The Use of Laboratory Findings in the Diagnosis of CEH–Pyometra Complex in the Bitch

Mustafa KAYMAZ, Ayhan BAŞTAN, Nil ERÜNAL, Selim ASLAN, Murat FINDIK
University of Ankara, Faculty of Veterinary Medicine, Department of Obstetrics and Gynaecology, Ankara-TURKEY

Abstract: The aim of this study was to research the effects of ultrasonography, vaginal cytology, a serum biochemical profile, complete blood count and blood gas analysis in 18 bitches in the diagnosis of cystic endometrial hyperplasia (CEH)–pyometra complex.

In transabdomimal ultrasonography, it was observed the the majority of anechongenic areas differed with the thickness of the uterine wall. Usually basal–parabasal type of cells appeared in vaginal cytologic examination, invasion of neutrophyl leucocytes and in some cases degenerative cell changes proved inflammatory changes. In bitches with CEH–pyometra complex there was a very significant increase in AST (Aspartate aminotransferase) and decrease in the ALT (Alanine aminotransferase). White blood cell (WBC) levels were higher than $12x10^3 xmm^3$. MCV count results showed that 93.3% of the cases were higher than the normal concentrations. The concentration of creatine and urea were found to be lower than the normal levels. Creatine concentrations were higher only in 30.7% of the animals and the GGT (Gama glutamyltransferase) levels to be higher in 33.3% of the animals. In 84.06% of the bitches with pyometra, serum albumin levels found to be lower than 4.1 g/dl. For all of the bitches, lactate dehydrogenase (LDH) levels were higher than 143–171 u/l. Triglycerides were found to be higher than 0.2–1.8 mmol/l in 70% of the bitches. It can be assumed that the normal level of serum alkaline phosphatase (ALP) shows the severity of low renal failure in 58.33% of the bitches. In the blood gas analysis it was determined that PO_2 levels in 90% of the bitches and HCO_3 levels in 60% of the bitches with pyometra were lower than 85–95 mmHg and 17–25 mmol/l respectively.

Key Words: Pyometra, bitch, laboratory diagnosis, vaginal cytology.

Köpeklerde CEH–Pyometra Kompleksinin Tanısında Laboratuvar Bulgularının Kullanılması

Özet: Bu çalışma, ultrasonografi, vaginal sitoloji, serum biyokimyasal analizleri, tam kan sayımı ve kan gazı analizlerinin köpeklerde CEH–pyometra kompleksi tanısında beraber kullanımını amaçlamıştır.

Transabdominal ultrasonografide kalınlaşmış uterus duvarıyla beraber, anekojenik alanların yoğunluğu tespit edilmiştir. Vaginal sitolojik muayenelerde bazal–parabazal tipte hücre yoğunluğu gözlenmiş ve nötrofil lökosit ve bazı olgularda dejeneratif hücre değişiklikleri yangısal değişikliklerin varlığını doğrulamıştır. CEH–pyometra kompleksli hayvanlarda AST'de belirgin bir artış ve ALT'de ise düşüş saptanmıştır. Bunun yanında WBC seviyesi $12x10^3 xmm^3$ ün üzerinde bulunmuştur. MCV sayımı sonucunda olguların %93.3'ünde normal değerlerin üzerinde veriler elde edilmiştir. Kreatin ve üre konsantrasyonları sırasıyla normal değerlerinden düşük bulunmuştur. Hayvanların %30.7'sinde kreatin ve %33.3'ünde ise GGT değerleri yüksek saptanmıştır. Pyometralı köpeklerin %84.06'sında albumin miktarı 4.1 g/dl'den düşük saptandı. LDH'ın çalışmadaki köpeklerin tamamında 143–171 u/l'den yüksek olduğu gözlendi. Trigliseridler hayvanların %70'inde 0.2–1.8 mmol/l'den yüksek bulunmuştur. ALP'nin %58.33 oranında normal sınırlar içerisinde saptanması böbreklerdeki yıkımlanmanın çok şiddetli olmadığını göstermiştir. Yapılan kan gazı analizlerinde köpeklerin %90'ında PO_2 değeri 85–95 mmHg'nin ve %60'ında ise HCO_3 değeri 17.0–25.0 mmol/l değerinin altında olduğu tespit edilmiştir.

