CASE REPORT

Occurrence of Severe Haematometra with CEH-Pyometra, Endometrial Polyps and Cystic Ovarian Disease in a Dog

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Haematometra (collection of blood contents in the uterus) or metrorrhagia (uterine bleeding) is an uncommon life threatening emergency clinical condition affecting dogs (Troxel *et al*., 2002). There are various etiologies documented for haematometra in dogs which are postpartum subinvolution of placental sites (Dickie and Arbeiter, 1993), anticoagulant rodenticide (warfarin) toxicity (Padgett *et al*., 1998), coagulation deficiency, uterine trauma, neoplasia, placental necrosis, idiopathic prepubertal metrorrhagia, uterine serosal inclusion cysts and postpartum endometritis (Feldman and Nelson, 1996). In haematometra, physical examination findings and clinical signs are inconclusive, but the dog can suffer from anemia with frank vulvar hemorrhage of an open-cervix type.

Canine pyometra is a disease of the uterus in intact, sexually mature female dogs usually diagnosed from 4 weeks to 4 months post-estrus. Cystic endometrial hyperplasia is usually associated with pyometra in dogs but can also cause haematometra (Troxtel *et al*., 2002). Endometrial cysts usually arise from the glandular epithelium of canine uterus and hyperplastic endometrium frequently become inflamed and infected leading to pyometra which is a life threatening disease (Schlafer and Gillford, 2008). Ultrasonographic examination could be useful and reliable tool for diagnosis of cystic endometrial hyperplasia (CEH) where a fluid filled organ with variable wall thickness and proliferative changes could be visualized (Bigliardi *et al*., 2004). CEH often predisposes the dog to pyometra due to over growth of normal vaginal flora (*E. coli*, *Staphylococci*, *Streptococci* and *Pseudomonas aeruginosa*) that enters the uterus at distress phase (Arora *et al*., 200l).

Endometrial polyps (EPs) are solitary, proliferating masses that originate from the endometrium as broad based sessile masses or pedunculated polyps with stalks with unknown specific etiology (Gumber *et al*., 2010) due to stimulation of cystic endometrial glands (Schlafer and Gillford, 2008). Usually small endometrial polyps are observed in dogs and mostly associated with senility. CEH-pyometra could also be a reason for the formation of endometrial polyps in dogs. Polycystic ovarian syndrome/disease (PCOS) accounts for more than 80% ovarian pathologies in canine (Dow, 1960) out of which luteal cysts are most common (Maya-Pulgarian *et al*., 2017; Knauf *et al*., 2018). During diestrus phase PCOS is commonly associated with CEH-pyometra. Presence of steroid producing cystic structures in the ovaries of dog predisposes them to uterine pathologies where CEH is most common one (Maya-Pulgarian *et al*., 2017). The present clinical report highlights the presence of severe haematometra in a 2 year old American Pit Bull Terrier female dog associated with CEH-pyometra, endometrial polyps as well as luteal cystic ovarian disease.

Case History and Observations

A 2 year old intact female American Pit Bull Terrier dog was presented at university teaching veterinary clinical complex (TVCC) of Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana (India) with history of mating 56 days back with signs of nesting behavior, milk let down in nipples, swollen vulvar lips and frank sanguineous vaginal discharge since last 2 days. On general physical examination, the dog was quiet, alert, responsive, and approximately 5% to 7% dehydrated, temperature 101^{o}F, normal body condition score and pale mucous membrane. The dog was afebrile, had a normal heart rate, and respiration rate with all lung fields normal on auscultation. The dog exhibited mild discomfort on abdominal palpation, but no other palpable abnormalities were detected. Profuse hemorrhagic discharge was noted from the vulva, and the dog occasionally passed long, thread-like blood clots through the vulva. Digital vaginal examination revealed no other abnormalities. Signs

of nesting behavior and milk let down revealed it might be pregnancy/nervous lactation but frank vaginal bleeding was also present. Complete blood count (CBC) and serum biochemistry parameters recorded are presented in Table 1.

