

Atrophic-pattern prostatic adenocarcinoma: a diagnostic pitfall

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Abstract

The atrophic pattern of prostatic adenocarcinoma is an uncommon histological pattern of acinar prostatic adenocarcinoma. Due to its deceptively benign histological appearance, it can be misdiagnosed as a benign entity. We report a case of atrophic pattern prostatic adenocarcinoma in an elderly male patient, highlighting key histopathological findings and prognostic implications. This pattern closely resembles benign atrophy, and we discuss the differences in architectural and cytological features, as well as the role of immunohistochemistry as a diagnostic adjunct. It is vital to recognise benign-appearing variants of prostatic adenocarcinoma to prevent misdiagnosis and ensure appropriate clinical management.

Keywords Benign atrophy; immunohistochemistry; needle biopsy; prostate cancer; urologic pathology; uropathology

Case report

A 72-year-old male presented with a six-month history of worsening lower urinary tract symptoms, including urinary frequency, reduced flow, and nocturia. Digital rectal examination revealed a smooth, enlarged prostate and serum prostate-specific antigen was elevated.

An MRI scan identified a 3.5 cm left mid-gland to apical peripheral zone T3a tumour, PI-RADS and Likert scores of 5, with no regional lymph node involvement. Nuclear medicine bone scan showed no bone metastases.

Targeted and systematic prostate biopsies revealed adenocarcinoma with Gleason scores of 3 + 4 = 7 (right posterior), 3 + 3 = 6 (right anterior), 4 + 5 = 9 (left prostate), corresponding to ISUP grade group 5. The area of interest for discussion was a focus measuring 3 mm in length from the right anterior prostate

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core. It showed small, separate, infiltrative acini with cells showing scant cytoplasm, prominent macronucleoli, and mildly enlarged nuclei (Figures 1 and 2). Immunohistochemistry for AMACR showed diffuse strong positivity in the atypical cells, whereas CK5 did not highlight any basal cells in the acini (Figures 3 and 4).

The final diagnosis was prostatic adenocarcinoma, Gleason score 4 + 5 = 9 (6/7 cores) T3a N0 Mx, Cambridge Prognostic Group 5. The patient was commenced on hormone therapy and considered for radical radiotherapy.

Discussion

Atrophic pattern prostatic adenocarcinoma is an uncommon histological pattern of prostatic acinar adenocarcinoma as recognised in the 5th edition of the WHO Classification of Urinary and Male Genital Tumours.¹ It represents a diagnostic pitfall in prostate pathology and is reported to be seen in up to 16% of radical prostatectomy specimens and 2% of needle biopsies.^{2,3} This pattern can arise sporadically, after radiotherapy or hormone treatment. The atrophic pattern is one of several uncommon histological patterns of prostatic acinar adenocarcinoma (atrophic, pseudohyperplastic, microcystic, foamy gland, mucinous). These patterns can mimic benign lesions and may lead to diagnostic challenges.^{1,3,4}

There is no literature on the macroscopic description of atrophic pattern adenocarcinoma. On microscopy, consistent with the case report, there is an invasive arrangement of glands with reduced cytoplasmic volume, mimicking benign atrophic glands. The cells have an amphophilic or eosinophilic cytoplasm, macronucleoli and nucleomegaly. However, nuclear atypia can be difficult to identify due to nuclear compression, which adds to the diagnostic difficulty. This focus of atrophic pattern is typically admixed with malignant glands of non-atrophic pattern usual acinar adenocarcinoma with a moderate amount of cytoplasm, averaging 16–25% of the total adenocarcinoma, with a broad range of 10–90% in needle core biopsies and 1–70% in radical prostatectomies.^{1–5} There have been no reported cases of pure atrophic pattern adenocarcinoma. Due to its resemblance to benign atrophic lesions (Figures 5 and 6), pure atrophic pattern adenocarcinoma should rarely be diagnosed on core biopsy specimens. The differential diagnosis for atrophic acini includes sclerosing atrophy, post-atrophic hyperplasia, and full or partial atrophy. Compared to these benign lesions, atrophic pattern

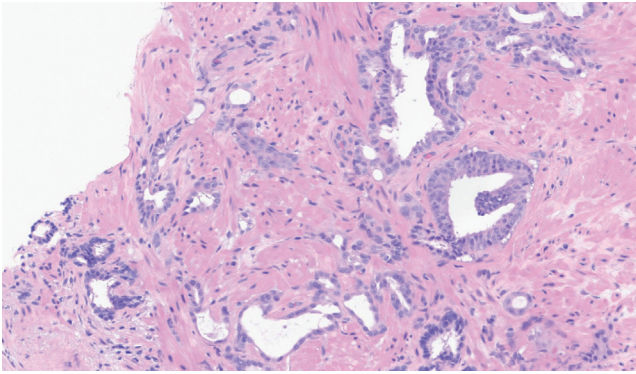


Figure 1 Prostatic acinar adenocarcinoma. Small infiltrative and atypical arrangement of atrophic glands admixed with usual acinar adenocarcinoma. H&E of prostate core biopsy on $\times 200$ magnification.

