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Objective—To describe the clinical features, surgical and histologic findings, biological behavior, and outcome of dogs with retroperitoneal sarcomas.

Design—Retrospective study.

Animals—14 dogs.

Procedures—Medical and pathology records from 1992 to 2002 of dogs with tumors originating in the retroperitoneal space were reviewed. Dogs with retroperitoneal tumors originating from the adrenal glands, kidneys, or ureters were excluded. Inclusion criteria included observation of a tumor arising from the retroperitoneal space during exploratory surgery or necropsy and histologic confirmation of tumor type. Details of clinical signs, diagnostic findings, survival management, and outcome were determined from medical records and telephone interviews with veterinarians and owners.

Results—Retroperitoneal sarcoma was diagnosed in 14 dogs, 2 at necropsy and 12 during exploratory surgery. Hemangiosarcoma was the most common histologic diagnosis. Seven dogs had regional extension of the sarcoma into adjacent organs, and 4 dogs had metastatic disease. Grossly complete resection was possible in 6 dogs. Cytoreductive surgery or incisional biopsy was performed in the remaining dogs. Two dogs were treated with palliative radiation therapy (1 intraoperatively and 1 postoperatively). Three dogs received adjunctive chemotherapy, although none completed the targeted course because of development of local recurrence or metastatic disease. Local recurrence was reported in 2 of 12 dogs and metastasis in 10 of 14 dogs. Thirteen dogs died or were euthanatized as a result of the retroperitoneal sarcoma; 1 dog was alive and disease-free 410 days after surgery. Median survival time was 375 days.

Conclusions and Clinical Relevance—In dogs, retroperitoneal sarcomas are aggressive tumors with a high rate of local recurrence and metastasis, and a poor survival time. (J Am Vet Med Assoc 2004;224:1471–1477)

The retroperitoneal space is a potential space within the abdominal cavity that contains fat, loose con-
achieve complete microscopic and macroscopic surgical resection.6,12,13 The 5-year survival rate of 69% to 92% for grade I RPSs is significantly better than 16% to 48% for grade II and III RPSs.6,8,11,13-20 Regardless of grade, complete excision results in a substantial survival benefit with a 41- to 103-month median survival time and 43% to 72% 5-year survival rate, compared with 9 to 18 months and 3% to 33%, respectively, following incomplete resection.6,11,16-20 The purpose of the study reported here was to describe the clinical features, surgical and histologic findings, biological behavior, and outcome of dogs with RPSs.

Criteria for Selection of Cases
Medical and pathology records of dogs with RPSs examined at Colorado State University Veterinary Teaching Hospital from January 1992 to June 2002 were reviewed. Inclusion criteria included observation of a tumor arising from the retroperitoneal space during exploratory surgery or necropsy and histologic confirmation of tumor type. Dogs were excluded from the study if the retroperitoneal tumor originated from the adrenal gland, kidney, or ureter.

Procedures
Details of signalment, clinical signs, physical examination findings, results of diagnostic tests performed before surgery, surgical findings, and outcome were recorded. Diagnostic tests performed before surgery included CBC, serum biochemical analyses, and urinalysis; radiography (left and right lateral and ventrodorsal views) of the thorax; and radiography, ultrasonography, and computed tomography (CT) of the abdomen.

Surgery and necropsy reports were reviewed to determine the side of retroperitoneal involvement, size of the tumor, evidence of local extension or metastatic disease, and gross assessment of the completeness of resection. Clinical stage was determined by use of a staging system (Appendix). Histologic samples were reviewed by a single pathologist (EJE) and tumor type and grade recorded. The number of dogs receiving chemotherapy and radiation therapy or radiation therapy alone was recorded, including chemotherapeutic drug, dose, and number of doses administered, and number of fractions and dose per fraction for radiation therapy.

Outcome after surgery was determined from medical records and telephone conversations with referring veterinarians and owners. Survival time was calculated from the time of surgery to death and did not include dogs in which RPS was diagnosed at necropsy. The cause of death was recorded as related or unrelated to RPSs. Dogs that died as a result of treatment for RPSs were included as a disease-related death.

