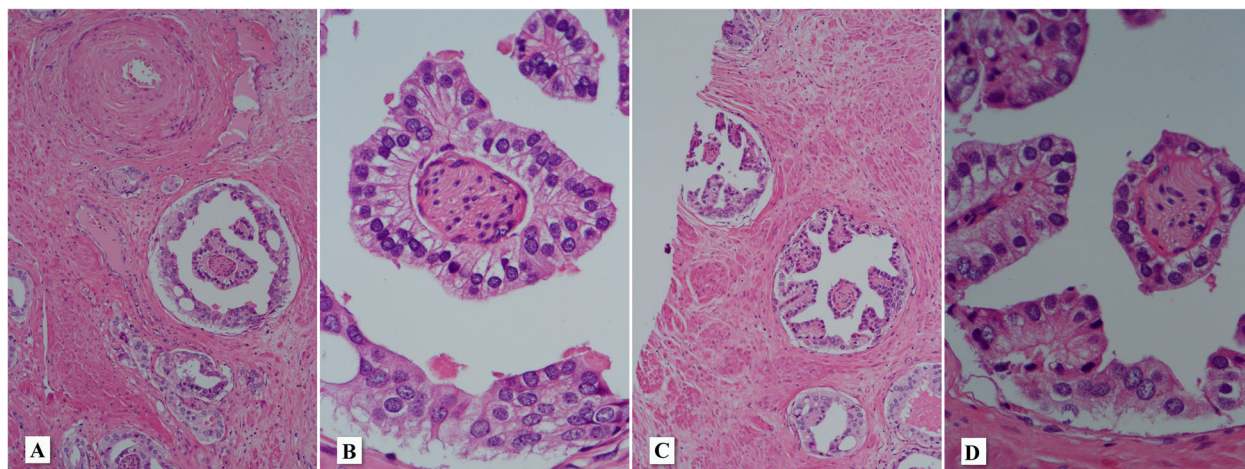


Fig. 3 Obvious perineural invasion by prostatic adenocarcinoma with pseudohyperplastic morphology and inverse polarity. Hematoxylin and eosin stain: A (100x), B (400x), C (100x) and D (400x)

(Paulk et al. 2018). Pseudohyperplastic variant shows dilated glands with papillary infolding which may be very reminiscent of benign glands. These glands are lined by a single layer of cells that show vesicular/round nuclei with macronucleoli or bland nuclei with deceptive benign appearance. Infiltrative pattern of growth, a high index of suspicion and awareness of this variant, and ancillary investigation of basal cells by immunohistochemistry are crucial for the diagnosis (Humphrey et al. 1998, Levi and Epstein 2000; Arista-Nasr et al. 2015; Humphrey 2018). These tumors are considered low-grade and graded as Gleason pattern 3 by consensus (Epstein et al. 2005). In contrast, ductal PIN-like

adenocarcinoma is characterized by the same architectural changes but show pseudostratified lining. By definition, ductal adenocarcinoma of the prostate is composed by columnar/tall cells and graded as Gleason pattern 4. Recent data suggest that ductal adenocarcinomas with PIN-like architecture (PIN-like ductal adenocarcinoma) show a more indolent behavior and, therefore, should be also graded as Gleason pattern 3 (Paulk et al. 2018; Zhou 2018).

Conclusions

This is the second report case of invasive prostatic adenocarcinoma with pseudohyperplastic morphology

