Diagnosis and medical treatment of pyometra in the queen

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Abstract

Although the incidence of feline pyometra is lower than canine, it can have devastating effects in breeding animals. Owners are requesting medical management of pyometra for valuable breeding animals more often and the practitioner must be able to provide recommendations and guidance. Pyometra is most often diagnosed in older animals, but there is now a disease process observed in animals as young as 9 - 10 months. Pathogenesis, clinical signs, diagnosis, and medical treatment are discussed.

Keywords: Pyometra, queen, cystic endometrial hyperplasia, endometritis

Introduction

Accumulation of purulent material within the uterus is referred to as pyometra. This occurs during the luteal phase when a corpus luteum (CL) is present. Because there is no pregnancy, this luteal phase is often called a 'pseudopregnancy' because it lasts 40 days rather than the full 63 days of pregnancy. Incidence of pyometra in the cat is much lower than the bitch where 20% of females will develop pyometra by age 10.[1] Pyometra developed in 2.2% European cats by the age of 13 years.[2] Lower incidence of pyometra in the cat is likely due to less overall prolonged progesterone exposure since they are induced ovulators, have a shorter nonpregnancy luteal phase (40 days) and are seasonal. Pyometra occurs in middle age or older queens, 3 - 4 weeks after ovulation (spontaneous, induced, or mated), and can be life threatening.

Pathogenesis

Most studies evaluated the pathogenesis of pyometra in dogs; sadly, it is inferred that development in cats is similar. Cystic endometrial hyperplasia (CEH) is an underlying uterine pathology that has been implicated as a precursor to the development of pyometra. When uterus is subjected to prolonged periods of progesterone exposure without pregnancy, progesterone induces changes in the endometrium. Progesterone decreases uterine contractions, causes thickening of the endometrium, proliferation of the endometrial glands, and increases glandular secretions.[3] Progesterone also decreases the ability of uterus to respond to bacterial assault by decreasing the inflammatory response. Changes within the uterus with CEH predispose the animal to development of pyometra. Once CEH has damaged the uterus and progesterone decreases uterine overall ability to eliminate infection, bacteria entering through the vaginal area and cervix are able to colonize and replicate. The most common bacteria isolated in queens is *Escherichia coli (E. coli)*, followed by *Streptococcus* spp and *Staphylococcus* spp.[4]

'Atypical' pyometra?

Although in past literature, CEH-pyometra complex has been long discussed as a single disease, there is increasing support that CEH and pyometra are actually 2 separate disease processes and although they often occur together, they can also occur separately. This is likely the case in young cats that develop pyometra. The author has observed this clinical presentation in her feline research colony. These queens are between 10 months and 2 years and some have not been bred by a male. Pyometra has been historically described as the sequalae to uterine changes following prolonged exposure to progesterone. Therefore, spontaneous ovulation must be considered in unmated queens presenting with pyometra. Spontaneous ovulation (ovulation without coitus) may occur in ~ one third of cats.[5] Incidence of spontaneous ovulation increased as body weight increased.[5] Although factors affecting spontaneous ovulation are not clearly known, they are observed more frequently in cats housed within the visual, olfactory, and auditory presence of an intact male. In group-housed queens, the incidence of spontaneous ovulation prior to addition of a male was 0 - 22% compared to 33 - 57% after a male was housed within olfactory, visual, and auditory presence in the room.[6]

Even with multiple spontaneous ovulations, uterine pathology does not seem to be the underlaying predisposition in this group of queens. Many queens are < 1 year and may have only been cyclic a few months. Their successful response to medical management and return to fertility indicates that the underlying uterus is not damaged. It is suspected that endometritis, inflammation within the endometrium, is occurring in the absence of permanent pathological changes. Endometritis

caused by the entry of ascending bacteria can be undetected until the queen is mated. Once the queen ovulates, progesterone closes the cervix, decreases the myometrial contractions, increases the glandular fluid, and reduces the inflammatory response within the uterus all allowing for prime bacterial growth.

The typical presentation of this group are young queens, either not yet bred (but in the same room as a male) or placed with a male for the first time. These queens remain bright and alert, systemically healthy, but may have a slight fever. Purulent vaginal discharge in their cage where they sit, or on their tail/vulva is the most consistent clinical sign observed. These queens remain stable, continue to eat and drink and do not require supportive care. Ultrasonography of the uterus confirms pyometra. Uterine loops distended with flocculent material can be observed in both uterine horns. Vaginal cytology will identify degenerative neutrophils in high numbers and progesterone concentrations > 2 ng/ml, indicating the presence of a CL.

These queens respond well to medical treatment (described in the next section) and often only require a few days of prostaglandin therapy to clear the uterus. These queens are allowed to rest for 1 month and then exposed to a male. Approximately 80 - 85% of cats will successfully produce a litter following treatment. Anecdotally, these queens are predisposed to another episode of pyometra later in their breeding career; however, this has not been confirmed by research. The author has had 2 valuable queens that were treated medically for pyometra twice in their breeding career and produce litters following both episodes. One queen was spayed following a litter after her second treatment and the other was spayed after producing 2 more litters and then being diagnosed with a third pyometra. Both queens were first diagnosed with pyometra at 11 - 12 months of age and neither was assessed for underlaying chronic endometritis at any time.

