Artykuł przeglądowy *Review*

Glandular cystic hyperplasia of endometrium/pyometra complex

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Summary

Glandular cystic hyperplasia of endometrium/pyometra complex (GCHE-PC) in bitches is a disease which presents several diagnostic and prognostic challenges. The complex pathological process and systemic manifestations of the disease, the potential need for emergency treatment and the owner's desire to maintain the breeding performance of the bitch, are all factors that should be taken into consideration. This review aimed at conducting a thorough diagnostic plan in order to achieve several parameters related to the monitoring and the subsequent treatment of cystic glandular hyperplasia of endometrium pyometra complex. Detailed information on the history and the clinical findings of sick bitches facilitated making an initial selection into two groups: those referred for surgical treatment and those referred for medical treatment. This selection was further clarified by ultrasonographic imaging procedure. USG was found to be an accurate diagnostic tool because of its high level of correlation to patho-anatomical findings. USG facilitates distinguishing densities of the uterine content, internal uterine wall structures and uterine wall thickness.In this study it was found to be a valuable tool in determining the ideal treatment programme and estimating the prognosis for each given case. Ultrasonography proved to be more precise and conclusive than roentgenology in determining the type and location of the pathological process and the extent of the lesion. This review recommends the most potent antibiotics that may be used either concurrently with prostaglandin therapy or in cases when emergency treatment is indicated in bitches with advanced GCHE-PC.

Keywords: glandular cystic hyperplasia, endometrium, bitch

Glandular cystic hyperplasia of endometrium – pyometra complex (GCHE – PC) is common and serious reproduction apparatus disorder of bitches. GCHE – PC is caused by two combined mechanisms exhibiting inflammation of uterus with or without vaginal discharge. First mechanism is induced by prolonged influence of progesterone that causes proliferation of endometrium and excessive secretion of endometrial glands. Second mechanism is based on the significant effect of bacterial growth with increased inhibition of leukocyte response previously reduced by endogenous progesterone.

In last decade significant increase of application of exogenous hormones, mainly progestagens and estrogens, has appeared in bitches, even in younger age categories. The purpose of this hormonal treatment is to prevent the nidation after mismating, delay or termination of estrus. This fact reduces average age of patient with GCHE – PC. Bitches in this age category are ideal for reproduction use. Unfortunately, in this period manipulation with reproductive cycle is most frequent. The success of medical or surgical treatment and recovery from GCH – PC is fully dependent on optimal immune system response.

Microbiological analyses

Microbiological findings from bitches surgically treated are variable and often non specific, presenting haemolytic coli bacteria, staphylococci and haemolytic streptococci as dominant findings and lower occurrence of mixed cultures. Cultures from section material support bacterial invasion of endometrium. Microbiological findings from bitches medically treated are less conclusive. A variety of strains are less conspicuous and findings of mixed cultures of staphylococci, *E. coli* are a little more pronounced. In a study done by Bjurstrom (2) it was found that *E. coli* was the main strain isolated from bitches with GCHE – PC followed by β haemolytic streptococci and staphylococci. Gandotra et al., (4) isolated pure cultures with a dominance of *Staphylococcus* ssp. and much lower isolates of *E. coli*. Vandeplassche et al., (11) also found *Escherichia coli* to be dominant in pure culture isolates. In our study differentiation was made between haemolytic and non haemolytic *E. coli* and findings presented a dominance of haemolytic *E. coli*. The results of the aerobic bacterial culture of the vagina confirms the observations of previous studies by

Tab. 1. Antibiotic sensitivity of bacterial strains isolated from vaginal smears and section material from bitches with glandular cystic hyperplasia of endometrium – pyometra complex

