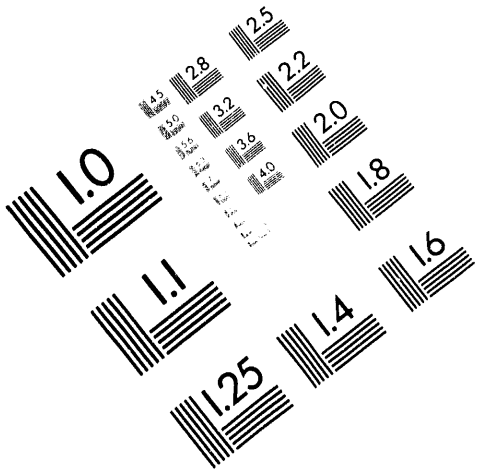

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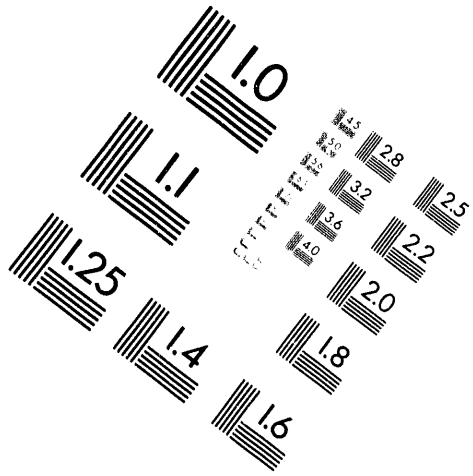

