tubular pattern.[4–6] The case described by Muñoz *et al.* has cystic architecture also.[7] Seethala *et al.* have described the variants of EMC of the salivary gland in their study; namely, the dedifferentiated EMC, oncocytic EMC, EMC ex pleomorphic adenoma, double-clear EMC, and EMC with myoepithelial anaplasia.[3] They reported a biphasic papillary pattern in a minority of salivary gland EMCs (7/61; 11.5%) in their study.[3] Our case had well-formed true papillae lined by TTF-1 negative and CK7 positive epithelial cells along with tubulo-glandular architecture. The abluminal myoepithelial cells can have varied morphologies including clear cells, spindled cells and amphophilic cytoplasm. Those seen in our case were predominantly clear cells which stained brightly with S-100, P-40 and SMA. These myoepithelial cells were also seen lining the papillary epithelium.

EMC has a broad range of differential diagnoses which depends on the predominance of the cells forming its architecture. The biphasic nature of this entity entails a differential of pleomorphic adenoma.[8] The absence of a chondromyxoid stroma and predominance of clear myoepithelial cells in our case helped in differentiating from this neoplasm. The second differential which arises is adenoid cystic carcinoma which can be distinguished by its infiltrative nature and cribriform architecture. The other close differential which may be considered is a metastatic salivary gland EMC to the lung. However, the patient had no such history in the past nor did she have any parotid or submandibular mass. In addition to these salivary gland type malignancies, endobronchial papillary tumours were added to the list of differential diagnoses due to a prominent papillary architecture in the current case. The primary endobronchial papillary tumours are rare and are commonly papillomas, cystadenomas or adenocarcinomas.[9,10] The index case, which was lined with TTF-1 negative epithelial cells, could be easily differentiated from the above lesions which originate from the surface epithelium and are in contrast TTF-1 positive. Rarely, the epithelial component of EMC shows pneumocytic differentiation giving rise to positive staining for TTF-1. The metastatic papillary tumours are the next common differentials, the likelihood of which was nullified by the histomorphology and the IHC characteristics of the present case. Some salivary gland tumours also rarely display a papillary architecture, such as mucoepidermoid carcinomas[11] and polymorphic low grade adenocarcinomas (PLGA).[12] Lack of squamous/transitional cells and mucin ruled out mucoepidermoid carcinoma and presence of a prominent abluminal myoepithelial component easily distinguished it from PLGA.

In conclusion, the present case highlights an unusual histomorphology of an endobronchial epithelial myoepithelial carcinoma bearing a papillary architecture. We also describe the gamut of differentials which needed consideration during the diagnosis of this lesion. We emphasise the importance of careful assessment of histomorphology and supportive immunohistochemistry which help in diagnosing complex cases.

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PSA-positive urethral adenocarcinoma of female genital tract

Sir,

A 75-year-old female presented with macroscopic haematuria and on examination was found to have a mass at the external urethral meatus. Her past medical history included severe emphysema, hypertension, dyslipidaemia and a 50 pack-year smoking history. A cystoscopy revealed a urethral tumour and also a separate exophytic bladder lesion overlying the right ureteric orifice. Contrast magnetic resonance imaging (MRI) of her pelvis showed a 3 cm mass with an enhancing peripheral rim in the posterior distal urethra extending both into the anterior vaginal wall inferiorly and into the urethra anteriorly.