Vaginal cytology examination stained with Leishman's stain revealed presence of red blood cells (RBCs), parabasal cells, small and large intermediate cells with neutrophils indicative of diestrus stage with hemorrhage and inflammation. Vaginal endoscopy revealed no gross anatomical abnormality or injury in the genital tract. X-ray/radiological examination done to rule out pregnancy was inconclusive while, abdominal Ultrasonography (USG) depicted distended uterine loops with presence of some echogenic contents (suspected blood clots).

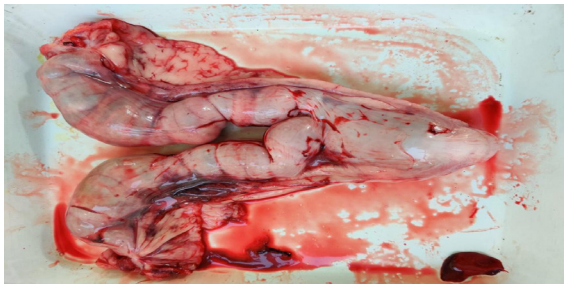
Table 1: Complete blood count and serum biochemical parameters of the dog before surgery

Parameter	Value	Reference range (Dabhi *et al.*, 2009)
Haemoglobin (g/dL)	9.0	12-18
Total Erythrocyte count ($\times10^6$/µL)	3.10	5.5-8.5
Packed Cell Volume (%)	30.6	37-55
Platelets count ($\times10^3$/µL)	286	200-500
Total Leucocyte count (/µL)	24500	6000-17000
Neutrophils (%)	88	60-77
Lymphocytes (%)	06	12-30
Eosinophils (%)	04	3-10
Monocytes (%)	02	2-10
Basophils (%)	0	0-1
ALT/SGPT (U/L)	13	8.2-57
AST/SGOT (U/L)	24	8.9-49
ALKP/ALP (U/L)	207	10.6-101
Creatinine (mg/dL)	0.4	0.3-1.6
BUN (mg/dL)	40	8.8-26
Blood glucose (mg/dL)	94	62-108

ALT, Alanine aminotransferase; SGPT, Serum glutamic-pyruvic transaminase; AST, Aspartate aminotransferase; SGOT, serum glutamic-oxaloacetic transaminase; ALKP/ALP, Alkaline phosphatase; BUN, Blood urea nitrogen

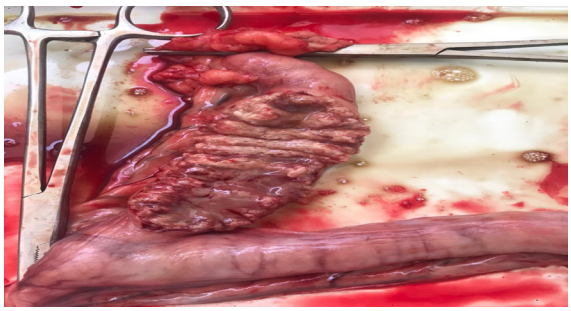
Emergency exploratory laparotomy was decided to be of choice for final diagnosis and treatment of the animal. After surgery the exteriorized hyperemic uterus (Fig. 1A) was incised and it revealed presence of around 350-400 mL of fresh and clotted blood (Fig. 1B). The gross examination of the uterus depicted presence of pus as well as cystic thickened corrugated endometrial wall (Fig. 1C).

A few small pieces of uterine and ovarian tissue from affected sites were immediately collected in 10% formalin for fixation. This was done to ensure optimal routine histopathological analysis. The fixed tissues were processed through ascending grades of alcohol followed by xylene and paraffin embedding as per the standard operating protocol. Tissue sections were obtained at 3-4 µm thickness and Hematoxylin and Eosin staining was performed. The stained slides were mounted with cover slip using DPX mountant and examined under bright field microscope for histopathological interpretations.



(1A)

(1B)



(1C)

Fig. 1: (**A**) Exteriorized hyperemic uterus. (**B**) Presence of around 350-400 mL of fresh and clotted blood in the exteriorized incised uterus. (**C**) Presence of pus as well as cystic thickened corrugated endometrial wall of uterus.

