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Canine Pyometra: Current Perspectives on Causes and Management – A Review

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Abstract

Canine pyometra is a pathological condition of endometrium which results in accumulation of purulent semisolid substance in uterus. Canine pyometra is a sequlae of cystic endometrial hyperplacia (CEH) which results from hormonal imbalance. Despite of enormous veterinary medical research and development, still its main aspect of etio-pathology is not fully known. Canine pyometra is mostly associated with other similar uterine pathological conditions, i.e., hydrometra, mucometra and chronic endomertitis.

Introduction

Canine pyometra is a common reproductive syndrome of intact, sexually mature bitches during met/diestrous stage with various clinical as well as pathological signs specific to reproductive system along with systemic signs (Fransson, 2003). Other terms to describe canine pyometra in relation to pathogenesis like chronic endometritis, chronic purulent metritis, cystic endometrial hyperplasia (CEH) or cystic endometrial hyperplasia - pyometra complex etc. also coined (Sandholm *et al*., 1975). Canine Pyometra can be categorized based on status of cervix as open-cervix or closed-cervix; however closed type is more serious condition, which needs surgical intervention so as to prevent concomitant sepsis and fatality (Smith, 2006).

Pyometra can be defined as pathological condition of uterus in which there is accumulation of purulent semisolid-liquid substance inside the uterus of intact bitches, generally during post-progesterone dominant phase of estrous cycle. Several authors suggested that pyometra should be classified as CEH- pyometra complex because of the fact that subacute endometritis later

develops as CEH is most important predisposing factor of pyometra (Sandholm *et al*., 1975). However, others classified both condition separately based on histopathology and clinical reports which profess pyometra without CEH (De Bosschere *et al*., 2002).

Etiology

Several researches indicated predominant role of reproductive hormones, i.e., progesterone and estrogen as predisposing factors for pyometra in which former being most dominant one. It is well established that progesterone stimulates endometrial glands secretions as well as suppresses myometrial contraction which is favorable for bacterial growth and colonization (Cox, 1970). Estrogen has indirect role as it enhances endometrial response to progesterone. Etiology of bacterial origin can be traced by most common presence of *E. coli* along with endotoxins (Hageman, 2004; Bondade *et al*., 2010) Virulence factor of *E. coli,* i.e., K antigen and cytotoxin necrotizing factor are associated with pathological conditions; however several other pathogenic bacteria are also identified as causative agent, i.e., *Klebsiella Spp.*, *Streptococci, Staphylococci*, anaerobic bacteria, *Pseudomonads* (Dhaliwal *et al*., 1998). Several workers narrated that susceptibility of host and pathogenic bacteria along with progesterone appears to be an important components leading to disease condition (Krekeler *et al*., 2012a; 2012b).

Prevalence, History and Clinical Findings

Canine pyometra is commonly reported from mature bithches ranging from 4 to 16 years, but most common at the age of 7.5 years with regular and repeated estrous cycle (Johnston *et al*., 2001). Recently disease occurrence was reported as 19% in bitches below 10 years of age and 20% in older female dogs (Jitpean *et al*., 2014). Breed susceptibility is also observed in this condition with high risk include Rottweiler, Saint Bernard, Chow chow, Golden Retriever, Miniature Schnauzer, Irish Terrier, Airedale Terrier, Cavalier King Charles Spaniel, Rough Collie, and Bernese Mountain dog (Smith, 2006). Moreover, a few breeds possess low risk like German Shepherd, Daschunds, and Swedish hounds. Breed susceptability strongly indicates the contribution of genotype towards increase or decrease risk of disease (Jitpean *et al.,* 2012).

Pathogenesis

During luteal phase of estrous cycle blood progesterone level increases which in turn leads to increased secretions from endometrial glands, increase proliferation of endometrium, reduced myometrial contraction and closure of cervix (Hardie, 1995) that favours occurrence of disease. Factors associated with bacteria as well as their receptor expression may lead to enhance bacterial attachment to endometrium (Gabriel *et al.,* 2016). Wijewardana *et al.* (2015) described negative correlation between progesterone on maturation of antigen presenting dendritic cells which may lead to reduction of cell mediated immunity (CMI). Gultiken *et al.* (2016) reported increased expression of 3β-hydroxysteroid dehydrogenase on endometrial tissue in bitches suffering from pyometra which further indicates influence of local production of progesterone on disease occurrence even at its normal range. Therefore reduced CMI due to progesterone dominance in luteal phase (Sugiura *et al*., 2004), along with suppressed local immunity is favorable uterine environment for pathogens leading to their enhanced growth and colonization.