The biopsy from the urethral tumour showed an invasive adenocarcinoma. Subsequently another cystoscopy was

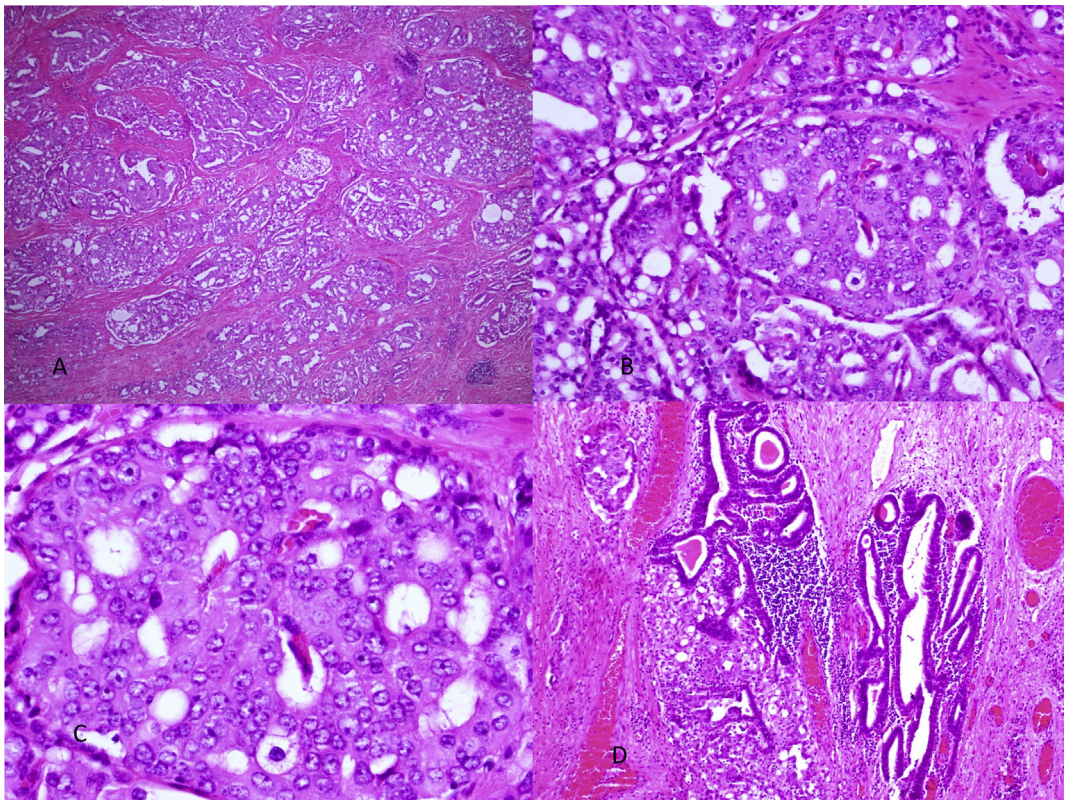

Fig. 1 Infiltrative malignant glands in (A) low, (B) medium and (C) high magnifications. (D) Association of malignancy to Skene's glands.

performed, the bladder lesion was resected and a repeat biopsy was also taken from the distal urethra mass. The bladder lesion was a papillary urothelial neoplasm of low malignant potential (PUNLMP), and morphologically dissimilar to the adenocarcinoma found in the urethra. The repeated biopsy taken from the urethral tumour showed features identical to those seen in the initial biopsy. She eventually underwent anterior exenteration, bilateral pelvic lymphadenectomy and formation of ileal conduit. Macroscopically, the 20 mm tumour was relatively demarcated, located at the posterior aspect of the distal urethra and showed solid and tan cut surfaces. Paraffin sections showed an adenocarcinoma comprising cribriform and back-to-back glands infiltrating amongst fibrous stroma (Fig. 1). The malignant cells were large and cuboidal with eosinophilic cytoplasm, open chromatin and conspicuous nucleoli. Frequent mitoses and apoptosis were present. Intraluminal mucin secretion and background stromal hyalinisation were present. Additionally, close association of adenocarcinoma with subepithelial Skene's glands and crypts were identified, reflecting the origin (Fig. 1). Lymphovascular and perineural invasion were present. No metastasis was found in the regional lymph nodes dissected from the pelvis and lower abdomen. The bladder did not show any residual urothelial neoplasm.