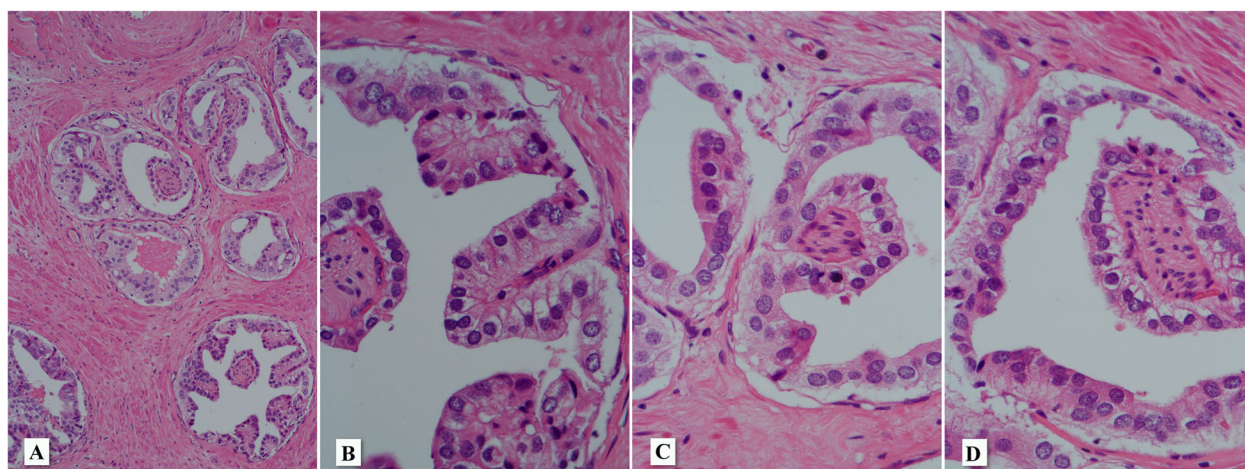


Fig. 4 Other illustrative areas of extensive perineural invasion by prostatic adenocarcinoma with pseudohyperplastic morphology and inverse polarity. Hematoxylin and eosin stain: A (100x), B (400x), C (100x) and D (400x)

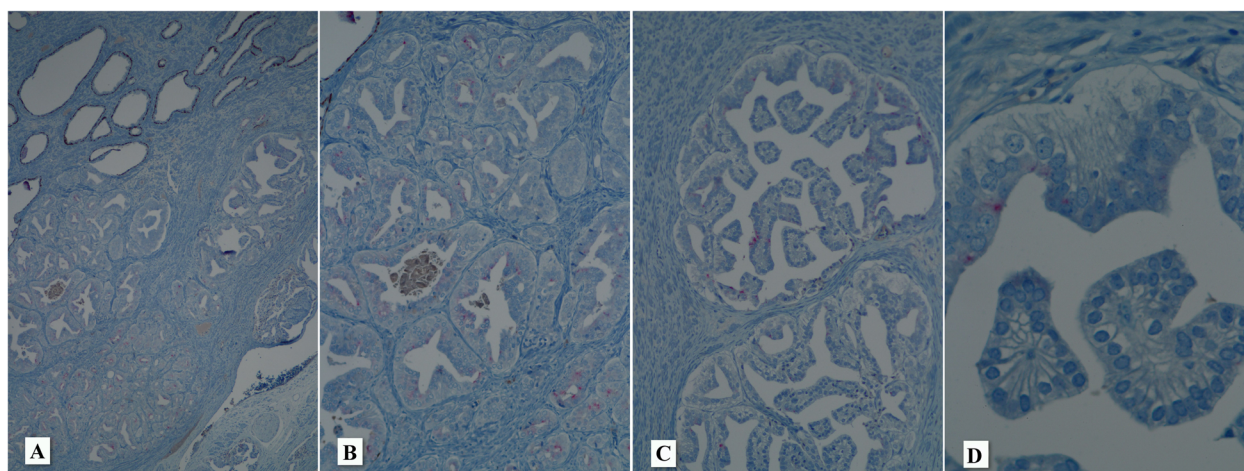


Fig. 5 Invasive prostatic adenocarcinoma with pseudohyperplastic morphology and inverse polarity showing absence of basal cells and weak cytoplasmic/luminal expression of alpha-methylacyl-CoA racemase. Immunohistochemical antibody cocktail staining – P63 and high molecular weight cytokeratins (peroxidase - brown) and alpha-methylacyl-CoA racemase (phosphatase - red): A (40x), B and C (100x) and D (400x)

and inverse polarity. Although pseudohyperplastic adenocarcinoma is believed to be a low-grade tumor to be graded as Gleason pattern 3, this particular tumor showed extensive extraprostatic extension and association with higher grade component. Awareness of this morphology is important to collect more information on its biologic behavior and clinical implication.

Abbreviations

AMACR: alpha-methylacyl-CoA racemase; HGPIN: Hematoxylin and eosin stain

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None.

Authors' contributions

DAA conceived the idea. DAA was the major contributor to the writing of the manuscript. DDA, MFS and MEPA diagnosed the cases. MSF and MEPA were major contributors for critically revising the manuscript for important intellectual content. The authors read and approved the final manuscript.

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Availability of data and materials

Supplementary data is available upon request.

Declarations

Ethics approval and consent to participate

Not applicable.

Written informed consent was obtained from the patient for participation in this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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