## DEP IN DIAGNOSTIC CYTOLOGY CASE STUDY

## URINE CYTOLOGY

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## Diploma of Expert Practice in Diagnostic Cytology

- Note the change in title it's not "Non-gynaecological cytology" anymore
- To undertake the training and qualification:
  - Member or fellow of the IBMS
  - HCPC registered
  - Five years post registration experience at least
    - At least 2 years practical experience in sample preparation and evaluation
  - Your lab should be
    - UKAS accredited
    - Have IBMS post registration training approval



### Structure

- Must have a nominated consultant pathologist Supervisor
- A log of *at least* 300 evaluated/ reported samples
- Evidence of review of at least 10% of each case type with the the supervising pathologist.
- Four different case studies that reflect the workload type.
- Record of training courses attended.
- 500 word (+/- 10%) evaluation of a reference paper.
- Details of in house assessment and audit of personal practice against local and national standards.
- Reflection on whole learning process
- So.... Quite a lot of work



## **INTRODUCTION TO CASE STUDY**

Urothelial carcinoma.

Anatomy of the Urinary Tract and cytology sampling.

Case study - Pre Analysis.

Cytology sample processing/BMS role. Microscopic analysis and The Paris System. Concurrent Histology. Surgical options. Multi-Disciplinary Meeting/shared decision making. Further investigations.

Post operative analysis.



### **Urothelial Carcinoma**

- One of the most common types of cancer in the UK
- Age 60 + (rare in people under 50).
- More common in males.

### **Risk factors:**

Smoking, overweight, high blood pressure. Working in the rubber and dye industry. Taking certain drugs e.g. Cyclophosphamine (chemo). Schistosomiasis – parasitic worm. Genetic abnormalities e.g. Lynch Syndrome.

#### Symptoms:

Haematuria, recurrent infections, increased urination, urinary tract pain, weight loss



### **Anatomy of the Urinary Tract**

- Urine passes from a system of ducts in the kidneys via the renal pelvis and is filtered through the ureter, bladder and finally the urethra before passing through the body.
- In men the urethra also passes through the prostate gland.
- Urothelium is multi-layered, impermeable to urine.
- Low exfoliation process can take up to a year to shed.





## **Cytology Urinary Tract Sampling**

Urine Cytology is used in the diagnosis of urinary tract cancers and follow up in patients with known malignant disease.

Types of samples: voided urine (not early morning), catheter urine, bladder washings, renal washings, ureteric, ileal conduit.

Methods used to obtain a sample have a significance on the appearance of the cells.

Cytology samples are usually more tumour-enriched than biopsies.

Locally urinary tract samples are pre-screened by Specialist Biomedical scientists.



## **DEP Case Study – Pre-analysis**

- 35-year old female in good health, smoker, phlebotomist.
- Episodes of visible haematuria first noticed 2 months previously.
- Referred by her GP to her local hospital: routine blood tests indicated normal kidney function with modest albuminuria found in her urine.
- A follow up cystoscopy unremarkable features.
- Haematuria persisted urgently referred to a specialist urology centre.
- CT scan reported a distended right renal pelvis filled with soft tissue that extended into the calyces.
- Flexible ureteroscopy to investigate the presumed source of the haematuria.



## **Cytology Laboratory**



- 7ml of bloodstained urine from the right kidney.
- This low volume specimen was centrifuged single cytofunnel slide and megafunnel slide was prepared from the centrifuged deposit.
- Both preparations were fixed in 95% alcohol and stained using the Papanicolaou method.
- All fresh material was handled in a class 1 cabinet.
- Residual fluid was stored in the laboratory fridge for potential further analysis or until the case was clinically approved.



### **BMS role - pre-screening**

**Cells:** urothelial, RBC's, neutrophil polymorphs, bacteria. Men: seminal vesicle cells, spermatozoa, prostatic epithelial cells. Women: glandular cells from the female genital tract.

### Pitfalls:

Collection method not stated by sender.

False positives/negatives: Low grade neoplasms – subtle changes.

Degenerate cells.

Benign changes: produces morphological changes in the urothelium that can be mistaken for carcinoma.

### Infections (benign):

Bacteria e.g. E.coli, fungi – candida, HSV – uncommon e.g. CMV – , TV – STI protozoa, polyoma virus, HPV.

### **Non-infectious findings:**

Casts and crystals, lithiasis, iatrogenic changes e.g. chemo, immunotherapy.





