



Florid Basal Cell Hyperplasia Mimicking Prostatic Carcinoma: Report of 2 Cases

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Abstract:

Basal cell hyperplasia, a common finding in benign prostatic hyperplasia, refers to proliferation of basal/reserve cells. However, occasionally it is so florid and extensive that it can be mistaken for carcinoma. Accurate distinction separating benign and malignant lesions is critical for appropriate management. We report two elderly gentlemen who presented with signs and symptoms of prostatomegaly, histology showed florid basal cell hyperplasia with pseudo-infiltrative pattern raising a doubt of carcinoma warranting a second opinion. Review of histopathology with multiplex immunohistochemistry panel combining basal cell, metabolic, proliferation and other markers proved the benign nature of the lesion. Thereby, we conclude that although morphologic criteria guide diagnosis, immunohistochemistry confirms the benign nature resolving the dilemma even on limited material.

Key words: Carcinoma, Hyperplasia, Immunohistochemistry, Prostatic Hyperplasia, Prostatic Neoplasms.

Introduction

Ordinary basal cell hyperplasia (BCH) is a common finding in benign prostatic hyperplasia (BPH); however, occasionally it is so florid and extensive that it can be mistaken for carcinoma [1]. Accurate distinction separating benign and malignant lesions is critical for an adequate treatment [2]. We present two cases highlighting the importance of histological features along with the rationale use of immunohistochemistry (IHC) panel including multiplex IHC (a combination of basal cell & metabolic markers) and proliferation markers to solve the dilemma.

Case Reports

Case 1

A 50 years old man presented with chronic retention of urine and bilateral hydronephrosis. The cystoscopy showed a moderately enlarged prostate gland (32 grams) with a papilla-like lesion projecting into the prostatic urethra from bladder neck on the left side. Serum PSA was within normal limits. The patient was catheterised to decompress the bladder, followed by transurethral resection of prostate (TUR-P) 3 weeks later.

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We received paraffin blocks for IHC with a prior diagnosis of possibility of a dual malignancy of co-existent basal cell carcinoma with an intraductal papillary transitional cell carcinoma. H & E examination showed florid basal cell hyperplasia with solid and cribriform patterns and pseudo-infiltrative appearance at places [Fig.1,2]. Few other fragments showed features of an inverted urothelial papilloma. Occasional mitotic figures were noted. There was no evidence of necrosis or perineural invasion. The multiplex IHC (AMACR + p63 + CK 5 + CK 14) showed an intact basal cell layer throughout the lesion and a dim AMACR ruling out prostatic adenocarcinoma [Fig.3]. BCL-2, SMA & S-100 were uniformly positive. Her-2neu was equivocal. PSA was positive in the luminal layer of the glands. Chromogranin was negative. Uroplakin highlighted the inverted papilloma. Ki-67 index was 9%-11%. The case was concluded as florid BCH of varying degrees and patterns along with an inverted papilloma and focal adenomatous hyperplasia with focal squamous metaplasia and prostatitis with no features of malignancy.

The patient has been followed up for 18 months and is asymptomatic.

Case 2

A 63 years old man presented with hematuria and was found to have an enlarged prostate on ultrasound. Serum PSA was 22.6 ng/mL. We received paraffin blocks of trucut biopsy of prostate with a primary diagnosis of benign prostatic hyperplasia, however adenocarcinoma needs exclusion by IHC. H & E showed foci of crowded glands of varying sizes lined by cells having clear cytoplasm and basally located bland nuclei.

The multiplex IHC demonstrated a maintained basal cell layer throughout with foci of reserve cell hyperplasia. No AMACR prominence was identified. This case was also concluded as benign prostatic enlargement.

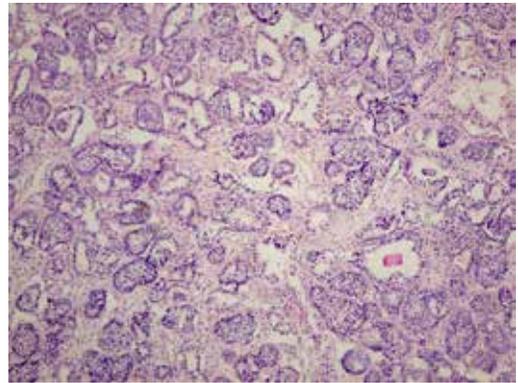


Fig.1: Florid basal cell hyperplasia (H & E stain, 100x).

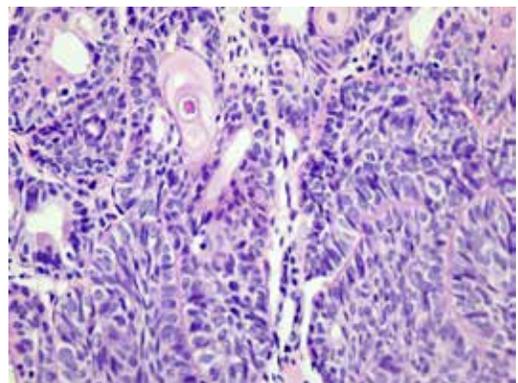


Fig.2: Florid basal cell hyperplasia (H & E stain, 400x).