Strain	Antibiotic														
	AMP	Eryt	CHF	Poly	STM	GTM	TTC	LIN	Sulfisoxazol	PNC	Baytril	Fur	Cefa	Colistin	Amx/ca
Haemolytic coli-bacteria	+		++	+++	++	+++	+		+		+	++	++	+++	+++
Non haemolytic *E. coli*	+		+++	+++	++	+++	++		+++		+++	+++	++	+++	++
Staphylococci	++	+++	++		++	+++	+	+++	+	++	+++	+	++		+++
Haemolytic streptococci	++	+++	+++		++	+++	+++	+++	+	+++		+	+++		++
Proteus ssp.	+		++	+++	+++	+++	+		++			++	++		++
Staphylococci + *E. coli*	+	+	++		++	+++	+		+			+	++		+++
Haemolytic streptococci + staphylococci	+	+++	++		+	+++	+	+++	+	++		+	++		++
Haemolytic streptococci + *Proteus* ssp.	+	+	++		+	+++	+		+			+	++		++
Broadest spectrum			≡			≡							≡		≡

Explanations: AMP – Ampicillin^R – beta-lactam antibiotic, ampicillin; Eryt – Erythromycin^R – makrolid antibiotic, erythromycin; CHF – Chloramphenicol^R – broad spectrum antibiotic, chloramphenicol; Poly – Aerosporin^R – polypeptid antibiotic, polymyxin; STM – Streptomycin – aminoglycosid antibiotic, streptomycin; GTM – Gentamycin^R – aminoglycosid antibiotic, gentamycin; TTC – Tetracyclin^R – tetracyclin antibiotic; LIN – Lincomycin^R – lincosamid antibiotic, lincomycin; Sulfisoxazol^R – sulfonamid, sulfafurazol; PNC – Penicillin G – penicillins, benzyl penicillin; Baytril^R – fluochinolons group, enrofloxacin; Fur – Furantoin^R – chemoterapeutic, nitrofurantoin; Cefa – Cefoclen^R – cefalosporin, cefalexin; Colistin – Colistin^R – polypeptide atb, colistin; Amx/ca – Amoksiklav^R – beta-lactam antibiotic, amoxicillin/clavulanic acid

Olson and Marther (9). In this study it was found that bacterial cultures recovered from diseased vaginas are closely similar to those found in healthy vaginas, suggesting that the pathogenesis of a chance invasion by opportunistic pathogens of a uterus already altered by an abnormal response to high progesterone levels.

Bacterial strains were most sensitive to gentamycin, chloramphenicol, cephalexin and amoxycillin with clavulanic acid (Tab. 1). Gilbert (5) recommended the use of amoxycillin with clavulanic acid as the treatment of choice concomitant to $PGF_2\alpha$ treatment. In this study owing to availability and pharmacodynamic consideration, gentamycin, dihydrostreptomycin – pencillin and chloramphenicol were used for antibacterical therapy. Microbiological evaluation used as a diagnostic procedure allowed isolation of the most frequently occuring bacterial strains in bitches with glandular cystic hyperplasia – pyometra complex. Based on antibiotic sensitivity tests, this review recommends the most potent antibiotics that may be used either concurrently with prostaglandin therapy or in cases when emergency treatment is indicated in bitches with advanced glandular cystic hyperplasia – pyometra complex.

Ultrasonography

Ultrasonographic imaging of the uterus was found to be a very important diagnostic procedure in the gynecology of bitches. Ultrasonographic measurements of three selected biometric parameters (internal diameter of the uterine horn, thickness of the uterine horn wall and external diameter of the uterine horn) of uterine horns behind bifurcation showed a high correlation with biometric measurement of these parameters in uterine horns after ovariohysterectomy.

A high correlation between ultrasonographic and pathological findings was also found by Zoldag et al (12, 13). It was found out that bitches, which recovered, had the average of the uterine horn lumen (internal diameter) 0.61 × 0.67 cm. The average of the uterine horn lumen (internal diameter) behind its bifurcation was in bitches that had to over go ovariohysterectomy 2.77 × 2.50 cm. It seems that also thickness of the uterine wall is very important for the process of healing up of reparable morphologically changed endometrium. Probably the thickness of the uterine horn wall requires the value above 0.30 cm in order the uterus could actively react to $PGF_2\alpha$ and by aid of Atb could cope with bacterial infection.

The value of mean total thickness of the uterine horn behind bifurcation (external diameter) is prognostically favourable for the choice of medical therapy probably only in lower values around 1.20 × 1.22 cm. Similarly, Renton et al., (10) measured the uterine horns by USG before application of $PGF_2\alpha$ as medical treatment and reported the mean diameter of the uterine horn around 1.5 cm.

