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PYOMETRA IN THE BITCH AND QUEEN

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Pyometra is a disease of the uterus mainly observed during diestrous or anoestrous (post-partum or not). Cystic endometrial hyperplasia (CEH), mediated by progesterone and potentially aggravated by estrogens, was usually suggested as the initiating lesion of pyometra in dogs. CEH is characterized by degenerative tissue changes (cystic distention of glands, fibrosis, etc.) that provide opportune conditions for establishment of uterine infections. The compromised uterus is then invaded by pathogens from the vagina which will extensively multiply, primarily due to the excessive amount of secretary fluids that have accumulated in its lumen and glands. The classical theory of the pathogenesis of the spontaneous pyometra disease thus involves the suppression of immune responses, stimulation of endometrial gland secretion (providing a suitable environment for bacterial growth), functional closure of the cervix (inhibiting drainage of uterine exudates) and, perhaps most importantly, cystic endometrial hyperplasia (all related to the influence of progesterone on the uterus). In the classical theory, progesterone-mediated degenerative processes facilitate the bacterial development and invasion of the uterus. A more recent theory suggests that this may not be so, and that a subtle (subclinical) uterine infection may occur first, providing the stimulus for excessive endometrial hypertrophy and hyperplasia (the so-called trophoblastic reaction based on the observed hyper-reaction of the uterus at implantation). The associated increased glandular secretions would exacerbate the infection leading to further secretion by endometrial glands and luminal epithelial cells progressing to pyometra. This hypothesis is supported by experiments done in dogs by Nomura and collaborators who have shown that during the luteal phase of the cycle, a variety of physical, biological, and chemical substances will cause the endometrium to proliferate. The exact role of progesterone in the susceptibility of pyometra is still controversial, however, it is clearly essential. In the classical theory, progesterone is responsible for the degenerative changes facilitating bacterial development, whereas in the new theory, progesterone is necessary to allow for the trophoblastic reaction to occur. Progesterone in the new theory is not the initial effector facilitating the development of the disease, but is still absolutely essential to allow the uterus to react to the stimulus induced by a local effector. Indeed, studies have clearly demonstrated that it is impossible to induce the trophoblastic reaction in the absence of progesterone.

The classical theory is probably the one which best explains the more common pyometra observed in older animals, whereas the new trophoblastic theory is interesting in that it more easily explains the occurrence of unilateral pyometra and pyometra in younger dogs.

CLINICAL SIGNS

The clinical signs of pyometra include vaginal discharge, lethargy, polyuria, polydipsia, emesis, and hyperthermia followed by hypothermia. However an extensive range of clinical signs may be observed. For example, some dogs may exhibit only abdominal distension or a stiff gait, while others may have only apathy and reduced appetite. Still other patients will show the whole range of clinical signs. There is no relation between the intensity of clinical signs and the severity of the lesions. Dogs may have no clinical signs except abdominal distension, whereas some dogs with a moderately developed pyometra may show dramatic clinical signs, including shock. The presence of a vaginal discharge allows for a distinction between open and closed pyometra.

TREATMENT

The traditional therapy for pyometra in both bitch and queen is surgical ovariohysterectomy. This remains the recommended treatment in all cases except where the owner strongly desires to breed the bitch. Because of the insidious onset of the disease and its often equivocal clinical signs, patients are often in poor condition for anesthesia and surgery. Although treatment should not be unduly delayed, patients should always be stabilized and treated for shock as needed prior to surgery. At the very least, broad spectrum antibiotics and intravenous fluids should be administered. CBC and chemistry should be evaluated as soon as possible and used as decisive parameters before surgery. In particular, the kidneys should be checked as animals with preexisting or induced kidney failure are never the best patients for surgery without previous stabilization. If kidney function cannot be improved before surgery, the prognosis is always guarded. Supportive measures should be continued during and after surgery; antibacterial therapy should be continued for at least 2 weeks following surgery. In spite of these precautions, some complications like DIC may be expected.