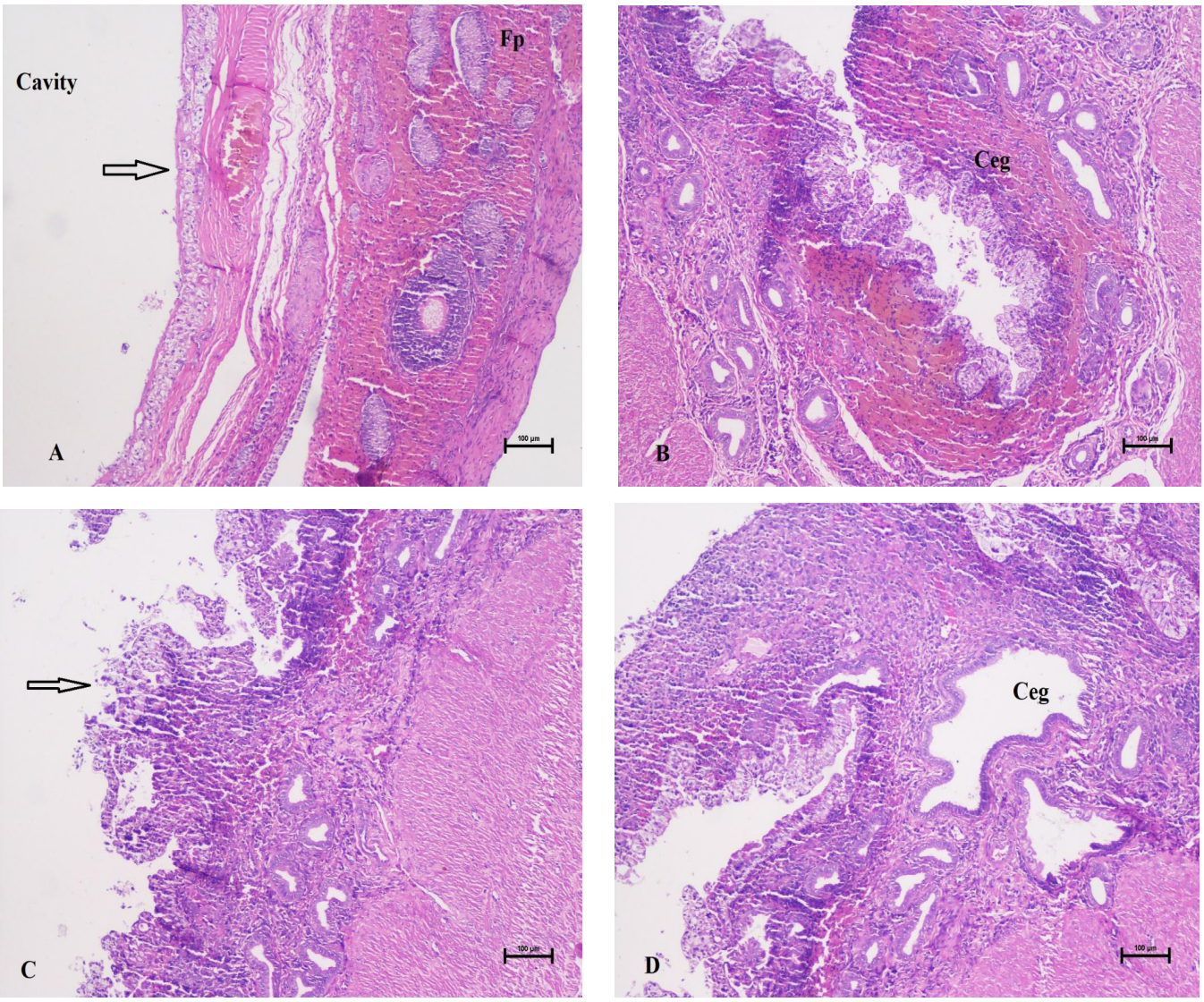
Treatment and Discussion

Before the surgery, the animal was administered with systemic antimicrobial (Ceftriaxone @ 10 mg/kg b.wt.), anti-inflammatory drug (Meloxicam @ 0.3 mg/kg b.wt.), antacid (Ranitidine @ 0.5 mg/kg b.wt.), haemostat (Adenochrome monosemicarbazone @ 2 mg) and fluid therapy consisting of Ringer's lactate and normal saline. The midline exploratory laparotomy was performed under general anesthesia and uterus was exteriorized. It revealed enlarged hyperemic uterine body and horns, hence ovariohysterectomy was performed in a routine manner. The animal was recovered from the anesthesia and was prescribed post-surgery medications as systemic antimicrobial, anti-inflammatory drug, antacid, hematinics, liver tonics and fluid therapy for 5 days. Antiseptic dressing of the wound was advised with

povidone iodine ointment. The animal recovered well and the skin sutures were removed 14 days post-surgery.