Anahtar Sözcükler: Pyometra, köpek, laboratuvar bulguları, vaginal smear.

Introduction

During early metestrus stage elevated progesterone levels decrease the resistance to infections and increase the risk of local infection. The increase in bacterial number and toxins released from them stimulates exudate accumulation in the endometrium so that inflammatory response develops, endometrium gradually thickens and pyometra occurs (1–4).

The clinical signs of pyometra vary with the severity and duration, of the condition of the occurence of bacterial infection, the existence of endotoxemia, the potency of the cervix and the animal's general health (5). The observation of symptoms such as anorexia, apathy, polyuria, polydipsia, lethargy and vomiting soon after estrus leads to suspicion of pyometra (2, 3, 5–8). Especially in iatrogenic pyometras most of the cases, bitches have never been pregnant or they have been pregnant several years prior to observation of clinical signs (9).

Due to leucopenia, fast and severe general health and immune system disorders occur (2, 8, 9).

Total white blood cell (WBC) count is usually between 38.000–45.000 cell/ml and is typical for pyometra. However, WBC count of the animals with pyometra can vary between 2.500 –> 100.000 cell/ml. About 26–60% cases of pyometra anemia have been reported. As pyometra is a chronic disease; normocytic, normochromic, nondegenerative anemia frequently develops. Initially pocket cell volume (PCV) is normal, but decreases later on. Anemia may be covered because of dehydration. Pyometra associated with anemia is generally related to inflammation (2, 3, 8).

Apart form the clinical changes in pyometra, disorders of cardiologic and circulatory system electrolyte balance occur. Thus, slight hypocalcemia and hyponatremia develop (8). Nephropathy is occasionally examined by toxins resorbed from uterus (2, 5, 6, 8, 10). The severity of renal insufficiency can be estimated by increased concentrations of serum urea, creatine and inorganic phosphate (10). Toxins increase blood flow to the kidneys and decrease Na levels. Because of prolonged pyometra, liver disorders which are determined with intrahepatic cholestase, increased AST and Creatine kinase occur. Continuous hipoalbuminemia is seen as acute phase reaction. While blood total protein level increases, hipoalbuminemia develops (2, 3, 6, 8). Depending on severity of pyometra, leucocytosis, degenerative left shift and rapid sedimentation rate can be detected (2, 6). Forty four percent of bitches with uterus disorders originating hormonal changes show AST increase (11).

Cholesterol, bilurubin, alkalen phosphatase (ALP) and lactate dehydrogenase (LDH) levels may be high. Significantly low alanine aminotransferase (ALT) levels in bitches with pyometra has been observed (2, 3, 7, 10, 12). After estrus, decreased serum ALT levels in bitches are of clinical importance in typical endometritis (10, 12).

In some cases, less then 36% of hematrocrit values indicate normocytic, normochromic anemia. The prognose in leucopenia and low body temperature (in severely toxemic patients) is not well (13).

Although vaginal cytology does not differentiate uterine disorders from each other, increase in neutrophyl and bacteria suggests inflammatory changes (2, 14). Severe degenerations are observed in neutrophyl leucocytosis in vaginal smear of bitches with open pyometra. Vacuols, macrophages, throphoblastic cells undergoing cytolysis and heavy bacterial growth may be usefull in diagnosis of pyometra (3).

Especially if sepsis and shock develop, acid–base balance spoils (2–5, 8, 15). Moreover, when abdominal pain is associated with pyometra, pulmoner functions can not fully work and respiratoric acidosis develops. Aside from respiratoric acidosis, metabolic acidosis can be observed because of prolonged anorexia (2, 15).