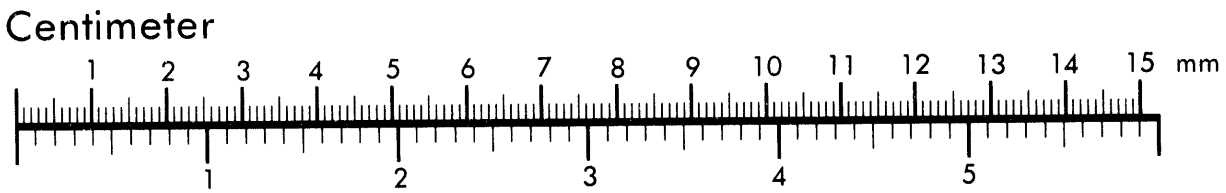

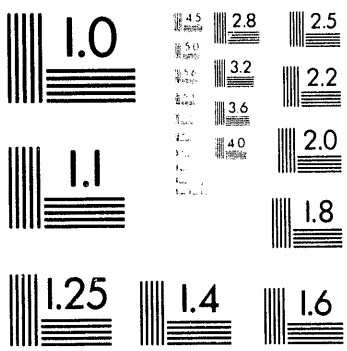

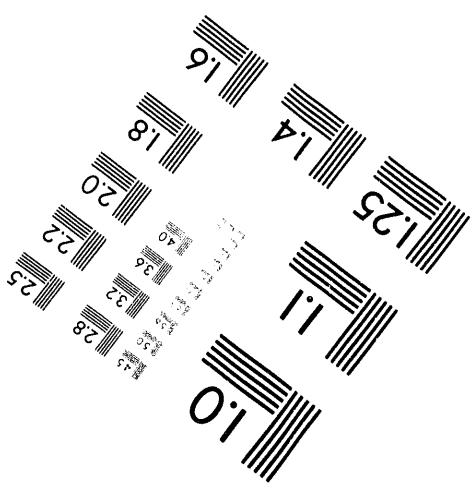

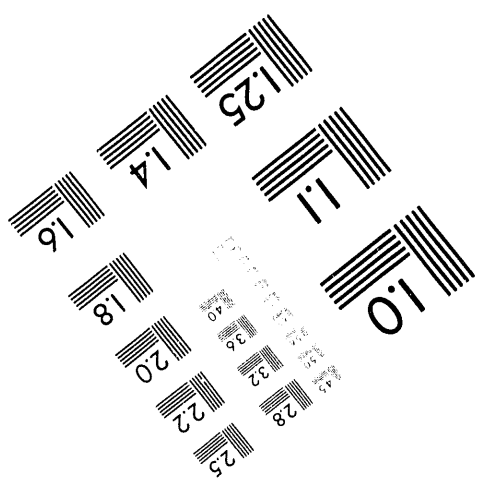

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UROGENITAL TUMORS

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MASTER

UROGENITAL TUMORS

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RENAL TUMORS

Primary renal tumors account for 0.7 to 1.7 per cent of canine tumors and 2.5 per cent of feline tumors. Adenocarcinoma is the most frequent primary renal tumor type in dogs. This tumor occurs in middle-aged and older dogs and more frequently in male dogs than in female dogs. The tumor metastasizes to the lungs and less frequently to the other kidney, lymph nodes, liver, spleen, brain, and bone.

Nephroblastoma (Wilm's tumor, embryonal nephroma) is a mixed renal tumor consisting of metanephric blastema and its stromal and epithelial derivatives in various stages of differentiation. The tumor may contain smooth muscle, skeletal muscle, cartilage, bone, and fat. In one report, 60 per cent of dogs with nephroblastomas were less than 1 year of age and 65 per cent had metastatic disease, most frequently to the lungs. Tumor cells can implant into peritoneal surfaces, omentum, and mesentery.

Hereditary multifocal renal cystadenocarcinomas associated with firm multiple nodular dermatofibrosis has been reported in

German shepherd dogs. The syndrome was found in necropsy specimens of 43 German shepherd dogs, with breeding data available for 37 affected dogs, all sharing a male ancestor. In addition to these tissue changes, multiple uterine tumors were found in 10 of 11 bitches.

Metastatic renal neoplasms are more common than primary tumors. Malignant lymphoma may originate in the kidney, particularly in cats, or be metastatic from other sites. Osteosarcoma, hemangiosarcoma, malignant lymphoma, mast cell tumors, and malignant melanomas are the most frequent metastatic tumor types in dogs.

Diagnosis

The signs associated with renal tumors are usually nonspecific and include anorexia, weight loss, and abdominal distension. Signs related to the urinary tract, such as hematuria, polyuria, and polydipsia, occur less frequently. Dyspnea may be caused by lung metastasis. Hypertrophic osteopathy has been reported in a dog with a renal cell carcinoma and lung metastasis, and in a dog with an atypical nephroblastoma and no apparent pulmonary lesions.

Urinalysis may reveal hematuria and rarely tumor cells. The animal may be anemic or polycythemic, possibly because of disturbances in erythropoietin production. Radiographic or ultrasonographic examination may show a cranial abdominal mass that could also be from enlargement of an adrenal gland, ovary,

liver, or pancreas instead of the kidney. Excretory urography will help localize the mass to the kidney and may help to estimate the degree of kidney involvement. Definitive diagnosis is based on cytologic and/or histologic examination of tumor tissue. Tissue can be obtained percutaneously by a fine-needle aspirate or needle biopsy, or during exploratory laparotomy by wedge biopsy.

Treatment

Nephroureterectomy is the treatment of choice for renal tumors with no evidence of metastasis or vascular invasion. The entire ureter should be removed. Surgery is complicated by extensive adhesions, local invasion, and the proximity of the caudal vena cava, aorta, and adrenal glands. A combined thoracoabdominal incision may be necessary to gain adequate exposure. It can be difficult to identify and isolate the renal vessels. Preoperative embolization or balloon-catheter occlusion of the renal artery is sometimes used in human patients to reduce the size of the tumorous mass and to decrease hemorrhage prior to ligation of the renal vessels. The renal artery should be ligated early to minimize the chances of vascular tumor emboli.

