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Pathology in Practice

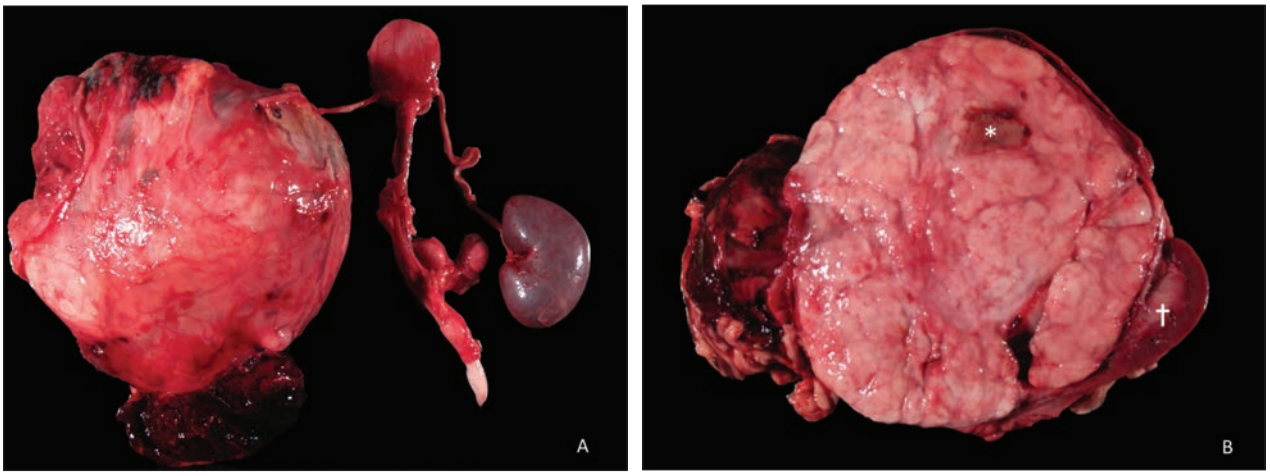

Figure 1—Photographs of the urogenital system (A) and cut section (B) of the left kidney of a 16-week-old sexually intact male Whippet. Notice that the left kidney is markedly enlarged (18 × 17 × 10 cm), compared with the size of the unaffected right kidney. On cut section, notice the tan lobulated mass with necrotic focus (asterisk) and residual normal renal tissue at the cranial pole (dagger).

History

A 16-week-old sexually intact male Whippet was evaluated because of a 1-week history of a firm abdominal swelling. The puppy had been obtained from a breeder at 9 weeks of age and had been healthy until the swelling was noticed.

Clinical and Gross Findings

Physical examination revealed a large, spherical, nonpainful mass that distorted the contour of the left flank area. The mass could not be palpated rectally, and both testicles were present in the scrotum. Abdominal ultrasonography revealed a 10-cm-diameter, internally lobulated, well-encapsulated mass originating from the caudal pole of the left kidney. There was no sonographic evidence of invasion of local vessels. A small amount of anechoic free fluid was evident adjacent to the mass. Ultrasound-guided fine-needle aspirate samples of the renal mass were obtained for cytologic examination. The owner declined surgery. One month later, the dog was reexamined because of signs of pain, particularly when defecating, and 1 episode of vomiting after eating grass; it was euthanized at that time.

At necropsy, the left kidney measured 18 × 17 × 10 cm and was distorted and largely replaced by a white to tan, lobulated mass (**Figure 1**) with two 2-cm foci of necrosis. Some residual grossly normal renal tissue was noted at the cranial pole. The right kidney was apparently normal. Samples of the renal mass, unaffected right kidney, and both adrenal glands were obtained for histologic examination.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

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Histologic and Pathologic Findings

