SHORT REPORT

Recurrent prostatic stromal sarcoma with massive high-grade prostatic intraepithelial neoplasia

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A unique case of prostatic stromal sarcoma (PSS) that recurred in the pelvic cavity with massive high-grade prostatic intraepithelial neoplasia is described. A 52-year-old man who presented with urinary retention underwent a radical cystoprostatectomy. Tumour tissues of the prostate showed an admixture of hyperplastic glands and markedly cellular stroma of spindle cells arranged in a fascicular pattern, and the tumour was diagnosed as PSS. 66 months after the operation, CT scans revealed three recurrent tumours around the bilateral obturator and left fore iliopsoas. The recurrent tumours were biphasic neoplasms, as before, but the epithelial component had grown prominent and manifested overt atypia in a manner resembling high-grade prostatic intraepithelial neoplasia. Our findings suggest that not only the stromal component but also and the epithelial components of PSS may have malignant potential.

Mixed epithelial–stromal tumour of the prostate is a rare lesion composed of spindle to pleomorphic stromal cells and an intervening benign glandular element.[1 2] In 1998, Gaudin *et al* classified sarcomas and related proliferative lesions of the specialised prostatic stroma, including prostatic phyllodes tumours, into two categories: prostatic stromal sarcoma (PSS) and prostatic stromal proliferation of uncertain malignant potential.[1 3] PSS and prostatic stromal proliferation of uncertain malignant potential often recur with increasing atypia of neoplastic stromal cells, especially after incomplete resection.[1 2 4–9] Less attention has been focused on the epithelial component of these tumours, a component that has been consistently considered non-neoplastic.[1] Here, we report a case of extraprostatic recurrent PSS in which the epithelial component represented massive high-grade prostatic intraepithelial neoplasia (HGPIN).

CASE HISTORY

A 52-year-old man presented with urinary retention. Digital rectal examination revealed a markedly enlarged prostate with soft consistency. The serum prostate-specific antigen (PSA) level was 7.25 ng/ml (normal: <4 ng/ml). CT showed a 7 cm mass in the posterior prostate, with some compression of both the bladder and rectum. A needle biopsy specimen was histologically diagnosed as prostatic sarcoma. The patient underwent a radical cystoprostatectomy and ileal conduit construction without a pelvic lymphadenectomy. The serum PSA fell to <0.1 ng/ml after the operation.

CT performed 66 months after the operation revealed three recurrent tumours around the bilateral obturator and left fore iliopsoas (fig 1). Serum PSA had risen to 3.3 ng/ml. The patient was diagnosed with recurrent prostatic sarcoma and treated with a combination chemotherapy (three cycles of cisplatin, pirarubicin and ifosfamide). The recurrent tumours were resected and the patient was discharged. The serum PSA fell to 0.2 ng/ml after the second operation; however, 12 months after the operation, the serum PSA rose again to 3.7 ng/ml and CT revealed a 4 cm recurrent tumour around the right obturator.

METHODS

Gross examination of the cystoprostatectomy specimen revealed a cavity in the posterior prostate from which the soft tumour material had flowed out during the operation. A fragmented, soft and greyish tumour was submitted separately. The recurrent tumours consisted of fragments of soft, grey to brown tissue. Whole portions of both of the primary and recurrent tumours were embedded in paraffin wax and examined histologically.

Immunostaining of formalin-fixed paraffin-wax-embedded sections of the tissue was performed by the labelled streptavidin using biotin method with an LSAB2 kit (DacoCytomation, Carpinteria, California, USA) and the following antibodies: PSA (polyclonal, DakoCytomation; prediluted), Ki-67 (MIB-1, Immunotech, Marseille, France; 1:200 dilution), high-molecular-weight cytokeratin (HMWCK) (34βE12, DakoCytomation; 1:100 dilution) and α-methylacyl-coenzyme A racemase (AMACR) (polyclonal, Diagnostic Biosystems, Pleasanton, California, USA; 1:100 dilution).

RESULTS

Primary tumour

Microscopically, the tumour was biphasic, with markedly cellular stroma interspersed with glands (fig 2A). The ratio between the epithelial and stromal components (E:S ratio) was about 1:4. The glands appeared hyperplastic, and no slit-like phyllodes pattern was apparent. Cribriform glands were also sporadically observed. The secretory cells had uniformly enlarged nuclei with inconspicuous nucleoli, with a lining of single-layered basal cells (fig 2B). A few glands manifested squamous metaplasia. The stroma was markedly cellular with spindle cells arranged in a fascicular pattern. The tumour was diagnosed as PSS based on the marked stromal cellularity and scattered mitotic figures (4 mitoses per 10 high-power fields).