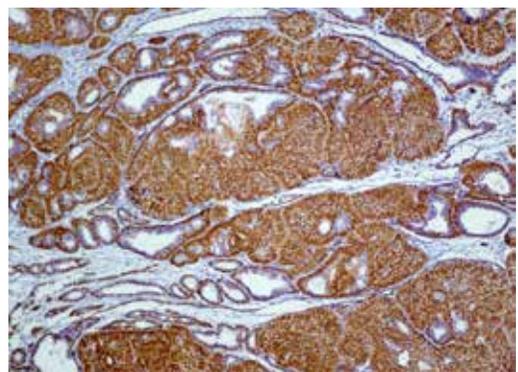


Fig.3: Multiplex IHC - intact basal cell layer highlighted by p63, CK 5, CK 14 and negative AMACR expression (100x).

Discussion

Basal cell proliferation in the prostate was first described in 1925. BCH resembles prostate acini seen in the fetus, accounting for the synonyms fetalisation and embryonal hyperplasia [3]. These arise from basal/reserve cells and are characterised by multilayering of the cells within the glands. It is important to recognise this pathological entity as it may be misdiagnosed as adenocarcinoma or high grade PIN, particularly when accompanied with cytological atypia or infiltrating patterns.

Young *et al.* [4] proposed a classification of benign BCH, which included complete BCH, incomplete BCH, atypical BCH, adenoid-cystic like BCH and atrophy associated BCH. Classic BCH may be confused with prostatic adenocarcinoma due to proliferation of small glands and occasional infiltrative appearance. Atypical BCH also mimics cancer and high grade PIN due to presence of nucleoli and mitotic figures [5]. These cases of atypical BCH are currently referred as “BCH with prominent nucleoli”. The adenoid-cystic like form of BCH requires distinction from basaloid carcinoma.

Other classification schemes include Bostwick's in which he separated BCH in four groups (complete and incomplete BCH, atypical BCH, basal cell adenoma and adenoid basal cell tumor) and suggested progression between these [6]. Grignon *et al.* [7] suggested a similar continuum of BCH, adenoid basal cell tumor an adenoid cystic carcinoma.

Four morphological findings of BCH have been reviewed by Rioux-Leclercq NC *et al.* [8]: intracytoplasmic globules, calcifications, squamous features and cribriform pattern. Our first case showed intracytoplasmic globules, squamous features in the form of squamous metaplasia and cribriform features. Intracytoplasmic globules, reported also by Yang *et al.* [9] has not been seen in other prostatic

lesions, especially prostatic adenocarcinoma or PIN. The knowledge of presence of squamous and cribriform features in BCH along with their light microscopic and IHC features can help to distinguish it from pre-neoplastic and neoplastic diseases. Van de Voorde and colleagues [10] described florid BCH as compact glandular proliferation with solid nests; the cytology in some areas looking disturbing because the cells have a moderately enlarged nucleus, often with a prominent nucleolus with few mitotic figures; the intervening stroma is scant and cellular; the lesions are not circumscribed and are intermingled with surrounding glands, giving the impression of infiltration. Both of our cases showed a similar morphology. Yang *et al.* [9] gave an additional criterion for florid BCH: extensive proliferation of basal cells involving more than 100 small crowded acini (in each section) forming a nodule.

Florid BCH especially with cribriform features and focal infiltrative patterns needs to be distinguished from basaloid cell carcinoma. The diagnostic criteria for basaloid cell carcinoma include: i) extensive infiltration between normal prostate glands, ii) extension out of prostate, iii) perineural invasion, or iv) necrosis [3,5,6]. Though there was a focal pseudo-infiltrative appearance, none of these features were seen in either of our cases.

Despite the well-characterised morphological features of BCH, the use of appropriate IHC markers is advantageous and helpful in arriving at the correct diagnosis, especially in florid BCH. A conventional prostatic adenocarcinoma shows AMACR positivity and loss of basal cell markers. The multiplex cocktail showed an intact basal cell layer (CK5, CK14 and p63 positive) and a dim or no AMACR staining in both our cases thereby ruling out prostatic adenocarcinoma. AMACR, also known as P504s is a molecular marker specific for prostate cancer. Yang *et al.* [1] observed AMACR positivity in

only in prostatic adenocarcinomas and in 2 possibly premalignant lesions, high grade PIN (50%) and atypical adenomatous hyperplasia (10-17.5%). Montirani *et al.* [3] have reported the expression of Her-2neu in basal cell proliferations whereas O.L. Bohn *et al.* [2] found a consistent negative expression in both hyperplastic and malignant cases. We found an equivocal Her-2neu expression. SMA and S-100 stains showed a uniform positivity confirming the basal myoepithelial differentiation that appears in BCPs, both benign and malignant [3,9,10]. Yang *et al.* [11] demonstrated a strong bcl-2 expression in basaloid carcinomas versus a negative to weak expression in BCH. We noted a weak reaction. Ki-67 index in our case was low, i.e., 9%-11% as also demonstrated by Yang *et al.* [9] and Montirani *et al.* [4] who got a Ki-67 index of 8%-25% and 11%-18% respectively in BCH. Chromogranin was negative in our case as also seen by Montirani *et al.* [3] Uroplakin highlighted the inverted papilloma as it is specific for urothelium.

Conclusion

An accurate diagnosis and appropriate management requires distinction between florid BCH from malignancies including conventional prostatic adenocarcinoma and basaloid carcinoma. Although morphologic criteria guide diagnosis, supplementing IHC markers prevents overtreatment.

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