Results
Retroperitoneal sarcomas were diagnosed in 15 dogs with 12 confirmed during exploratory surgery and 2 confirmed at necropsy. One dog was excluded from further analysis because a retroperitoneal OSA was diagnosed via fine-needle aspirate only, and this was not confirmed by histologic examination. Median age was 9 years (range, 2 to 13 years). Of the 14 dogs, 7 were female and 7 were male. The majority of dogs were large breeds; breeds included mixed-breed (n = 4), Golden Retriever (4), Labrador Retriever (2), and 1 each of Australian Shepherd, Brittany Spaniel, Cocker Spaniel, and Great Pyrenees. Median weight of dogs was 27.7 kg (60.9 lb; range, 13.6 to 42.7 kg [29.9 to 93.9 lb]).

Clinical signs were nonspecific or neurologic. Nonspecific clinical signs included inappetence (n = 8), lethargy or collapse (7), and weight loss (2). Lower motor neuron hind limb lameness was detected in 4 dogs, and 2 of those had neurogenic urinary incontinence. Median duration of clinical signs before evaluation was 1 day (range, 1 to 42 days). An abdominal mass was detected in 6 dogs, and signs of abdominal or retroperitoneal pain were detected in 5 dogs during physical examination.

Complete blood count and serum biochemical analyses were performed in all dogs. Abnormalities identified on the CBC included leukocytosis (n = 6 dogs); mature neutrophilia (7), lymphopenia (8), anemia (10), of which 6 were regenerative; and thrombocytopenia (5). Morphologic abnormalities of RBCs, such as schistocytes, acanthocytes, echinocytes, and polychromasia, were detected in 7 dogs. Serum biochemical abnormalities included high activities of creatine kinase (CK; n = 7), alkaline phosphatase (4), alanine amino transferase (3), aspartate aminotransferase (AST; 9), and γ-glutamyltransferase (2). Hypokalemia (n = 5), hyponatremia (3), and hypochloremia (4) were commonly detected electrolyte disturbances. Urinalysis was performed in 9 dogs, and abnormal findings included hyposthenuria (n = 6), microscopic or macroscopic hematuria (5), and proteinuria (2).

Abdominal imaging was performed in all dogs. A retroperitoneal mass was detected in all dogs examined with radiography (n = 7), ultrasonography (12), and CT (2; Fig 1). A large radiopaque mass in the dorsal portion of the abdomen was a consistent finding and...
caused ventral and lateral displacement of the ipsilateral kidney, bladder, and small and large intestine on radiography (Fig 2). Ultrasonography of the abdomen was often required to differentiate between a renal and retroperitoneal mass. Ultrasonographic appearance of a retroperitoneal mass varied, although most were hyperechoic, compared with the adjacent renal cortex, spleen, and liver, and occasionally contained multifocal anechoic areas (Fig 3). Regional metastasis was suspected in 1 dog on the basis of multifocal anechoic to hypoechoic lesions observed in the spleen and liver.

Radiography of the thorax was performed in 11 dogs for the purpose of staging the RPS, and pulmonary metastases were detected in 3 dogs.

Exploratory surgery of the abdomen was performed in 12 dogs, and necropsy was performed in 2 dogs. A retroperitoneal mass originating from the retroperitoneal space (n = 5) or epaxial muscles (9) within the retroperitoneal space was confirmed in all dogs. The side of retroperitoneal involvement was recorded in 13 dogs and included the left side (n = 9), right side (3), and midline (1). The location of the RPS was identified in the caudal retroperitoneal space (n = 1), extending from the pelvic inlet to the level of the bladder (3) or kidneys (2), extending from the bladder to the kidney (2), or pararenal (6). The size of the RPS was > 5 cm (n = 12 dogs), > 10 cm (7), and > 15 cm (2) in diameter. Local extension of the retroperitoneal mass into the ipsilateral kidney (n = 3), aorta (2), paravertebral muscles (3), caudal vena cava (1), adrenal gland (1), and the root of the mesentry (1) was observed in 7 dogs. In these dogs, RPSs were diagnosed rather than a primary renal or adrenal tumor because the volume of the tumor was much greater in the retroperitoneal space than the kidney or aorta, and these organs only had focal rather than diffuse involvement. Rupture of a retroperitoneal HSA and hemoperitoneum was observed in 1 dog. Multiple metastatic lesions to the omentum and peritoneum were observed in 2 dogs, and 1 dog had a colocolonic intussusception secondary to a metastatic lesion in the colon with concurrent metastatic lesions in the liver. One dog with suspected hepatic and splenic metastases on abdominal ultrasound examination had nodular hyperplasia of the liver and no gross splenic abnormalities.