Further research is necessary with these young queens to determine the cause of pyometra in relation to uterine pathology. However, if this is observed commonly in a colony, subclinical endometritis should be suspected.

Diagnosis

Pyometra can be suspected based on history (placed with a male 3 - 4 weeks ago), signalment (older intact queen), and/or clinical signs. Clinical signs include any of the following and depend on severity of the disease: purulent vaginal discharge, pyrexia, anorexia, lethargy, and abdominal distension. Abdominal radiographs may reveal soft tissue mass opacity; however, radiographs alone are not diagnostic. Ultrasonography is the most ideal diagnostic tool for identifying pyometra. By scanning the uterus starting near the bladder and extending cranially, fluid-filled loops of uterus become visible. Pyometra causes segmental enlargement of uterus in cat, unlike in bitch where the uterus is uniformly enlarged. Pyometra must be differentiated from pregnancy. Uterine distension caused by pyometra is often not uniform and there will be areas with various fluid diameters within the uterus. In pregnancy, all fluid-filled structures should measure similarly. Echogenicity of the fluid may also give an indication; inflammatory debris within the uterus with pyometra will appear flocculent. Pockets of uterine fluid should be measured along each uterine horn to assess uterine distension. Those same pockets should be remeasured daily to assess response to treatment. Vaginal cytology should be performed to confirm the presence of inflammatory cells within the discharge. Huge numbers of degenerative neutrophils will be present along with a few parabasal or small intermediate cells in cases of pyometra.

Additional testing prior to and throughout treatment may include complete blood count and serum chemistry to assess the severity of systemic disease and response to treatment. Acute phase proteins (e.g., serum amyloid A, serum Hp, and serum albumin) were higher in cats affected with pyometra when compared to normal cats. Following surgical correction (ovariohysterectomy), the acute phase proteins returned to normal concentrations within 2 weeks. This suggested that measurement of acute phase proteins may be used as a biomarker for response to treatment.[7] Determination of serum progesterone concentrations is necessary; however, it can wait a few days into treatment. Documentation that progesterone concentrations are baseline following initiation of treatment is more important than knowing the initial value.

Medical treatment

When considering medical treatment of pyometra, the overall health status of the queen must be evaluated. If there is comorbidity including peritonitis or sepsis, medical therapy is not recommended. Medical treatment should only be attempted when the queen is not systemically compromised, a valuable breeding animal, has not exhibited signs of infertility with past mating attempts, and preferably young (< 4 years of age). Supportive care and stabilization are essential when treating a pyometra in any species. Queen tends not to be as systemically ill as the bitch, but the severity of clinical signs in the queen is directly correlated to the amount of uterine distension.[8]

Medical treatment begins with antibiotic therapy. The most common bacteria isolated in cases of feline pyometra is *E. coli*, followed by *Streptococcus* spp., *Staphylococcus aureus*, *Klebsiella* spp., and other fecal bacteria. Antibiotics should be chosen based on vaginal culture and susceptibility results. Since these results are not available immediately, broad spectrum antibiotics that especially target *E. coli* should be initiated immediately. Amoxicillin/clavulanic acid (15 - 25 mg/kg orally twice a day or intravenously 3 times a day) is an option as the initial treatment of choice. This author prefers initiating treatment with enrofloxacin (5 mg/kg orally or subcutaneously every 24 hours) to target the uterus directly. Since enrofloxacin caused retinal degeneration in cats at higher doses,[9] other fluroquinolones (e.g., pradofloxacin) may be substituted. Antibiotic therapy should be adjusted once final culture and susceptibility patterns are known. Therapy should be continued for 10 - 14 days after uterine distension has resolved.

Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) therapy is essential by lysing the CL, opening the cervix, and inducing uterine contractions. Two forms of $PGF_{2\alpha}$ are available; native prostaglandin (dinoprost tromethamine) that is marked through Zoetis as Lutalyse, and cloprostenol, a synthetic prostaglandin marketed by Merck

as Estrumate. Both are considered off-label in companion animals. Side effects are largely dose dependent and include vocalization, salivation, panting, restlessness, vomiting, diarrhea, excessive grooming, and tenesmus. Signs begin shortly after treatment and continue for no more than 1 hour.[10] Cats should be hospitalized and monitored continuously when first treated with prostaglandins and with each increasing dose to observe an individual's side effects. If extensive side effects are observed, decreasing the dose or switching to the other form of $PGF_{2\alpha}$ may be helpful. Lutalyse treatment should start at 10 -15 µg/kg subcutaneously 3 - 4 times a day for the first day, followed by 25 µg/kg subcutaneously 3 - 4 times a day on day 2, and increasing to 50 µg/kg subcutaneously 2 - 4 times a day on day 3 until uterine clearance and luteolysis is complete. Cloprostenol given subcutaneously at 5 µg/kg once a day for 3 days was effective in treating open pyometra.[11] Cloprostenol has a longer half-life and may have a longer duration of efficacy making dosing frequency less. Although cloprostenol may cause fewer side effects, Lutalyse is preferred by this author because it causes stronger uterine contractions and faster emptying of the uterus. Starting with a low dose and increasing both dose and frequency over time minimizes side effects. With the described dosage, transient hypersalivation, vomiting, and diarrhea are the most common side effects observed.

