

PYOMETRA AND ENDOMETRITIS IN THE BITCH

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Introduction

Pyometra is a life-threatening uterine infection of mainly intact middle-aged bitches in dioestrus. Ovariohysterectomy is often the treatment of choice. This presents a significant financial loss to the dog breeder. Here, the pathogenesis and treatment options are emphasized.

Background

Pyometra is an important disease in the canine species as up to 24% of intact bitches develop a pyometra before ten years of age. Originally cystic endometrial hyperplasia (CEH) and pyometra were defined as one disease entity. It was believed that the condition of CEH arose first and therefore predisposed the uterus to a secondary bacterial infection, which resulted in a pyometra.

More recently the question has been raised if pyometra and cystic endometrial hyperplasia are two separate disease entities. Although, both diseases bear many similarities with each other and can be found as subsequent events, the conditions have the potential to derive *de novo*. Any stimulus in a progesterone-influenced uterus can lead to CEH and therefore the presence of CEH in pyometra could merely be the result of a uterine reaction to the bacterial infection.

The pathogenesis of pyometra is not thoroughly understood. Many factors, such as the influence of age, ovarian hormones, breed, parity, and treatment with exogenous hormones have been shown to play a role in the development of the disease.

Pyometra has initially been described as a condition of older, ovary-intact bitches that still undergo estrous cycles. The mean age is reported to be between 7 to 8.5 years, although a range from 4 months to 18 years has been reported.

A breed predisposition has been described for the Golden Retriever, Cavalier King Charles Spaniel, Miniature Schnauzer, Irish Terrier, rough Saint Bernard, Leonberger, Airedale Terrier, rough Collie and Rottweiler. On the other hand, Dachshounds and Fox Terriers were underrepresented.

Pyometra is believed to be facilitated by the unique canine oestrous cycle, during which an oestrogen phase is followed by a relatively long progesterone dominated phase (dioestrus). The length of the dioestrous phase in a non-pregnant bitch is not significantly shorter than that of a pregnant bitch. This is suggesting that a luteolytic mechanism, as present in other domestic species, is missing in the dog.

Studies show that the overwhelming proportion of affected bitches present within 8-12 weeks of their last heat. Leukocyte inhibition and decreased myometrial contractions, in the progesterone influenced uterus facilitate bacterial growth. The progesterone influence in dioestrus results in uterine stromal and glandular epithelial proliferation and increased glandular secretion. These effects are cumulative. Therefore, the risk of uterine disease increases with each estrous cycle.

Although there is no evidence of abnormal ovarian hormone concentrations in the pathogenesis of pyometra it has been shown that progesterone is necessary to initiate a CEH reaction and oestrogen potentiates the effect by upregulating the expression of progesterone receptors. Exogenous hormone administration, especially of oestradiol early in diestrus ("mismating shot"), can be linked to an increased risk in developing the disease.

In dioestrus, the most common time for the diagnosis of pyometra, the uterus of healthy bitches has been found to be free of bacterial growth. Uropathogenic *E. coli* is the most commonly isolated pathogen from canine uteri with pyometra (> 90 % of cases).

The role of the bitch's immune response has recently been emphasized by the diagnosis of endometritis in the bitch. It was widely believed that endometritis did not exist in the canine species and a bacterial infection would always result in pyometra. Latest studies, however, show that bacteria can be isolated from subfertile bitches that do not show the hallmarks of pyometra. Interestingly, the mean age of these bitches was lower than in those with pyometra. This suggests that bitches might contain bacteria in the form of subclinical endometritis for some time before unknown factors allow bacterial proliferation and subsequent pyometra.

Clinical signs

Vulvar discharge varies with patency of the cervix but often also present in closed-cervix pyometra. In open-cervix pyometra, bitches present with more copious amounts of vulvar discharge and are often less clinically ill. Bitches with closed-cervix pyometra are almost always systemically ill. Vomiting and depression are often presenting complaints along with fever, polyuria/ polydipsia, and abdominal distention mediated by septicaemia, bacteraemia and/ or endotoxaemia.

Diagnosis

- **Ultrasonography:** thin-walled tubular uterus filled with hypoechoic fluid +/- flocculent material; wall can appear thick if severe CEH changes are present.
- **Laboratory findings:** White blood cell count is most commonly > 35,000 cells/ μ l (neutrophilia with left shift and toxic change). But normoleukocytosis and leukopenia are possible and do not necessarily exclude the disease; anaemia, elevated ALP and prerenal/ renal azotemia are common.

