Non-invasive carcinoma (Required)

Reason/Evidentiary Support

The majority of patients with urothelial carcinoma present initially with non-invasive disease. Most of these have a non-invasive papillary tumour and much less frequently have urothelial any identifiable urothelial component no matter how small and including urothelial carcinoma (CIS) as the initial diagnosis. Non-invasive papillary tumours account for 70% to 75% of newly diagnosed cases with over one-half being in the lower grade categories (papillary urothelial neoplasm of low malignant potential, low grade papillary carcinoma).[1,2] Urothelial CIS in its pure form counts for 1% to 3% of newly diagnosed urothelial tumours and is by definition high grade.[3] Much more often it coexists with high grade papillary urothelial carcinoma and is found in association with invasive urothelial carcinoma in up to 65% of cases.[3-5] Papillary tumours range from benign (papilloma, papillary urothelial neoplasm of low malignant potential) to low and high grade carcinomas. CIS and papillary carcinoma develop by different genetic pathways and have different biologic behaviour and so are considered as different entities within the non-invasive category.[6]

Classification of non-invasive urothelial tumours into the papillary and in situ categories has both prognostic and management implications. Further the identification of CIS coexisting with papillary carcinoma also has significance for prognosis and treatment. In biopsy and transurethral resection of bladder tumour (TURBT) specimens both diagnoses can be rendered when the papillary carcinoma and the CIS are present on different tissue fragments or in specimens submitted from different sites. When flat lesion is present adjacent to and in continuity with a papillary tumour the question becomes whether the flat part represents a “shoulder” of the papillary tumour or coexisting CIS. There are no generally accepted criteria for making this decision even though the diagnosis does have clinical significance. We would recommend making the diagnosis of associated CIS in this situation if (i) there is a gap of normal urothelium between the papillary tumour and the flat lesion or (ii) if the morphology of the flat lesion is different than that of the epithelium on the surface of papillary fronds.

For patients presenting with invasive urothelial carcinoma the recognition and documentation of an associated non-invasive papillary carcinoma and/or CIS remains important. For patients with T1 disease the presence of CIS indicates a significantly increased risk of subsequent recurrence and of progression to muscle invasive disease. For patients with CIS of the bladder unresponsive to Bacillus Calmette-Guerin (BCG) therapy this is an indication for early cystectomy.[7-9] The presence of associated CIS in newly diagnosed high grade T1 disease may also be used to support early cystectomy.[7,10] For patients presenting with invasive urothelial carcinoma there are data that such cases arising through the “papillary” pathway have stage for stage a better prognosis that those developing via the “flat” pathway.[11,12]

There is also evidence that the extensiveness of the CIS is significant and so distinguishing between a single focus and diffuse (or multifocal) disease is important. For the purpose of this dataset, diffuse is defined as the presence of CIS in more than one site as indicated by biopsies submitted separately or involving more than one tissue fragment in a TURBT specimen.

Lastly non-urothelial CIS can also occur in the urinary tract. Most frequently this is squamous cell CIS typically in association with keratinizing squamous metaplasia. This can be identified in patients with

invasive squamous cell carcinoma but also can be diagnosed in the absence of invasive disease. Adenocarcinoma in situ is not a well-defined lesion in the urinary tract. In cases of intestinal metaplasia varying degrees of atypia can be seen up to high grade dysplasia, a term we would prefer rather than adenocarcinoma in situ. Urothelial CIS can show areas of squamous and glandular differentiation and these should not be diagnosed as squamous or adenocarcinoma in situ respectively.

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