Depending on pyometra's phase, there are changes in both uterus and other internal organs. Therefore both pre–and post–operative precautions need to be taken by evaluating various laboratory results.

In this study, our objective was to determine the importance of laboratory results which support the diagnosis and therapy of pyometra.

Materials and Methods

From January to July 1996, 18 privately owned bitches in different breeds which were 8.0±2.8 years old were referred to the Gynaecology Clinic of the Veterinary Faculty of Ankara University (Türkiye) for the treatment of CEH–Pyometra complex.

The owners were questioned about feeding, environment, general health conditions and preious estrus cycles.

After general examination (body temperature, heart rate, respiratory rate, evidence of dehydration), gynaecological examination was performed.

In gynaecological examination; oedema at the vulva, the character of the vulvar discharge and mucosal changes were inspected. Digital palpation of the uterus through the abdominal wall performed gently because of the friability of an affected uterus. Vaginoscopy was used to determine the changes of the cervix and the discharge in the orificium uteri externa. Soon after that, vaginal smear samples were taken. The samples were stained according to Papanicolau staining precedure.

Ultrasonography was perfomed by using B–Mode Real time 3.5 MHz linear transducer. The patient was positioned in dorsal recumbency. The abdomen and especially uterus were scanned firstly.

Blood samples were collected by puncture of cephalic vein, in both clean–dry and heparinised glass vials fitted with polyethylene stoppers and were allowed to coagulate at room temperature for approximately 30 minutes in dry galss vials. Then, the nonheparinised samples were centrifuged and the serum transferred into a chemically clean tube. A complete blood count (RBC, MCV Hct, WBC and Hb), a serum biochemical profile (Glucose, urea, creatine, uric acid, total protein, albumin, alanine

aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), triglyceride, total cholesterol, natrium, potassium, γ–glutamyltransferase (GGT), total bilurin and blood gas parameters (pH, PCO_2, PO_2, HCO_3, O_2–SAT, BE) were determined from the samples obtained from 18 bitches.

Statistical analysis were performed by using Minitab.

Results

Results of history from the bitches which were brought to our clinic are shown in Table 1.

In transabdominal ultrasonograhy, it was observed that the majority of anechogenic areas differed with the thickness of uterine wall.

Complete blood count results showed that particularly averages of MCV and WBC were higher than the normal values (Table 2). These parameters show that 93.3% of the bitches with pyometra had higher MCV and and 73.3% of them had higher WBC.

In vaginal cytologic examination mostly basal and parabasal cells were dominant. The invasion of neutrophyl leucocytes and in some cases degenerative cell changes prove imflamatory changes (Table 5).

Blood serum biochemical results show that uric cacid (53.8±36.4), total protein (71.6±9.2), AST (49.5±22.9), LDH (512±271), triglyceride (2.6±0.9), T–bilurubin (17.6±12.6) concentrations are higher than the normal levels (Tablo 4).

Aspartate aminotransferase, LDH, triglycerides, T–bilurubin concentrations in bitches were higher 84.6%, 100%, 70% and 66% respectively. Mean albumin concentration was measured to be lower (2.7±1.2) than normal values. This lower concentration was observed in %84 of the bitches. About 69.2% of the bitches with pyometra had lower creatine (38.7±30.4) and ALT (31.6±21.1) concentrations.

Blood gas analysis results of the present study showed that PO_2 was lover in 90% of the cases, however BE (base excess) was higher in all the cases (100%) (Table 3).

Discussion

Cystic endometrial hyperplasia–pyometra complex, generally occurs in middle age or aged bitches during progestative stage of estrus cycle (6). Especially for bitches older than 8 years of age pyometra cases

Table 1.   Information received from owners.

	Number of Bitches	Age	Birth	Polydipsia	General Health Condition	Vaginal Discharge	Last estrus date (week)	Pseudo– pregnancy %
					HISTORY			
Results	18	8.0±2.8	(+) 13.3% (−) 86.6%	(+) %85.7 (−) %14.3	(↓) % 92.8 (N) %7.2	6.9±3.0 %72.2 (−) %27	(+) 61.1 min:2.0 max: 12.0	(−) 38.9

(+): Presence, (−): absence, (↓): Poor condition, (N): Normal.

