invasive ductal carcinoma. The current case is unique as disease is bilateral and multicentric arising in multiple radial scars and a CSL.

Complete excision is the required form of treatment as recurrence occurs relatively frequently, presumably due to incomplete or marginal excision. The current case suggests another reason for a high recurrence rate may be tumour multifocality. Although LGASC is rarely metastasising, mastectomy may be required due to locally aggressive behaviour[1–3] and in the instance of multiple tumours. Mastectomy was clearly the correct choice in the current case. As the histology of LGASC is so subtle, careful assessment of margins is required. Adjuvant therapies such as chemotherapy and radiotherapy may have no role, following adequate local excision.[3]

Acknowledgements: Great thanks are owed to Drs Elizabeth Sinclair, Ivan Burchett and Ian Burgess.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: 10.1097/PAT.0000000000000034

A low grade PIN-like neoplasm of the transition zone immunohistochemically negative for basal cell markers: a possible example of low grade adenocarcinoma with stratified epithelium

Sir,
In 2003 Amin *et al.* reported in a conference abstract a potential pitfall in the recognition of invasive prostatic adenocarcinoma, i.e., circumferential perineural invasion seen in adenocarcinoma with the features of micropapillary high grade prostatic intraepithelial neoplasia (HGPIN).[1–3] In 2006 Hameed and Humphrey were the first to fully describe an unusual subset of prostatic adenocarcinoma composed of single glands lined by stratified non-cribriform epithelium and to highlight that this lesion mimics HGPIN.[4] In 2008 Tavora and Epstein termed this pattern as 'PIN-like prostatic duct adenocarcinoma'.[5]

We report herein a case of low grade PIN-like lesion of the transition zone of the prostate associated with benign prostatic hyperplasia (BPH) and immunohistochemically negative for basal cell markers. We believe that it could be an example of low grade adenocarcinoma with stratified epithelium.

The case was a 73-year-old man with a clinical diagnosis of bladder outlet obstruction and with progressive worsening of the urinary symptoms. The total serum prostate specific antigen (PSA) was 4.21 ng/mL with a free-to-total ratio of 20%. Digital rectal examination (DRE) was negative. Transrectal ultrasound (TRUS) evaluation did not show hypoechoic lesions. The patient refused any pharmacological treatment for fear of side effects, such as impotency. Suprapubic simple prostatectomy was performed to relieve the patient from the urinary symptoms. The patient was followed up for 5 years after the operation. The urinary symptoms improved. The PSA decreased to 1.2 ng/mL and remained stable until he was last seen by the clinicians. DRE remained negative. TRUS did not show changes in the residual prostate.

The diameters of the surgical specimen were $7 \times 5 \times 4$ cm and the weight was 80 g (the volume of the corresponding ellipsoid was 87.92 cc). The specimen was totally sliced at an interval of 4 mm. On the cut surface the parenchyma was whitish in colour, nodular in appearance with microcystic areas. A well demarcated yellow nodule measuring 6×4 mm (volume 0.4 cc) was seen in one of the slices. The area was 5 mm away from external surface of the specimen. Initial generous sampling of the specimen was carried out, including the entire yellow area. Additional sampling was performed before signing out the pathology report. Histologically, the initial and additional tissue samples showed the features of BPH with focal cystic dilatation of the glands. Mild focal chronic inflammation was present in the periglandular stroma.

The yellow nodule seen macroscopically was composed of tightly packed glands, separated by little stroma, and with a well-defined peripheral border (Fig. 1A). The mean greatest external diameter of the glands was 269 μm, the diameter being below 300 μm in 80% of the glands, smaller than that of the non-cystically dilated non-neoplastic glands of the surrounding parenchyma (mean greatest external diameter 526 μm; greater than 300 μm in all glands). The glands, none of them dilated, were lined by epithelium 3-to-4 cells thick, the cells showing crowded nuclei and scant cytoplasm (Fig. 1B,C). The epithelial architecture was flat, tufted and micropapillary in 60%, 30% and 10% of the glands, respectively (some with more than one pattern). The nuclei were mostly round, with a mean greatest diameter of 9.28 μm (the diameter of the nuclei in the non-neoplastic nuclei being 7.29 μm, and 8.57 μm in a HGPIN case not part of this study) (see Table 1 and Fig. 2A–F for additional comparisons) and showed an irregularly distributed chromatin. The nucleoli, visible in approximately 40% of the nuclei, were small and prominent in 3% of the nuclei (Fig. 1B,C). The lumen of 10% of the glands contained pink dense secretion. Necrosis was not present. Rare mitoses were seen (Fig. 1C).

