

Atypical pyometra in a canine with hyperadrenocorticism and endocardiosis: a clinical case

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ABSTRACT

The aim of this report was to document the presentation of a 12-week-old pyometra in an 11-year-old female Chihuahua with hyperadrenocorticism and endocardiosis. The patient presented with clinical and paraclinical signs consistent with chronic hyperadrenocorticism. An adrenocorticotrophic hormone (ACTH) stimulation test confirmed the hyperadrenocorticism (post-stimulation cortisol of 27.79 µg/dl). However, the progression of subclinical pyometra was evident at 12 weeks of evolution (Acute Patient Physiologic and Laboratory Evaluation – fast [APPLE-fast] of 15; Quick Sequential Organ Failure Assessment [qSOFA] of 1) with additional signs of pulmonary edema secondary to endocardiosis. At 48 hours post-surgery, the patient exhibited lethargy, anorexia, an APPLE-fast of 26, and clinical criteria of SIRS-3. After the therapeutic failure of the previous approach with enrofloxacin plus ampicillin/sulbactam, and later cefovecin, it was decided to administer gentamicin for 3 days, with a favorable clinical and paraclinical response, and an APPLE-fast of 19. The result of the urine culture revealed the presence of enterohemorrhagic *Escherichia coli* (EHEC) with a multidrug-resistant profile suggestive of extended spectrum beta-lactamase (ESBL). At the clinical follow-up 4 weeks after starting trilostane post-discharge, the tutor reported improvement in clinical signs of chronic polydipsia, polyuria, and polyphagia, with an appropriate quality of life score for monitoring hyperadrenocorticism. It is presumed that the classic clinical expression of pyometra and infectious cystitis was mitigated by the uncontrolled underlying hyperadrenocorticism, and the clinical course of the disease progressed to sepsis due to EHEC with apparent production of ESBL.

Keywords: canine syndrome of Cushing, pyometra, extended spectrum beta-lactamase producing *E. coli*.

Piíometra atípico en canino con hiperadrenocorticismo y endocardiosis: caso clínico

RESUMEN

El objetivo de este reporte fue documentar la presentación de piíometra de doce semanas de evolución en una hembra Chihuahua de once años con hiperadrenocorticismo y

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endocardiosis. Se recibió la paciente reseñada, con signos clínicos y paraclínicos manifiestos consistentes con hiperadrenocorticismo crónico. Una prueba de estimulación con hormona adrenocorticotrópica (ACTH, por sus siglas en inglés) comprobó el hiperadrenocorticismo (cortisol postestimulación de 27,79 µg/dl). No obstante, el progreso de un piometra subclínico fue evidente a las doce semanas de evolución (APPLE-*fast* de 15; qSOFA de 1) con signos adicionales de edema pulmonar secundario a endocardiosis. A las 48 horas del posquirúrgico, la paciente manifestó decaimiento, anorexia y un APPLE-*fast* de 26 con criterios clínicos de SIRS-3; tras la falla terapéutica del abordaje previo con enrofloxacin más ampicilina/sulbactam y posteriormente cefovecina, se decidió suministrar gentamicina durante tres días, con respuesta favorable clínica y paraclínica del animal y APPLE-*fast* de 19. El resultado del urocultivo reveló la presencia de *E. coli* enterohemorrágica (EHEC, por sus siglas en inglés) con un perfil de multirresistencia sugerente de betalactamasas de espectro extendido (BLEE). Al control clínico cuatro semanas después de inicio del trilostano al alta médica, la tutora reportó mejoría de signos clínicos de polidipsia, poliurea, polifagia crónicos, con un puntaje de calidad de vida adecuado para el seguimiento del hiperadrenocorticismo. Se presume que la expresión clínica clásica de piometra y cistitis infecciosa se mitigó por el hiperadrenocorticismo no controlado de base y el curso clínico de la enfermedad progresó a sepsis por EHEC con aparente producción de BLEE.

Palabras clave: síndrome de Cushing canino, piometra, *E. coli* con betalactamasas de espectro extendido.