Parameters	Normal Ranges (Min–Max)	Results X±S	(Min–Max)
RBC (10^6 mm^3)	5.5–7.8	5.8±1.3	(3.5–8.5)
MCV (μm^3)	60–70	82.6±8.7	(67.0–97.0)
Hct (%)	42–52	49±13	(27–79)
WBC (10^3 mm^3)	6–12	32.05±19.5	(2.4–62.8)
Hb (gr/100 ml)	12–18	14.3±3.3	(8.5–20.9)

Table 2.   Complete blood count results (n=18).

Table 3.   Blood gas analysis results (n=18).

Parameters	Normal Ranges (Min–Max)	Results X±S (Min–Max)
Ph	7.37–7.51 (7.44)	7.2±0.08 (7.1–7.4)
PCO$_2$ (mmHg)	24.0–38.0 (31)	34.0±7.4 (26.8–53.1)
PO$_2$ (mmHg)	85–95	53.5±36.8 (22.0–153.6)
HCO$_3$ (mmol/l)	17.0–25.0 (21)	15.5±3.4 (10.5–20.3)
O$_2$ (SAT%)	99.2–99.4	133.8±202.5 (28.9–707.0)
BE (–mmol/l)	0 (–2.0–2.0)	–9.6±4.5 (–15.5*–3.0)

constituted about 50–60% of all gynaecologic disorders (3, 5, 6, 12, 16, 17). In our study, it was determined that the average age and last estrus date were 8.0±2.8 years and 6.9±3.0 weeks respectively. Dumon et al., (18) state that pseudo–pregnancy may lead to poliuria, polidipsia, mucometra, pyometra and or cystic endometrial hyperplasia. In this study, it was determined that in 11 bitches (61.1%) pseudopregnancy had occured in previous estrus cycles.

Diagnosis of pyometra in bitches is quite easy by using ultrasonography (2, 14, 19, 20). Chronic endometritis and pyometra cases may be determined by mild or high anechogen secret in uterus lumen and anechogen uterine walls reflection to the monitor (2, 14, 19).

In ultrasonographic examinations, the parallel data has been obtained with those of other researchers.

The preparation of cytologic samples together with vaginoscope helps determine vaginal discharge. However

CEH–Pyometra complex not always presents as vaginal discharge. In the study carried out, the proportion of the cases which no discharge was seen is 27% (n=5), while in 72.2% of the cases (n=13) discharge could be observed easily. Vaginal cytology is a useful method so as to determine the increase in WBC numbers. Though WBC is not a specific finding for uterine diseases, it indicates an extraordinary situation in the genital tract (2). On the other hand, in this study, the absence of leucocyts on the cytologic samples, in 4 cases of 5 showing close cervix pyometra, drew attention, whereas in the cases with discharge there were a large amount of degenerated and normal leucocyts. Feldman and Nelson (3) reported that vaginal smear of a bitch with open cervix pyometra frequently includes degenerated neutrophyl cells. Feldman and Nelson (3) noted the presence of cells degenerations such as degenerated cytoplasmic wall, distortion, cytolysis and karyolysis in epitel cells. Correspondingly, in this study too, the similar cell degenerations have been determined in 66.6% of the samples. Christiansen (6) reported that there were basal and parabasal cells in pyometra cases. In the same way, our study showed basal–parabasal cells to be the dominant cell types seen in vaginal cytologic examinations in 83.3% of the cases (n=5). In two bitches, although the last estrus was seen 12–14 weeks before the samples were taken, the dominance of keratinized and superficial cells has been observed and following ovariohysterectomie, in one dog ovarian cyst and in the other granulose cell tumour occured. Similarly, Hosken et al. (14) reported that they found cornification up to

Table 4.   Biochemical findings from the serum (n=18).