On histopathology, the ovarian tissue revealed abnormally enlarged classical lutein cysts compressing the available stroma with thick connective tissues with embedded atrophied follicles (Fig. 2A). Extravasations of blood vessels were prominent owing to compression, thus accounted for large accumulation of RBCs within stroma and also resulted in massive congestion of intact blood vessels. The cysts were lined typically with thin layer of fibrin from the inner surface over the granulosa cells, while at an outer surface, an inconspicuous thin layer of theca cells surrounding the moderately thick fibrous layer over the cyst was observed. The cyst had spherical central cavity with no content in it. The uterine tissue exhibited massive areas of mucosal haemorrhages with loss of mucosal lining along with cystic endometrial glands at several to many places (Fig. 2B). At some places, thinning of endometrium due to sloughing off of necrotic mucosal surface tissues along with exposed subepithelial tissues was evident (Fig. 2C). Apart from 'glandular crowding' across the reduced endometrial surfaces (Fig. 2D) some highly dilated endometrial glands also possessed large accumulation of blood mixed purulent exudates (Fig. 2E). A generalized thickening of myometrium due to downstream expansion of inflammatory edema and cellular infiltration was noticed.

Evidence of multiple giant adenomyomatous endometrial polyps was an interesting finding that was characterized by scanty to profuse secretory contents and attenuated endometrial surface from 3 sides bordering with smooth muscle fibres (Fig. 2F). Additionally such endometrial polyps possessed highly irregular papillary epithelial projections within its central cavity that has contributed towards formation of sero-mucous exudates (Fig. 2G). Intriguingly, few small sized adenomyomatous polyps were also observed that had interspersed with smooth muscle fibres. Areas of profuse haemorhages both at endometrial region as well as