INTRODUCTION

Canine hyperadrenocorticism is an endocrine disorder with a relatively frequent occurrence, and its diagnosis has been increasing in recent years (Schofield *et al.* 2022). The typical presentation profile includes dogs over six years of age and predisposed breeds such as Poodles, Terriers, Beagles, German Shepherds, and Boxers (Bennaïm *et al.* 2019a). The clinical presentation is characterized by classic signs such as polydipsia, polyuria, polyphagia, and varying degrees of sarcopenia and pendulous abdomen due to myopathy and abdominal organomegaly (secondary hepatopathy, distended bladder, reduced abdominal pressure, and increased mesenteric fat deposition). Additionally, dermatological signs are often present in these patients. These are characterized

by non-pruritic, bilateral, truncal, and symmetrical alopecia, thin, dry, and inelastic skin, phlebectasia, comedones, and other less common signs (Kooistra & Galac 2010). The paraclinical profile is marked by varying degrees of stress leukogram, thrombocytosis, and mild relative polycythemia in the blood count, with a moderate to severe elevation of alkaline phosphatase (ALP), proportionately higher than the elevation of other liver enzymes (which may range from mild to moderate). Additionally, there is an elevation of triglycerides (VLDL), cholesterol (LDL, HDL), mild hyperglycemia, and sustained hyposthenuria to isosthenuria. The most common comorbidities include systemic hypertension, proteinuria, dyslipidemia, insulin resistance, biliary mucocele, steroid hepatopathy, tendon laxity, and calcium

oxalate uroliths (Kooistra & Galac 2010). Diagnosis is obtained through a consistent combination of the patient profile, clinical signs, and paraclinical findings, along with the confirmation of chronic hypercortisolism in a low-dose dexamethasone suppression test or through ACTH stimulation (Behrend *et al.* 2013).

Given the anti-inflammatory and immunosuppressive effects of chronic hypercortisolemia, urinary or dermatological infections are common, even without the manifestation of a typical clinical picture (Bennaim *et al.* 2019a). The aim of this clinical case report was to document the presentation of a 12-week-old pyometra in an 11-year-old female Chihuahua with underlying hyperadrenocorticism that only showed systemic signs of sepsis late in the course of the disease, possibly due to the chronic influence of cortisol mitigating the classical presentation of pyometra.

CASE REPORT PRESENTATION

Patient overview and reason for consultation

A 11-year-old intact female Chihuahua canine was brought to the outpatient clinic at the University of La Salle for constant panting and a heart murmur detected during a previous veterinary examination.

Anamnesis and physical examination

During the anamnesis, marked polyphagia, polydipsia, and polyuria were reported, with an approximate evolution of 8-12 months. Additionally, there had been scanty and intermittent mucous-yellowish vulvar discharges in the last 12 weeks, with the clinical manifestation of proestrus occurring about 14 weeks ago. The results of paraclinical tests conducted since

the onset of the disease revealed relative polycythemia, monocytosis, and hyperglobulinemia in the complete blood count, without abnormalities in the measured blood biochemistry (ALT, creatinine). Furthermore, an anamnestic ultrasound revealed a reduced corticomedullary differentiation and ratio with hyperechoic cortex compared to the spleen. The liver parenchyma appeared heterogeneous and hyperechoic, along with marked hepatomegaly. The gallbladder volume was measured at 24.5 ml. Additionally, bilateral adrenomegaly was identified (0.79 and 1.15 cm, respectively). The vaccination history of the patient was up-to-date, and the reported nutritional plan was balanced. The initial physical examination findings are presented in table 1.

Initial diagnostic and therapeutic plan

The initial paraclinical results, detailed in table 2, indicated a stress leukogram, severe increase in ALP, mild elevation in filtration and induction liver enzymes, increased preprandial bile acids, hypercholesterolemia, hyperphosphatemia, hyposthenuria, active sediment, and post-glomerular proteinuria. These results were obtained after a 12-hour fasting period. The urinary cortisol:creatinine ratio was used as a screening test for hyperadrenocorticism, following protocols by Behrend *et al.* (2013) and Smiley & Peterson (1993). The low-dose dexamethasone suppression test, recommended by the American College of Veterinary Internal Medicine (ACVIM) consensus (Behrend *et al.* 2013), was canceled due to syncope, potentially leading to a false positive. Hyperadrenocorticism was later confirmed by an ACTH stimulation test, showing post-stimulation cortisol levels of 27.79 µg/dl.