Complete resection of the RPS was attempted in 6 dogs, cytoreductive surgery was performed in 4 dogs, and incisional biopsy only was performed in 2 dogs. Colonic resection and end-to-end anastomosis was performed in the dog with intussusception secondary to a metastatic lesion in the colon with concurrent metastatic lesions in the liver. An adrenalectomy was also performed in this dog, despite no evidence of gross adrenal abnormalities, because an adrenal pheochromocytoma was suspected due to preoperative hypertension (170 mm Hg; reference range, 92 to 116 mm Hg) and retroperitoneal hemorrhage. Incisional biopsy of the retroperitoneal mass resulted in profuse hemorrhage, and aggressive resection was not attempted. Treatment was not attempted in another dog because the tumor involved the root of the mesentery. Intraoperative radiation therapy was performed in 1 dog after debulking the tumor. This dog was transported from surgery to the radiation suite. The dog was redraped using an aseptic technique, and the retroperitoneal mass was isolated with laparotomy sponges ensuring adequate retraction of the intestines, kidneys, and ureters. An 8-cm diameter, sterile, circular plexiglass cone was positioned over the isolated retroperitoneal mass and 1 cm bolus of isotonic saline (0.9% NaCl) solution added to the cone. The cone was then docked to a 6-MV linear accelerator, which was used to deliver 20 Gy radiation, with 12 MeV to the retroperitoneal mass. Radiation dose was calculated by use of skin-to-surface distance geometry with a 90% isodose of reference. Following IORT, the dog was transported back to surgery for abdominal lavage and routine closure of the linea alba, subcutaneous tissue, and skin.

Retroperitoneal sarcoma was confirmed histologically in all dogs. Sarcoma types included HSA (n = 9), OSA (2), and 1 each of leiomyosarcoma, myxoid-type peripheral nerve sheath tumor (PNST), and hemangiopericytoma (HPC). These RPSs were graded as...
grade II (n = 5; 1 leiomyosarcoma, 1 PNST, and 3 HSA), or grade III (8; 1 HPC, 2 OSA, and 5 HSA). On the basis of imaging, surgical, and necropsy findings, tumors were clinically staged as T2b-N0-M0 (n = 10) or T2b-N0-M1 (4) RPSs. When combined with histologic grading, 6 dogs had stage I, 4 dogs had stage III, and 4 dogs had stage IV disease (Appendix). All 4 dogs with metastasis at diagnosis (stage IV) had grade III tumors (3 HSA and 1 HPC).

Adjuvant chemotherapy was administered to 3 dogs. No dog completed the targeted number of doses because of local recurrence or metastasis. One dog with extraskeletal OSA received 3 of 5 targeted doses of doxorubicin prior to local recurrence and distant metastasis, 1 dose of cisplatin after detection of local recurrence, and then no further chemotherapy because of progressive disease. Two dogs with residual gross HSA received adjuvant chemotherapy. One dog received 3 of 6 targeted doses of vincristine and cyclophosphamide before detection of progressive disease and metastasis. The other dog received 1 of 5 targeted doses of doxorubicin before ultrasonographic evidence of progressive disease was identified and was then treated with metronomic chemotherapy, consisting of piroxicam, doxycycline, and cyclophosphamide and palliative EBRT, with 4 doses of 6 Gy on days 0, 7, 14, and 28.