Parameters	Normal Ranges (Min–Max)	Results X±S (Min–Max)
Glucose	3.7–8.2 mmol/l	2.1±1.2 (0.6–5.3)
Urea	42.8–59.9 mg/dl	40.3±26.7 (13.0–97.0)
Creatine	44–133 µmol/l	38.7±30.4 (10.3–106.7)
Uric Acid	24 µmol/	53.8±36.4 (7.8–124.3)
Total Protein	48–66 g/l	71.6±9.2 (55.0–85.0)
Albumin	4.1 g/dl	2.7±1.2 (0.6–4.3)
Alt (Gpt)	3–50 u/l	31.6±21.1 (9.0–85.0)
Ast (Got)	1–37 u/l	49.5±22.9 (15.0–91.0)
Alp	20–155 u/l	141.6±137.6 (18–472)
Ldh	143–171 u/l	512±271 (290–943)
Triglyceride	0.2–1.8 mmol/l	2.6±0.9 (0.7–3.6)
Total Cholesterol	3.3–9.3 mmol/l	6.83±2.84 (2.43–11.57)
Na	138–148 mmol/l	149.1±22.9 (129.0–196.0)
K	3.5–5.0 mmol/l	4.5±1.0 (3.2–6.5)
Ggt	5–25 u/l	14.3±17.0 (1.0–39.0)
Total Bilurubin	2–10 µmol/l	17.6±12.6 (7.7–41.6)

Table 5.   The results of vaginal smear and vaginoscopy.

No	Discharge	Dominant cell type seen in the smear	Leucocyte presence/ absence	Eritrocyte presence/ absence	Mucus presence/ absence	Cellular degeneration*
I	–	all of basal (B) and parabasal (PB)	+	–	+	–
II	+/bloody-mucous	B–PB	+++/ degenerated*	++++	+	–
III	pinky in appearance, seromucous	B–PB, a few intermedier	++++/ degenerated	–	++	–
IV	–	B–PB, a few intermedier	–	–	+++	+
V	chocolate like appearance, bad odourfull	B–PB	++++/ degenerated	–	+	+
VI	+	B–PB	++++	–	+	+
VII	+	B–PB	++++/ degenerated	–	+	–
VIII	–	B–PB, intermedier	–	–	+	–
IX	+	B–PB	++++/ degenerated	–	++	–
X	+/bloody	B–PB Intermedier	++++	++++	+	+
XI	+/mucous	B–PB %60 Interm. % 30 Low superficial (Supf.) %10	+	–	–	–
XII	+/bloody, prulent	B–PB	++	+++	–	+
XIII	+/prulent	B–PB	++++	–	++++	+
XIV	–	Supf. %70 Interm. %30	–	–	–	–
XV	+/prulent	Cornified Supf. % 80 Supf. %20	–	–	+	Cell clusters
XVI	+/bloody	B–PB, a few intermedier	++++	++++	+	+
XVII	+/sero mucous	B–PB	++++	–	+	+
XVIII	–	P–PB	–	–	–	++

* Cellular degeneration; Nuclear clusters without cytoplasm, Degenerations such as cytolysis and karyolysis in nucleus and cytoplasm, Cellular distortion and cells containing vacuol in cytoplasm.

100% in epithelial cells in a bitch with endometrial hyperplasia and follicular cyst.

It has been reported that (2, 3, 5–8) polidipsia, anorexia and apathy soon after estrus lead to the suspicion of pyometra. Polidipsia was observed in 85.7% and anorexia and apathy were observed in 92.8% of the bitches with pyometra.

Kuntze and Aurich (9) reported that in most of the cases with pyometra, bitches have never been pregnant or they have been pregnant several times before the

onset of clinical signs. In our study it was detected that 86.6% of the animals had never been pregnant. This data was similar with the results of researchers.

Medulla spinalis responses to inflammation by increasing leucocytes. About 60% of the bitches with pyometra have over 12.000 leucocytes/ml (2, 3, 8, 17). However, normal or close to normal WBC values have been observed (2, 17).