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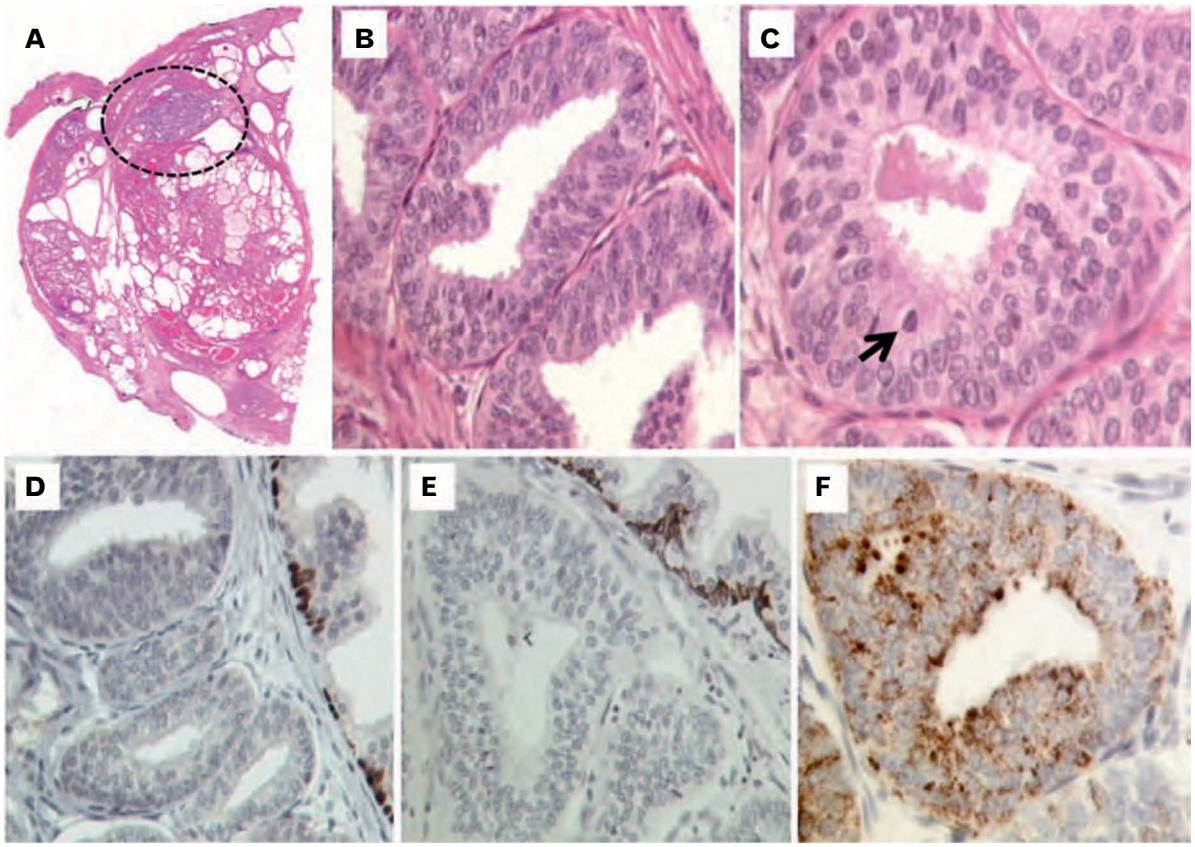

Fig. 1 (A) Histological section showing the lesion that macroscopically appeared of yellow colour (dotted circle). The parenchyma surrounding the circled area shows the features of benign prostatic hyperplasia (BPH) with cystically dilated glands. (B) Glands separated by scant stroma and lined by stratified epithelium with tufted and flat patterns. (C) Gland lined by stratified epithelium with a mitotic figure (arrowed). The nuclei are mostly round in shape with chromatin irregularly distributed and small nucleoli. Pink secretion is present in the lumen. (D) p63 immunohistochemistry. The glands are negative, i.e., a basal cell layer is not present. p63 positive cells are present in the normal gland adjacent to the negative cells (positive internal control). (E) 34βE12 immunohistochemistry. The glands are negative, i.e., a basal cell layer is not present. 34βE12 positive cells are present in the normal gland adjacent to the negative cells (positive internal control). (F) AMACR immunohistochemistry. The gland shows strong cytoplasmic staining.

The immunohistochemical investigation showed that the epithelial lining was PSA positive and it was negative for the basal cell markers p63, high molecular weight cytokeratin (34βE12) (Fig. 1D,E) and cytokeratin 5/6. The normal glands in the surrounding parenchyma or entrapped within the lesion showed variable expression of the basal cell markers in cells in basal position. The cells were alpha-methylacyl coenzyme A racemase (AMACR) positive in a dot-like fashion in 90% of glands (Fig. 1F), the surrounding BPH tissue being negative. S100 and smooth muscle actin were negative.

The initial differential diagnosis was low grade PIN versus basal cell hyperplasia. However, the results of the immunohistochemical studies did not support the diagnosis of low grade PIN and excluded that of basal cell hyperplasia for the lack of basal cell marker expression. A diagnosis of 'low grade PIN-like adenocarcinoma of the transition zone, occupying less than 5% of the specimen' was made, based on the literature on the differential diagnosis and mimickers of PIN.[2–5] The Gleason score was not included in the pathology report, even though a comment

Table 1 Quantitative analysis in the current case and in the surrounding BPH tissue

Type of lesion	Mean greatest external diameter of the glands, μm	Mean nuclear greatest diameter*, μm (SD)	% of nuclei with prominent nucleoli
BPH (from the current case) (Fig. 2A)	526	7.29 (0.78)	<1%
Lesion in current case (Fig. 2B)	269	9.28 (0.85)	10%
Low grade PIN (Fig. 2C)	397	7.74 (0.7)	5%
High grade PIN (Fig. 2D)	384	8.57 (0.96)	70%
Acinar adenocarcinoma, Gleason score 2 + 2 = 4 (Fig. 2E)	158	9.72 (1.05)	80%
Ductal adenocarcinoma (Fig. 2F)	Not calculated	12.63 (1.19)	90%

Results of valuation on low and high grade PIN, usual acinar adenocarcinoma and ductal adenocarcinoma are also shown for comparison, performed on lesions from the archives of one of the authors (RM).

* Several images representative of the lesions were recorded with a Nikon digital camera mounted on a Nikon Eclipse E800 microscope (Nikon, Japan) at the objective magnification of 20×. The greatest diameter (unit of measurement, μm; calibration was based on the measurement of nuclei with known diameter) was then analysed with the LabVIEW software (National Instruments, USA) by one of the authors (MAM). Typical images of the lesions measured for this study are shown in Fig. 2A–F).

BPH, benign prostatic hyperplasia; PIN, prostatic intraepithelial neoplasia; SD, standard deviation.

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