



## Clear Cell Cribriform Hyperplasia of the Prostate: A Potential Diagnostic Pitfall

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### Abstract:

Cribriform lesions of the prostate can be of difficult histological interpretation and have diagnostic pitfalls. We discuss the case of a patient presenting with urinary obstruction symptoms for which he underwent transurethral prostatic resection. Histology of the prostate chips revealed a cribriform lesion which posed a challenging differential diagnosis between benign hyperplastic lesion, prostatic intraepithelial neoplasia and possibly a malignant lesion. The careful examination of the cytology of the lesion, the use of immunohistochemistry and peer review of the case helped excluding cribriform prostatic carcinoma and cribriform intraepithelial neoplasia. We diagnosed this case as clear cell cribriform hyperplasia, an uncommon variant of benign prostatic hyperplasia which does not carry any malignant potential. Awareness about this entity is essential to avoid misdiagnosis which can potentially lead to a wrong clinical management.

**Key words:** Prostatic Hyperplasia, Adenocarcinoma, Prostatic Intraepithelial Neoplasia, Prostatic Neoplasms, Humans.

### Introduction

Clear cell cribriform hyperplasia of the prostate is an uncommon variant of benign prostatic hyperplasia which can be misdiagnosed as prostatic cancer or prostatic intraepithelial neoplasia, potentially leading to a wrong clinical management of the patient.

### Case Report

A 70 years old man presented to the urology clinic for regular follow up of a Gleason grade 3+3 prostatic carcinoma, diagnosed 5 years before. PSA level at diagnosis was 2.1 µg/L and 4.45

µg/L on the last clinic appointment. He complained of urinary obstruction symptoms despite treatment with Tamsulosin. Urodynamic tests were essentially equivocal but due to ongoing symptoms a cystoscopy was performed. The patient was found to have a moderately enlarged occlusive prostate which was treated with transurethral resection. Prostate chippings were sent for histological assessment as per protocol.

Histology of the prostate chips revealed a lesion characterized by a crowded proliferation of complex glands with many cells containing

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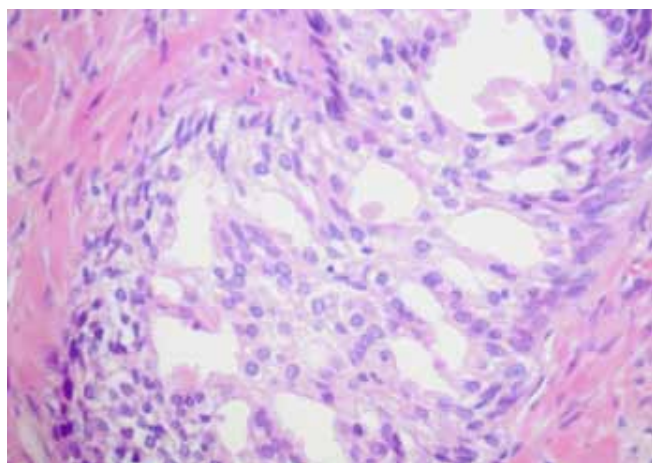
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clear cytoplasm [Fig.1]. Differential diagnoses considered were: clear cell cribriform hyperplasia, prostatic intraepithelial neoplasia and Gleason grade 4 cribriform prostatic adenocarcinoma. Immunohistochemistry was performed for cytokeratin 5/6 and 34 beta E12 [Fig.2]. These stain highlighted a basal cell layer around the glands in the periphery, ruling out prostatic adenocarcinoma. The differentiation between prostatic intraepithelial neoplasia and cribriform hyperplasia was done on the basis of cellular atypia and presence of nucleoli which are absent in this case. Moreover immunostaining with P504S showed weak staining pattern supporting a benign lesion in contrast to a strong reaction pattern expected in prostatic intraepithelial neoplasia [Fig.3].

Patient continued to follow the scheduled surveillance urology appointments.

## Discussion

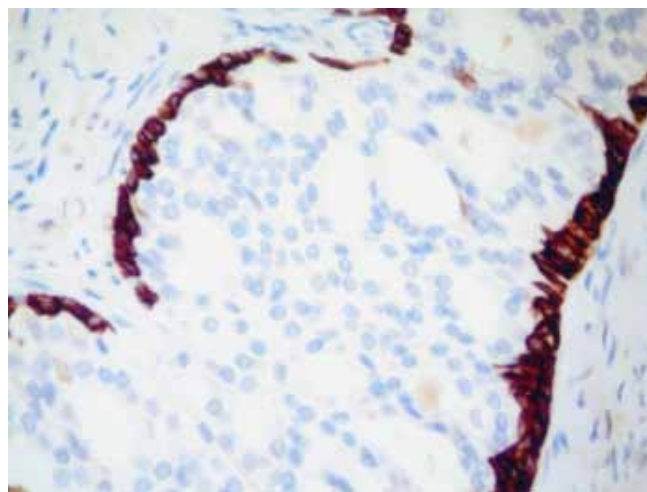
Analysis of prostatic core biopsies or prostatic chips