Median survival time for dogs with RPSs was 37.5 days (range, 2 to 498 days). One dog with a grade II leiomyosarcoma was alive and disease-free 410 days after surgery. The remaining 13 dogs died or were euthanatized because of progressive local disease (n = 6), local recurrence (2), or distant metastasis (10). The lungs were the site of distant metastasis in all cases; other metastatic sites included the peritoneum (n = 2), intestines (1), liver (1), heart (1), and brain (1).

Discussion

Retroperitoneal sarcomas are mesenchymal tumors originating from within the retroperitoneal space but not primarily involving retroperitoneal organs, such as the adrenal glands, kidneys, or ureters. RPSs are rarely diagnosed in dogs, and the lack of clinical signs had RPSs. In contrast, HSA was the most common RPS in dogs, accounting for 9 of the 14 cases reported in the present series. Similarly, RPSs are not well recognized in dogs, with only 3 cases reported in the veterinary literature since 1969. In the study reported here, 14 dogs had RPSs during a 10-year period, which emphasizes the rarity of this tumor and provides information to potentially improve the diagnosis, management, and outcome of dogs with RPSs.

The most common histologic types of RPSs in humans are liposarcoma, leiomyosarcoma, and malignant fibrous histiocytoma. In contrast, HSA was the most common RPS in dogs, accounting for 9 of the 14 cases, followed by extraskeletal OSA. Retroperitoneal HSA and OSA are rare in humans. Nonvisceral leiomyosarcoma is rare in the dog, although 1 case was reported in the present series.

Clinical signs of dogs and humans with RPSs were similar. Most dogs had nonspecific clinical signs such as inappetence, weight loss, lethargy, signs of abdominal pain, and an abdominal mass. These clinical signs are also common in dogs with a variety of other intra-abdominal neoplasms including hepatic, renal, and splenic tumors. Tumors originating in the retroperitoneal space are bordered by the vertebral column, paravertebral musculature, and abdominal organs. As a result, RPSs can become very large prior to detection, and these clinical signs are most likely the result of tumor size, compression or invasion of adjacent anatomic structures, and distension of the peritoneum. In some dogs, it was difficult to classify retroperitoneal masses as an RPS because of renal or adrenal involvement. In these dogs, RPS was diagnosed because tumor volume was greater in the retroperitoneal space and organ involvement was focal rather than diffuse.

Four dogs with hind limb lameness had monoparesis or unilateral sciatic neuropathy. A malignant PNST is suspected until proven otherwise in humans with RPSs and neurologic signs. In contrast, in the study reported here, peripheral neuropathy was presumably associated with compression or invasion of the vertebral nerve roots of the sciatic nerve and not tumor type because none of the 4 dogs with neurologic signs had PNST. The lumbosacral plexus, femoral nerve, and obturator nerve can also be affected in humans with RPSs. Lower motor neuron paralysis of the bladder was detected in 2 dogs with sciatic neuropathy, and this finding is consistent with multiple nerve root involvement, especially if the tumor extends into the caudal retroperitoneal space and invades the paravertebral muscles adjacent to the caudal lumbar and sacral vertebral bodies, or vertebral canal.

Anemia, morphologic changes in RBC, and thrombocytopenia were frequent hematologic abnormalities in dogs with RPSs. These findings are commonly reported in dogs with visceral HSA. Proposed causes of morphologic changes in RBCs include chronic iron deficiency, altered hepatic lipoprotein metabolism, disseminated intravascular coagulation, and sluggish flow through abnormal vascular channels causing increased membrane fragility. In dogs with HSA, anemia and thrombocytopenia develop secondary to blood loss from tumor rupture, disseminated intravascular coagulation, or Kasabach-Merritt syndrome. Serum biochemical abnormalities included increases in CK and AST. Aspartate aminotransferase can be increased in dogs with liver or muscle disease, whereas CK is a muscle-specific enzyme. Increases in CK and AST activity without concomitant liver enzyme abnormalities are indicative of muscle damage. This is an important consideration in the surgical management of dogs with RPSs because the ability to achieve complete resection of RPSs is limited by invasion into the paravertebral muscles. Dogs with RPSs and high CK or AST activity may be poor surgical candidates.