The efficacy of chemotherapy, radiation therapy, or immunotherapy for the treatment of renal tumors in the dog and cat has not been established. Systemic chemotherapy may provide palliation of signs and prolongation of life, for lymphoma

primarily or secondarily affecting the kidney (see Dra. Jeglum's chapter on Hematopoietic Neoplasms).

URINARY BLADDER TUMORS

Urinary bladder tumors comprise less than 0.5 per cent of all canine tumors and are rare in the cat. The frequency increases with age, with most affected dogs and cats being over eight years of age. In human subjects tumors of the urinary bladder are three times more common in males, whereas in dogs urinary bladder tumors are more common in females. Neutered dogs appear to be at greater risk for bladder cancer as do Airedale terriers, beagles, and Scottish terriers. Urinary bladder tumors are also more common in older dogs weighing greater than 10 kg.

The etiology of primary bladder cancer in dogs is unknown. Endogenous carcinogens, exogenous carcinogens, chronic inflammation, and viruses have been incriminated. Aromatic amino metabolites of tryptophan, which are excreted in large quantities in the urine of dogs, have been implicated. Cats metabolize tryptophan by a different method than dogs, and their urine has only very small quantities of tryptophan metabolites. Bladder tumors have been induced in dogs by the oral administration of 2-naphthylamine for 2 to 24 months. Because the metabolism of analine dyes produces naphthylene and related compounds, environmental carcinogens may be associated with the development of urinary bladder cancer. In one study, a significant positive correlation was seen between the proportional morbidity ratios

for canine bladder cancer and the overall level of industrial activity in the host country of the hospital.

Transitional cell carcinomas have been reported in three dogs following treatment with oral cyclophosphamide. It would appear that there is a causal relationship.

Most urinary bladder tumors are transitional cell carcinomas (TCC). Tumors originating from the transitional epithelium of the ureters and urethra are rare even though they are lined with by the same type of epithelium as the bladder. Retention of urine in the bladder may account for the rarity of neoplasia in the transitional epithelium elsewhere in the urinary tract. Other tumors of epithelial origin include squamous cell carcinoma and adenocarcinoma. Seventy-seven per cent of primary canine bladder tumors are of epithelial origin. Malignant mesenchymal tumors include fibrosarcoma, leiomyosarcoma, rhabdomyosarcoma, and myxosarcoma. Benign epithelial tumors (papillomas) are more common than benign mesenchymal tumors such as leiomyomas, fibromas, or rhabdomyomas.

Embryonal rhabdomyosarcoma (botryoid rhabdomyosarcoma) of the canine urinary bladder is a rare tumor that tends to occur in large breed dogs of less than 2 years of age. The tumor invades the neck of the bladder and does not appear to metastasize, however, it has been commonly associated with the development of hypertrophic osteopathy in the absence of lung metastasis.

Diagnosis

Clinical signs associated with neoplasia of the urinary bladder include hematuria, dysuria, pollakiuria, and only rarely a palpable mass. Anorexia and weight loss can be observed in the latter stages of the disease.

Cytologic examination of the urine may reveal tumor cells. In one study, seven of ten dogs with urinary bladder tumors had tumor cells in the urine sediment. Caution is advised in making a definitive diagnosis by cytology alone, because atypical transitional cells may appear in some dogs with cystitis. The urine cytology may reveal only numerous red blood cells. Complete blood cell counts and serum biochemistries are not diagnostic.

Survey radiographs may reveal a space-occupying mass in the caudal abdomen, sublumbar lymphadenopathy, or metastases to bone. Thoracic radiographs should also be examined. Urinary bladder neoplasms are difficult to demonstrate by noncontrast radiographic studies. A double-contrast cystogram and urethrogram is recommended to visualization of the lower urinary tract. Pyogranulomatous masses and polypoid cystitis, which have fair to good prognoses, may have the same radiographic and gross appearance as urinary bladder neoplasms.

