

HYPERESTROGENISM AND NONRESPONSIVE CEH-PYOMETRA COMPLEX IN A GERMAN SHEPHERD DOG WITH BILATERAL OVARIAN FOLLICULAR CYSTS

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SUMMARY

An eleven-year-old nulliparous German Shepherd Dog (GSD) was presented with a complaint of purulent vaginal discharge. Haematological analysis revealed leucocytosis, anaemia and thrombocytopenia. Sonographic examination unveiled cystic endometrial hyperplasia and ovarian cyst. The flank region exhibited bilateral nonpruritic alopecia. The serum progesterone and estradiol concentrations were 22.97 ng/mL and 134.96 pg/mL respectively. Medical management started with mifepristone and cabergoline along with systemic antibiotic and supportive therapy. Even though improvement was observed during the first week, the condition worsened during the next week and an emergency ovariohysterectomy was performed. During ovariohysterectomy, multiple follicular cysts and ulcerated, corrugated and haemorrhagic endometrium was noticed. Following the surgery, the animal received antibiotic treatment and experienced a smooth and uncomplicated recovery.

Keywords: Canine, Cystic endometrial hyperplasia-pyometra complex, Follicular cysts, Hyperestrogenism

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Cystic endometrial hyperplasia (CEH)-pyometra complex is an acute or chronic, polysystemic, dioestral disorder of intact dog, characterised by hyperplasia of the endometrium, gradual development of CEH, infiltration of inflammatory cells, accumulation of pus in the uterus and finally bring about CEH-pyometra complex (Jitpean *et al.*, 2017). The most common infecting agent is *Escherichia coli*. The disease is associated with endotoxemia, systemic inflammatory response syndrome and further progress to disseminated intravascular coagulation, multi-organ failure, shock and death with a mortality rate of 3-4 per cent in dogs (Hagman *et al.*, 2006).

Concurrent diseases reported in dogs affected with cystic endometrial hyperplasia (CEH)-pyometra complex is ovarian cysts (Johnston *et al.*, 2001). Estrogen will increase the sensitivity of endometrium towards progesterone (Chen *et al.*, 2001) and progesterone will potentiate the hyperplastic effects on endometrium which leads to endometrial proliferation and pyometra (Shukla, 2012). Estrogen from the follicular cyst will cause an estrogen-induced myelotoxic effect on the hematopoietic system which can lead to anaemia and loss of condition (Suttorp *et al.*, 2002).

Pyometra can be managed by medical treatment, but always there is a risk of recurrence (Verstegen *et al.*, 2008). The presence of ovarian cysts and CEH can aggravate the disease and may cause recurrence or non-responsiveness to treatment (Trasch *et al.*, 2003). The treatment of choice for a dog with degenerative cystic uterine diseases or

pyometra which is not intended for breeding in future or the animal not responding to medical therapy is ovariohysterectomy (Kumar *et al.*, 2019). The present case was dealing with management of CEH-pyometra complex in a German Shepherd dog with bilateral ovarian follicular cysts.

An eleven-year-old nulliparous German Shepherd dog was presented to Teaching Veterinary Clinical Complex, College of Veterinary and Animal Sciences, Mannuthy, Kerala. The dog was presented with a complaint of purulent vaginal discharge persisting for three days. The animal had a history of oestrous signs four weeks back, reduced food intake and hyperthermia (103° F) was noticed in the last three days. Haematological analysis revealed leucocytosis, anaemia and thrombocytopenia (Table 1). Serum creatinine and BUN values were within the normal physiological range (0.81 and 13.07 mg/dl, respectively). The Sonographic examination divulged the presence of hypoechoic uterine sacculations and cystic endometrial hyperplasia, with an average wall thickness measuring 10.3 mm and a lumen diameter of 16.25 mm. The serum progesterone concentration was observed as 22.97 ng/mL and Gram-positive cocci were isolated from the vaginal discharge. Based on the clinico-gynaecological examination, the case was diagnosed as CEH-pyometra complex. Since the animal was aged with deteriorating blood value, medical management was initiated with mifepristone @ 2.5 mg/kg body weight BID for 5 days PO and cabergoline @ 5 µg/kg body weight OD for 7 days per orally along with systemic antibiotic and supportive

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Table1. Haematological analysis of a German Shepherd Dog affected with Follicular cyst complicated CEH-pyometra complex before and after surgery.

Day of sample collection	Haematological values			
	Leucocyte count (10 ³ /μL)	Erythrocyte count (10 ⁶ /μL)	Haemoglobin (g/dL)	Thrombocyte (10 ³ /μL)
On the day of admission	25.8	4.02	8.6	99
Before surgery	25.6	3.06	7.7	51
Two weeks after surgery	17.1	4.08	9.8	146

therapy.