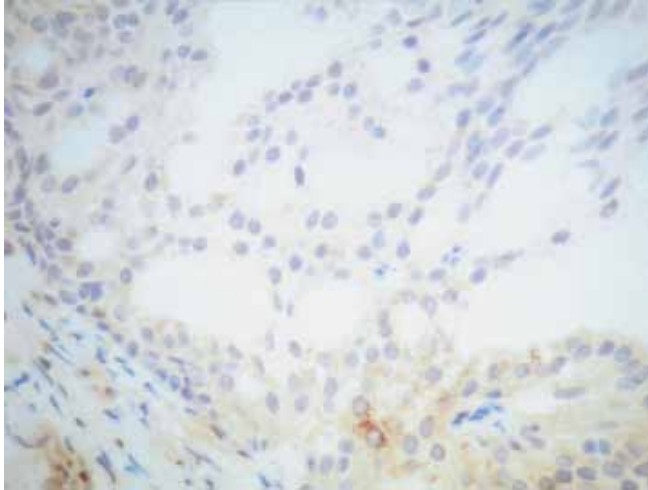
**Fig.1:** Clear cell cribriform hyperplasia. High power view of a crowded proliferation of glands with cribriform architecture. Cells have clear cytoplasm, uniform nuclei and lack nucleoli. (haematoxylin and eosin, original magnification x40).

can be problematic when facing benign condition that mimics prostatic intraepithelial neoplasia and prostatic adenocarcinoma. One of these mimics is represented by clear cell cribriform hyperplasia. This lesion is usually seen in the transitional zone as part of benign nodular epithelial hyperplasia. It is characterised by a crowded proliferation of complex glands without significant cytological atypia. In most instances, the cribriform glands have uniform round lumina and clear cytoplasm, hence the name “clear cell cribriform hyperplasia”. At low power the lesion generally has a nodular appearance and intervening cellular stroma is seen. The cells comprising the central cribriform areas are cuboidal to low columnar secretory-type cells with uniform round nuclei and clear cytoplasm. They lack nuclear atypia and nucleolar enlargement. Basal cells are prominently displayed around the periphery [1].

Clear cell cribriform hyperplasia enters the differential diagnosis of Gleason grade 4 cribriform prostatic carcinoma. The distinction of clear cell cribriform hyperplasia from cribriform



**Fig.2:** Positivity of the basal cell layer for 34 beta E12 anti-high-molecular-weight keratin antibody (immunoperoxidase with haematoxylin counterstain, original magnification x40).



**Fig.3:** Weak pattern of stain of the cells for P504S antibody (immunoperoxidase with haematoxylin counterstain, original magnificationx40).

carcinoma is based on the 'low power' nodularity, cellular stroma, presence of basal cells and lack of significant cytological atypia [1,2]. It is possible to demonstrate a basal cell layer with the use of the 34 beta E12 anti-high-molecular-weight keratin antibody that reacts with the basal cells but not with the acinar cells of the prostate. A continuous basal cell layer is not evident in presence of a prostatic adenocarcinoma [2].

Basal cell markers are not very helpful in discriminating cribriform hyperplasia from architectural similar foci of high grade PIN since both entities may present a patchy peripheral basal cell layer and focal or absent basal myoepithelial cells in the bridges of the cribriform duct. The discrimination of the two lesions is therefore based on the evaluation of nuclear atypia, which lacks in the hyperplastic glands and is present in PIN [3,4]. Immunostain for P504S can also be of support since the pattern of staining is circumferential luminal and diffuse granular cytoplasmic in high grade PIN and prostatic adenocarcinoma but patchy weak in benign lesion [5].

It is important to notice that a misdiagnosis of Gleason grade 4 prostatic carcinoma would have resulted in the patient been offered a radical prostatectomy or radical radiotherapy resulting in an unnecessary treatment. Moreover a misdiagnosis of high grade PIN would have been followed by unnecessary repeat prostatic biopsies. In this case instead the patient continued with his yearly PSA level monitoring.

## Conclusion

Cribriform hyperplasia is a form of benign prostatic hyperplasia that can be misdiagnosed for prostatic carcinoma or cribriform PIN. An immunohistochemical panel with 34betaE12, CK5/6, and P504S can help in reaching the correct diagnosis. Awareness of this histological entity is important for correct diagnosis and consequent patient management.

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