tumor remained free of disease 13 months after nephrectomy and the one with T3N0M0 tumor remained free of disease at 17 months. A patient with a T3N+M+ tumor experienced progression at 1 month, local recurrence at 17 months and was then lost to followup. The 2 other patients with T3N+M0 and T3N+M+ disease, respectively, progressed rapidly and were lost to followup after 5 months. One patient with a T3N+M0 neoplasm received immunotherapy and died after 24 months, while the other with T3N+M0 disease was treated with oral prednisolone and died after 5 months. Finally, 2 patients with T3N+M+ disease received chemotherapy, consisting of 1,250 mg/m2 gemcitabine on days 1 and 8, and 70 mg/m2 cisplatin on day 1. Each patient achieved an objective response after 3 chemotherapy cycles and remained disease-free 27 and 9 months after nephrectomy, respectively.

Conclusions: CDC is an aggressive variety of kidney neoplasm that is often associated with nodal and visceral metastases at presentation. Our data suggest that combined gemcitabine and cisplatin chemotherapy may be the best therapeutic option for patients with this tumor.

Editorial Comment

Collecting duct carcinoma accounts for approximately 1 per cent of renal cell neoplasms. In spite of its rarity is considered one of the most aggressive variants of renal tumors. No consistent pattern of genetic abnormalities has been established. The morphologic features are characterized by irregular tubules reminiscent of the Bellini collecting ducts set in a desmoplastic stroma. An affinity for the Ulex europaeus lectin supports a collecting duct origin for this tumor.

A differential diagnosis is with renal urothelial carcinoma with glandular differentiation. Favors this latter diagnosis squamous differentiation and dysplastic epithelium or in situ carcinoma in the pelvic urothelium. Another differential diagnosis is the recently described low-grade mucinous and spindle cell carcinoma of the kidney (Mod Pathol. 2002; 15: 182A). Microscopically, it shows tubular structures reminiscent of the thin segment of the loop of Henle. It is a tumor with good prognosis and a striking female preponderance. The immunohistochemistry displays proximal and distal nephronic markers.

A variant of collecting duct carcinoma is the medullary carcinoma of the kidney. This variant was described by Davis, Mostofi and Sesterhen (Am J Surg Pathol. 1995; 19: 1-11) which is believed to arise from the collecting ducts of the renal medulla and is associated with sickle cell trait. The authors coined this tumor as the seventh sickle cell nephropathy. The other 6 are hematuria, papillary necrosis, nephrotic syndrome, renal infarction, inability to concentrate urine and pyelonephritis.

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INVESTIGATIVE UROLOGY

Analysis of the modifications in the composition of bladder glycosaminoglycan and collagen as a consequence of changes in sex hormones associated with puberty or oophorectomy in female rats

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Purpose: The effects of female sex hormones on rat vesical extracellular matrix were evaluated by analyzing glycosaminoglycan (GAG) and collagen composition under different hormonal conditions.

Materials and Methods: Bladders were obtained from Wistar rats, including young prepubertal females at age 30 days (YF), and adult intact females (AF), adult oophorectomized females (AOF), adult males and adult sham operated females at age 120 days. Oophorectomy and sham operation were performed at age 30 days. Bladders were analyzed for total GAG and collagen concentration per mg dry tissue and for the contents of GAG species, as determined by agarose electrophoresis and reported as the percent of total sulfated GAG.

Results: Collagen concentration in AF (54.80 +/- 4.60 microg/mg) was different from that in YF (34.52 +/- 5.29 microg/mg, $p < 0.001$) and AOF (63.25 +/- 3.51 microg/mg, $p < 0.001$). GAG concentration in AF (0.71 +/- 0.18 microg/mg) was different from that in YF (0.45 +/- 0.07 microg/mg, $p < 0.001$) and males (0.46 +/- 0.10 microg/mg, $p < 0.001$). The GAG species detected were dermatan sulfate and heparan sulfate. Dermatan sulfate content in AF (90.9% +/- 2.8%) was different from that in YF (86.6% +/- 2.4%, $p < 0.005$), AOF (87.9% +/- 2.1%, $p < 0.005$) and males (87.7% +/- 4.7%, $p < 0.005$). Heparan sulfate content in AF was 9.1% +/- 2.8%, which differed from that in YF (13.4% +/- 2.4%, $p < 0.025$) and AOF (11.2% +/- 2.9%, $p < 0.025$).