Ultrasound-guided fine-needle aspirate samples of the renal mass that were obtained at initial evaluation underwent microscopic examination. Cytologically, smears of the samples were hemodiluted but contained numerous large atypical round cells (**Figure 2**). Cells were present singly or occasionally in cohesive clusters that suggested rosette formation; scant light pink matrix was seen in the background. Rarely, more extensive lakes of extracellular material contained embedded cell clusters. Individual cells were characterized by scant to moderately abundant basophilic cytoplasm that often contained a few small, clear cytoplasmic vacuoles and a single nucleus with round to oval to sometimes undulating nuclear margins; the chromatin was finely stippled. In the background, scattered macrophages with phagocytized cellular debris were evident; cytoplasmic fragments were not present. The cytologic diagnosis was anaplastic round cell tumor, consistent with nephroblastoma or, less likely, lymphoma. The presence of matrix and cell cohesion and the absence of cytoplasmic fragments were thought to be most consistent with the diagnosis of nephroblastoma (Wilms tumor).

During necropsy, renal mass samples were collected for histologic examination. Histologically, the renal tumor was composed of epithelial, stromal, and blastemal components (**Figure 3**). Epithelial cells were arranged in small cohesive irregular nests or in trabeculae, sometimes forming extracellular lumina and occasionally projecting tufts into lumina (primitive glomeruli). Epithelial cells were cuboidal to columnar with sparse to moderate amounts of eosinophilic cytoplasm, irregularly round to oval nuclei with densely clumped chromatin, and 1 to 2 nucleoli. Rare epithelial cells had evidence of squamous differentiation. Stromal elements consisted of elongated fibroblast-like cells with a scant amount of eosinophilic fibrillary cytoplasm; oval to elongated nuclei had stippled chromatin and 1 to 2 nucleoli. Rare cells had skeletal muscle differentiation with elongated eosinophilic cytoplasm and cross striations. Small, undifferentiated blastematous cells had high nuclear-to-cytoplasmic ratios, grew in loosely cohesive groups, and blended subtly into the epithelial and stromal components. Microscopic examination of samples of the unaffected right kidney and both adrenal glands revealed no abnormalities.

Samples of the renal mass underwent immunohistochemical analysis, and skeletal muscle elements were confirmed by detection of reactivity for muscle-specific actin, desmin, and myogenin. Epithelial components stained for cytokeratin AE1/AE3, and lumen-forming clusters also stained for cytokeratin Lu5. Nonepithelial components were positive for vimentin. Staining for neurofilaments and neuron-specific enolase revealed numerous nerve fibers and ganglion cells. Focal weak staining with Wilms tumor antigen 1 (WT1) of some tumor cells was interpreted as negative.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: nephroblastoma, triphasic, predominantly mesenchymal and epithelial with minor blastemal components, and heterologous elements including squamous epithelium, skeletal muscle, and ganglion cells (so-called teratoid nephroblastoma).

Case summary: renal nephroblastoma in a young dog.