Results of medical treatment for canine pyometra using prostaglandin F2alpha (PGF2alpha) are encouraging. Apart from its luteolytic effect, PGF2a is believed to promote myometrial contraction and to mediate functional opening of the cervix to permit drainage of exudates, though experimental evidence for this is lacking in the bitch. The use of PgE2 to open the cervix before inducing uterine contraction is also possible. Furthermore, to hasten luteolysis and improve the overall immunologic condition of the animal, the use of a dopamine-agonist inhibiting prolactin secretion (like bromocryptine or cabergoline) has also been consistently described with significant results.

Prostaglandins used to treat pyometra are generally dependant on natural prostaglandins to take benefit of their utero-tonic and luteolytic effects. Synthetic prostaglandins are interesting due to their long half-life and reduced side-effects, however their reduced ability to contract the uterus make them less clinically interesting to empty the infected uterus. Doses of 0.01 to 0.05 mg/kg of natural PgF2 alpha, administered twice to five times daily for 3 to 7 days, have been used successfully in association with 5 µg/kg of cabergoline or 25 µg/kg bromocryptine. Great care should be exercised in calculating the dose as the therapeutic index is relatively small (LD50 in dogs is approximately 5 mg/kg) and side effects are quite severe as soon as doses over 30-50 microgram per kg are used. The once a day high dose (from 100 to 250 µg/kg) previously advocated are NO LONGER recommended as associated with many side effects and, when used in closed pyometra, risk of uterine rupture. The lowest repeated doses allow for a progressive opening of the uterus and continuous contraction facilitating pus expulsion.

The condition of animals treated with PGF2alpha at low doses does not always improve during the first 48 hours after onset of treatment and may sometime deteriorate, however substantial increases in uterine discharges should be observed rapidly in open pyometra, and later (24 to 36 hours) in closed pyometra. DIC can be observed when treatment is begun in chronic cases and no significant responses are observed after a few days. It is the author's habit to systematically check for PDGF degradation products, di-dimeres and changes in platelets counts. A prophylactic injection of 100 to 500 UI of heparin is always indicated. Initial response to PGF2 treatment includes a transient increase in the amount of vaginal exudates, followed by a change in its character (to serous), and its eventual cessation. The leukogram returns to normal, although leukocytosis may be aggravated initially in some cases. In successful treatment, a 50% reduction of the uterine diameter is generally observed in 2 to 4 days. The treatment is discontinued when the uterine size has returned to normal. If there is no significant change in the uterine diameter after 2 to 4 days, the prognosis is poor and other treatment should be considered.

Concomitant broad spectrum antimicrobial therapy should be administered during PGF2a treatment. Some bitches with pyometra are bacteriemic and it is reasonable to assume that increased uterine contractile activity may predispose bitches to further bacteriemia or septicemia. Many different antimicrobials have been used successfully, but *in vitro* sensitivity studies and clinical evidence suggest that amoxycillin, amoxycillin plus clavulanic acid, cephalosporins or potentiated sulfonamides are good choices. It is recommended that the antimicrobial therapy be continued for 10 to 14 days minimum after the end of PgF2alpha treatment. The bitch should be re-evaluated 2 weeks after completion of the treatment. Pyometra is prone to recur in treated bitches and is most likely to recur during subsequent periods of diestrus. Breeding should be attempted at the first estrus following treatment and at every subsequent estrus until the desired number of offspring has been obtained or until recurrence, when retreatment or ovariohysterectomy should be considered. Ultrasonography should always be used to make the diagnosis and evaluate the prognosis. Particular attention should be addressed to the level of CEH detected at sonography, as CEH inversely correlates to fertility results after treatment. Mibolerone has been given with success by some clinicians including our team to prevent an early return to estrus and allow for better uterine regeneration before the next cycle.

Anti-progestin agents have been proposed alone or in combination with PgF2 to treat pyometra. The results appear promising particularly in cases of closed pyometra. However, there is still much controversy concerning their mode of action (diestrous versus anestrous pyometra) and this type of drug is not available in the United-States. The authors have recently developed a new transcervical endoscopic catheterization technique (TECT) of the uterus which is used to treat pyometra after infusion of some specific cocktails. This promising approach allows for the treatment of highly valuable animals with a rapid resolution and treatment of the disease (mean 2 to 3 days).

References available from the authors upon request.