TABLE 1. Admission physical examination of a canine patient with endocardiosis and concurrent hyperadrenocorticism accompanied by a 12-week evolution of pyometra

Examined Constant	Identified Finding	Examined System	Identified Finding
Temperament	Docile	Skin inspection	The skin of the abdominal region presents as thin, dry, and inelastic, exhibiting phlebotectasia, comedones, mild generalized scaling, bilateral hypotrichosis in a multifocal pattern, and alopecia of the nasal bridge along with moderate xeromycteria. No vulvar discharge was identified upon initial physical examination.
Attitude	Mild depression	Ocular Inspection	Bilateral corneal dystrophy (well-circumscribed whitish opacity appearing as circular halos on the cornea) with negative fluorescein staining.
Body condition	5/9		
Muscle score	2/4	Musculoskeletal System Inspection	Sarcopenia and cranio-lateral patellar displacement during gait associated with 3/4 lameness in the right hind limb, varus knee; positive drawer and tibial compression tests.
Weight	3.7 Kg		
Dehydration	< 6%	Abdominal Palpation	Pendulous abdomen, severe hepatomegaly, and plethoric bladder upon abdominal palpation
Heart rate	124 beats per minute		
Respiratory rate	29 breaths per minute	Thoracic Auscultation	Normal bronchial and respiratory sounds, regular cardiac rhythm, 4/6 left-sided murmur with the point of greatest intensity between the 3rd and 5th intercostal space, apparently associated with the cardiac base.
Rectal temperature	38.2 °C		
Pulse	Strong, symmetrical, concordant	Oral Inspection	Grade III/IV periodontal disease.

Source: own elaboration.

Echocardiographic assessment revealed mitral valve degeneration without pulmonary hypertension and cardiac remodeling, classifying the patient in stage B2 (Keene *et al.* 2019). Thoracic radiography confirmed left atrial cardiomegaly with a subtle broncho-interstitial pattern in the perihilar region. Systolic blood pressure

measured by vascular Doppler averaged 110 mmHg from five readings in right lateral recumbency. No abnormalities were found in the electrical conduction of the heart on the electrocardiogram. The initial therapeutic protocol included oral pimobendan at 0.25 mg/kg every 12 hours.

TABLE 2. Paraclinical evolution of an intact 11-year-old female Chihuahua with hyperadrenocorticism and endocardiosis, developing a 12-week progression pyometra and subsequent emergence of sepsis signs in the postoperative period

Analyte	Initial outpatient consultation	Hospitalization (days)				Follow-up at hospital discharge (day)	
		1	3	5	7	2	8
Blood/plasma							
Erythrocytes (x 10 ⁶ cel/ul)	6.8	7.4	6	5.5	4.7	5.8	5.8
Hemoglobin (g/dl)	15	13.5	11.8	9.8	8.6	11.3	12
Hematocrit (%)	48	46	38	33	28	38	40
MCV (fl)	70.6	62.2	63.3	60	59.6	65.5	69
MCHC (g/dl)	31.3	29.3	31.1	29.7	30.7	29.7	30
Leukocytes (x 10 ³ cel/ul)	20.4	27.1	40.1	44.8	54	37.4	27.9
Neutrophils (x 10 ³ cel/ul)	18	22	34.9	37.6	47	31	21.2
Bands (x 10 ³ cel/ul)	0.6	0.5	0.4	1.8	1.1	1.1	0.6
Toxic Neutrophils	+	++	++	+	+	+	+
Lymphocytes (x 10 ³ cel/ul)	0.4	0.8	2.4	1.8	1.6	2.2	3.9
Macrophages (x 10 ³ cel/ul)	1	2.2	1.6	2.2	1.6	2.6	1.4
Eosinophils (x 10 ³ cel/ul)	0.4	1.1	0.4	0.4	1.1	0.4	0.3
Basophils (x 10 ³ cel/ul)	0	1	0	1	1	0	0
Platelets (x 10 ³ cel/ul)	420	160	698	634	847	609	567
Total Proteins (g/dl)	6.4	8.4	8.4	7.6	7.2	8	8.6
Globulins (g/dl)	3.3						
Albumin (g/dl)	3.1						
Creatinine (mg/dl)	0.2			0.53	0.52	0.39	
BUN (mg/dl)	11.2				14		
Calcium (mg/dl)	9.01						
Phosphorus (mg/dl)	11.3						
Glucose (mg/dl)	95			129	194	102	
Total Bilirubin (mg/dl)	0.1						
GGT (U/L)	315						
ALP (U/L)	>1300						
ALT (U/L)	373						
AST (U/L)	34						
Bile Acids (umol/L)	24.6						