Abdominal imaging was performed by use of radiography, ultrasonography, or CT. Similar to humans with RPSs, a retroperitoneal mass was always imaged regardless of the technique. There are minor differences in the radiographic appearance of RPSs in dogs and humans. In humans, RPSs often appear as a heterogeneous mass, primarily solid with areas of liquefaction, whereas RPSs in dogs are solid and radiopaque. Displacement of adjacent abdominal organs, such as the liver, gastrointestinal...
tract, kidneys, or urinary bladder, is a common radiographic finding in dogs and humans with RPSs. Abdominal ultrasonography and CT were useful in planning the surgical management of RPSs by differentiating retroperitoneal and renal masses and defining the extent of disease. In humans, the presence of a retroperitoneal mass on abdominal imaging is suggestive of RPSs. Ultrasonography, CT-guided aspirates, or needle-core biopsies are not recommended in humans because of the high risk of tumor seeding and increased potential for local recurrence and decreased survival time.

Surgery is the principal form of treatment for humans with RPSs. Curative-intent surgery is recommended if local resection is possible and there is no evidence of metastatic disease. However, as there is no survival benefit to incomplete resection, surgery is not recommended if complete excision is considered unlikely. Complete excision is complicated by adherence, enmass, or invasion of RPSs into adjacent structures in 31% to 75% of cases. The rate of complete resection, which varies between 35% to 100%, is dramatically improved by an aggressive approach involving en bloc resection of adjacent organs, muscle, and osseous structures, including segments of the vertebral bodies and pelvis. In the present study, adjacent anatomic structures were involved with the RPS in 7 of 14 dogs, and the RPS was completely excised in 6 of the 12 dogs treated with surgery. These poor results reflect early reports in the human literature when a more tentative surgical approach was often used by means of surgical biopsy or tumor debulking rather than curative-intent resection. However, in contrast to RPSs in humans, the most common type of RPS in dogs was HSA, and these often originated from and diffusely involved the paravertebral musculature, which compromised the ability to achieve complete resection.

The biological behavior of retroperitoneal HSA in dogs is similar to stage III cutaneous HSA, defined as a primary HSA with underlying muscular involvement, with poorly defined margins, low rate of complete excision, and high rates of local recurrence and metastasis. In dogs with stage III cutaneous HSA, complete excision was only achieved with wide surgical resection. Radical excision of RPS with diffuse paravertebral muscle involvement would involve removal of segments of lumbar and sacral vertebral bodies resulting in a decreased quality of life with the risk of vertebral column instability and neurologic dysfunction. The rate of complete resection in the study reported here was low because, unlike RPS in humans, resection was not limited by invasion of adjacent abdominal organs but rather diffuse involvement of paravertebral musculature. Local recurrence is the most common cause of death following surgical resection of RPSs. In humans, local recurrence is reported in 20% to 85% of cases, which is similar to the 17% of dogs with local recurrence in the present study. The most likely cause of local recurrence in dogs with RPSs was incomplete excision as recurrent disease is common following incomplete excision of stage III cutaneous HSA in dogs. In humans, the rate of local recurrence is the same following complete and incomplete resection, although the disease-free interval is substantially longer following complete excision. Because only 6 of 12 dogs had complete gross resection of the RPS, a conclusion cannot be made on whether local recurrence rates differ with the completeness of resection in dogs. In humans, recurrent disease is treated with a second attempt at surgical resection as the rate of complete resection, local recurrence, and survival time is similar to initial surgical management of RPSs.