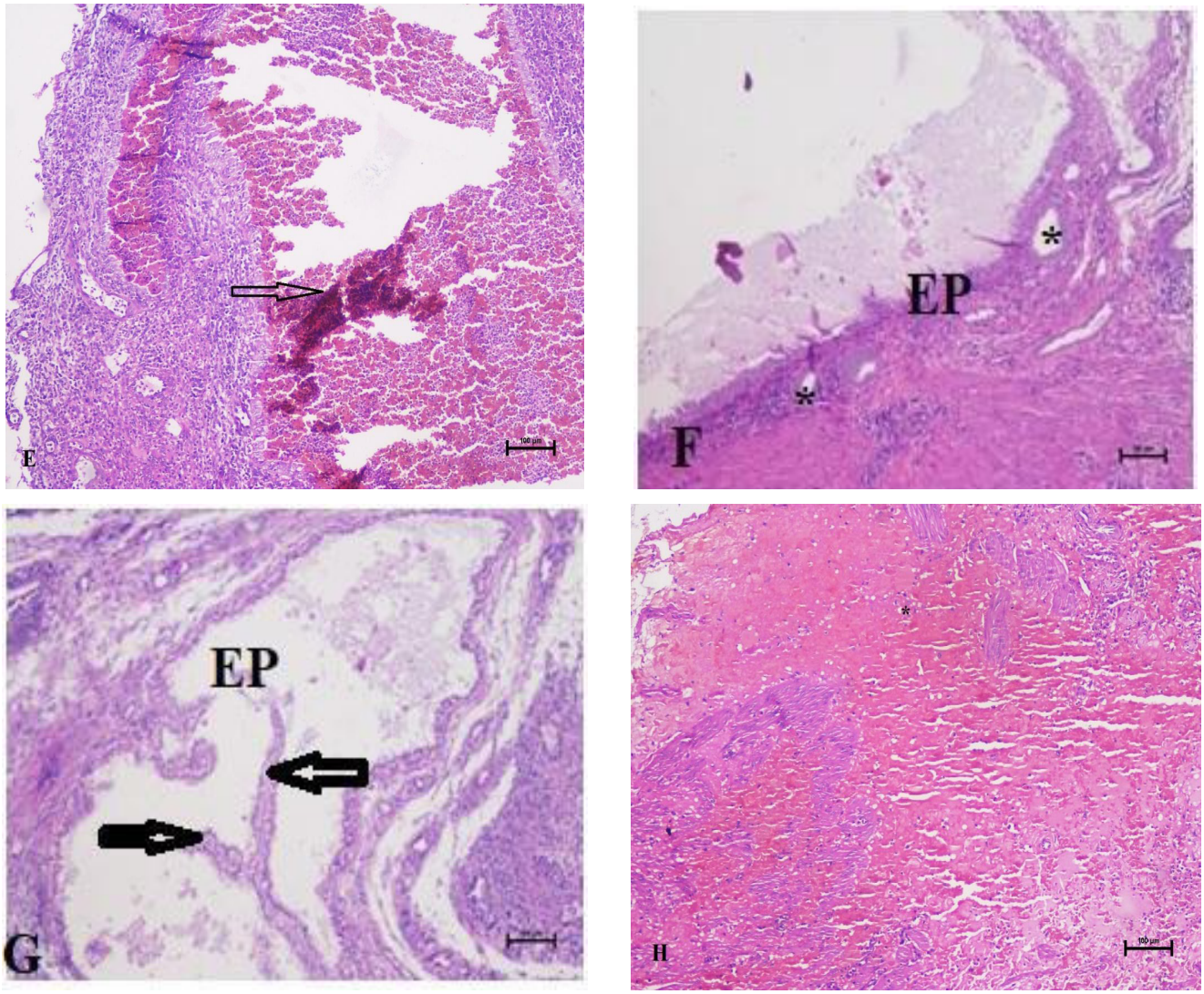


Fig. 2: Microscopic changes in ovarian and uterine tissues. **A**. Luteal cyst lined with few layers of granulosa cells over laid with extremely thin, fragile fibrous layer (arrows) at an innermost surface of central cavity (C). Note the beleaguered atrophied follicle (*fp*) with widespread areas of vascular congestion and haemorhages. **B**. Uterine mucosa with massive sub-epithelial haemorhages and many cystic endometrial glands (*Ceg*). **C**. Endometrial surface with necrotic musocal epithelium (arrow) and prominent 'glandular crowding'. **D**. Endometrium with some prominent cystic endometrial glands (*Ceg*). ***E***. (same magnification): Highly dilated endometrial glands with profuse presence of blood mixed purulent exudates (arrows). **F.** Endometrial polyps with central cavity containing scanty mucous contents (arrow)*. Note the endometrial glands (*asterisks*) peripheral to polyps embedded within muscular stroma (*adenomyomatous polyps*). **G**. Endometrial polyps (*Ep*) with papillary projected epithelial lining with moderate presence of mucous secretions. **H**. Myometrium revealing large areas of blood filled spaces resembling to peliosis (*asterisk*).

in myometrium (unnatural blood filled cavity-*peliosis*) had ensured profuse bleeding in the given case (Fig. 2H).

Cystic endometrial hyperplasia is a progressive pathological disorder of canine reproductive tract caused by thickening of the endometrium due to hyperplasia as well as hypertrophy of the endometrial glands (Dow, 1960), which was also consistent in the present case. Diagnosis of pyometra can be done by routine physical examination, CBC, biochemical profile and USG of the dog (Rautela and Katiyar, 2019) but in the present case no clinical symptoms were seen and exploratory laparotomy was only treatment of choice. Cystic uterine changes observed after OHE were later confirmed by histopathology to be a severe case of CEH/pyometra complex along with endometrial polyps and luteal cysts. Many of the common clinical findings associated with pyometra were not present in this case. Physical examination findings were also inconclusive, as the dog was afebrile; quiet, but not lethargic or depressed; had frank hemorrhagic vaginal discharge, rather than serosanguineous or mucopurulent discharge; and was not polyuric or polydipsic. Abdominal radiographs failed to demonstrate a fluid-filled uterus in the caudal abdomen.