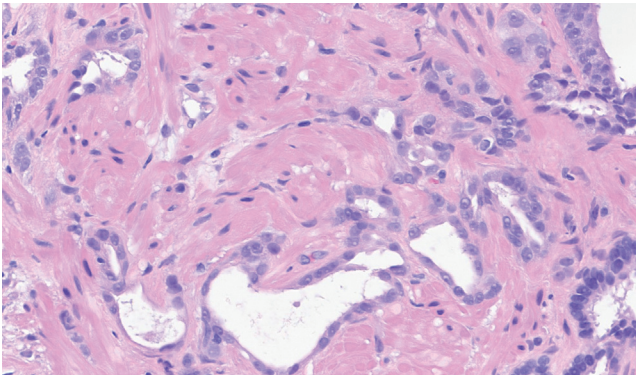


Figure 2 Prostatic acinar adenocarcinoma. Malignant atrophic glands have cytoplasmic volume loss, prominent macronucleoli, and occasional hyperchromatic and enlarged nuclei. H&E of prostate core biopsy on $\times 400$ magnification.

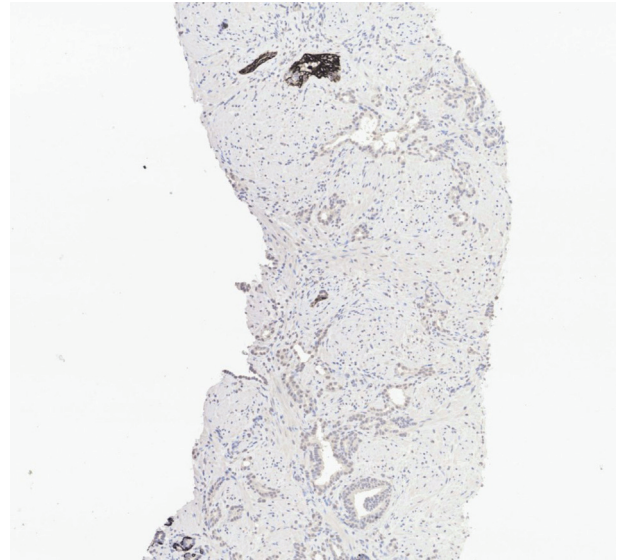


Figure 4 Prostatic acinar adenocarcinoma. Small malignant atrophic glands showing negative staining for CK5 on immunohistochemistry.

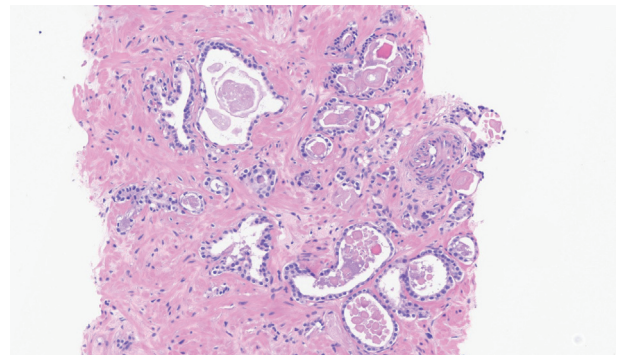


Figure 5 Prostatic acinar adenocarcinoma. An example of atrophic pattern prostatic adenocarcinoma. Intraluminal eosinophilic secretions and crystalloids are present within malignant atrophic glands. H&E of prostate core biopsy on $\times 200$ magnification.

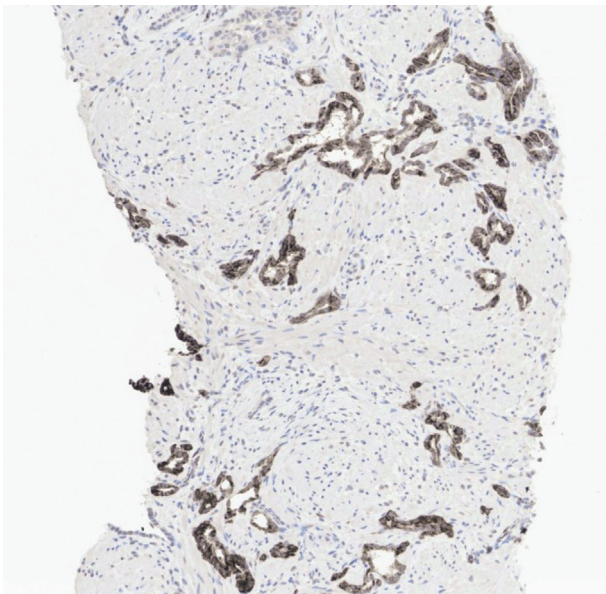


Figure 3 Prostatic acinar adenocarcinoma. Small malignant atrophic glands showing positive staining for AMACR on immunohistochemistry.

