



Visualisation at it best

Update series on bladder endoscopy and pathology. Part I: non-muscle invasive bladder cancer. Prof. Dr Bernard Malavaud - Dr Catherine Mazerolles, Toulouse (France)

Stage	White light	PDD	Pathology	Pathology	Pathology
pTA LMP					
pTA LG					
pTA HG					
pTI HG					
pTI HG					
CIS					
CIS					
CIS					
CIS					

History

Case 1:

76 yo. Male, first cystoscopy for gross haematuria shows two small (5mm) papillary lesions that are faintly fluorescent. Washout cytology is not suspicious of urothelial carcinoma.

Case 2:

First diagnosis of pT1aLG one year before followed by 8 cycles of MMC. First recurrence 8 months later (pTaLG with small foci of pTaHG (10%) treated by BCGx6. Present follow-up cystoscopy shows multiple areas of papillary lesions with indiscriminate borders that are faintly fluorescent. Cytology was not evocative of HG tumour.

Case 3:

53 yo male, Cystoscopy for gross haematuria, shows multiple (>20) slightly raised and intensely fluorescent lesions with wide insertion onto the bladder wall.

Case 4:

53 yo male, non-smoking, first cystoscopy for gross haematuria shows a massive (3cm wide) and intensely fluorescent tumour in the bladder base, with two flat lesions in the vicinity that proved to be CIS.

Case 5:

81 yo Male, previous history of recurrent "superficial cancer" in another centre. Cystoscopy shows two papillary lesions on the right aspect of the bladder wall with a large (5-cm wide) fluorescent flat lesion on the bladder dome that proved to be CIS. Cytology was unevocative due to associated inflammatory cells.

Case 4 (continued):

Discrete area that is slightly raised and intensely fluorescent in the vicinity of a single exophytic high-grade lesion (pT1HG).

Case 5 (continued):

A slightly uneven surface in white light cystoscopy that was intensely fluorescent in blue light was harvested by cold cup biopsy.

Case 6:

71 yo male, EBRT for prostate cancer 7 years ago. Positive cytology with no evidence of disease on white light cystoscopy. Blue light shows a faint irregular signal on the right bladder wall.

Case 7:

70 yo male with history of pT1G3 treated by BCG + maintenance. Positive cytology but unevocative white light cystoscopy spurred two successive random biopsies that failed to show any significant abnormalities. Blue light showed three large flat and fluorescent areas whose detached urothelium was intensely fluorescent (inset).

Pathology

This tumour shows discrete and not fused papillary stalks that are covered by a multilayered urothelium with minimal atypia. Note the presence of terminally-differentiated umbrella cells (arrowhead) and the absence of mitotic figures.

Coalescent papillary stalks with orderly but variable (x10 power) organization of the urothelium layer that befits the WHO 2004 definition of Low Grade tumour (WHO1973 Grade I). Note one mitose (arrowhead) that is not located in the basal layer.

Short and wide papillary stalks are focally fused with intense angiogenesis close to the basal membrane (arrowhead). Loss of superficial layer maturation with marked architectural disorders and significant cell atypias, as evident compared to normal urothelium in a Brun nest (*). MIB1 shows high proliferative activity. While classified as High Grade in the WHO 2004 classification atypias are not intense enough to qualify for Grade 3 in the 1973 WHO classification. It is then recommended to report in the two grading systems: HG WHO 2004, Grade 2 WHO 1973.

Massive and coalescent papillae with invasion of the superficial stromal layer by high-grade carcinoma, as shown by anticytokeratine immunostaining (AE1AE3). Note the high microvessel density, evident on H&E staining and confirmed by anti CD31 staining.

Despite thin and well-formed papillary stalks, invasion of the superficial stromal layer is evident on HE staining (box). High power shows frank cell atypias with marked pleiomorphism and hyperchromasia. The infiltrative component exhibits a rare microkystic variant with well-formed cysts (arrowhead).

Pleiomorphic cells with hyperchromatic nuclei are found underneath the most superficial layer of the mucosa that retains terminal differentiation (arrowhead) as reported in the Amin's classification (AmJSurg Pathol 2001) as an "undermining" variant of *carcinoma in situ*. Note intense p53 staining in this contingent.

Low power is evocative of the erosive form of *carcinoma in situ* as the urothelial layer is detached (arrowhead) or denuded (*). At high power large pleiomorphic cells with abundant cytoplasm are grouped in clusters and remain attached to the basal layer (arrowhead).

The urothelial layer is thin and disorganised. Note the presence of large proliferative cells with prominent nuclei (arrowhead). Proliferative cells (MIB1) are interspersed between normal cells in a *pagetoid variant of carcinoma in situ*.

Low power shows denuded areas (arrowhead), when present (*) the urothelium is normal looking. High power (box) shows faint abnormalities in the guise of slight architectural disorganisation and presence of large nuclei that were not sufficient to characterise *carcinoma in situ*. However, intense and discrete p53 staining confirms malignancy.