Radiographic imaging

Radiographic imaging of the uterus may be used as a diagnostic tool in the detection of pyometra but should be backed up by other diagnostic procedures. Localized uterine enlargement may suggest a number of diseases including neoplasia, cystic endometrial hyperplasia, localized pyometra, hydrometra or mucometra, uterine stump granuloma or abscess, cystic

uterine remnant and uterine adenomyosis (1). In comparison with a lot of different diagnoses attributed to radiographic findings, ultrasonographic imaging of the uterus presents a much more specific technique which allows not only the type of pyometra to be recorded (showing whether it is localized, segmental or uniform tubular in nature) but also integrity of uterine wall and content type (7). The differential diagnosis for fluid filled uterus includes hydrometra and mucometra. Those pathologics may be suspected if the luminal contents are anechoic and the uterine wall is thin. Degrees of echogenesity of fluid in pyometra indicate serous (hypoechogenic) to viscid (hyperechogenic) content (5, 8). Degrees in echogenesity were not conclusive between surgically and medically treated bitches suggesting that serous to viscid fluid may be present in both groups.

Ultrasonography as a diagnostic tool plays a major role in distinguishing the pathologic stage of cystic glandular hyperplasia – pyometra complex, besides allowing one to rule out other differential diagnoses such as pregnancy with or without fetal death or peritonitis. As reported by Fayrer et al., (3), ultrasonography can be used to make diagnosis of pyometra prior to any appearance of clinical signs, when monitoring bitches subjected to hormonal therapy for treatment of mismating or estrus suppression or when monitoring bitches exhibiting ovarian acyclicity.

Imunodeficiency rate

Haematological parameters including high white blood cells counts and neutrophilia indicated significantly alterated condition of patients with GCHE-PC (4, 6). Improvement of these abnormal parameters occurs after treatment and correlates with improvement of clinical status of bitches.

Phagocytes play a crucial role in the defence mechanism of an acute inflammatory process. Their function is to catch and destroy foreign antigenic material and to cooperate with functions of other cells in the immune system. Functional ability of phagocytising cells is one of the important parameters of cell mediated immunity and resistance of the organism. Acquired defect in phagocytic function (defective chemotaxis or ingestion) results in an increased susceptibility to opportunistic pathogens and the consequence may be severe inflammation. Transient decreases in phagocytosis occur following severe trauma and thermal injury. Diminished phagocytic activity was observed in canine patients with inflammation (GCHE – PC). Decreased phagocytic activity and ingestion capacity of leukocytes and neutrophiles are in indirect relation with neutrophilia. Impaired phagocytic activity of neutrophiles in the bitch with GCHE – PC is reported also by Vandeplassche et al. (11). The possible explanation of this depression of phagocytic activity observed in affected dogs is that the disease – mediated prolonged exposure of neutrophiles to high concentration of inflammatory mediators that could result in the generalized deactivation of all cellular functions due to receptor down regulation. Mitogen induced lymphocyte blastogenesis is widely used as an indicator of the functional status of lymphocytes. The lymphocyte response to mitogen was depressed in dogs with pyometra in comparison with those in healthy dogs. The response of the blood lymphocytes is dependent on a number of regulatory factors, which obviously vary slightly with time and considerably with infectious disease. The diseases with extensive bacterial infiltration of the tissues, such as inflammatory diseases due to mixed infections, or juvenile pyodermas, suppurative dermatitis, suppurative osteomyelitis, peritonitis in dogs are usually associated with the presence of serum lymphocyte mitogenesis suppressing factors, which depresses stimulation index of lymphocytes in autologus serum. Decreased stimulation index of lymphocytes found in course of numerous infectious diseases can be caused not only by the presence of serum immunosuppressive factors but also by the decreased response of lymphocytes to mitogens.

A thorough immunological analysis provides specific information on the severity of the inflammatory process and animal health status during the course of the illness. Furthermore, it contributes to better monitoring of the clinical status of patients in the recovery period and facilitates the choice of suitable therapy of GCHE-PC.

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