Immunohistochemically, the malignant cells identified in all specimens showed positive expression of prostatic alkaline phosphatase (PAP) and prostatic specific antigen (PSA) using monoclonal antibody clone 35H9 (ready to use; Leica, Germany). There was focal positivity of progesterone receptor. P16 was also performed due to its association with many epithelial tumours of the lower female genito-urinary tract. The stain was patchy in only a small subset of the malignant cells and therefore interpreted as negative (Fig. 2). Other negative stains included CK7, CK20, 34E12, PAX8, p53, CEA, GATA-3 and CD34.

Both morphology and immunophenotype are reminiscent of a prostatic acinar adenocarcinoma, and its female equivalent is a urethral adenocarcinoma arising from a Skene's gland. A staging whole body bone scan with SPECT/CT of the pelvis and lower spine was negative for metastatic disease. Pre-operative serum follicle-stimulating hormone (FSH) and luteinising hormone (LH) were high, 44.8 U/L and 15.4 U/L, respectively, as expected in menopause. The oestradiol and testosterone levels were normal, <44 pmol/L and 0.1 nmol/L, respectively. Interestingly, a high serum PSA of 22.82 ng/mL was detected, reflecting PSA immunostain positivity of the tumour cells.

In view of the clear surgical margins and negative regional lymph nodes, it was decided not to give adjuvant chemotherapy or radiotherapy. Interestingly, the patient's serum PSA has been undetectable since 6 weeks post-surgery. She developed ureteroileal anastomotic stricture 10 months post-exenteration for which a unilateral ureteroileal reimplantation was performed. She has been followed up by imaging and serum PSA levels, and the last follow up was 2 years post-operation with no evidence of tumour recurrence.

Urethral carcinoma is among the rarest neoplasms of the urogenital tract and corresponds to 0.003% of all malignant neoplasms occurring in the female urogenital tract.[1] Squamous cell carcinoma and transitional carcinoma are the most common histological types of female urethral carcinomas, accounting for 70% and 20% of all cases, respectively, while adenocarcinoma is relatively less common, accounting for 8−10%. Other rarer types of female urethral neoplasms include lymphoma, neuroendocrine carcinoma,

