The use of fibrin sealants in urology has been particularly popular recently, due to its use in laparoscopic kidney surgery. With the expanding role of laparoscopy for partial nephrectomy, methods to better control urinary leak or bleeding have been explored. Aside from direct suturing of the collecting system and vessels, fibrin sealants have been the "suspenders" to the "belts" of suturing. The current commercially available sealants are Tisseel "fibrin sealant", (by Baxter, a mix of fibrinogen aprotonin solution, Factor XIII, and human derived thrombin), FloSeal "gelatin matrix" (by Baxter, a mix of human derived thrombin and bovine derived gelatin matrix), and BioGlue "surgical adhesive" (by Cryolife, a mix of bovine serum albumin and gluteraldehyde).

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PATHOLOGY

Xp11.2 Translocation Renal Cell Carcinoma with Very Aggressive Course in Five Adult Patients

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Background: Renal cell carcinomas (RCC) associated with Xp11.2 translocations (TFE3 gene fusions) are rare tumors occurring predominantly in children and young adults. Although, thus far, only limited data is available, these tumors are believed to be rather indolent even when diagnosed at advanced stages.
Design: Five cases of TFE3-RCC were evaluated in patients aged 18 or older (mean age 31). Diagnosis was confirmed by IHC detection of increased TFE3 fusion protein. Morphology was examined by HE, IHC and electron microscopy (EM) and correlated with clinical picture.
Results: HE showed clear cells, arranged in a pseudopapillary architecture, with retention of morphology in the metastatic tumor deposits. By IHC there was strong nuclear positivity for TFE3 in all cases and focal stain for AE3 and vimentin; stains for HMB45, calretinin, pankeratin and AE1 were all negative. By EM (2/5 cases examined) there were junctional complexes and rudimentary microvilli. In one case there were abundant lipid droplets and glycogen; in a second case, rare rhomboid crystals, similar to those seen in alveolar soft part sarcoma, were present. All patients (3 Caucasian, 2 Hispanic) presented with innocuous complaints, abdominal/flank pain and hematuria, and lacked any significant prior history. All but one patient presented with distant metastases at the time of diagnosis, and all patients were diagnosed with additional metastases or tumor recurrence within 5 months of presentation. Treatments included tumor resection, interleukin-2 therapy, combination chemotherapy, and radiation therapy, all with minimal success. Patients followed a rapidly terminal course, with a mean survival of 15 months post-diagnosis (range 10-20 months). One patient is currently undergoing chemotherapy at 13 months post-diagnosis (with brain metastasis), and another patient is alive at 6 months post-diagnosis, with metastases.
Conclusions: The patients presented here were older than typically described for TFE3-RCC. Although tumor morphology was similar to pediatric patients, these adult patients had a very aggressive clinical course compared to pediatric TFE3-RCC and even to conventional, adult-type RCC. Consistent use of antibodies against TFE3 in all tumors, regardless of patient age, may expand the spectrum of Xp11.2 translocation RCC with respect to age, clinical behavior and molecular abnormalities.

Editorial Comment

These carcinomas are defined by several different translocations involving chromosome Xp11.2. The t(X; 1) (p11.2; q21) translocation results in the fusion of TFE3 gene in chromosome X to PRCC gene in chromosome 1; the t(X; 17) (p11.2; q25) translocation results in the fusion of TFE3 gene in chromosome X with the ASPL gene in chromosome 17. This latter translocation is also seen in the alveolar soft part sarcoma.

These carcinomas predominantly affect children and adolescents and are believed to be rather indolent even when diagnosed at advanced stages. The most distinctive histopathologic appearance is that of a carcinoma with papillary architecture comprised of voluminous clear to eosinophilic cytoplasm, discrete cell borders, vesicular chromatin and prominent nucleoli. Scattered hyaline nodules and psammomatous bodies can be seen. The most distinctive immunohistochemical feature of these tumors is nuclear immunoreactivity for the chimerical (mutant) TFE3 protein (1).

The present study by Meyer et al. reported 5 patients of TFE3 renal cell carcinoma aged 18 or older (mean age 31). All but one patient presented with distant metastases at the time of diagnosis, and all patients were diagnosed with additional metastases or tumor recurrence within 5 months of presentation. The authors emphasize the fact that although tumor morphology was similar to children and adolescents, these adult patients had a very aggressive course. It is noteworthy a Brazilian female 58-year old recently reported with renal cell carcinoma associated with Xp11.2 translocation TFE3 (ASPL-TFE3) gene fusion (2). Metastases were seen in 3 of the 6 dissected lymph nodes, thus determining a final staging (TNM, 2002) pT1b, pN2, pMX (stage IV). After approximately 6 months of follow-up, the patient showed favorable outcome, without manifesting disease or any other signs or symptoms.

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Papillary Renal Cell Carcinoma: Assessment of Clear Cell Change and Clinicopathologic Correlation

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Background: Papillary renal cell carcinoma with clear cell change and chromosome 3p21 aberration has been described. The significance of this finding, however, remains unclear. We perform the first study to investigate the significance of clear cell change and its clinicopathologic correlation.

