Canine Pyometra

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Introduction

Canine Pyometra is a common reproductive disorder of intact, diestrual bitch which affects nearly one fourth of all female dogs before they reach ten years of age . By definition it is the accumulation of pus within the uterine lumen, typically occurring during or immediately following a period of progesterone dominance. It can be classified as open cervix or close cervix pyometra. Closed cervix pyometra is particularly dangerous, so it needs early recognition, diagnosis and appropriate treatment to avoid any disastrous consequences i.e death of patient due to septicemia and toxaemia . Despite modern treatment the mortality rate due to pyometra is about 4% .

Etiological factors

Age : Pyometra occurs at any age after the first estrus, typically a condition of the middle aged to older bitch. Reported mean age of 7.25 yrs as young as 4 months to as old as 16 years of age. Spontaneous disease occurs most frequently in bitches over 6 yrs of age. It also affects younger animals with a mean age of approximately 2 yrs.

Parity : Previously it was suggested that nulliparity, abnormal estrous cycle and pseudopregnancy increase the risk of pyometra. But recent literature has suggested that there is no association between pseudopregnancy and abnormal estrus cycle and pyometra. However there is a modest relationship between nulliparity and pyometra.

Stages of estrous cycle: Most bitches present to pyometra within 8 weeks of last estrous. However, it may occur at any stage of estrous cycle or during pregnancy.

Hormone: Progesterone has a role in initiating the pathogenesis of cystic endometrial hyperplasia(CEH)-Pyometra complex. Endometrial hyperplasia that resulted into CEH caused by progesterone is more pronounced when it has been primed with estrogen. Thus administration of estrogen when progesterone levels high may predispose bitches to pyometra. Estrogen keeps the cervix relaxed for longer period in the luteal phase and also enhancing the stimulatory effects of progesterone on the uterus. The hormonal therapies that include either progesterone for estrous suppression or estrogen for estrous induction or pregnancy termination may explain the development of pyometra in young bitches. Thus estrogen being an important factor in young animals and endogenous progesterone being crucial in older animal. Evidence suggests that there is increase risk for pyometra in 1-2 years old age group due to estrogen administration but no significant association between progesterone therapy and pyometra.

Higher concentration of IGF-1 located in surrounding epithelial cells of the endometrium in dogs with may play important role in the development of CEH-Pyometra complex.

Breed: Breeds reported to be predisposed to pyometra includes the Rottweiler, Saint Bernard, Chow Chow, Golden Retriever, Miniature Schnaeger, Irish terrier, Spanish, Callie etc. Breeds with low risk for pyometra includes Drevers, German Shepherd, Daschunds, Swedish hounds etc.

Pathophysiology

Pyometra in the bitch is a hormonally mediated disease. Prolonged or repeated stimulation of endometrium by progesterone produces CEH, if bacterial infection occurs at that time leads to pyometra. After ovulation increase progesterone concentration (> 40 ng/ml) promotes endometrial (endometrial hyperplasia) growth and glandular secretion leads to accumulation of uterine glandular secretion which provides excellent media for bacterial growth. In the progesterone primed uterus leucocyte response to infection also inhibited. But recent research suggested that CEH and pyometra complex are not necessarily sequent events, but each may develop independently. In endometrial hyperplasia, endometrial gland secretion results in an accumulation of fluid within lumen of uterus lead to hydrometra or mucometra but these conditions are sterile.

Estrogen by itself doesn't produce CEH but it enhance the stimulatory effects of progesterone on the uterus. Estrogen induces proliferation of the

endometrial glands and progesterone does branching and coiling of the glands, responsible for onset of secretion.

Exogenous or endogenous concentration of circulating steroid hormones particularly estrogen and progesterone influence the distribution of steroid receptors within the uterus of bitches. Regulation of estrogen and progesterone receptor expression in endometrial glands may play an important role in pathogenesis of pyometra complex in the bitch. In normal estrous cycle progesterone induces downregulation of estrogen receptors in endometrium so proliferative process halted but this mechanism failed in CEH. Due to increase expression of estrogen receptor, the endometrium remain receptive to even low levels of circulating estrogen. So simultaneous action of estrogen and progesterone could explain the CEH and pyometra complex pathway. Bacterial infection plays an important role in pathogenesis of pyometra. Progesterone sensitized endometrium and myometrium had an affinity for E. coli i.e commonly isolated from uterine fluid as part of the normal vaginal and vulval microflora Endometrium develop E. coli receptors during early metestrus. If infection results during this time then there is colonization of bacteria in the uterus leads to pyometra.

Clinical signs

Onset of clinical signs in case of pyometra is gradual and insidious. Clinical signs in case of pyometra depends upon patency of cervix. In open cervix pyometra, bitches are less systemically ill than closed cervix pyometra. Common clinical signs includes mucopurullent discharge, lethargy, depression, inappetence, polyurea, polydypsia, vomiting and diarrhoea. Bitches with closed cervix pyometra generally are very ill at presentation, death may occure due to toxaemia alone or may be associated with peritonitis due to rupture of uterus. In some cases, there may be intermittant opening of cervix, with relative good health following discharge of pus and malaise during intervening period.

Fever may or may not be present in case of open cervix pyometra, but in closed cervix pyometra is commonly associated with fever. Those bitches associated with toxaemia, may be hypothermic.

Character of vulval discharge may be variable in consistency and light chocolate brown in colour and malodorous. Sometimes yellow colour and often blood tinged and watery to creamy consistency.Vulva is generally enlarged and there may be discolouration or scalding of perivulval tissues and perineum.

Physical examination

It may be difficult to palplate uterine enlargement, especially in case of open-cervix pyometra and in case of large and obese bitch. In case of closed cervix pyometra the degree of uterine distention is greater and may be associated with visible enlargement.