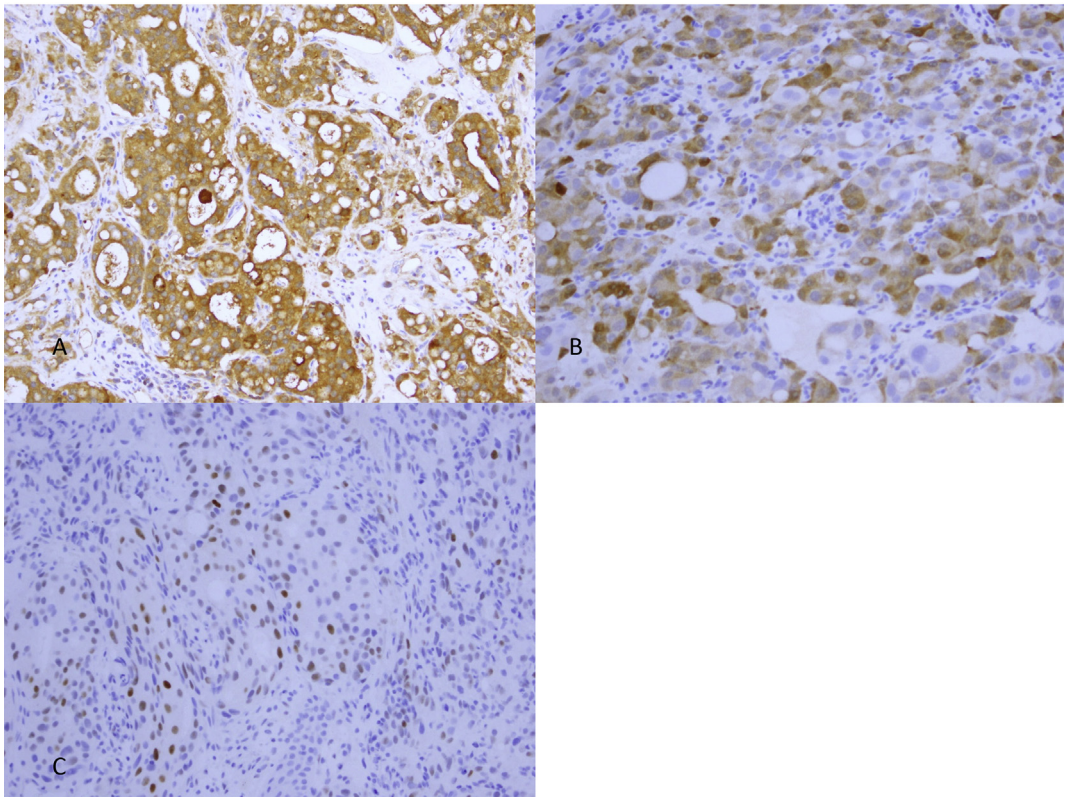

Fig. 2 (A) Diffuse and strong PSA positivity. (B) P16 was patchy and (C) progesterone receptor was focally positive.

sarcomas, paragangliomas, melanoma and metastasis.[2] Urethral adenocarcinomas can be subdivided into mucinous, nephrogenic, clear-cell and Skene's gland derivative. Female Skene's glands have the same embryological origin and ultra-structural appearance as the male prostate gland.[3] This finding is reflected by PSA immunoreactivity in some of these adenocarcinomas and also a post-operative decline in the serum PSA level after complete removal of the tumour. However, only a few cases reported in literature documented pre-operative and post-operative PSA levels as in our case.[1,4] At least to some extent, this rarity could be a result of not performing serum PSA test in female patients, since PSA is recognised in general as an exclusive male antigen.

Reis *et al.*[5] have thoroughly studied the immunohistochemical profile of the female urethral mucosa and the underlying subepithelial Skene's glands. The female urethral mucosa is mostly lined by a non-keratinising squamous epithelium (CEA and AE1/AE3 positive) which is continuous with the invaginated Skene's duct showing an abrupt substitution with a transitional epithelium (P63 and 34bE12 positive). The luminal border of this transitional epithelium has columnar eosinophilic cells which are CK7 positive. Ultimately at the very end of the Skene's gland duct, the columnar cells form alveolar out-pouching of clear cells which are positive for PAS, Alcian blue PAS at PH 2.5 (ABPAS) and colloidal iron. Only scattered secretory clear cells in the epithelium of some glands show PSA positivity in the luminal part of the cytoplasm. Since the epithelial lining of the Skene's gland shows heterogenic immunoperoxidase reactivity at different parts,[5] and many cells in the normal structure of these glands are PSA negative, some adenocarcinomas which originate from Skene's glands may not express PSA. Reis *et al.*[5] reported two PSA-negative adenocarcinomas which were favoured to be of Skene's gland origin due to the gross findings and also cytochemical and immunohistochemical similarities with normal Skene's glands.

There are some other rare morphological types of female urethral adenocarcinomas which should be considered amongst the differential diagnosis of any adenocarcinoma in this location. Mucinous adenocarcinoma is most often composed of colonic-type glandular epithelium and may contain abundant extracellular mucin, resembling their colon counterparts.[6] This type of urethral adenocarcinoma is rare with only 25 cases reported in the English literature.[7–9] Reis *et al.*[5] also describe a case of clear cell adenocarcinoma in the female urethra. Immunopositivity with CK7 and 34bE12 and ABPAS at pH2.5 suggested Skene's gland origin in that case. Nephrogenic adenoma in which no marked nuclear pleomorphism, mitotic activity or infiltrative growth can be seen is among the differential diagnosis.[10] Although very rare, metastatic adenocarcinoma should be considered, and in our case was ruled out by clinical correlation.

