cervix, or upper vagina, entering the anterior vagina, or on mobilizing or suturing the vaginal vault. If a bladder injury is noted at this time, it can usually be easily managed by a 2 or 3 layer closure. Retrograde bladder filling with blue colored saline facilitates bladder injury diagnosis. Undiagnosed intraoperative injuries to the bladder typically present days to weeks after surgery. In patients with prior pelvic irradiation, fistulas can present months to even years after hysterectomy.

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PATHOLOGY

Renal cell carcinomas with papillary architecture and clear cell components: the utility of immunohistochemical and cytogenetical analyses in differential diagnosis

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Although histologic features enable an accurate diagnosis in most renal carcinomas, overlapping morphologic findings between some renal neoplasms make subclassification difficult. Some renal carcinomas show papillary architecture but are composed extensively of cells with clear cytoplasm, and it is unclear whether they should be classified as clear cell renal cell carcinomas or papillary renal cell carcinomas. We analyzed the immunohistochemical profiles and the cytogenetic patterns of 14 renal carcinomas showing papillary architecture in which there were variable amounts of cells with clear cytoplasm. The patients were 8 women and 6 men (mean age: 54 y). Immunohistochemistry and fluorescence in situ hybridization analysis distinguished 2 different groups. The first consisted of 10 renal cell carcinomas with strong immunoreactivity for alpha-methyl coenzyme A racemase, of which 9 also expressed cytokeratin 7. All of these neoplasms showed gains of chromosome 7 or 17 and chromosome Y was lost in all the male patients whereas 3p deletion was detected only in one case. In the other 4 renal cell carcinomas, cytokeratin 7 was not detected and alpha-methylacyl-CoA racemase was positive in only 1. In these neoplasms, no gain of chromosome 7 or 17 and no loss of chromosome Y were observed, whereas 3p deletion was detected in 3 of them. None of the 14 neoplasms showed immunoreactivity for TFE3. The combined use of immunohistochemistry and cytogenetics enabled us to provide a definitive diagnosis for 12 of 14 renal cell carcinomas with papillary architecture and clear cell components: 9 cases were confirmed to be papillary renal cell carcinomas and 3 cases were confirmed to be clear cell renal cell carcinomas. Despite these ancillary techniques, 2 cases remained unclassified. Our study establishes the utility of these procedures in accurately classifying the great majority of renal cell carcinomas with these findings.

Editorial Comment

In some tumors, the pathologist finds clear cell component in an otherwise papillary tumor. The usual papillary renal cell carcinoma may be either type I or II. In the former, the cells have scant cytoplasm and due

to this cytological feature, the tumor has a blue tinge in the microscopic examination. Type II tumors have abundant eosinophilic cytoplasm. In case there is a clear cell component, the differential diagnosis is papillary renal cell carcinoma with clear cell component vs. clear cell (conventional) renal cell carcinoma with papillary features. The study by Gobbo et al. shows that immunohistochemical and cytogenetical analyses are important for the differential diagnosis.

Two other tumors that may have papillary architecture with clear cell component must be recognized: the renal carcinoma associated with Xp11.2 translocations/TFE3 gene fusions (1) and the renal cell carcinoma associated with acquired cystic kidney disease (2). The latter is easily diagnosed due to the association with patients submitted to hemodialysis. To exclude the former it is necessary that TFE3 is negative in immunohistochemistry.

It is controversial the significance of a clear cell component when the diagnosis is the usual papillary renal cell carcinoma. Some consider these tumors to have a good prognosis, which goes along with their low nuclear grade. Others, however, have shown that a clear cell component is associated with a higher stage (3-5).

In spite of this controversy, it is important that the practicing pathologist adds to his pathology report the finding of a clear cell component in cases of usual papillary renal cell carcinoma.

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The role of pathologic prognostic factors in squamous cell carcinoma of the penis

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Purpose: The aim of this review was to identify prognostic pathologic factors which are independent from other clinical or molecular variables.
Methods: We reviewed the literature on morphological prognostic factors emphasizing our personal experience.

Results: We found that for a proper evaluation of prognostic factors a familiarity with penile complex anatomy is required. A biopsy of the primary tumor is not useful for a complete evaluation of prognostic factors other than malignancy and a resected specimen should be utilized. Penile carcinomas have a fairly predictable pattern of local, regional and systemic spread. Pathologic factors affecting patients outcome are multiple but it is difficult from the available studies using heterogeneous pathologic methodologies, different therapeutic approaches and ecologically variable patient populations to ascertain the independent validity of these factors. Invasion of perineural spaces by tumor, lymphatic-venous embolization and histological grade appear to be the most important pathologic predictors of nodal spread and cancer mortality. Other commonly cited factors influencing prognosis are tumor depth or thickness, anatomical site and size of the primary tumor, patterns of growth, irregular front of invasion, pathologic subtypes of the SCC, positive margins of resection and urethral invasion. A combination of two factors, histological grade and depth has been reported as significant predictor of cancer regional spread. After a preselection of significant factors, nomograms have been constructed to collectively evaluate the predictive power of various clinical and pathological indicators.
Conclusions: Among various factors perineurial invasion, vascular invasion and high histological grade appear to be the most important adverse pathological prognostic factors.

Editorial Comment

This is a very comprehensive review on a tumor that is very important in Brazil. A very recent article in Int Braz J Urol has shown the epidemiologic characteristics of penile cancer in this country (1). It is a very frequent tumor, predominantly affecting low income, non-neonatal circumcised males, Caucasian patients living in North and Northeast regions of Brazil where there may be a delay in obtaining specialized medical assistance.

Dr. Cubilla is an expert on penile carcinoma living in a country (Paraguay) also with a very high frequency of this tumor. He reviews the prognostic factors in squamous cell carcinoma. Among various factors, perineural invasion, vascular invasion and high histological grade appear to be the most important adverse pathological prognostic factors and should be reported by the pathologist. He also emphasizes the importance of the gross examination of the surgical specimen.

The grading of squamous cell carcinoma of the penis is based on the production of keratin. Abundant keratin production characterizes well differentiated tumors; keratinization of isolated cells moderately differentiated tumors; and, no production of keratin undifferentiated tumors.

The histopathologic subtypes are also important in prognosis. Verrucous carcinoma is a very well differentiated variant, the base is broad in all cases with pushing, regular borders composed of broad bulbous projections, which are usually restricted to the lamina propria but may extend deeper. They are slowly growing, locally infiltrative but do not metastasize. In some reports in the literature, this tumor is erroneously called giant condyloma. Verrucous carcinomas lack the HPV-related cellular changes characteristically seen in giant condyloma, and are not causally related to HPV, unlike giant condyloma (2).

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