## **Case Study - Microscopy**

Urine Cytology is a useful diagnostic test as it is highly sensitive in the detection of high-grade disease.

Highly cellular fluid containing many abnormal urothelial cells both singly and in groups.

These cells had increased nucleocytoplasmic ratios >0.7.

There were irregular nuclear outlines with nuclear hyperchromasia and coarse chromatin.

The appearances were those of a high-grade urothelial carcinoma (HGUC – Paris system of reporting).

NB: Upper tract lesions require a second opinion from another Consultant.





## The Paris System (TPS)

The Paris System for Reporting Urine Cytology (TPS) was released in 2016.

Designed to simplify and standardise the cytomorphologic criteria and terminology with a focus on **HGUC** diagnosis.

- Patient treatment can be more accurate.
- Improve correlation with histology and ancillary testing
- Reduces atypia reporting category
- Rule out high grade malignancy
- Clear reporting terminology linked to clinical management

Cytology **LGUC** does not exhibit enough morphological changes to distinguish between reactive and normal urothelium.

Alternatively, flat HGUC lesions which are detected by cytology are not always easy to visualise on cystoscopy.

### The Paris system



Image by Mikael Häggström. Reference: Wojcik, EM; Kurtycz, DFI; Rosenthal, DL (2022). Journal of the American Society of Cytopathology. 11 (2): 62–66.

### **Case Study**

Cells showed increased nucleocytoplasmic ratios 0.7

- Hyperchromasia
- Coarse Chromatin
- Irregular nuclear outlines
- Many abnormal groups and single cells.

British Association for Cytopathology

BAC

• HGUC

# Assessing the Nuclear to cytoplasmic ratio (NCR)

NCR



0.3	It can be tricky to interpret
0.4	the differences in sizes of the NCR's.
0.5	Zhang, ML <i>et al</i> . Cancer Cytopathology,
0.6	(2010). 009-077.
0.7	
0.8	



## **Case Study: Histology Biopsy**

A right kidney biopsy taken at the time of the ureteroscopy, was received in Histology.

- Three tiny off-white pieces of tissue measuring less than 1mm in diameter.
- Final biopsy diagnosis: consistent with papillary urothelial carcinoma, high grade (G2), stage pTa.

There were no requirements for further ancillary testing on either the cytology fluid or histology biopsy.

No indication of a differential diagnosis.

The outcome of both tests correlated with the CT scan results.



### **Surgical Options**

Surgical options depend upon the stage (CT), location of the cancer and health of the patient.

Stage 1 and 2 – located in the kidney (stage depends upon lesion size).

Partial Nephrectomy + lymph nodes – smaller tumours, patients with reduced kidney function.

Radical nephrectomy + lymph nodes – larger tumours, more than one, central part of the kidney.

Stage 3 – spread to nearby lymph nodes or large veins.

Radical nephrectomy and removal of nearby metastasis/lymph nodes.

**Stage 4** – Cancer spread to other parts of the body.

Remove kidney and metastasis, remove kidney only, palliative care



## **Multidisciplinary Meeting**

The case was discussed at the weekly uropathology multidisciplinary meeting.

Consultants, surgeons, nurses, Radiologists, Consultant Pathologist etc.

### Agreed plan

- Right nephroureterectomy removal of the whole kidney.
- Chemotherapy Intravesical Treatment: Mitomycin C (MMC).
- Genetic testing (Lynch syndrome).

Previous tests had also revealed that it was anticipated the remaining left kidney would continue to function normally.



## **Planned Surgery**

### **Routine pre op tests:**

Normal except...... high serum Human Chorionic Gonadotropin (HCG) Pregnancy test performed – positive. Operation postponed.

Discussion with patient revealed:

- recently had a period 3 weeks ago.
- partner had a vasectomy a few years ago, failed vasectomy possible...

RVI gynaecology team consulted: transabdominal scan performed.

No definite gestation and unremarkable ovaries. As there had been a recent last menstrual period (LMP), a pregnancy may be too early to diagnose.



## Gynaecology/Urology team collaboration

HCG levels still increased over 3 consecutive days of testing – another scan no embryo.

?HCG levels due to tumour – highly unlikely.

Results discussed with patient:

- this type of cancer is aggressive.
- if left untreated, may be incurable.