The role of radiation therapy in reducing the incidence of local recurrence is controversial and conflicting. Disease-free intervals are improved with adjuvant EBRT in certain reports. However, this effect is dose-dependent, and the cumulative doses of radiation required to substantially reduce local recurrence rates result in unacceptably high rates of radiation-induced enteritis and peripheral neuropathy. Neoadjuvant EBRT warrants investigation as potential benefits include decreased risk of acute toxicity because of downstaging of disease resulting in a greater ability to completely resect RPSs, and sterilization of tumor cells that decreases the risk of tumor seeding and local recurrence. An alternative and promising approach is the use of IORT in combination with moderate doses of fractionated EBRT. Radiation therapy was used in 2 dogs in the present study with no apparent survival benefit; IORT was performed in 1 dog with incompletely resected retroperitoneal HSA, and palliative EBRT was performed in another dog with local recurrence. A conclusion cannot be made on the benefit of radiation therapy in dogs with RPSs on the basis of these 2 dogs with suboptimal doses of radiation. Adjuvant chemotherapy is not beneficial in reducing the rate of local recurrence or improving survival time in humans with RPSs. Chemotherapy, consisting of doxorubicin or vincristine and cyclophosphamide, was administered to 1 dog with extraskeletal OSA and 2 dogs with HSA, but did not have an apparent impact on local recurrence, metastasis, or survival. In the present study, 9 dogs had HSA and 2 dogs had OSA. Adjuvant chemotherapy substantially improves survival times in dogs with extraskeletal OSA and non-metastatic visceral HSA following complete resection. Hence, chemotherapy is recommended in dogs with RPS, especially after complete gross resection of a retroperitoneal HSA or OSA.

Tumor grade and complete gross resection are the most important and consistent prognostic factors in humans with RPSs. Age, histologic type of tumor other than liposarcoma, tumor necrosis secondary to infection from contamination from intestinal contents or hematogenous spread, incomplete microscopic excision, large tumor size, tumor invasion into retroperitoneal structures, and metastasis at the time of diagnosis are other less commonly reported prognostic factors. Statistical analysis was not performed to identify prognostic factors in dogs with RPSs as all deaths were related to the RPS and the sample population was small. However, neoplastic extension into the sublumbar muscles and histologic type and grade of the tumor appeared to influence survival in dogs with RPSs. Neoplastic invasion into adjacent structures, particularly sublumbar muscles, limited the ability to achieve complete surgical resection and resulted in local recurrence or progressive...
disease. Hemangiosarcoma accounted for 8 of the 10 dogs with metastatic RPSs, and metastasis was present in 8 of the 9 dogs with retroperitoneal HSA, of which 5 were grade III. Grade III RPSs were diagnosed in all 4 dogs with metastasis at diagnosis and in 6 of 8 dogs that developed metastasis during the course of disease.

Median survival time of dogs with RPSs was 37.5 days. Thirteen dogs died from disease- or treatment-related causes, and only 1 dog was alive and disease-free after a follow-up time of 410 days. Local recurrence was reported in 2 of 12 dogs and metastasis in 10 of 14 dogs. The metastatic rate in dogs is higher than that reported in humans with RPSs and dogs with cutaneous STS.6-20,33,35-37 This may be because of the different types of sarcomas diagnosed in dogs with RPSs. The biological behavior of RPSs in humans is similar to STSs on the extremities, with a high rate of local recurrence and a low metastatic rate.6,20-35-37 In contrast, HSA and OSA were the most common types of RPSs diagnosed in dogs in our study. Hemangiosarcoma and extraskeletal OSA have a different and more aggressive biological behavior with a poorer prognosis than other types of STSs, which may account for the higher metastatic rate in dogs with RPSs.28,30-33,39,39

In dogs, the histologic types of RPSs are different from that in humans. Hemangiosarcoma was the most common tumor type, compared with liposarcoma, leiomyosarcoma, and malignant fibrous histiocytoma in humans.6-10 The difference in histologic types of RPSs may account for the aggressive behavior of RPS in dogs, with frequent invasion into regional structures, difficulty in achieving complete surgical resection, poor response to adjuvant therapy, high rate of distant metastasis, and poor survival times. Treatment recommendations for RPSs in dogs are difficult to determine on the basis of these findings; however, multimodality management with surgery, IORT, EBRT, and chemotherapy warrants consideration.

Appendix

Staging criteria for retroperitoneal sarcomas in dogs

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Clinical staging

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*Knapp DW, School of Veterinary Medicine, Purdue University, West Lafayette, Ind. Personal communication, 2003.

References