Design: Nineteen cases of papillary renal cell carcinoma between 1992 and 2005 were retrieved from the slide archives in the Department of Pathology, Westchester Medical Center. Cytogenetic findings were obtained in 2 cases. All tumors were subclassified as type 1 or 2 and were evaluated for clear cell change and Fuhrman nuclear grade. American Joint Committee on Cancer TNM Staging of Renal Cell Carcinoma (2002) was used and clinical charts were reviewed retrospectively to obtain clinical stage.
Results: The patient age ranged from 11 to 77 years (mean 56). Sixteen patients were males and 3 were females. Tumor size ranged from 1.8 to 10 cm (mean 4.6 cm). All tumors contained clear cells ranged from 0 to 85%. Of the 12 tumors with 0 to 25% clear cells, 9 cases presented with stage I, 2 with stage II, and 1 with stage III disease. Seven tumors possessed clear cell change ranged from 30 to 85%. Of these 7 patients, 2 cases presented with stage I, 1 with stage II, 3 with stage III, and 1 with stage IV. Cytogenetics findings in a tumor with 30% clear cells revealed 49-50X,-X, der(3)add(3)(p21),+7,+17,-19,+21 and the case with 5% clear cells showed 57,XXY,+2,+3,+4,+7,+8,+12,+16,+17,+20. Nine cases (47%) were classified as type 1 and 10 cases (53%) type 2. Of the 9 type 1 tumors, 2 cases had grade 1 nuclei, 6 grade 2, and 1 grade 1. Six of these patients presented with stage I, 2 with stage 2, and 1 with stage IV. In comparison to type 1, 5 cases of type 2 lesions had a nuclear grade of 2 and 5 had grade 3 nuclei. Five patients presented with stage I, 1 with stage II, and 4 with stage III disease.
Conclusions: Type 2 papillary renal cell carcinomas have higher nuclear grade and stage than that of type 1 lesions. Type 2 lesions have poorer prognosis than type 1. Patients bearing tumors with greater than 30% clear cells present with higher stage of disease. Therefore, clear cell change may be a useful pathologic prognosticator in evaluating clinical behavior of these tumors.

Editorial Comment

Papillary renal cell carcinoma has a tendency to present at a lower stage, but with a distinct potential for progression and aggressive behavior (1). Papillary renal cell carcinomas comprise approximately 10% of renal cell carcinoma in large surgical series. The tumor is characterized by malignant epithelial cells forming varying proportions of papillae and tubules. The tumor papillae contain a delicate fibrovascular core and aggregates of foamy macrophages and cholesterol crystals may be present. Solid variants consist of tubules or short papillae resembling glomeruli.

Two morphological types of papillary renal cell carcinoma have been described (2). Type 1 tumors have papillae covered by small cells with scanty cytoplasm, arranged in a single layer on the papillary basement membrane. Type 2 tumor cells are often of higher nuclear grade with eosinophilic cytoplasm and pseudostratified nuclei on papillary cores. Type 1 tumors are more frequently multifocal. Sarcomatoid dedifferentiation is seen in approximately 5% of these tumors and has been associated with both type 1 and type 2 tumors. In series of papillary renal cell carcinoma containing both type 1 and 2 tumors, five year survivals for all stages range from 49% to 84% with tumor grade, stage at presentation and the presence of sarcomatoid dedifferentiation being correlated with outcome. Longer survivals have been demonstrated for type 1 when compared with type 2 on both univariate and multivariate analysis that included both tumor stage and grade.

Uropathologists are aware of the fact that some papillary renal cell carcinomas show clear cell differentiation. Torres-Cabala et al. (3) showed that some of papillary renal cell carcinomas with clear cell differentiation show 3p deletion that is a common finding in conventional clear cell carcinoma. They suggested that this finding might represent an early event in tumor progression to conventional clear cell carcinoma. The study of Dasgupta and Yeh is a further evidence that clear cell differentiation in papillary renal cell carcinomas may have prognostic implications. Patients bearing tumors with greater than 30% clear cells presented with higher stage of disease. Pathologists should report on presence of clear cell differentiation in papillary renal cell carcinomas.

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INVESTIGATIVE UROLOGY

Immunohistochemical Distribution of cAMP- and cGMP-Phosphodiesterase (PDE) Isoenzymes in the Human Prostate

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Objectives: With the introduction of sildenafil citrate (VIAGRA trade mark), the concept of phosphodiesterase (PDE) inhibition has gained tremendous interest in the field of urology. Cyclic nucleotide second messengers cGMP and cAMP have been assumed to be involved in the control of the normal function of the prostate. The aim of the present study was to evaluate by means of immunohistochemistry the expression and distribution of some cAMP- and cGMP-PDE isoenzymes in the prostate.
Material & Methods: Cryostat sections (10muM) of formaldehyde-fixated tissue segments excised from the transition zone of human prostates were incubated with primary antibodies directed against the PDE isoenzymes 3, 4, 5, and 11. Then, sections were exposed to either fluorescein isothiocyanate- (FITC) or Texas Red- (TR) labeled secondary antibodies and visualization was commenced by means of laser fluorescence microscopy.
Results: TR-immunofluorescence indicating the presence of PDE4 (cAMP-PDE) was abundantly observed in the fibromuscular stroma as well as in glandular structures of the transition zone. In contrast to the distribution of PDE4, immunoactivity indicating PDE5 (cGMP-PDE) and 11 (dual substrate PDE) was mainly observed in glandular and subglandular areas. No immunostaining for PDE3 (cGMP-inhibited PDE) was detected.
Conclusion: Our results confirm the presence of PDE isoenzymes 4, 5 and 11 in the transition zone of the human prostate and present evidence that these isoenzymes are not evenly distributed. These findings are in support of the hypothesis that there might be a rationale for the use of PDE inhibitors in the pharmacotherapy of BPH and LUTS.