Analyte	Initial outpatient consultation	Hospitalization (days)				Follow-up at hospital discharge (day)	
		1	3	5	7	2	8
Cholesterol (mg/dl)	404						
Baseline Cortisol (ug/dl)	14.81						
Cortisol 4 hours post-LDDST (ug/dl)	17.68						
Cortisol 8 hours post-LDDST (ug/dl)	---						
Cortisol post-ACTH (ug/dl)		27.79					
Lactate (mmol/L)				5.89	10.4	8.13	
APPLE fast	15		26		19		
Urine							
Specific gravity	1006	1016		1011			1016
pH	6	6		5			6
Bilirubin	negative	negative					
Ketones	negative	negative					
Glucose	negative	negative					
Protein (mg/dl)	30	100		15			15
UPCR	5.7						
UCCR (x 10 ⁻⁶)	29.4						
Urinary Sediment							
Erythrocytes	4-7	4-7		0-4			4-7
Leukocytes (per HPF)	8-10	0-3		3-5			0-3
Bacteria (per HPF)	++	-		+			-
Tran.EC (per HPF)	1-3	1-		0			0
SEC (per HPF)	1	1-5		0-3			1-5
Casts (per HPF)	Hyaline 1	Hyaline 1 Granular 4		Granular 2			Hyaline 1 Granular 4

*UPCR: urine protein-creatinine ratio; UCCR: urinary cortisol-creatinine ratio; HPF: high-power field; Tran.EC: transitional epithelial cells; SEC: squamous epithelial cells.

Source: own elaboration.

Clinical progression and follow-up plan

Two days later, the patient was admitted for hospitalization due to the sudden onset of a new syncope episode, along with intensified lung sounds associated with bilateral crackles and mixed dyspnea. Follow-up blood analysis showed a significant increase in leukocytosis with bandemia and additional toxic changes (table 2). Additionally, poikilocytosis secondary to chronic hepatopathy (codocytes, acanthocytes, and eccentrocytes) was evident. Upon admission to hospitalization, abdominal ultrasound confirmed hepatomegaly and adrenomegaly, along with renal structural abnormalities. Furthermore, intraluminal anechoic content was detected in the uterus, suggestive of pyometra, mucometra, or hematometra (figure 1). These findings in the uterus were not identified in the ultrasound reported in the anamnesis conducted eight weeks earlier, after four weeks of worsening systemic signs of disease and with a history of scanty mucoid vulvar discharge.

In the hospitalization treatment plan, intravenous furosemide at 2 mg/kg every

8 hours and oxygen therapy at an approximate FiO2 of 28% were added based on the differential diagnosis of pulmonary edema associated with left heart failure. Additionally, subcutaneous enrofloxacin at 5 mg/kg every 24 hours and intravenous ampicillin-sulbactam at 20 mg/kg every 8 hours were initiated due to the presence of an infectious origin inflammatory leukogram (neutrophilia with a left shift regenerative) with a probable focus in the uterus. Because of cardiovascular instability that contraindicated surgical intervention at that time, subcutaneous aglepristone at 10 mg/kg was also added to the therapy. The analgesic plan was initiated with dipyron at 25 mg/kg every 8 hours and tramadol at 3 mg/kg every 8 hours, in conjunction with supportive nursing care.