Clinical pathology

Vaginal cytology examination is an initial tool in diagnosis of canine pyometra. Intracellular and extracellular bacteria may be seen on cytological examination with pyometra. Common clinical findings is peripheral leukocytosis, often exceeding 30,000 cells/mm3, degenerative left shift with toxic neutrophils are oftenly seen. But the degree is much less marked in cases of open cervix pyometra. A mild normocytic, normochromic nondegenerative anemic (PCV within 30-35%) condition reflects chronic nature of disease and toxic suppression of bone marrow.

In pyometra abnormal serum chemistry includes hyperproteinemia and hyperglobinemia may result due to dehydration and chronic antigenic stimulation of the immune system. These changes reflect hepatocellular damage due to toxaemia or diminished hepatic circulation and cellular hypoxia due to dehydration.

Clinical blood chemistry includes-mild to moderate increase of Alanine aminotransferase (ALT) and Alkalinephosphatase (AP) concentration app. 50-75% cases. Toxaemic condition develop due to bacterial infection especially *E. coli* impair the collecting tubules reabsorbing ability, insensitive to the action of ADH resulting in further loss of urinary concentrating ability.

Immune complex deposits in glomeruli causes a mixed membrano glomerulo-nephropathy and leads to proteinuria. This proteinuria gradually resolves with correction of pyometra.

Diagnostic imaging

The diagnosis of pyometra is best made with the aid of ultrasonography and radiology. Ultrasonographic findings includes an enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid. The diagnosis of uterus may vary depending upon whether the cervix is open or closed. The uterine wall is usually relatively hypoechoic and increase in thickness. The luminal contents are usually homogenous and filled with anechoic flud, although small echogenic particles may be identified. Radiography may also be used as an aid in diagnosis of pyometra in the bitch . In pyometra radiographically, a fluid dome, tubular structure should be seen in the ventral and caudal abdomen, displacing loops of intestine dorsally and cranically. In open cervix pyometra with significant drainage of uterine contents through vagina, uterus may not visualize radiographically. So inability to radiographically visualize the uterus does not rule out pyometra.

Treatment

Ovariohysterectomy is the choice of treatment for

older bitches, closed cervix pyometra or in cases where owner has no strong desire to breed bitches presented at early course of the disease surgical risk is low and success rates upto 92%. In toxaemic cases, lower success rate may be obtained. Before surgery bitches should be stabilized with fluid therapy and broad spectrum antibiotics. Surgical removal of the uterus will resolve the septic state of the bitch. 7 days after hysterectomy altered haematological parameters returned to normal levels. The main advantage of Ovariohysterectomy is the exclusion of any risk of reccurrence. However, surgical treatment has its limits when the risk of anaesthesia and surgery are life threatening

Medical treatment: If condition is not life threatening and the animal is particularly valuable, in such cases, restoration of fertility may be done with medical treatment.

Principles of treatment

Induction of luteolysis or prevention of progesterone binding to its receptors for prevention of progesterone effects. Now-a-days PGF2alpha used either alone or in combination with other drugs like prolactin inhibitor or progesterone receptor blocker for this effect. Expulsion of the uterine contents by allowing cervical relaxation in closed pyometra either by the use of Prostaglandins or progesterone receptor blocker.

Induction of uterine contraction and emptying either by the use of Prostaglandins or progesterone receptor blocker. Use of broad-spectrum antibiotics for inhibition of bacterial growth and development. Facilitating uterine regeneration by prolonging anestrus.

PGF2alpha treatment is a practical treatment for pyometra when reproduction is desired. PGF2alpha brings lysis of CL, cervical relaxation which permits drainage of exudate and promotes myometrial contraction. These action are depending on the dosage, route and frequency of administration. PG therapy is not approved for use in dog, so clients consent must be taken before its use. PGF2alpha should be used with caution in case of closed cervix pyometra because of the chance of uterine rupture.

PGF2alpha have been used successfully for treatment of pyometra. Natural prostaglandin @ 10-50 mg, 3-5 times daily for 3-7 days have been used. One should start with lower dosage to avoid side effects and then slowly increase the dosage to reach higher dosage. One should careful for side effects of PG treatment. Initially, the bitch may be restless, may begin pacing, hypersalivation, panting, vomition and defaecation may occur. These reactions subsided within 20-60 minutes of treatment. This drug is not ideal for severely ill animals. Use of synthetic PG such as cloprosterol instead natural PG associated with reduced side effects and prolonged activity resulting in slower evacuation of the uterine contents.

In bitch, prolactin is important luteotropic hormone. So Dopamine agonists or prolactin inhibitors such as bromocriptine (20 mcg/kg) or cabergoline (@ 5 mcg/kg) are used in combination with natural or synthetic Prostagalndin to treat pyometra. These combinations potentiates the luteolysis effects of each drug and results in rapid luteolysis.

Progesterone receptor blocker like Aglepristone competitively prevents progesterone from binding to its receptor. There is controversy of its use, to induce uterine contractions if used alone. The combination of aglepristone with cloprostenol more effective in medical treatment of open and closed cervix pyometra than aglepristone alone.

Antimicrobial treatment involves broad spectrum antibiotics necessary to combate from infectious agents. Before starting treatment antibiotic sensitivity test should be done for selection of antibiotics. Antibiotics like amoxicillin, amoxicillin plus clauvanic acid and cephalosporins or potentiated sulfonamides are choice for initial treatment.

To avoid recurrence of the pyometra, it is necessary to facilitate uterine regeneration during the post treatment anestrus. This prolongation of anestrus allows apoptosis and regeneration of endometrium, this can be done by administration of androgen receptor agonist, postponing the estrus for 2-3 month.

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