Extent of invasion (Required)

Reason/Evidentiary Support

Reporting the extent of invasion is a critical part of the assessment of carcinomas arising in the urinary tract. The elements included reflect the anatomic landmarks that are essential to the pathologic staging of each tumour and vary by site within the urinary tract.[1] It is not appropriate to assign pathologic stage on biopsy or transurethral resection (TUR) specimens and pathologic stage is not an element within this dataset. It is however possible, based on the assessment of the extent of invasion to recognise the least pathological stage possible in a given case.

The diagnosis of invasion can be challenging. Throughout the urothelial tract histologic features that are indicative of stromal invasion include individual tumour cells, irregular nests or cords of cells, retraction artefact around nests, increased cytoplasmic eosinophilia and a myxoid or desmoplastic stromal response.[2,3] Several studies have documented the difficulty with the diagnosis of invasion.[4-6] Two large studies based on central review of patients being entered on clinical trials have demonstrated the over diagnosis of invasion in 35% to 53% of cases.[7,8] Studies have also demonstrated lack of agreement among pathologists with special interest in urologic pathology.[9] In some cases immunohistochemistry with a pan cytokeratin marker is helpful in identifying individual cells particularly when there is a heavy inflammatory infiltrate present. Following the principles of the American Joint Committee on Cancer (AJCC) TNM staging system the diagnosis of invasion should be limited to cases with unequivocal invasion.[1]

Identification of invasion of smooth muscle fibres in specimens from the renal pelvis, ureter and urethra all indicate T2 disease. In the urinary bladder the presence of the muscularis mucosae complicates the interpretation as involvement of these fibres still represents a T1 tumour.[10] Muscularis mucosae fibres can be present throughout the bladder.[11] The trigone/bladder neck region least often has recognisable muscularis mucosae fibres and from a practical perspective involvement of smooth muscle in this location essentially always indicates muscularis propria invasion. Muscularis mucosae fibres are typically thin and wispy forming small bundles that taper at the ends and usually are only a few cells thick. They lack the dense eosinophilic cytoplasm characteristic of muscularis propria. Often the fibres are seen in association with a layer of thick walled blood vessels. The muscularis mucosae can however occasionally be thickened and better defined, more closely mimicking muscularis propria. Smoothelin, a cytoskeletal protein is differentially expressed in the muscularis propria and not the muscularis mucosae.[12] Application in challenging cases can be helpful but for the most part the marker has not gained widespread application.[13,14] Regarding the use of smoothelin for staging, the International Society of Urological Pathology (ISUP) states “limited experience and conflicting data preclude smoothelin or vimentin to be recommended routinely for subclassifying muscle type at this time.”[15] In some cases it is not possible to be certain if the smooth muscle involvement represents muscularis mucosae or muscularis propria. In those cases this should be specifically commented upon. Repeat TUR on these cases is necessary to determine the true depth of involvement.[14]

Assessment of the presence or absence of muscularis propria invasion can also be hampered by cautery artefact. This can result in stromal changes that mimic smooth muscle leading to over staging or make muscularis propria unrecognisable leading to under staging.[16] Pathologists have

used histochemistry (trichrome stain) or immunohistochemistry (desmin) to help determine if muscle is represented in cauterized tissue but no controlled studies of the reliability of these approaches is available.

Urothelial carcinoma can be primary in the prostatic urethra but in the majority of cases involvement is seen in association with a bladder tumour.[17-19] Among all male patients with bladder cancer the prostate is involved in approximately 4% of cases.[20] Prostatic involvement is found in 15% to 48% of patients undergoing cystoprostatectomy for urothelial carcinoma of the bladder.[21-24] Involvement is usually by urothelial CIS but occasionally papillary tumours are seen. Extension into the prostatic ducts is frequently present in these cases and should not be mistaken for invasion. Inflammation can be present around the ducts in the absence of invasion. Usually invasion of the subepithelial connective tissue or the prostatic stroma elicits a desmoplastic response. Immunohistochemistry is frequently required to distinguish urothelial carcinoma from high grade prostatic carcinoma.[15] Glandular and or squamous differentiation can be present as with urothelial carcinoma elsewhere.

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