Pathology in Practice

In collaboration with the American College of Veterinary Pathologists

History

An 11-year-old sexually intact female Yorkshire Terrier was presented to the referring veterinarian because of a 24-hour history of vomiting and a distended abdomen. Radiography revealed an abdominal mass adjacent to the caudal pole of the left kidney. The dog was treated with maropitant, cyclosporine, and carprofen and referred to The Ohio State University Veterinary Medical Center for evaluation of the abdominal mass.

Clinical and Clinicopathologic Findings

Heart rate and respiratory rate were within reference limits, but rectal temperature was mildly high (39.8 °C). The dog was 6% dehydrated, with pink, tacky mucous membranes and a clinically normal capillary refill time. Small amounts of mucoid, green ocular discharge were present in both eyes. The abdomen was distended and tense, and signs of pain were elicited on palpation, precluding adequate palpation. Mucoid, loose feces were present on rectal examination. Incidental findings included a 2.5 X 3.5-cm ulcerated, alopecic mass on the right second mammary gland and a 1-cm round, firm cutaneous mass present on the left mid thorax. The remaining findings on physical examination were within reference limits.

The dog underwent CT, which revealed a 3.1 X 3.0 X 2.5-cm soft tissue–attenuating, heterogeneously contrast-enhancing mass of apparent ovarian origin that appeared to completely efface the right ovarian parenchyma. The uterus was diffusely dilated and contained segmental accumulation of fluid. Some of

Figure 1—Photomicrograph of a direct smear of peritoneal fluid from an 11-year-old sexually intact female Yorkshire Terrier with a 24-hour history of vomiting and a distended abdomen and a radiographically evident abdominal mass adjacent to the caudal pole of the left kidney. Numerous degenerate neutrophils contain large, intracellular rod-shaped structures (arrowhead). A cluster of round to polygonal epithelial cells, characterized by moderate anisocytosis and anisokaryosis and a moderate nuclear-to-cytoplasmic ratio, is also seen (arrow). Wright-Giemsa stain; bar = 10 μ m.

the fluid pockets appeared encapsulated within circular soft tissue structures whereas other pockets of fluid appeared luminal. A small amount of peritoneal effusion was present. Abdominocentesis yielded approximately 2 mL of cloudy, yellow fluid that was submitted for cytologic examination (**Figure 1**).

Formulate differential diagnoses, then continue reading.

Cytologic Findings

The abdominal fluid had a total protein concentration of 4.9 g/dL (reference limit, < 2.5 g/dL) and a WBC count of 112,280 cells/ μ L (reference limit < 1,000 cells/ μ L). Direct smears were markedly cellular with a mildly bloody, light pink, proteinaceous background. The predominant nucleated cells were markedly degenerate neutrophils, which often contained large, intracellular rod-shaped structures. Rare large mononuclear cells and a mixed population of predominantly small and occasional intermediate lymphocytes were seen. There also were numerous, variably sized clusters of round to polygonal epithelial

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Figure 2—Photomicrograph of a direct smear of peritoneal fluid from the same dog, showing clusters of round to polygonal epithelial cells with similar characteristics as described in Figure 1 and rare binucleation (arrow). Often the clusters have a papillary (long, often branching) appearance. Wright-Giemsa stain; bar = 100 μ m.

cells characterized by moderate anisocytosis and anisokaryosis, a moderate nuclear-to-cytoplasmic ratio, and rare binucleation (**Figure 2**). Often these clusters of epithelial cells had a papillary (long, often branching) appearance. These polygonal epithelial cells also had moderate amounts of light to medium blue cytoplasm. Nuclei were oval and pericentrally placed with finely stippled chromatin and 0 to 3 round, small, faint nucleoli.

Interpretation and Case Summary

The WBC count and total protein concentration of the abdominal fluid were consistent with an exudate. The intracellular large rod-shaped structures were interpreted as bacteria, and the clusters of anaplastic epithelial cells were interpreted as neoplastic. The cytologic diagnosis was a neutrophilic exudate with evidence of bacterial infection (septic suppurative inflammation) and malignant epithelial neoplasia in a peritoneal effusion in a dog.