Cystoscopy is a method for diagnosis used routinely in human medicine for direct visualization of the mucosal surface of the bladder; small patient size often precludes routine use of the cystoscope in veterinary practice. Other diagnostic and staging

methods used for pelvic neoplasms in human medicine rely to a large extent on imaging examinations; these methods include arteriography, ultrasonography, lymphangiography, computerized tomography, guided thin needle biopsy, and nuclear magnetic resonance scanning. These methods do have merit for clinical staging of those patients for whom treatment is planned, although they are not routinely available in veterinary practice. Ultrasonography is routinely used and allows identification of an intravesical mass, its extension through the muscularis into perivesical fat, invasion of adjacent organs, and enlarged lymph nodes. Biopsy and histopathologic examination are necessary for the definitive diagnosis of a urinary bladder mass.

Staging of urinary bladder tumors is recommended and may help in the evaluation of treatment protocols.

Treatment

The best treatment modality for urinary bladder cancer is not known. Concurrent urinary tract infections should be treated with appropriate antibiotics based on urine culture and sensitivity.

At the present time, partial cystectomy remains the most common treatment for canine and feline urinary bladder tumors. If there is insufficient bladder following excision of the tumor, and if the trigone is not tumorous, a trigone-colonic anastomosis can be done. Unfortunately, most urinary bladder tumors requiring extensive resection also involve the trigone.

Ureterocolonic anastomosis and complete cystectomy is being investigated as a means of urinary diversion following complete cystectomy.

When marked hematuria is present, chemical cauterization should be considered. Moderate bleeding may be minimized by treatment with methenamine mandelate (10 mg/kg orally every six hours to effect). Severe hematuria may require instillation of a dilute (1 per cent) formalin solution.

Adjuvant therapy, including radiation therapy, systemic chemotherapy, hyperthermia, and intravesicular therapy, is being investigated at several veterinary centers. The role of radiation therapy in humans has not been firmly established and its value is controversial. The outcome of adjuvant chemotherapy in treatment of canine bladder cancer cannot be determined with any certainty. Doxorubicin, cisplatin, cyclophosphamide, vincristine, 5-fluorouracil, and triethylene thiophosphoramide (Thiotepa, Lederle) are among the agents that have been used. Doxorubicin may have some treatment efficacy when combined with surgery, and cisplatin has been shown to have beneficial antitumor effects in dogs with TCC. At present, however, specific recommendations cannot be made.

Carcinomas tend to spread by direct extension into surrounding structures such as the prostate gland, urethra, ureters, rectum, vagina, and uterus. The frequency of metastasis is unknown. Fifty per cent of TCC and 9 per cent of squamous cell carcinoma metastasized in a study of 130 dogs with primary bladder cancer. The prognosis for bladder tumors is poor.

The future challenge will be to find effective therapy for the control of micrometastatic disease as well as achievement of permanent local control.

PROSTATIC NEOPLASIA

Prostatic neoplasia occurs in older male dogs. It very rarely occurs in cats. Most primary prostatic neoplasms are adenocarcinomas. Other tumors such as transitional cell carcinoma, rectal and colonic adenocarcinoma, and rectal and colonic squamous cell carcinoma can locally invade the prostate. Malignant lymphoma and perianal adenocarcinoma can metastasize to the prostate. The correlation between benign prostatic hyperplasia and prostatic adenocarcinoma is unclear. Estimates of the proportion of male dogs affected with prostatic adenocarcinoma (PAC) have ranged from 0.29 to 0.6 per cent in studies based on necropsy material. The etiology of PAC remains unknown. It has been shown to be an androgen-responsive tumor in men and male dogs, although one study reported that castration of male dogs at any age failed to demonstrate a sparing effect on the risk of development of PAC. This suggests that the etiology of PAC in the dog may not be exclusively related to testicular hormones. Work in humans suggests that the adrenal and pituitary glands play a significant role in the disease. Preliminary work in dogs supports the view that nontesticular androgens exert a significant influence on the canine prostate.

