Pathology in Practice

History

A 3.5-year-old spayed female Blanc de Hotot rabbit was referred to the University of Georgia Small Animal Teaching Hospital because of anorexia and lethargy of 1 week's duration, dyspnea of 3 days' duration, and a suspected thoracic mass.

Clinical and Gross Findings

At the referral evaluation, the rabbit was dyspneic with slightly cyanotic mucous membranes. Via auscultation, increased bronchovesicular sounds, which were more pronounced on the left side, were audible. Thoracic radiography revealed pleural effusion and a mass that was obscuring the normal architecture of the lungs primarily on the left side. Cytologic examination of an ultrasound-guided fine-needle aspirate of the thoracic mass revealed numerous, variably sized clusters of well-differentiated epithelial cells that were often associated with abundant, brightly eosinophilic, amorphous to fibrillar material (Figure 1). Individual cells were round to angular with indistinct cell borders, deeply basophilic and occasionally vacuolated cytoplasm, and round to oval nuclei with finely granular chromatin. There was mild anisocytosis and anisokaryosis. Thoracic computed tomography was performed to assess whether the mass could be surgically resected. Because of the presence of a nonresectable mass in the thoracic cavity, the rabbit was euthanatized and necropsy was performed.

At necropsy, the thorax contained approximately 8 mL of serosanguineous fluid. The lungs were diffusely reddened and wet, and the pericardial sac was adhered to the left pleura. An irregularly round (3.0 × 2.5 × 1.0 cm) mass (3.5 × 3.0 × 1.5 cm) that was adhered to the pleural surface of the left cranial lung lobe, a mass (3.5 × 3.0 × 1.5 cm) that was adhered to the pleural surface of the left cranial lung lobe, and a raised mass (0.5 cm in diameter) on the surface of the right caudal lung lobe. Additional similar masses were detected in the thoracic cavity; these included a mass (2.0 × 1.4 × 0.9 cm) in the left cranial lung lobe, a mass (3.5 × 3.0 × 1.5 cm) that was adhered to the pleural surface of the left cranial lung lobe, and a raised mass (0.5 cm in diameter) on the surface of the right caudal lung lobe. The abdomen contained approximately 10 mL of fluid. A multilobulated (1.75 × 1.0 × 0.75-cm) mass was located cranial to the urinary bladder. Additional smaller masses were detected in the abdomen; these included a multilobulated, white, firm mass was present on the abdominal surface of the diaphragm. Similar smaller masses were detected in the abdomen; these included a multilobulated, white, firm mass in the mesentery; a mass on the tip of the spleen; and a mass on the serosal surface of the cecum. A multilobulated (5.25 × 3.50 × 2.75-cm), tan to pink mass was located cranial to the urinary bladder.

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

Figure 1—Photomicrograph of a slide prepared from a fine-needle aspirate specimen obtained from a mass in the cranial portion of the thoracic cavity (A) and photograph of a mass in the caudal portion of the abdomen (B) of a 3.5-year-old rabbit that was evaluated because of anorexia and lethargy of 1 week's duration, dyspnea of 3 days' duration, and a suspected thoracic mass. In the aspirate specimen, notice the tight clusters of well-differentiated epithelial cells that are closely associated with brightly eosinophilic, amorphous to fibrillar material that was interpreted to be a secretory product. The multilobulated abdominal mass is located just cranial to the urinary bladder (cranial is to the right in this image). Panel A, modified Wright-Giemsa stain; bar = 50 µm.
Histopathologic Findings