During the first-week animal was responded to treatment with increased food intake and reduced vaginal discharge. However, the condition was worsened on next week, the animal became inactive, food intake was reduced and vaginal discharge noticed. Bilateral alopecia was noticed on the flank region (Fig. 1). Skin scraping examination was negative for dermatophytes, parasites and yeasts. Haematological analysis revealed leucocytosis, severe anaemia and thrombocytopenia (Table). Detailed ultrasound examination revealed the presence of multiple cystic follicles within the ovaries caudal to kidney with an average diameter of 15.12 mm (Fig. 2). Hypoechoic uterine content with endometrial hyperplasia was also noticed (Fig. 3). The serum estradiol concentration was observed as 134.96 pg/mL which was higher than the normal range 60-70 pg/ml (Hill, 1998). The cause of nonresponsive CEH-pyometra complex was tentatively diagnosed as multiple follicular cysts. Since the animal was not responded to medical management, emergency ovariohysterectomy was performed to save the animal.

An exploratory laparotomy was performed under general anesthesia with ketamine (5 mg/kg body weight, IM) following preanaesthetic medication with atropine sulphate (0.045 mg/kg body weight, SC), xylazine HCl (1mg/kg body weight, IM) and diazepam (0.5 mg/kg body weight, IV). Anaesthesia was maintained with two per cent isoflurane. Following ovariohystorectomy, tissue samples of uterus and ovaries were collected for gross and histopathological examination. The selected specimens were fixed in ten per cent buffered formalin (pH = 7.2) and then sectioned at 5 μm and stained with hematoxylin and eosin. Grossly, the endometrium was thickened, haemorrhagic, corrugated and ulcerated (Fig. 4). Both the ovaries contained large multiple follicles more than 15 follicles were observed in each ovary, few corpus luteum and a parovarian cyst (Fig. 5) was present in right ovary. Fluid inside the cyst was straw coloured indicative of follicular cyst. Histopathological studies of the ovary revealed multiple, large-sized follicles with sclerosed wall and pyknotic changes in the oocyte and cumulus cells (Fig. 6). The follicular cysts were lined with a single layer of

cuboidal to columnar cells with a residue of the oocyte (Fig. 7). Histopathological study of the uterus showed moderate congestion, area of haemorrhage, enlarged cystic endometrial glands and mononuclear cell infiltration involving the endometrial stroma and thrombosis of blood vessels (Fig. 8). Post-operative medical management was given for two weeks. The serum estradiol and progesterone values came to basal level on 14th day. Furthermore, complete blood cell count indicated positive response to treatment (Table 1).

The cystic endometrial hyperplasia-pyometra complex is a purulent inflammatory and hyperplastic condition of the uterus affecting intact, sexually mature middle-aged dogs (Hagman *et al.*, 2006). The endometrial epithelium showed hyperplastic proliferation and endometrial glands showed cystic dilatation and hyperplasia along with neutrophils in its lumen (Younis *et al.*, 2014). Ultrasonographic examination in the present study revealed fluid-filled uterus with variable wall thickness and proliferative changes.

Pyometra is the most common disease diagnosed in dogs with ovarian cyst; it may be due to prolonged exposure of the endometrium to elevated serum estrogen concentrations which in turn induce cystic endometrial hyperplasia (Knauf *et al.*, 2018). The present case report describes a nulliparous eleven-year-old German shepherd dog suffering from CEH as a complication of a follicular cyst. This can be correlated with the findings that dogs with ovarian cysts and associated reproductive perturbations are common in nulliparous, large breeds with an average of occurrence as 9.5 ± 3 years (Devi *et al.*, 2021 and Knauf *et al.*, 2018).

Other than reproductive system, hyperestrogenism can affect bone marrow and hair growth. Progressive, nonpruritic, bilaterally symmetrical alopecia of the neck, trunk, and perineum, with associated lichenification and hyperkeratosis and anaemia were noticed in dog with hyperestrogenism. Estrogen in high doses has a toxic effect on bone marrow, resulting in an estrogen-induced myelotoxic effect on the hematopoietic system and leading to anaemia and thrombocytopenia (Suttorp *et al.*, 2002). Bilateral alopecia and severe anaemia observed in the