Recurrent tumours

Microscopically, the tumours were biphasic, as before, with an admixture of glands and cellular stroma (fig 2C). In contrast to the primary tumour, however, the glandular component was predominant (the E:S ratio was about 3:2). Cribriform glands were frequently observed. Moreover, the epithelial cells exhibited a diffuse pattern of prominent atypia with dense stratification and prominent nucleoli (fig 2D). A distinct layer

Abbreviations: AMACR, α-methylacyl-coenzyme A racemase; HGPIN, high-grade prostatic intraepithelial neoplasia; PSA, prostate-specific antigen; PSS, prostatic stromal sarcoma

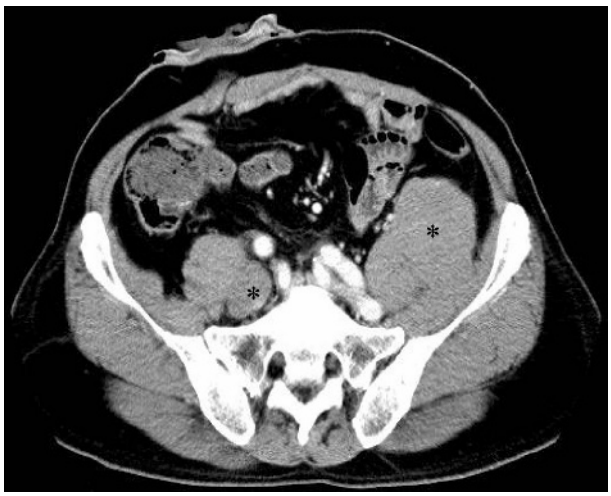

Figure 1 CT scans shows two recurrent tumours (*) around the bilateral psoas major muscles.

of basal cells still remained, although often obscurely. The stromal component, on the other had, closely resembled that of the primary tumour with some degeneration. No lymph node examined was involved by the tumour.

Immunohistochemistry

The epithelial cells of both primary and recurrent tumours were diffusely immunoreactive for PSA. Three of the findings in the epithelia differed considerably between the primary tumour and recurrent tumours, however: (1) a marked increase of the Ki-67 labelling index from 1.2% in the primary tumour to 17.1% in the recurrent tumour (fig 2E); (2) a discontinuous pattern of basal cell layer in HMWCK staining of the recurrent tumours (fig 2F) versus continuous staining in the primary tumour; (3) a weak immunoreactivity for AMACR in the recurrent tumours versus no immunoreactivity in the primary tumour.

DISCUSSION

In the present case, the whole epithelia in the recurrent tumours manifested prominent structural and nuclear atypia suggestive of HGPIN. The following immunohistochemical results in the