A third type of treatment is a dopamine agonist. Cabergoline and bromocriptine are prolactin antagonists and therefore have an antiluteotropic effect on the CL. This therapy should be used in combination with $PGF_{2\alpha}$ to remove the CL and open the cervix. Cabergoline is preferred because side effects are minimal. Cabergoline can be obtained from most human pharmacies and prescribed at a dose of 5 µg/kg orally once daily. Bromocriptine is more cost effective but requires more frequent dosing and has higher incidence of side effects such as vomiting, lethargy, and diarrhea. The dose for bromocriptine is 10 - 25 µg/kg orally every 8 hours.[12] Treatment with either medication should be continued for 5 - 7 days and can be discontinued once progesterone concentrations remain baseline.

Nonsurgical uterine lavage (transcervical) has been described in large nondomestic feline species as a treatment for pyometra..[13] This technique is gaining popularity in the dog; however, it is still not practical in domestic cat due to the small size of the vaginal canal.

Monitoring response to treatment

Aggressive therapy is important if return to fertility is desired. Monitoring medical management should be an intense process with daily examinations, ultrasonography, and assessments of the queen overall. Even if medical management is initiated, the queen may not respond and still require ovariohysterectomy. Daily physical examination is important to assess overall wellbeing of the queen. Some can be very stoic and subtle signs indicating systemic compromise may be missed. Once medical management is initiated, the cat should be held in the hospital for about 2 - 3 hours to assess reaction to medications. If the queen is systemically stable, hydrated, and eating and drinking normally, the queen can return home for outpatient treatment. If the queen is compromised, dehydrated, or has moderate to severe clinical signs associated with $PGF_{2\alpha}$ treatment, hospitalization is necessary. Daily ultrasonography of the uterus should be performed for contents and measurement of uterine diameter. With treatment, a 50% decrease in uterine fluid and an increase in the amount of vaginal discharge is expected within 2 days. If uterine diameter is not decreasing despite treatment, the frequency of Lutalyse can be increased up to 4 times daily.

Serum progesterone concentrations should be determined 2 - 3 days after initial treatment. Progesterone concentrations should return to baseline (< 2 ng/ml). Feline CL is more refractory to prostaglandins than canine CL and may require longer treatment to fully lyse the CL. Once baseline progesterone concentrations are reached (and the uterus is free of fluid), prostaglandin therapy should be continued for another 24 hours. Serum progesterone concentrations can be determined again (2 - 4 days later) to make sure that the concentrations are still baseline and the CL has not rebounded.

Medical treatment can be considered effective if uterus is reducing in diameter, free fluid is resolving, vaginal discharge that initially increased is reducing, and the inflammatory leukogram is improving. Once these are occurring, prostaglandin and cabergoline therapy can be discontinued. Antibiotic therapy should be continued for 10 - 14 days after resolution of clinical signs. Final ultrasonography of the uterus to assess the presence of intraluminal fluid is necessary at the end of antibiotic therapy. Medical treatment is considered a failure if there is minimal or no decrease in uterine diameter within 4 - 5 days after starting treatment, the queen becomes systemically compromised, or uterine pathology is observed over the course of treatment. In these cases, ovariohysterectomy should be performed. Prognosis for future fertility decreases the longer the treatment is required.

Prognosis

If queen responds well to medical treatment, return to fertility will depend on underlaying uterine pathology. Younger queens are more likely to return to a successful breeding career than older queens because underlaying CEH is more prevalent as queens age. Regardless, queens should be bred ~ 4 weeks after resolution of clinical signs. They should be kept away from intact males until ready for breeding to decrease the incidence of spontaneous ovulation. If queen fails to become pregnant with mating, a relapse of pyometra is more likely. If endometritis is suspected in a queen, treatment with antibiotics around mating may reduce the chance of development of pyometra. This should be instituted only on a case-by-case basis to prevent unnecessary and overuse of antibiotics. After mating, the queen should be monitored closely via abdominal ultrasonography starting 20 - 30 days to assess for either pregnancy or pyometra. Once the queen is no longer needed for breeding, ovariohysterectomy should be performed. Uterus must be removed (versus ovariectomy) to prevent any possibility of recurrence should the queen be exposed to hormones later.

Conclusion

Pyometra is less common in queen than in bitch. However, medical management is similar. With aggressive therapy, prognosis is positive and a return to fertility is possible in the right case.

Conflict of interest

None to declare.

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