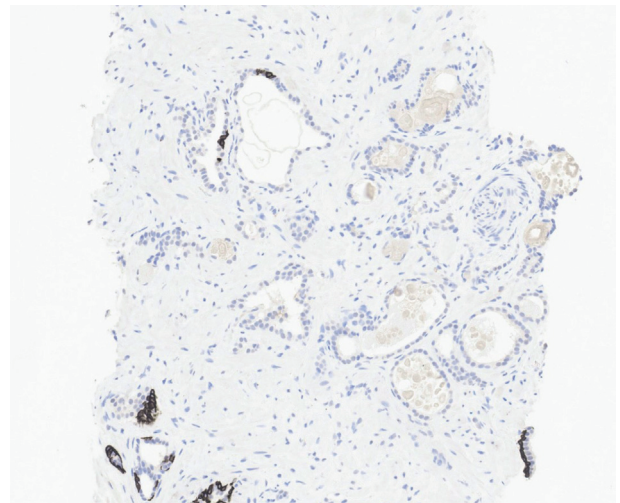


Figure 6 Prostatic acinar adenocarcinoma. An example of atrophic pattern prostatic adenocarcinoma glands showing negative staining for CK5 on immunohistochemistry.

adenocarcinoma is characterised by infiltrative growth, rigid luminal borders, nuclear atypia, and a complete, diffuse absence of basal cells. In some cases, additional features such as intraluminal eosinophilic secretions, intraluminal wispy blue mucin, intraluminal crystalloids, and perineural invasion may also be present.⁶

Immunohistochemistry is a valuable adjunct in most cases but should not be solely relied upon. The acini in atrophic pattern adenocarcinoma consistently demonstrate a complete loss of basal cells as evidenced by negative staining for p63 or high-molecular-weight cytokeratins such as CK5. It is important to note that expression of AMACR is diminished in atrophic pattern adenocarcinoma with 70% of cases being positive as compared to approximately 90% of usual acinar adenocarcinoma cases. This shows that a negative AMACR immunostain is not informative in differentiating between atrophic adenocarcinoma and benign atrophy. AMACR can also be positive in 4% of benign atrophy and up to 79% of partial atrophy. ERG has limited diagnostic value in distinguishing atrophic pattern adenocarcinoma from benign atrophy. While benign atrophy is consistently negative for ERG, approximately 50% of prostatic adenocarcinomas demonstrate expression for ERG.⁴

Atrophic pattern adenocarcinoma is often classified as a proliferative Gleason pattern 3. The associated usual acinar adenocarcinoma is typically pattern 3, although in approximately 13% of cases, a high-grade pattern 4 component is present. The proliferation index of atrophic pattern adenocarcinoma (4%) is comparable to that of usual acinar adenocarcinoma (5%), with apoptosis being infrequent in both. Clinically, the presence or absence of atrophic change does not affect prognosis since prognosis is primarily determined by Gleason score and tumour stage.^{2,4}

Atrophic pattern adenocarcinoma, as an uncommon histological pattern, represents one of several potential diagnostic pitfalls in the histological assessment of prostate biopsies.⁷ Given the limited tissue available in prostate core biopsies, histological examination remains the main part of cancer diagnosis, significantly influencing patient management and prognosis. Therefore, awareness of potential diagnostic pitfalls is essential to prevent misdiagnosis and ensure timely, appropriate treatment.

Conclusion

This case report describes a 72-year-old male diagnosed with prostatic adenocarcinoma, including an uncommon atrophic pattern on histology. Atrophic pattern prostatic adenocarcinoma can be mistaken for benign atrophy, potentially leading to delayed or inappropriate treatment. This report discusses the histological features distinguishing malignant from benign atrophic acini and highlights the role of immunohistochemical stains as useful adjuncts in diagnosis. ◆

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Practice points

- Atrophic pattern prostatic adenocarcinoma is an uncommon histological pattern of prostatic acinar adenocarcinoma, which can be interpreted as benign atrophy in clinical practice
 - Maintain a high degree of suspicion if there are foci of hyperplastic and atrophic glands showing degrees of distorted and infiltrative architecture
 - Besides atrophic pattern, be aware of other benign-appearing histological variants, such as pseudohyperplastic, microcystic, foamy gland, and mucinous
- Histological features consistent with atrophic pattern prostatic adenocarcinoma:
 - Invasive glandular growth pattern
 - Cells demonstrate an amphophilic cytoplasm with the presence of macronucleoli and nucleomegaly
- Immunohistochemistry is useful but be mindful of its limitations:
 - AMACR overexpression is seen in the malignant glands, however, compared to 90% of usual acinar adenocarcinoma staining positive on immunohistochemistry, only 70% of atrophic pattern adenocarcinoma stain positive
 - p63 or high-molecular-weight cytokeratin such as CK5 will show a lack of basal cells within the glands

Self-assessment questions

1. Which of the following is NOT a histological pattern of prostatic acinar adenocarcinoma from the WHO classification?

- A. Atrophic
- B. Microcystic
- C. Mucinous
- D. Anaplastic

Answer: D

2. What is the typical Gleason pattern in atrophic adenocarcinoma?

- A. 2
- B. 3
- C. 4
- D. 5

Answer: B

3. Which of the following immunohistochemical marker is the MOST useful in confirming the malignant nature of atrophic glands?

- A. AMACR
- B. CK5
- C. PSA
- D. NKX3.1

Answer: B