In the clinical progression within the 48 hours following hospitalization, the patient appeared slightly lethargic with polyphagia, polydipsia, polyuria, abdominal distension, temperature ranging from 37.1-38.7 °C, respiratory rate between 44 and 52 rpm, heart rate between 96 and 116 bpm, systolic blood pressure between

FIGURE 1. Bilateral adrenomegaly present in a 12-year-old Chihuahua with hyperadrenocorticism, pyometra, and endocardiosis. The caudal pole of the right adrenal gland measured 1.25 cm and the left adrenal gland measured 1.1 cm.



Source: own elaboration.

106-141 mmHg, well-hydrated, with an APPLE-fast score of 15 (Hayes *et al.* 2010) and a qSOFA score of 1 (Donati *et al.* 2022). Furthermore, the blood count at 48 hours after the start of antibiotic therapy revealed a progression of the systemic inflammatory curve with no favorable response. Therefore, after achieving cardiovascular clinical stabilization following therapy with furosemide and pimobendan, it was decided to perform an ovariohysterectomy. In accordance with the recommendations for prudent and rational use of antimicrobials (Weese *et al.* 2015), de-escalation was performed by discontinuing enrofloxacin and ampicillin-sulbactam from the therapy. It was then considered to add cefovecin (8 mg/kg, subcutaneous, single dose) to the therapy, which covered the potential spectrum of bacteria epidemiologically more involved in the development of pyometra, namely *Escherichia coli* and *Staphylococcus* spp. (Hagman, 2022). At that time, N-acetylcysteine and Ursodeoxycholic acid were also added to the therapeutic plan. All drugs administered were provided at doses adjusted for hepatic metabolism and renal excretion.

The anesthetic procedure was performed with acepromazine and fentanyl in the premedication, and 1% Propofol for induction. Maintenance was carried out with 1.5% isoflurane and a continuous infusion of fentanyl. Anesthesia depth was monitored using conventional multi-parameter monitor. No complications associated with anesthesia or surgical technique were encountered during the procedure. Surgical findings confirmed the presence of pyometra with a moderate amount of accumulation in the uterine horns and body. The approximate surgical time was 30 minutes.

In the clinical progression following the surgical removal of the pyometra, the mood remained mildly to moderately depressed, with hyporexia, polydipsia, polyuria, and abdominal distension/pain. The temperature ranged between 37.1-38.7 °C, respiratory rate between 44 and 52 rpm, heart rate between 142 and 181 bpm, and systolic blood pressure between 100-113 mmHg. The patient remained well-hydrated, with an APPLE-fast score of 26 and met the criteria for SIRS3 (Donati *et al.* 2022). However, the white blood cell count continued to show a progressive uncontrolled systemic inflammation curve (table 2). Therefore, it was decided to perform urine and blood cultures, in addition to initiating intravenous therapy with gentamicin at 6 mg/kg every 24 hours for 3 days, taking precautions to classify the patient as at risk of AKI II/V (Ross 2011). Additionally, with the patient clinically well-hydrated, renal perfusion was planned with fluid therapy according to the protocols described for renal failure (Langston 2008) before gentamicin infusion, and diuresis and hydration parameters were carefully monitored. At 72 hours, no microbial growth was detected in the blood culture; however, EHEC was isolated from the urine culture. The multidrug resistance profile is shown in table 3.

Following treatment with gentamicin, the patient showed significant clinical improvement, appearing alert, more interactive, and displaying a return to playfulness. However, polydipsia, polyuria, polyphagia, abdominal distension, and dermatological findings persisted. Physiological parameters remained within acceptable ranges, with a temperature ranging between 37.4-37.8 °C, respiratory rate between 23 and 28 rpm, heart rate between 110 and 131 bpm, and

TABLE 3. Multidrug resistance profile of EHEC isolated from urine culture taken 48 hours after surgical correction of pyometra in a canine with hyperadrenocorticism

Sensitive	Intermediate	Resistant
Ciprofloxacin	Neomycin	Ampicilin
Streptomycin	Erythromycin	Amoxicillin-clavulanic acid
Gentamicin		Sulfamethoxazole/trimethoprim
		Novobiocin
		Cefoxitin

Source: own elaboration.

systolic blood pressure between 125 and 146 mmHg. The patient remained well-hydrated, with an APPLE-fast score of 19. Therefore, it was decided to discharge the patient with clinical monitoring of temperature and physiological parameters at home.