Histologically, the tissue associated with the mass located cranial to the urinary bladder was consistent with uterine tissue. Microscopic examination of sections of the mass revealed a moderately cellular, unencapsulated, poorly demarcated neoplasm that faced the endometrium, infiltrated the myometrium, and extended to the serosal surface of the uterine stump (Figure 2). The neoplasm consisted of closely apposed tubulocentric structures that were supported by a moderate fibrovascular to myxomatous stroma (Figure 3). The tubulocentric structures were lined by 1 to 5 polygonal cells that had distinct cell borders, moderate eosinophilic cytoplasm, round to oval nuclei with finely stippled chromatin, and 1 to 2 small magenta nucleoli (Figure 4). Cells often contained a palely basophilic, stringy material or a homogenous to granular eosinophilic material. There was mild anisocytosis and anisokaryosis; few mitotic figures were observed. Throughout the neoplasm, there were large foci of necrosis, occasional foci of hemorrhage, and a low number of heterophils. A similar neoplasm had replaced most of the left lung tissue and a small area of the right caudal lung lobe; adjacent tissues were compressed. Histologic examination of sections of this lung mass revealed 3 mitoses/hpf (40X). There were extensive foci of necrosis and hemorrhage and moderate numbers of heterophils with perivascular collections of moderate numbers of plasma cells and lymphocytes throughout the neoplasm. Alveoli were filled with large numbers of foamy alveolar macrophages and a pale, eosinophilic, homogenous material that was interpreted as pulmonary edema. Nodules in the diaphragm, spleen, mesentery, and cecum were histologically similar to the uterine and pulmonary neoplasms.

Morphologic Diagnosis

Uterine adenocarcinoma with metastasis to the lungs, diaphragm, spleen, mesentery, and cecum.

Comments

Uterine adenocarcinoma is the most common neoplasm in sexually intact female rabbits, and age appears to be the most important risk factor in its development.1,2 The incidence of uterine adenocarcinoma may be as high as 60% in rabbits > 4 years old and up to 80% in rabbits of certain breeds, such as Tan, French silver, Havana, and Dutch.1,2 Clinical signs that are typically associated with uterine adenocarcinoma in rabbits include intermittent or cyclic hematuria, bloody vaginal discharge, and weight loss.3–5 Uterine hemorrhage may be sufficiently severe to be life-threatening.3 Signs that develop later as the adenocarcinoma metastasizes to the lungs may include lethargy, anorexia, pale mucous membranes, and dyspnea.3 Clinicopathologic findings may include anemia if hemorrhage is severe; in instances of liver metastasis, serum concentrations of liver enzymes are often elevated.3 Radiography generally reveals a soft tissue...
mass in the caudal portion of the abdomen and often ascites. Typically, affected rabbits die 12 to 24 months after clinical signs appear.  

Uterine adenocarcinomas in rabbits often develop as globular, polypoid masses and are generally multicentric and involve both uterine horns. Historically, the tumors are well differentiated and may have necrotic or hemorrhagic centers, or they may secrete mucus. They usually grow slowly and eventually metastasize locally into the peritoneum, myometrium, local lymph nodes, and abdominal organs. Hematogenous spread of the neoplasm to the eyes, liver, brain, skin, bones, and lungs can also occur. Local invasion of myometrium and adjacent peritoneum occurs early in the development of the tumor; 1 to 2 years may elapse before there is detectable evidence of hematogenous dissemination.  

Uterine adenocarcinomas are associated with age-related changes in the endometrium, including increased endometrial collagen content and decreased cellularity (senile atrophy). As in humans, uterine polyps may progress to cystic hyperplasia, followed by adenomatous hyperplasia and eventually adenocarcinoma in rabbits.  

Generally, ovariohysterectomy is curative once the neoplasm is identified, unless local invasion or distant metastasis has already occurred. However, it is advisable to reexamine an affected rabbit every 6 months for several years after the procedure to check for metastases in the lungs or other sites. Hypertrophic osteopathy associated with pulmonary metastasis from a uterine adenocarcinoma in a rabbit that was spayed 9 months earlier has been reported. Thus, even after ovariohysterectomy, it is important that uterine adenocarcinoma remain a differential diagnosis for rabbits that develop abdominal or lung masses. When performing an ovariohysterectomy in a rabbit, the uterus may be ligated cranial or caudal to the cervices at the level of the vagina. However, given the possibility of development of uterine stump adenocarcinoma, it is recommended that the uterus be resected at the vaginal side of the cervices. In the rabbit of this report, it is likely that a uterine remnant remained following ovariohysterectomy, which allowed development of a uterine adenocarcinoma and subsequent metastasis. Development of uterine adenocarcinoma from the uterine stump is not unique to rabbits; there is also a report of uterine stump adenocarcinoma in a cat that had been spayed at 6 months of age. Similarly, women who have undergone subtotal hysterectomy occasionally develop carcinoma from the cervical stump.  

References  