Comments

The presence of a peritoneal exudate characterized by marked neutrophilic inflammation and intracellular bacteria combined with the CT findings of a fluid-filled uterus is most consistent with a ruptured pyometra. Pyometra is common in middle-aged to older intact female dogs, and some studies have found an increased incidence in nulliparous bitches.^{1,2} Unfortunately, the parity status of this dog was unknown. The pathogenesis of pyometra is complex and not completely understood but thought to involve repeated and prolonged exposure to estrogen followed by sustained exposure to progesterone. These hormone changes cause increased endometrial

glandular secretion, decreased uterine contractions, and closure of the cervix, predisposing the uterus to bacterial colonization and infection of the endometrium.^{1,3,4} Of interest to this case, 1 study⁵ found that of 58 dogs with ovarian tumors, 39 (67%) had cystic endometrial hyperplasia, which may lead to pyometra, as noted in the present case.^{1,3-5} It was possible the dog of the present report had pyometra secondary to the presence of an ovarian tumor.

The most common bacteria in pyometra is *Escherichia coli*, which is consistent with the rod-shaped appearance of the organisms that were seen on cytology in this case.³ Culture is necessary for confirmation, but in this case ancillary diagnostics were not performed.

The concurrent presence of malignant epithelial cells in the fluid most likely occurred from exfoliation of neoplastic cells from the ovarian mass. In an attempt to rule in the diagnosis of ovarian carcinoma, the peritoneal fluid of this patient was screened for mutations in the B-raf (BRAF) proto-oncogene, as BRAF mutations have been detected in some human ovarian carcinomas.^{6,7} No mutations in the *BRAF* gene were detected in the peritoneal fluid of this patient; however, this does not rule out the diagnosis of ovarian neoplasia.⁷ One study⁸ found that cytologically evaluating effusions in dogs with these tumors has been found to be useful in diagnosing epithelial neoplasia, as seen in this case, although biopsy with histopathology is necessary for definitive characterization.⁸⁻¹¹ Due to poor prognosis, the dog was euthanized, but the owner declined an autopsy.

Canine ovarian tumors are uncommon and represent only 1.04% of all tumors in dogs.¹⁰ Ovarian neoplasia occurs in intact bitches, in bitches that have undergone ovary-sparing hysterectomies, and in bitches with ovarian remnants present.¹² Ovarian tumors are most common in older animals, except for teratomas, which are more common in young animals.⁵ Primary canine ovarian tumors include papillary adenocarcinoma, papillary adenoma, granulosa cell tumor, dysgerminoma, luteoma, and teratoma; of these tumors, papillary adenocarcinomas, adenomas, and granulosa cell tumors are most common.^{5,6,10,12} Cytologically, the cells seen in the peritoneal fluid were most consistent with ovarian papillary adenocarcinoma given the papillary (long, often branching) clustering of the neoplastic epithelial cells.

Papillary adenocarcinomas arise from the surface epithelium of ovaries that extends into the ovarian cortex and are often bilateral in dogs.¹¹ One study⁵ found that 48% of dogs with papillary adenocarcinoma had metastasis at diagnosis, and these tumors are frequently detected after the development of effusion.^{5,11-13} Treatment is typically surgical.^{5,14-16} At least 2 instances of intraperitoneal chemotherapy for metastatic ovarian papillary adenocarcinoma have been reported in the dog.^{15,16}

In the present case, neither the presence of a septic exudate nor malignant cells was unexpected

based on clinical and imaging findings. Careful cytologic assessment of the peritoneal fluid sample allowed confirmation of a septic process, as well as the presence of malignant epithelial cells. This is of additional importance given that epithelial ovarian tumors carry a different prognosis than other ovarian tumor types, such as germ cell tumors.¹² Ultimately, these findings contributed to the poor prognosis and the owner's decision for humane euthanasia. This case is an example of how thorough evaluation of cytology samples can help the clinician to make the best diagnosis, offer the most realistic prognosis, and institute the most appropriate treatment.

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