Two and seven days after hospital discharge, the patient continued to show favorable clinical progress, and the hemogram suggested progressive control of systemic inflammation, along with inactive sediment and the disappearance of asymptomatic bacteriuria in the urine analysis (table 2). At that point, oral trilostane therapy was initiated at a dose of 1 mg/kg every 12 hours. Four weeks into the follow-up, during a clinical check-up, the owner reported a reduction in polydipsia-polyuria and persistent panting. Additionally, there was increased activity, and a moderate improvement in polyphagia control, despite the expected persistence of dermatological findings and pendulous abdomen.

DISCUSSION

In this canine patient, its profile, clinical presentation, as well as the paraclinical and ultrasound findings together were consistent

with the suspicion of hyperadrenocorticism, apparently of pituitary origin. Given that the specificity of low-dose dexamethasone suppression is low (44-73%) (Lathan 2023), and even more so when a disease with persistent inflammatory focus is present, it was not considered as the ideal test for the confirmatory diagnosis of hyperadrenocorticism in this patient. On the other hand, ACTH stimulation has lower chances of false positives and is less influenced by environmental stress or non-adrenal disease (Bennaim *et al.* 2019b), despite having lower sensitivity (60%-80%) (Lathan 2023). Furthermore, although progestogens can suppress the hypothalamic-pituitary-adrenal axis (Behrend *et al.* 2013; Bennaim *et al.* 2019b), for this patient, the cortisol range following ACTH stimulation was considered confirmatory for hyperadrenocorticism given the congruent clinical scenario (Bennaim *et al.* 2019b). The urine cortisol-to-creatinine ratio was not considered diagnostic for the condition, due to its low specificity (20%-25%) and high likelihood of false positives while a non-adrenal disease is ongoing (Lathan 2023).

The classic signs of pyometra include lethargy/depression (63%-100%),

polydipsia-polyuria (73%-89%), depression, anorexia (42%-87%), vomiting (13%-38%), abdominal distension/pain (5%-80%), dehydration (15%-94%), fever (32%-50%), and signs of Systemic Inflammatory Response Syndrome (SIRS) (57%-61%) in a female in estrus. The presence of vulvar discharge may or may not be present (57%-88%) depending on whether the cervix allows drainage (Hagman 2022). Due to the similarity of some of these signs with hyperadrenocorticism (HAC) and the anti-inflammatory and immunosuppressive effects of cortisol (Bennaim *et al.* 2019a), which could have masked symptoms such as anorexia, depression/lethargy, and fever, it appears likely that the coexistence of HAC may have influenced the clarity of the diagnosis of this condition, which only became evident after twelve weeks of intermittent vulvar discharge. However, it is interesting that the manifestation of sepsis signs from the uterine pyogenic focus did not occur at that point, and the survival of the animal without treatment did not deteriorate during that period.

Aglepristone is a competitive antagonist of progesterone receptors indicated for the medical treatment of pyometra when surgical intervention is not the first viable option. Different protocols, either alone or in combination with cloprostenol and oxytocin, have been described for open pyometra without signs of SIRS, with a relative success rate (46%-100%) and moderate recurrence (12%-48%) (Gogny & Fiéni 2016; Hagman 2022). Given the initial cardiovascular condition with which this patient presented, aglepristone was considered as the initial treatment; however, due to clinical deterioration and the clear onset of signs of sepsis (with an

increased APPLE-fast score of 26), surgical intervention became necessary.

The occurrence of *E. coli* with ESBL as a common pathogen in the urine of canines is well-documented (Dierikx *et al.* 2012). Given the multidrug resistance profile of the *E. coli* isolate in the urine of this patient, it is feasible that the presence of ESBL contributed to the therapeutic failure of the combination of enrofloxacin and ampicillin/sulbactam initiated as soon as sepsis was identified. In line with this, the lack of clinical and paraclinical response to the addition of ceftiofur (despite being a third generation extended-spectrum cephalosporin with activity against *E. coli*) may also indicate the presence of this mechanism of multidrug resistance due to prior exposure of the enteric microbiota to third generation cephalosporins or enrofloxacin, which is a recognized potential mechanism for inducing ESBL (Weese *et al.* 2015; Weese *et al.* 2019). Additionally, since even in human medicine, the de-escalation strategy has not been associated with a negative clinical impact, this strategy was applied to mitigate the potential further induction of multidrug resistance in other enterobacteria (Weese *et al.* 2015).