Diagnosis

Prostatic neoplasia must be differentiated from benign prostatic hyperplasia, prostatic cysts, and prostatitis. The presenting signs are not specific for prostatic neoplasia (rear-limb lameness, lumbar pain, dysuria, dyschezia, hematuria). Digital rectal examination reveals an enlarged, firm, and irregular prostate gland. The gland may be immovable and firmly attached to the pubis.

Radiographic changes are not specific for prostate neoplasia. A retrograde urethrogram may reveal circumferential asymmetry and an asymmetric shape of the prostate around the urethra. Reflux of contrast material into the prostate parenchyma is not specific for prostatic neoplasia. The lumbar spine, pelvis, and lungs should be radiographed to check for metastasis. Ultrasonographic evaluation of the abdomen has proven to a useful, noninvasive method for imaging the prostate, and differentiation between cystic and solid prostatic enlargement is possible. Loss of marginal smoothness due to neoplastic invasion of the capsule is suggestive of malignancy, but this finding may be equivocal and other methods may be necessary to allow a definitive diagnosis to be made. Various imaging procedures have been used for external detection and definition of the lymphatic drainage of the prostate. These methods are useful for detection of occult lymph node metastases and may be used alternate to lymph node dissection. Visualization of the canine prostatic lymph nodes following

intraprostatic injection of technetium-99-m-antimony colloid has been accomplished in the dog; the simplicity of the procedure should prompt use of this diagnostic method in veterinary clinical practice.

Hemogram and blood chemistry findings are not diagnostic for prostatic tumors. Examination of urine sediment, ejaculate, or prostatic massage fluid occasionally reveals neoplastic cells. The measurement of prostate-specific antigen (PSA) has utility in human patients with prostatic cancer, but measurement of PSA has not yet been evaluated in dogs with prostatic neoplasms.

The definitive diagnosis is based on histopathologic findings. A perirectal biopsy technique has been described. A blind biopsy may give a misleading diagnosis when the tumor is nodular and/or associated with abscesses or benign prostatic hyperplasia. Abdominal exploratory and direct viewing of the prostate will enable the surgeon to choose the site of biopsy and take multiple biopsies if necessary.

If diagnosed before metastasis has occurred, surgical extirpation may be curative. Intraoperative radiotherapeutic methods may be useful for local tumors control or palliation. Unfortunately, early diagnosis is rare. Palliative therapy may include castration, estrogen therapy, and a cystostomy to divert urine from an obstructed urethra. The results of chemotherapeutic protocols have not been reported.

TESTICULAR TUMORS

Primary tumors of the canine testes have been frequently described in the veterinary literature. Testicular neoplasms are frequently recognized in the dog, representing 5 to 15 per cent of all tumors reported in male dogs. The incidence of testicular neoplasms is higher in the dog than in any other species, including man. Whereas testicular neoplasms of men are often malignant, benign tumors predominate in the dog. Neoplasms include seminomas (SEM) derived from the germinal seminiferous epithelial cell, and sertoli cell (SCT) and interstitial cell (ICT) neoplasms derived from the gonadal stroma. The most common tumor of the canine testis is the interstitial cell tumor (Leydig cell tumor). It has been shown that the incidence of TN increases with age, and usually occurs in dogs over 7 years of age. Metastatic disease has been described in 10 to 15 per cent of dogs with malignant SEM or SCT.

Associated clinical changes found in male dogs with testicular neoplasia include cryptorchism, perianal gland neoplasia, and inguinal hernia. The relationship between cryptorchidism and canine testicular neoplasia has been recognized for many years. In human subjects, similarly, the major risk factor for testicular cancer is the undescended testis. Cryptorchid dogs have been shown to have risk 13.6 times higher for testicular tumors than normal dogs. In addition, male dogs with inguinal hernia also have a risk estimated at 4.7 times higher than dogs without hernias for testicular neoplasms.