Clinical Signs and Diagnosis

Clinical signs of pyometra include endotoxaemia, septic shock, peritonitis and multi-organ failure. Jitpean *et al.* (2014) described peritonitis as most common finding in pyometra which ranges 10% of total cases. Cytological examination of vaginal discharge generally shows neutrophilia with more number of degenerative neutrophils. Bacteria may be seen in vaginal discharge.

Biochemical analysis shows considerable increase in serum urea nitrogen, creatinine, ALT, AST, ALP, globulin; however albumin level decreases highly significantly thus causing enhanced ratio of globulin:albumin in pyometra cases (Jitpean *et al*., 2014). Destruction of tissue due to effect of endotoxin can be attributed to elevated levels of serum urea nitrogen and creatinine. Hypoalbuminaemia and hyperglobulinaemia can be a result of acute phase reaction and dehydration respectively (Patil *et al*., 2013; Shah *et al.,* 2017).

Haematological evaluation shows erythrocytopenia, reduced level of haemoglobin (Hb), decreased packed cell volume (PCV), azotemia and leucocytosis with neutrophilia as consistent findings associated with disease (Patil *et al.,* 2013). Gupta and Dhami. (2013) explained that reduced level of Hb, PCV, total erythrocyte count (TEC) and platelets along with elevated level of erythrocyte sedimentation rate (ESR), total leucocytes count (TLC) and polymorphonuclear (PMN) cells indicates toxaemia whereas raised level of leucocytes, PMN cells and declining lymphocytes point out recovery from toxemia. Therefore these altered hematological values can be used as aid to diagnosis as well as prognosis of canine pyometra (Mohan *et al*., 2015). Most common finding in bitches affected with closed cervix pyometra shows leucocytosis with shift to left. (Nath *et al*., 2009). Anaemia in bitches can be sequelae of erythrocyte diapedesis into uterine lumen along with depression of erythropoiesis in the bone marrow associated with toxaemia (Nath *et al*., 2009). The azotaemia follows glomerulonephritis which occurs due to deposition of antigen-antibody complex on basement membrane of glomerulus; moreover this condition is further aggravated by pre-renal azotaemia (Pretzer, 2008).

Advanced diagnostic techniques like ultrasonographic imaging is one of the best diagnostic tool in which uterus is observed as enlarged and hypoechoic tubular organ containing echogenic fluid (Gupta *et al*., 2013), however sometimes pus shows slow, whirlpool like pattern (Bigliardi *et al*., 2004).

X ray can be another mode of diagnosis, but with some limitation as observation is sometime misdiagnosed with pregnancy especially of pre-mineralization stage (less than 45 days) (Pretzer, 2008).

Treatment

Surgical Approach

Spaying remains the choice of treatment for majority of obstetrician, however recently Laparoscopic Assisted Ovariohysterectomy (LAOVH) is advocated for treatment of select cases of canine pyometra, which is proved to be efficacious over conventional open method with careful case selection in order to improve success rate (Adamovich Rippe *et al*., 2013; Wallace *et al.,* 2015; Becher-Deichsel *et al.,* 2016).

Medical Approach

Medical approach mainly aims at systemic and intrauterine application of medicines. Subcutaneous administration of prostaglandin ($PGF_2\alpha$) at the dose rate of 150-200 µg/kg/day for more than 10 days showed 100% results (Myhre, 2016), which may be due the fact that $PGF_2\alpha$ causes luteolysis which leads to progesterone block (Renton *et al*., 1993). Another protocol with combination of cabergoline (@ 5 Pg/kg PO once daily) and cloprostenol (@ 1 Pg/kg once daily) for seven days was found enthusiastic. However, in recent times use of progesterone blockers such as mifepristone (Hoffman and Schuler, 2000) or aglepristone (Wehrend and Traschbostedt, 2003; Arnold *et al*., 2006) has proved better protocol of choice. Further Contri *et al*. (2015) successfully used a protocol in which aglepristone combined with a short duration (6 days) antibiotic cover proved efficacious. Another recent protocol used for the treatment of pyometra is administration of third generation GnRH antagonist acyline @ 330 µg/kg orally (single dose) with amoxicillin- clavulanate @ 12.5 mg/kg twice a day, orally for seven days provided promising results (Batista *et al.,* 2016),

Conclusion

In spite of greater pace of veterinary pharmacological and pathological advancement in research and innovation, satisfactory treatment for canine pyometra is still not formulized. One of the several reasons for this condition can be narrated as lack of complete and detailed information regarding etio-pathology of canine pyometra due to very complex nature of disease. It is need of the hour to find well established medical treatment with maximum recovery rate which can be used as alternative to stressful, costly and laborious surgical approach.

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Conflict of interest:

All authors declare no conflict of interest.

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