Female urethral carcinomas including adenocarcinomas are more likely to present at a high clinical stage and may extend into the bladder and/or vagina. In our case, the carcinoma extended into vaginal submucosa but the bladder was spared. Due to rarity of the condition, there is no absolute management guideline for these patients. There was a case report of successful treatment with definitive external beam radiotherapy for a PSA positive urethral adenocarcinoma, similar to organ-confined prostate cancer treatment, reserving exenterative surgery for disease progression.[4] In advanced cases, a combination of chemotherapy, radiation therapy and surgery has been recommended for optimal local and distant

disease control. Our case appears to have been successfully managed by radical surgical excision alone and there was no detectable serum PSA or evidence of tumour recurrence in clinical examination and imaging studies during the 2 year follow up period.

This rare case emphasises keeping an open mind in approaching an adenocarcinoma in the female urethro-genital region. Serum PSA level and PSA immunohistochemical staining should be considered in any case of urethro-genital adenocarcinoma in female patients. PSA positivity, if detected, not only demonstrates the possibility of Skene's gland origin but also provides a non-invasive long term follow up method by serum PSA monitoring.

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Imposter mucin: awareness of an important cytology artefact

Sir,

A mucin-mimicking artefact produced in surgical suction canister liner bags made from thick, opaque material has been identified in the setting of peritoneal washing cytology. This poses a potential problem in the misdiagnosis of mucin in peritoneal washing cytology specimens. An increasing number of different collection devices are now documented to contribute to this artefact. We report the finding of mucin-like artefact with Receptal branded liner bags (Amsino International, USA).

Our laboratory independently identified this artefact, and subsequently found similarities with other laboratory descriptions of this finding.[1–3] Laboratory staff were alerted to the issue by the presence of white flakes suspended in fluid contained within Receptal liner bags (Fig. 1). Empty liner bags were flushed with saline and cytospins and cell blocks prepared to support the hypothesis that the material was a contaminant. The artefact is generally abundant, staining purple on Papanicolaou stain, with sharp to soft fibrillary edges and multiple central laminations (Fig. 2A). In contrast, true mucin is pale blue to orange on Papanicolaou stain (Fig. 2C), and has hazy, ill-defined edges without laminations (Fig. 2C,D). In cell block preparations, the artefact has a less defined, dispersed and bubbly appearance (Fig. 2B).

Cytological assessment of peritoneal fluid is important for identification of intraperitoneal spread of malignant cells. The presence of abundant extracellular mucin is a significant abnormal finding in peritoneal washings.[1] The exogenous artefact described above can lead to misdiagnosis by obscuring diagnostic material or by mimicking extracellular mucin. Van

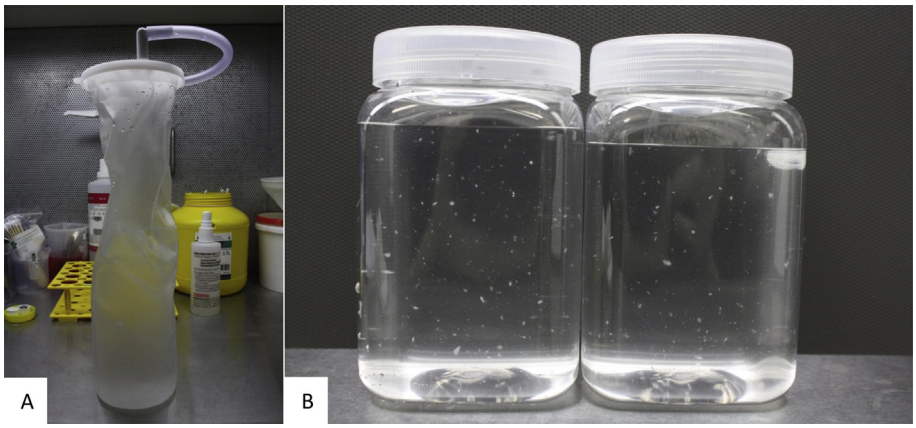

Fig. 1 (A) Receptal suction canister liner bag. (B) White flakes suspended in fluid from liner bag.