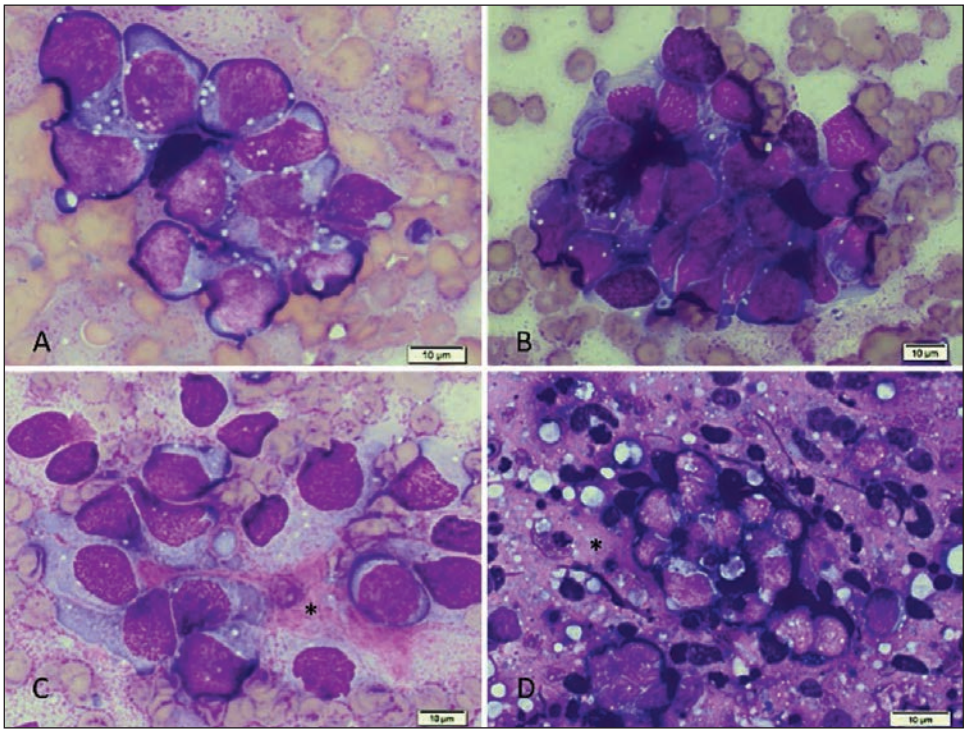

Figure 2—Photomicrographs of fine-needle aspirate samples of the renal mass obtained from the dog in Figure 1 at the initial evaluation. A—Aggregate of round cells with small cytoplasmic vacuoles and a mitotic figure. B—Cohesive group of cells with high nuclear-to-cytoplasmic ratio and a mitotic figure. C—Individual round to slightly elongated cells with a small amount of extracellular eosinophilic material (asterisk). D—Cohesive group of cells and several individual round cells; notice the abundant extracellular eosinophilic material in the background (asterisk). Scattered small, darkly stained cells correspond to blastemal cells. Modified Wright stain; bar = 10 µm.

Comments

Nephroblastomas are tumors that are derived from embryonic metanephric blastema. Nephroblastomas in dogs,[1] cats,[2] horses,[3] pigs,[4,5] cows,[6] and chickens[7] have been reported; in dogs, they develop as primary renal tumors and as spinal tumors that usually have an intradural, extramedullary location. Most cases in dogs reported in the literature involve spinal tumors; in 1 study[1] in dogs, 5 of 61 primary renal tumors examined were nephroblastomas. Most nephroblastomas are diagnosed in young dogs (age range, 3 months to 4 years); however, they have been diagnosed in dogs up to 12 years of age.[1] In children, most nephroblastomas are curable and the prognosis for patients who undergo surgery, chemotherapy, or radiation therapy is good. Information