Conclusions: Extracellular matrix of the female rat bladder undergoes marked remodeling during normal growth up to early adulthood with important consequences for vesical viscoelastic properties. Also, oophorectomy performed at a prepubertal age may lead to greater vesical wall stiffness.

Editorial Comment

Sex hormones have been shown to variously affect the synthesis of extracellular matrix (ECM) molecules by mesenchymal cells such as fibroblasts and smooth muscles cells, both in vivo and in vitro. This effect is exerted on several tissues and organs and has, in many cases, a normal regulatory role. The ECM may also undergo abnormal modifications, and these have been implicated with many diseases, including urinary tract disorders. In the present study, the effects of female sex hormones on the biochemical composition of vesical glycosaminoglycans (GAG) and collagen in rats under different hormonal conditions were evaluated.

The results show that variations in the plasma levels of female sex hormones parallel different changes in the ECM composition of the rat bladder wall. During the normal growth of the female rat from a pre-pubertal age to early adulthood, there are marked increases in both total GAG and collagen concentrations, together with a small increase in dermatan sulfate and a more important decrease in heparan sulfate. Compared to the intact adult females, the bladders from oophorectomized adult females had a slightly higher collagen concentration but presented no change in total GAG, whereas the dermatan sulfate and heparan sulfate contents were decreased and increased, respectively, which may lead to greater vesical wall stiffness. Bladders from adult males differ from those of females of comparable age in that they have less total GAG, and hence a higher collagen: GAG ratio, and slightly less dermatan sulfate. In conclusion, this work demonstrates that the ECM of the female rat bladder undergoes a marked remodeling during normal growth up, which can lead to important consequences for vesical viscoelastic properties.

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Experimental varicocele induces testicular germ cell apoptosis in the rat

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Purpose: We evaluated the impact of experimentally created varicocele on ipsilateral and contralateral testicular germ cells in the rat.

Materials and Methods: Experimental left varicocele was created by partial ligation of the left renal vein in 17 adult male Sprague-Dawley rats. An additional 5 rats that underwent laparotomy and renal vein handling without ligation served as sham surgical controls. Five rats that underwent no surgical or other intervention served as a control group. Rats were sacrificed 7 (5), 14 (5) or 28 (7) days following varicocele creation. Germ cell apoptosis was quantified using a TUNEL assay. The results of this assay are expressed as the number of apoptotic germ cell nuclei per seminiferous tubular cross section. The presence of apoptosis was confirmed by cellular ultrastructure evaluation using transmission electron microscopy.

Results: Control and sham animals were found to have a mean of 0.05 and 0.15 apoptotic germ cells per seminiferous tubular cross section, respectively. Rats sacrificed 7, 14 and 28 days after varicocele creation were found to have 0.15, 0.23 and 0.27 apoptotic germ cells per tubule in the ipsilateral testis, and 0.14, 0.16 and 0.17 apoptotic germ cells per tubule in the contralateral testis, respectively. Compared with control animals a statistically significant increase in the number of apoptotic germ cells per tubular cross section was noted 14 days following varicocele creation in the ipsilateral testis ($p < 0.05$).

Conclusions: The creation of experimental varicocele generated an increase in germ cell apoptosis in the ipsilateral testis at 14 days compared with control animals.

Editorial Comment

Until now, a precise relationship between varicocele and infertility is yet to be clarified. The present study analyzed the testicular germ cell apoptosis in the rat as consequence of experimentally induced varicocele.

The authors used an established animal model for the creation of testicular varicocele for assessing the time impact of such a lesion on germ cell apoptosis. The findings confirmed that the normal Sprague-Dawley rat demonstrates low levels of germ cell apoptosis (0.05 apoptotic germ cells per tubular cross section). Also, the animals subjected to laparotomy without partial ligation of the renal vein demonstrated germ cell apoptosis that was not statistically different from that in normal controls. On the other hand, rats that underwent experimental varicocele creation showed significantly increased levels of germ cell apoptosis in the ipsilateral testis 14 days following varicocele creation.

Although the animal model of varicocele clearly differs from the clinical varicocele seen in humans, the findings of the present study indicate that experimental varicocele creation in the rat generates a time dependent increase in germ cell apoptosis in the ipsilateral testis. These findings may be the explanation of the mechanism by which varicocele exerts a pathological influence on testicular function in a clinical setting.

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