Prognosis

The prognosis for survival is good with medical and surgical treatment if uterine rupture has not occurred. In regard to future reproductive performance it should be noted that the disease can reoccur and it is strongly recommended to breed the bitch in the next cycle and have her ultrasonographically examined for pregnancy 28 days after the LH surge; however, reoccurrence rate is dependent on age, parity and preexisting uterine pathology; most commonly it is reported to be ~20% within 12-14 months of diagnosis; it is possible that she will have a new infection at that stage and if that is the case ovariohysterectomy should be strongly recommended. It has been shown that dogs that do not respond well to medical treatment within 5 days have a very poor prognosis to retain their breeding potential and ovariohysterectomy should be elected; clinical improvement should be noted within 2 days and resolution of the disease should occur within 7 to 10 days.

Treatment

- **Surgical treatment:**

Ovariohysterectomy is the treatment of choice in all non-breeding animals. Owners of breeding animals should also be informed about the likelihood of recurrence. Patients are often in poor condition for surgery and should be stabilized with intravenous fluids and antibiotics before the procedure.

- **Medical treatment:**

Medical treatment is a valid choice in breeding animals. The rationale behind medical treatment is two fold:

- removal of progesterone allows cervical opening
- drainage of pus and elimination of bacteria through an open cervix aided by uterine contractions

1) Prostaglandin F_{2α} (PGF_{2α}): not registered/ approved for the use in dogs! Can be used off-label; main advantage is luteolytic effect and ecboic effect; very inexpensive! Especially in the case of closed-cervix pyometra it is paramount to start with low doses of PGF_{2α} in order to minimize the ecboic effect of the drug and reduce the risk of uterine rupture. Once luteolysis occurs and the cervix opens the dose can be increased and evacuation of the uterus is a desired effect of treatment.

- **dinoprost:** non-synthetic, inexpensive

dose:

10-15 µg/kg three times a day (TID) for 2 days subcutaneously (SC)

25 µg/kg TID for 2 days SC

50 µg/kg TID for 5 days SC

the dose can be adjusted to sensitivity of the bitch; some dogs are more sensitive and react with more side effects; others might need dose up to 100 µg/kg for 2 to 3 days.

side effects: side effects are dose dependent and diminish after several injections; they include: tachypnoea, vomiting, diarrhea, urination, anxiety; start about 20 min after treatment; walking the dog for 15 min after administration seems to alleviate the side effects; dog should be hospitalized for at least one hour after treatment to observe side effects.

- **cloprostenol:** synthetic PGF_{2α} analogue, slightly more expensive but less side effects; less uterine contractions than with dinoprost; reported to be 100 % effective if given at a dose of 1 µg/kg once a day for 10 days

2) Aglepristone: progesterone-antagonist; competitively prevents progesterone binding to its receptor; more expensive than prostaglandin; no side effects; causes luteolysis but poor uterine contractions; works well in combination with prostaglandins in closed-cervix pyometra; aglepristone is given first and prostaglandin treatment can be started 36 to 48 hours later; cervix will open 26 hours (+/- 13 hours) after first aglepristone injection;

dose: 10 mg/kg given twice 24 hours apart; can follow with an injection 8 days later.

3) Antimicrobial therapy: should be initiated immediately with a wide-spectrum antibiotic. Culture and sensitivity should be performed but therapy has to be started at time of diagnosis. Excellent results have been achieved with amoxicillin/clavulanic acid, cephalosporins and potentiated sulfonamides. If oral antibiotics are given care must be taken to give the drugs at a different time as the prostaglandin, which will often lead to vomiting. Antimicrobial therapy should be continued for at least 14 days after resolution of vulvar discharge.

Follow-up care

- weekly blood cell counts should be performed to demonstrate decreasing neutrophilia (left shift should be no longer present).
- ultrasonography is recommended; visible reduction in lumen size after 5 to 7 days
- serum progesterone levels; although levels can be hard to interpret if aglepristone is used; if prostaglandins are used reduction within 48 hours
- breeding management in next cycle and early pregnancy diagnosis by ultrasonography to exclude recurrence of the disease; note that treatment will often lead to shortened interoestrous interval; can be lengthened with mibolerone in order to allow for sufficient time for uterus to remodel; start one month after end of medical treatment and keep administering it for 2 to 3 months.

References

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