In this study, 73.3% of WBC count was found to be over 12.000/ml and this was assessed as leucocytes response to inflammation in bitches with pyometra. Elevated levels of MCV is described as macrocytosis. In this case formation is destructed (21). Depending on increased medulla spinalis activity, large number of reticulocytes are included into blood circulation. This is a symptom of macrocyter hyperchromic megaloblaster anemia (22, 23). Findings from laboratory MCV count results showed that 93.3% of the cases were higher than the normal concentrations.

ALT, AST, ALP and GGT are the liver enzymes used clinically to evaluate the presence of hepatic disease. Measurement of increased serum concentrations of these substances may suggest hepato–biliary disease. When ALT is decreased, about 60% of the bitches with pyometra have higher AST levels (9, 11). In this study, 69.2% of the bitches with pyometra had lower ALT and 84.6% of them had higher AST levels supporting the observations listed above.

In the pyometra cases, bitches have higher levels of urea and creatine (6, 9). Schepper et al. (10), reported that the renal failure with a rather high urea and creatine ratio was suggestive of a pre–renal disfunction.

In this study, depending on the lower concentrations of creatine and urea and higher levels of GGT, it can be deduced that no severe renal failure occured. The rise of GGT in the serum has shown hepatic failure. Creatine concentrations were only higher in 33.3% of the animals. Similar creatine concentrations have also been reported elsewhere (6, 17).

While total protein increases, hipoalbuminemia has been reported (6, 9). Hipoalbuminemia has been observed in severe liver insufficiency cases (22). Serum albumin levels tend to fall in hepatic diseases. We think that, this happens as a result of the accumulation of albumin into the extravascular tissue, because of the rise in capillary permeability or the expansion of extravascular tissue. The detection of hipoalbuminemia and the rise in total protein in 84% and 38.46% bitches with pyometra

respectively were in accordance with the findings of other researchers. Because hipoalbuminemia occurs together with higher total protein levels, in response to acute inflammatory reaction (9), it has important role in laboratory findings.

Cholesterol, bilirubin, ALP and LDH levels may be found higher than the normal (6, 9). Serum ALP levels were found normal in 84% and in 33.3% of the cases no serious renal destruction was seen. In this study, 100% of the cases had higher LDH, 66% of the cases had higher total bilirubin. These findings are similar with those of other researchers. The same researchers report that the cholesterol concentrations may be high while our findings showed that the cholesterol concentrations were in normal range in 63.33% of the bitches with pyometra.

Higher hematocrit levels confirm normocytic normochromic anemia (9). Although in the present study 26.6% of the cases had higher hematocrit concentrations, these values must be considered.

About 70% higher triglyceride levels showed hepatopathies.

The increase in the concentration of T–bilurubin showed hepatocellular damage. T–bilurubin levels were found to be higher than 2–10 µmol/l in 66.6% of the bitches. Under the considerations of hepatic enzymes, this result supports hepatocellular damage.

Tobias and Wheaton (24) reported that, increased arterial pH and decreases in PCO_2, PO_2 and HCO_3 are often found on blood gas analysis. These changes are classified as primary respiratory alkalosis with metabolic compensation and may be associated with hyperventilation from septicemia and endotoxemia. Metabolic acidosis indicates a more serious condition with mortality rate of 44.4% when HCO_3 is less than 15 mmol/l.

In the study carried out, the metabolic acidosis has been confirmed by having obtained low levels of PO_2 and HCO_3. However, HCO_3 levels not having been decreased under 15 mmol/l posed the low mortality rate. Our data parallels literatures on this subject.

Consequently, total blood and serum biochemical tests, blood gas analysis, vaginal cytologic and ultrasonographic examinations, for patients which have been found suspicious of CEH–pyometra complex, play an important role in diagnosis and the results would change treatment procedure and prognosis of the disease to a great extent in a positive way.

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