Vaginal cytology and vaginal endoscopy were also non-conclusive in the present case. Ultrasonography finally aided in identifying intraluminal uterine fluid (echogenic contents suspected blood clots) but cystic changes in the

uterine wall were not diagnosed properly which might be due to completely blood filled uterus. Finally, the decision to perform an exploratory laparotomy was taken and after exteriorization histopathology revealed CEH/ pyometra and ruled out other causes of haematometra. When haematometra is suspected, ovariohysterectomy (OHE) should be performed as soon as possible due to life threatening complications associated with bacteremia and endotoxemia (Troxtel *et al*., 2002).

Haematometra or metrorrhagia is an uncommon clinical presentation and many reported etiologies could be reason. The histological findings of cystic endometrial hyperplasia, endometrial polyps as well as luteal cysts on either of ovaries could be documented as one of the reasons for severe haematometra. Routine blood work aids in the diagnosis, but abnormalities are not definitive for pyometra or are nonspecific. Complete blood count results can vary, often showing an absolute neutrophillia with variable degrees of left shift. Presence of an absolute leukocytosis is also variable. A mild normocytic, normochromic, non-regenerative anemia often develops secondary to chronic disease and generally resolves following treatment (Gumber *et al*., 2010). Hyperproteinemia and hyperglobulinemia are possible secondary to dehydration or antigenic stimulation. Pre-renal azotemia is likely if dehydration is present. Mild to moderately elevated liver enzymes (*i.e.,* alanine transferase and alkaline phosphatase) are possible due to hepatocellular damage secondary to bacteremia/ endotoxemia, hepatocellular hypoxia secondary to decreased hepatic circulation with dehydration, or both. Low haemoglobin along with low PCV and TEC value was indicative of normocytic normochromic anaemia in the pyometra affected bitches (Dabhi *et al*., 2009).

Functional ovarian cysts could be found as single or multiple cystic structures of variable sizes on either of the ovary (Jisna *et al*., 2021). The presence of these functionally active steroid hormones secreting structures on the ovaries could be a cause for establishment of CEH-pyometra in dogs. The luteal cysts have been found to be of largest occurrence (23.8%) among all cystic conditions in dogs (Maya-Pulgarian *et al*., 2017; Knauf *et al*., 2018) and these cysts are responsible for contionuos production of progesterone and could be reason for hyperplastic as well as hypertrophic changes in the endometrium as reported in the present case. No single report could be isolated from the available literature with concurrent occurrence of PCOS and haematometra. The previous reports have documented smooth ovaries in case of haematometra (Troxtel *et al*., 2002; Gumber *et al*., 2010).

Endometrial polyps (EPs) have also been documented in previous reports along with sanguineous vaginal discharge (Gumber *et al*., 2010; Marino *et al*., 2013) but severe haematometra has never been reported in dogs with EPs. These EPs have been found to be associated with senility but presence of multiple EPs in a 2 year old dog is an unusual finding in the present report. Presence of EPs in the cases of CEH has been reported earlier but presence of luteal cyst in either of ovary in the current case is a novel finding. Kennedy *et al*. (1998) reported that these EPs are consisting of endometrial glands as well as the stromal connective tissue which is also consistent with the present finding.

The present case describes the concurrent occurrence of CEH-pyometra, endometrial polyps with hypertrophy of the endometrium, polycystic ovarian syndrome with multiple luteal cysts on either of the ovary along with severe haematometra. Solitary reports of these findings have been found in the available literature but the novelty of the case is about regressive diagnosis of multiple disorders and their common pathology.

In general, CEH-pyometra is a common disorder of diestrus phase of canines but haematometra is a very rare clinical emergency, which could not be diagnosed until the exploratory laparotomy is made. Multiple reasons could be involved in the occurrence of life threatening haematometra. The occurrence of multiple endometrial polyps along with PCOS is also a rare finding and could be found associated with CEH-pyometra and haematometra. Emergency elective ovariohysterectomy is treatment of choice for such critical cases.

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