Prostatic disease is a common finding in dogs with testicular tumor(s), although it is usually evenly divided among

the different tumor types. Benign and cystic prostatic hyperplasia are the most frequently diagnosed diseases. Benign prostatic hyperplasia in dogs is associated with advancing age. Prostatic disease and perianal gland neoplasia have been described in conjunction with canine testicular neoplasms. Both conditions are believed to be hormone-dependent, requiring the presence of functioning testes. Perianal gland adenomas and adenocarcinomas and prostatic disease were identified in 10 per cent of male dogs with testicular neoplasms in our closed beagle colony, although neither of these diseases was significantly correlated to any testicular tumor type. This would tend to support suggestions that all canine testicular tumors may be hormonally functional and more common than believed. Dogs with SCT, and less commonly with SEM may present with signs of hyperestrogenism. Signs of feminization may be caused by de novo synthesis of estrogen, conversion of testosterone or its precursors to estrogen, or relative changes in the quantity of estrogen. Bone marrow hypoplasia with anemia, leukopenia, and thrombocytopenia has also been reported.

Published data relating the size of canine testicular neoplasms is scarce. It is generally accepted that ICT is usually of small size compared to SCT and SEM. Our data indicated that in order of decreasing size (volume), SEM > ICT > SCT. Mean tumor volume was 0.35 cm^3, 2.58 cm^3, and 5.79 cm^3 for SCT, ICT, and SEM, respectively.

Several breeds of dogs have been shown to be at excessive relative risk (R > 1) for testicular neoplasms including the

Boxer, Shetland sheepdog, Weimaraner, and German shepherd dog, while the beagle, Dachshund, and mixed breeds are considered to be at low risk ($R \leq 1$).

Diagnosis

Enlargement of the testis and/or a discrete nodule within the testicular parenchyma is sometimes palpated. Diagnosis can be facilitated by fine-needle aspiration cytology of palpable masses, ultrasonography, and ultrasound-guided biopsy. Work conducted at our laboratory suggests that serum LDH concentration might serve as a biomarker for seminoma.

Treatment

The treatment of choice for testicular tumors is castration with removal of as much spermatic cord as possible. Bilateral castration is recommended based on a report that bilateral testicular tumors occurred in 50 per cent of affected dogs. The tumor in the opposite testicle was clinically apparent in only 12 per cent of the dogs. Little information is available about treatment of metastatic testicular tumors in dogs. Canine metastatic seminoma has been treated with combinations of actinomycin, chlorambucil, and mithramycin with no clinical response. Cisplatin-based chemotherapy has significantly improved the management and prognosis of nonseminomatous germ cell neoplasms and has also shown striking success in the

treatment of seminomas in humans. Four dogs with metastatic seminoma were treated with cesium 137 teleradiotherapy resulting in tumor regression in all four dogs.

CANINE TRANSMISSIBLE VENEREAL TUMOR

Transmissible venereal tumor (TVT) occurs most commonly on the external genitalia of dogs. Oral and nasal lesions have also been reported. Generally, the tumor is transmitted from dog to dog by exfoliation and implantation of cells into traumatized vaginal or penile epithelium during coitus. Spontaneous regression of naturally occurring TVT has not been reported. Metastasis to regional lymph nodes and other organs or direct invasion of the cervix, uterus, and fallopian tubes rarely occurs.

Diagnosis

A serosanguineous preputial or vaginal discharge may be the only sign. Careful examination will reveal multiple nodules or a cauliflower-like mass. The surface may be friable and hemorrhagic. The penis should be totally extended, because most penile TVTs are located around the glans penis.

The gross appearance of the tumor may be similar to a papilloma or squamous-cell carcinoma. Definitive diagnosis is based on cytologic or histopathologic examination.

Treatment

Surgical excision can be attempted if the tumor is small and can be completely resected. Because incomplete resection and recurrence are common, surgical excision is rarely the treatment of choice.