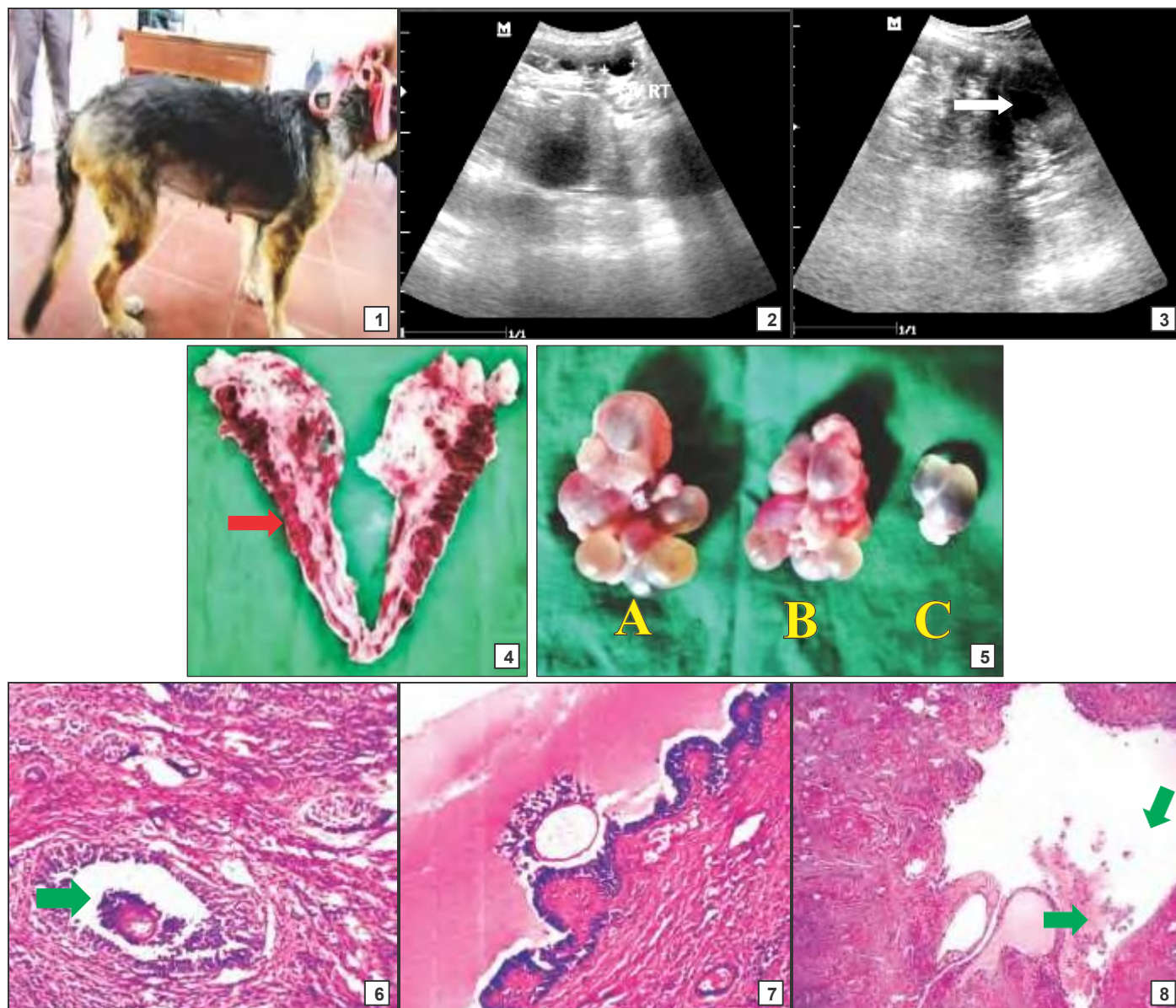


Fig. 1-8. (1) Bilateral Alopecia in the flank; (2) Ultrasound image of right ovary showing the follicular cyst; (3) Ultrasound image of uterus showing the sacculations; (4) Image at OHE, showing haemorrhagic endometrium with ulcer and corrugation; (5) Image at OHE, showing multiple large follicles in the ovaries (A&B), along with parovarian cyst (C); (6) Microphotograph of ovarian section showing pyknotic changes in the oocyte and cumulus cells; (7) Microphotograph of ovarian section showing cysts were lined with a single layer of cells with a residue of oocyte; (8) Microphotograph of uterine section showing congestion, haemorrhage, inflammatory cells and cystic dilatation in the endometrium

present case and estradiol concentration was 134.96 pg/ml. Serum estradiol concentration of more than 60-70 pg/ml (Feldman and Nelson, 1987) is an indication of hyperestrogenism and it may be due to an ovarian cyst or tumour (Frank, 2006).

The conservative therapy measures of cycle aberrations with hormone therapy may fail due to the simultaneous occurrence of luteal cysts and follicular cysts (Knauf *et al.*, 2018). In this case, the conservative treatment of pyometra with antiprogesterin is failed due to simultaneous presence of hormonally active corpus luteum and ovarian. Ovariohysterectomy is the treatment of choice for a dog

with a potentially lethal CEH-pyometra complex, which is not responding to medical management (Kumar *et al.*, 2019).

The present case report concluded that dogs affected with bilateral follicular cyst-complicated CEH pyometra, which is not responding to medical treatment can effectively treated with ovariohysterectomy.

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