The patient accepted the risks of a miscarriage and decided to continue with the procedure.



## Shared decision making – NICE guidelines

### **Shared decision making**

- Joint process healthcare professional works together with a patient to reach a decision about care.
- It involves choosing tests and treatments based both on evidence and on the person's individual preferences, beliefs and values.
- It makes sure the person understands the risks, benefits and possible consequences of different options through discussion and information sharing.

### **Benefits**

- Discuss and share information.
- This makes sure people have a good understanding of the benefits, harms and possible outcomes of different options.
- It empowers people to make decisions about the treatment and care that is right for them at that time.
- It allows people the opportunity to choose to what degree they want to engage in decision making.



### **Right Robotic Nephroureterectomy - Histology**

- A right nephroureterectomy was performed and forwarded to Histology for analysis.
- Results confirmed a high-grade urothelial carcinoma with complete excision.
- Stage 2 therefore no evidence it had spread to nearly lymph nodes or organs.
- Unusual HCG levels and no confirmed pregnancy
  HCG ancillary testing was performed on the tumour.
- This was found to be positive! Rare.







### **Post Operative Analysis**

Post-operative serum tests showed:

- dramatic decreased levels of HCG
- transvaginal scan showed no evidence of a pregnancy.

The diagnosis of a high-grade urothelial carcinoma in a 35-year-old female patient suggests this a rare case.

The complexity of a possible pregnancy diagnosis added to the cancer diagnosis led to a difficult management decision by the clinicians and the patient/family.

In this case, the patient history and all scans pointed to a false pregnancy, which was supported by

- ICC testing.
- Sharp decrease in serum HCG after the nephrectomy.



## CONCLUSION

Following surgery and chemotherapy:

Ultrasound examination was carried out - tumour was completely resolved.

No evidence of metastatic disease or pregnancy.

Genetic testing showed no abnormalities associated to Lynch syndrome.

The five-year survival rate for stage 2 kidney cancer is ~74% therefore; surveillance will be necessary due to an increased risk of recurrence.

Cystoscopic follow-up with cytology washings at least 3 months and 12 months after diagnosis for up to 5 years.

09/01/2024 Cytology bladder washings negative.



### REFERENCES

Institute of Biomedical Science Higher and Expert Qualifications <u>https://www.ibms.org/education/higher-and-expert-gualifications/diploma-of-expert-practice/diagnostic-cytopathology/</u> Accessed 24<sup>th</sup> May 2025

Cross, P: Chandra, A: Maddox, A: Narine, N and Giles, T (2019) Tissue pathways for Diagnostic Cytopathology [online], Available at: <u>Microsoft Word - G086 Tissue pathways for diagnostic cytopathology For Publication.docx</u> (rcpath.org). Accessed 14<sup>th</sup> May 2023.

NICE (2015) Nice guidelines for bladder cancer diagnosis and management ]online], Available at: <u>https://www.nice.org.uk/guidance/ng2/chapter/1-recommendations#follow-up-after-treatment-for-non-muscle-invasive-bladder-cancer-2</u>. Accessed 14<sup>th</sup> May 2023.

NICE (2023) Shared Decision Making [online], Available at: Shared decision making | NICE guidelines | NICE guidelines | NICE, guidance | Our programmes | What we do | About | NICE, Accessed 14<sup>th</sup> May 2023.

OCS (2021) Cancer Registration Statistics, England 2017 [online], Available at: <u>Cancer registration statistics</u>, <u>England - Office for National Statistics</u>, Accessed on: 23<sup>rd</sup> October 2022.

Scelo, G and Larose, T L (2018) Epidemiology and Risk Factors for Kidney Cancer. *Journal of Clinical Oncology*, 36(36), pp3574–3581.

Soni, S; Menon, MC; Bhaskaran, M; Jhaveri, KD; Molmenti, E; Muoio, V (2013) Elevated human chorionic gonadotropin levels in patients with chronic kidney disease. Indian Journal of Nephrology, 23(6), pp424-427.





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for Cytopathology



#### 28TH MAY 2025

## Members lunchtime slide club (May 2025)



### Free to BAC members!

Register to join the new monthly BAC Members Lunchtime Slide Club.

If you have a camera and microscope set up to live stream your case or have digital images please bring them to this session.

Talk through, share or showcase any interesting or challenging cases you might have.

This is an informal space for members to learn, grow and interact with experts.

Register today!