Overall, the most effective and practical therapy is chemotherapy. In the presence of metastatic disease, chemotherapy is the only reasonable choice. The most effective chemotherapeutic agents are vincristine and doxorubicin. Results of treatment with cyclophosphamide, methotrexate, or cyclophosphamide with predisone have been inconsistent. Doxorubicin should be reserved for the occasional tumor that is refractory to vincristine. Combination chemotherapy has been use with good results, however, single agent vincristine is just as effective as combination therapy and is associated with fewer side effects. Chemotherapeutic management of TVT using vincristine has been reported. Weekly treatments were administered intravenously at a dosage of 0.025 mg/kg. The investigators observed that 39 of 41 dogs had complete response following an average of 3.3 treatments per dog (range, 2 to 7). Metastatic TVT involving the central nervous system my be treatable with intrathecal cytosine arabinoside, or methotrexate.

Intraocular metastases may be effectively treated with systemic vincristine. Although used less frequently, a single dose of 10 Gy radiation is effective in curing most dogs with TVT.

OVARIAN TUMORS

Ovarian tumors are reported more frequently in older, nulliparous bitches. Granulosa cell tumors are the most common tumors of the ovary in bitches and queens. Papillary cystadenomas and cystadenocarcinomas occur only in the bitch.

Diagnosis

Ovarian tumors, irrespective of type, may occasionally stimulate the luteinization of theca cells with concomitant production of progesterone. Signs associated with prolonged progesterone stimulation include cystic endometrial hyperplasia or pyometra. Larger tumors may be palpable in the cranial right or left abdominal quadrant. They can produce signs consistent with a cranial abdominal space-occupying mass (vomiting, for example). Radiographic evaluation may reveal a soft-tissue density mass in the same area.

Bitches with granulosa cell tumors may show signs of prolonged estrogen stimulation such as hyperplasia and cornification of the vaginal epithelium. Cystadenomas usually cause no derangement of the estrous cycles, cystic endometrial hyperplasia, or ascites.

Treatment

The surgical therapy for a granulosa cell tumor is an ovariohysterectomy. It may be necessary to dissect the ovarian tumor from the body wall. A unilateral nephrectomy is indicated when the tumor has invaded the kidney.

Cystadenomas are either unilocular, varying in size from 0.8 to 1.5 cm, or multilocular, varying in size from 6 to 8 cm. They are thin-walled. Careful surgical excision by ovariohysterectomy should be curative.

Cystadenocarcinomas vary from microscopic size to 10 cm or more in diameter. When the tumor is confined within the ovarian bursa, the papillae are compressed and they have a cauliflower-like appearance. Once the papillae outgrow the bursa, their papillary nature becomes apparent and peritoneal implantation readily occurs. The presence of papillae indicates malignancy. Cysts of varying size are usually scattered throughout the neoplastic mass.

Surgical treatment for a confined papillary cystadenocarcinoma is an ovariohysterectomy. Because they frequently have peritoneal implants and lung metastasis, the prognosis is poor. Adjuvant therapy following surgical extirpation has not been reported for veterinary patients.

VAGINAL AND VULVAR TUMORS

Vaginal and vulvar tumors account for about 2.4 to 3 per cent of tumors in dogs. They are very rare in cats. Benign tumors are much more common than malignant tumors. If TVT is excluded, 81 per cent to 93 per cent of vaginal and vulvar tumors have been reported as benign. The benign tumors are most often leiomyomas, fibromas, and polyps, which occur in older, intact female dogs. Lipomas can also occur in this region. The more common malignant tumors include leiomyosarcoma and squamous cell carcinoma.

Diagnosis

The most common sign associated with benign tumors of the vagina and vulva is the sudden protrusion of a pedunculated mass through the lips of the vulva. Vulvar bleeding or discharge may be apparent. A mass in the perineal or vulvar region may be palpable. The definitive diagnosis is based on histopathologic examination.

Treatment

The treatment of choice for benign, nonlipomatous tumors is surgical resection and ovariohysterectomy. The malignant tumors tend not to be pedunculated, are more difficult to completely

excise, and tend to recur. Surgical excision and biopsy should be attempted, because the efficacy of other treatment modalities is unknown.

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