The clinical manifestation of signs of pulmonary edema, along with the therapeutic response to furosemide, suggests the presence of secondary left-sided heart failure due to endocardiosis. However, the clinical and echocardiographic evaluations of the animal were not entirely consistent with the progression to stage C heart failure (Keene *et al.* 2019), and the resolution of adventitious sounds after furosemide does not necessarily correspond to a diagnosis of cardiogenic pulmonary edema. Additionally, the occurrence of syncope could not be associated with a clear cause, and no

abnormalities in cardiac rhythm conduction were detected. However, syncope episodes could be related to the development of reentry arrhythmias in patients with pyometra-associated sepsis, considering that it is common (79.4%) and can be explained by myocardial injury, electrolyte disturbances, or underlying endotoxemia (Pugliese *et al.* 2020).

The leukogram indicating uncontrolled systemic inflammation along with hyperlactatemia exceeding 10 mmol/l are negative prognostic markers for the outcome of dogs with pyometra (Donati *et al.* 2022; Hagman 2022). However, the use of quantitative scoring systems that assess the risk of fatality and the severity of the disease in a hospitalized animal allows for a more accurate prognosis by objectively correlating multiple parameters, which is better than assessing them individually (Donati *et al.* 2022; Hayes *et al.* 2010). For instance, the APPLE-fast score has been validated in dogs as an index that categorizes the severity of disease in hospitalized dogs, aiming to provide a prognosis and protocol-based critical care therapeutic intervention (Hayes *et al.* 2010). Additionally, a qSOFA score >2 implies a 6.5 times higher odds ratio for the risk of death in dogs with pyometra (Donati *et al.* 2022).

In line with the aforementioned information, despite the leukogram and hyperlactatemia in the described patient, the medical outcome was favorable following the administration of gentamicin and control of the septic focus. Consistently, the presentation of a qSOFA score <2 was associated with a lower risk of fatality. The qSOFA score in dogs with pyometra has been proposed as a tool to stratify the risk of mortality and prolonged hospital

stays (Donati *et al.* 2022). In this report, this marker was consistent with a qSOFA score of 1 during the hospital stay, despite the complication of sepsis due to bacteremia with *E. coli*. Additionally, this is consistent with the assignment of a low to intermediate APPLE-fast score (19 to 26), which was associated with a positive prognosis, given the sensitivity of 67.1% and specificity of 85.3% of the scale in predicting the risk of death when a score of 25/50 is exceeded (Hayes *et al.* 2010).

Finally, the management of hyperadrenocorticism in this patient involved dose adjustment of trilostane based on pre-trilostane and three-hour post-trilostane cortisol levels (Cook & Bond 2010; MacFarlane *et al.* 2016), parameters of quality of life (Schofield *et al.* 2019), as well as addressing dyslipidemia, proteinuria, hypertension, and hepatopathy as therapeutic targets that affect life expectancy.

CONCLUSION

This report documents the presentation of pyometra in a female dog with a previous history of hyperadrenocorticism and endocardiosis. Although the clinical course of pyometra spanned 12 weeks, the expression of pyometra-associated sepsis occurred after this period and persisted even after the surgical removal of the pyogenic focus. This may be associated with the persistence of EHEC, apparently producing ESBL in the urine of the dog, without being associated with signs of bacterial cystitis. It is hypothesized that the underlying diagnosis of hyperadrenocorticism could have mitigated or delayed the expression of classical clinical signs of pyometra and urinary infection, which later represented a septic focus for the animal.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

ETHICAL APPROVAL STATEMENT

The publication of this case report did not require the approval of an ethics committee, the tutor of the patient consented to the scientific disclosure of the case report.

ARTIFICIAL INTELLIGENCE STATEMENT

It is declared that artificial intelligence technologies were not used in the construction of this case report.

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