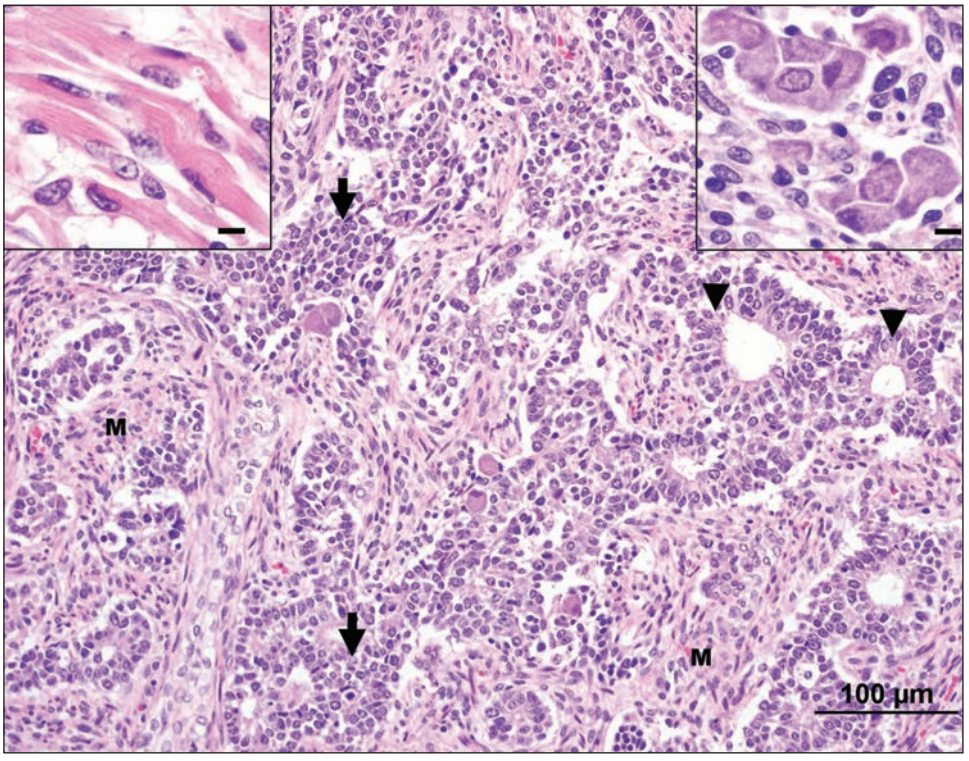

Figure 3—Photomicrographs of tissue sections obtained from the renal nephroblastoma in the dog in Figure 1. The neoplastic mass is composed of poorly defined cellular aggregates of solid blastemal cells (arrows), which blend with epithelial components arranged in branching and infolded tubules (arrowheads) and embryonic mesenchyme composed of spindle cells (M) admixed with cells with skeletal muscle differentiation (upper left inset) and neurons (upper right inset). H&E stain; in main image, bar = 100 µm; in insets, bar = 10 µm.

regarding prognosis for affected dogs following similar treatments is more limited, but dogs with spinal nephroblastomas have a fair prognosis after surgery alone.[1]

Among humans, teratoid nephroblastomas develop mostly in children and are responsive to treatment, similar to classic nephroblastomas. Teratoid nephroblastomas are rare, with only 25 pediatric and 1 adult case reported in the literature.[8] Among those 26 tumors, evidence of skeletal muscle differentiation was common (15 [58%] tumors); cartilage and bone was observed in 9 (35%) tumors, and neural differentiation was detected in 3 (12%) tumors.[8] Seven of the 25 (29%) children were bilaterally affected. The frequency of bilateralism is of interest because nonteratoid tumor variants are bilateral in only 5% of cases. The frequency of anaplasia in teratoid tumors (4%) is lower than that in nonteratoid tumors (9%). Treatment of the teratoid nephroblastomas is generally similar to that of classic nephroblastoma. Survival rate among children with teratoid nephroblastoma is good, with a reported 5-year survival rate of 86%.[8] No reports of teratoid nephroblastoma in dogs are available, to our knowledge.

Histologic diagnosis of nephroblastoma relies on the characteristic triphasic appearance with epithelial, mesenchymal, and blastemal components.[9] The relative proportion of each component within a nephroblastoma can be highly variable. In addition to classic triphasic components, these tumors may include heterologous elements (defined by some authors as composing > 50% of the tumor)[8] and can include skeletal muscle, adipose tissue, glial tissue, neurons, and squamous or mucinous epithelium. In the dog of this report, the large number of neuronal cells, skeletal muscle differentiation, and squamous epithelium were consistent with a teratoid variant. Differentiation between nephroblastoma with heterologous elements (teratoid Wilms tumor) and teratoma of the kidney relies on the fact that teratomas have organized (organ-like) differentiation of the various components into structures that resemble bronchial wall, skin with adnexa, retina, and teeth, whereas in teratoid Wilms tumors, the various tissue types are distributed haphazardly and do not have such a complex degree of spatial organization. Furthermore, the presence of characteristic components, including nephrogenic blastema, tubular differentiation, and other nephrogenic patterns, supports the diagnosis of Wilms tumor. To our knowledge, no cases of renal teratoma in dogs have been reported.

Positive results of immunohistochemical staining of biopsy specimens for WT1, a protein that is aberrantly overexpressed in nephroblastomas, can confirm the diagnosis. A recent study[10] investigated staining for WT1 in samples of spinal nephroblastomas obtained from dogs and revealed that 9 of 11 tumors were positive for WT1.

The cytologic features of nephroblastomas in humans and dogs are variable. In the dog of this report, the presence of occasional cell clusters without neuropil, elongated cells, and extracellular matrix were most consistent with the cytologic diagnosis of nephroblastoma. Preoperative cytologic examination of fine-needle aspirate samples may provide useful information for prognosis and treatment.

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