# Urethral Washings

Small Cell Neuroendocrine Carcinoma

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### Patient History and Clinical Information

- 79 year old male with previous cystoprostectomy for recurrent high risk bladder carcinoma in 2002 and an incidental finding of adenocarcinoma prostate
- Attended GP indicating daily visible blood from urethral meatus which was painful at night
- Ex-smoker
- Some UTIs in distant past but follow up ultrasounds have been normal



### Patient History and Clinical Information

- Urostomy bag clear on presentation to Day Procedure Unit clinic no evidence of haematuria
- Flexible urethroscopy small papillary outgrowth from wall of urethra with distributed red spots around it – max diameter of largest one 0.3 cm
- Referred for red flag GA urethroscopy and urethral biopsy
- Ureteric washings for cytology obtained and biopsy also taken



- 5 ml of blood stained urethral washings received in laboratory
- One ThinPrep urocyte slide is made and stained with Papanicoloau stain



ThinPrep Pap Magnification x10



 Hypercellular sample comprising occasional benign urothelial cells surrounded by plentiful abnormal hyperchromatic cells throughout



ThinPrep Pap Magnification x20



- Appearances are those of malignant cells with little or no cytoplasm, stippled chromatin and some nuclear moulding noted
- Make cytoblock to determine origin of tumour cells





ThinPrep Pap Magnification x40



 Cytoblock shows numerous malignant cells scattered throughout the section – as in the ThinPrep Pap slide



H&E of cytoblock preparation from urethral washings Magnification x20



Immunohistochemistry on cytoblock



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#### GATA3 (-)

- An occasional background urothelial cell staining positive
- Rules out high grade urothelial carcinoma

#### LCA (-)

- An occasional background lymphocyte staining positive
- Rules out lymphoid origin





#### AE1/AE3 (+)

- Benign urothelial cells showing strong cytoplasmic/membranous staining with the lesional cells showing dot like positive staining
- Confirms epithelial origin and dot-like staining is suggestive of neuroendocrine origin.



#### CD56 (+)

• Stains positive in small cell carcinoma





#### Synaptophysin (+)

• Confirms neuroendocrine differentiation



#### Chromogranin (Focal +)

 Both neuroendocrine markers may not always be positive



#### • Correlating Urethral biopsy



H&E Magnification x20

• Sheets of similar malignant cells to those seen in the urethral wash sample



# Diagnosis

- Morphologic and immunohistochemical appearances in keeping with a small cell neuroendocrine carcinoma
- Correlates with urethral biopsy diagnosis



- Very important to confirm type of malignancy and not assume this is a high grade urothelial carcinoma, particularly in view of previous history albeit more than 20 years previously.
- Consider cell type and morphologic features present especially if not conforming to usual morphologic appearance of high grade urothelial carcinoma.
- Cell size, stippled chromatin pattern, little/no cytoplasm, some nuclear moulding need to consider neuroendocrine origin in differentials.
- Small cell carcinoma confirmed with immunohistochemical staining. TTF-1 in this instance would not be helpful as it could be positive or negative and disease burden did not support a lung origin.



- Neuroendocrine tumours (NETs) of the urinary tract are rare and the urinary bladder is the most common primary site. <sup>(I)</sup>
- Primary small cell neuroendocrine carcinoma in the urinary tract represents less than 0.05% of urinary tract cancers<sup>(2)</sup>
- Small cell neuroendocrine carcinoma arises from pluripotent stem cells that have differentiated into neuroendocrine cells. <sup>(2)</sup>
- Among the different tumors arising in the male urethra, squamous cell cancer is the most frequently occurring histologic type (80%), the remaining being mainly transitional cell carcinoma\* (15%) and adenocarcinoma or undifferentiated carcinomas (5%). <sup>(3)</sup>

\*Please note the older terminology in reference to transitional cell carcinoma which nowadays would be referred to as urothelial carcinoma



- Concerning the male genital tract, focal neuroendocrine differentiation in a conventional prostatic adenocarcinoma is not uncommon, but small-cell carcinomas in the prostate are relatively rare. Carcinoids are not uncommon in the testis and should be distinguished from metastatic tumors; however, carcinoids are extremely rare elsewhere in the male genital tract.<sup>(3)</sup>
- Small-cell neuroendocrine carcinomas have been reported in the scrotal or penile skin (as Merkel cell carcinoma) but are extremely rare in the penile urethra.<sup>(3)</sup>

- Only a few cases of urethral neuroendocrine carcinoma appear in literature and I could only find one other that referred to a case with a history of transitional cell carcinoma and orthoptic bladder substitution <sup>(4)</sup>
- Patient is an ex-smoker and smoking has been implicated in the etiology of bladder small cell neuroendocrine carcinomas<sup>(5) (6)</sup>



### Treatment

- CT shows metastatic disease in liver, lung and pancreas
  – patient has good
  performance status and will begin palliative chemotherapy of Carboplatin Etoposide.
- Discussed at lung MDM and pattern of disease burden supports urogenital primary rather than lung.
- Surgery not an option in this instance.

### References

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