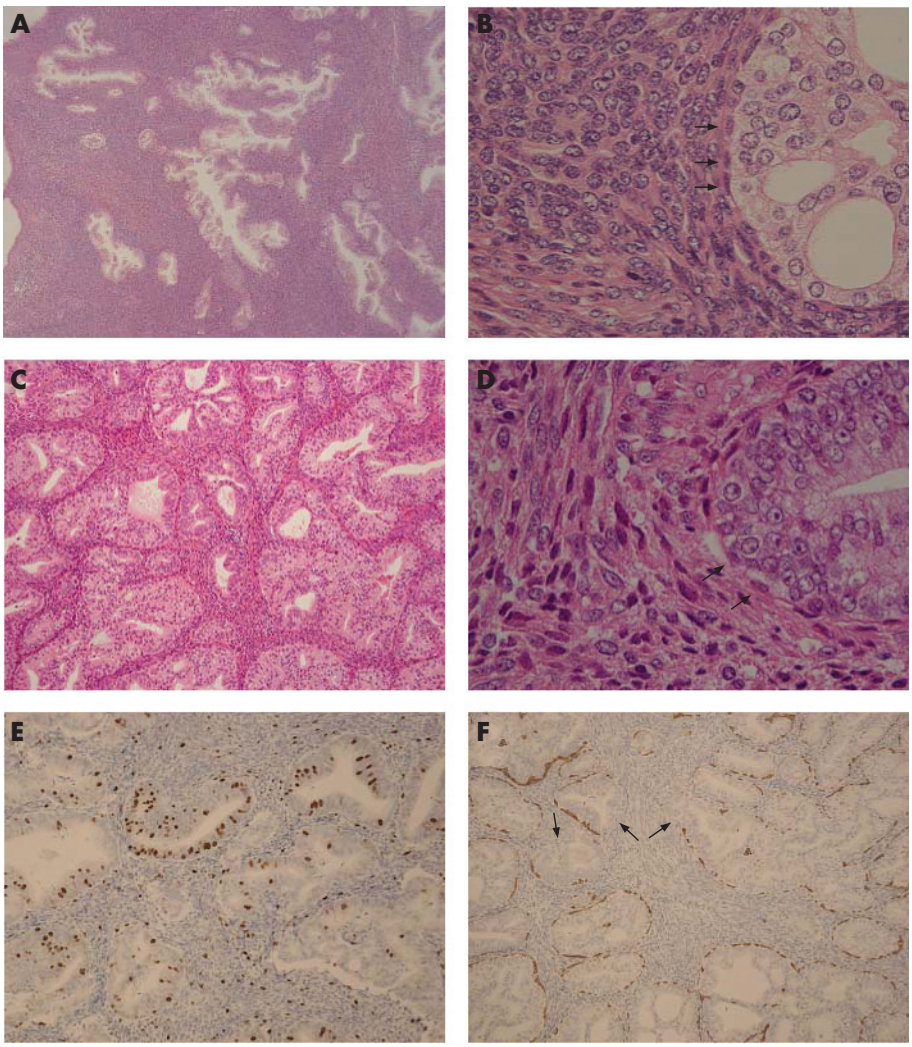

Figure 2 (A,B) Histological findings of the primary tumour. (A) Admixture of glands and highly cellular stroma. (B) Cribriform glands were sporadically observed. The secretory cells have uniformly enlarged nuclei and inconspicuous nucleoli, with a lining of single-layered basal cells (arrowheads). (C,D) Histological findings of the recurrent tumour. (C) Admixture of glands and cellular stroma; the former is predominant and cribriform glands were frequently observed. (D) The secretory cells are densely stratified and have prominent nucleoli, with a lining of single-layered basal cells (arrowheads). (E,F) Immunostaining in the recurrent tumour. (E) More Ki-67 immunoreactive nuclei are observed in the epithelia than in the stroma. (F) Immunostaining for high-molecular-weight cytokeratin demonstrates a partly discontinuous pattern of basal cell reactivity (arrowheads).

Take-home message

Prostatic stromal sarcoma is not simply a stromal neoplasm as previously believed. Not only the stromal component but also the epithelial component may have a malignant potential.

epithelia of the recurrent tumours were compatible with HGPIN: (1) markedly higher levels of Ki-67 labelling index (which rises higher in prostatic adenocarcinoma and HGPIN than in benign glands[10 11]) in the epithelia; (2) discontinuous staining for HMWCK (a staining pattern typical of HGPIN[12]); (3) weak staining for AMACR (which stains the majority of prostatic adenocarcinoma and HGPIN[13]). The malignant transformation of the epithelia surrounded by malignant stromal cells implies the existence of an epithelial–stromal interaction—that is, an aberrant stromal microenvironment promoted malignant transformation of the epithelia.[14]

Another remarkable finding in the present case was that basal cells, in addition to atypical stromal and secretory cells, existed in multiple recurrent tumours outside the prostate. Although a recent molecular genetic study has demonstrated that both epithelial and stromal components of prostatic phyllodes tumours are clonal,[15] the clonality of basal cells in prostatic stromal tumours has not been examined. In a previous study, McCarthy *et al* concluded that epithelial and stromal components might have different clonal origins.[15] Contrary to McCarthy *et al*'s study, our finding raises the possibility that both components, including basal cells, have a common clonal origin.

In summary, we report a previously unreported case of extraprostatic recurrent PSS in which the epithelial component represented massive HGPIN. It is important to note that mixed epithelial–stromal tumour of the prostate is not solely a stromal neoplasm as previously believed, and that not only the stromal but also the epithelial component of this tumour may have a malignant potential.

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Squamous differentiation in primary urothelial carcinoma of the urinary tract as seen by MAC387 immunohistochemistry

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Squamous differentiation (SqD) is variably present in urinary tract tumours, but its significance remains unclear. In this study, SqD was assessed by immunohistochemistry using the monoclonal antibody Mac387 in 145 urothelial tumours (bladder, n = 115; renal pelvis, n = 30). Mac387 detects the myelomonocytic L1 antigen; a member of the calgranulin family shared by epithelial cells and keratinocytes. L1 antigen was shown in SqD in urothelial carcinomas of the bladder or the renal pelvis, including 11 cases with focal SqD unrecognised by conventional analysis. SqD is more frequent in renal pelvic tumours (p = 0.027) and increases with grade/stage mainly in bladder carcinoma (grade, p = 0.05; stage, p = 0.005). Stage Ta/T1 bladder carcinomas with SqD recurred more (p = 0.021). In conclusion, Mac387 efficiently shows SqD in urothelial tumours.

Abbreviations: SqD, squamous differentiation