

Case Report

An incidence of cystic endometrial hyperplasia - pyometra complex in a Nigerian local breed bitch treated with medroxyprogesterone acetate (MPA) as a contraceptive

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A four year-old Nigerian local breed bitch was presented to the Small Animal Unit of the Ahmadu Bello University Veterinary Teaching Hospital (ABUVTH) Zaria, with distended abdomen despite decreased appetite and persistent vaginal discharge, pale mucus membrane, fever and vomiting, after medroxyprogesterone acetate (MPA) treatment. Hematological examination revealed anemia, neutrophilia, hypoproteinemia and increased serum progesterone concentration on assay. There were abundant neutrophils and few intermediate cells on exfoliative vaginal cytology. *Streptococcus* spp was isolated from the vaginal discharge on bacterial culture. Ovariohysterectomy was performed and the gross findings were enlarged uterus with thickened wall, gray to tan sticky material in the lumen of the uterus. Histopathologically, there was hyperplasia of the surface of the endometrium, infiltration of the endometrial stroma with inflammatory cells and fibrosis of the myometrium.

Key words: Cystic endometrial hyperplasia (CEH), pyometra, bitch, medroxyprogesterone acetate, contraceptive.

INTRODUCTION

Cystic endometrial hyperplasia (CEH) and pyometra in the bitch are luteal phase syndromes, supposed to be caused by hormonal disturbances and changes in endometrial steroid hormone (Kim and Kim, 2005). They are also associated with progestins administration (Concannon and Verstegen, 2005). During the luteal phase of the estrous cycle, serum progesterone concentration rises in pregnant and non pregnant bitches (Goodman, 2001). Progesterone stimulates the endometrial glands secretion, formation of cystic structures which are very important for feeding the embryos, and if the female is not pregnant they normally regress towards the end of the luteal phase leaving the endometrium to

to regenerate and be ready for the next chance for a pregnancy (Romagnoli, 2003).

However, repeated progestational stimulation (as it occurs with age in the bitch and queen) may lead to areas of the endometrium with these cystic structures not re-gaining normal status during the last part of diestrus and anestrus (Romagnoli and Concannon, 2003). These accumulated effects after several cycles explain the higher incidence of CEH in females of middle and advance age. CEH is thought to predispose to pyometra, as both can occur independently of the other. Although CEH usually precedes the development of pyometra, the CEH does not inevitably progress to pyometra in all

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bitches, the same way, while all bitches develop CEH with age, only some of them develop pyometra (Angulo, 2009). CEH is an incidental finding, and its natural incidence is not known. Exposure of the endometrium to progestin causes proliferation of the superficial layers of the endometrium with increased secretory activity of the endometrial glands, which can lead to CEH (Romagnoli and Concannon, 2003). Subclinical infection or a uterine endometrial irritation by foreign bodies during the end of estrus or early diestrus may stimulate an exaggerated hypertrophy-hyperplasia of the endometrium, similar to what occurs during the implantation (Angulo, 2009). Progesterone also reduces endometrial resistance which encourages bacterial proliferation (Noakes and Allen, 1986; Concannon and Romagnoli, 2003). CEH often predisposes the dog to pyometra (Feldman, 2000; Angulo, 2009) due to movement of normal vaginal bacterial flora into the uterus when the cervix is still open at the beginning of diestrus (Kustritz, 2005). The bacteria most frequently isolated in cases of pyometra is *Escherichia coli*, but *Staphylococcus* spp., *Streptococcus* spp., *Pseudomonas* spp., *Proteus* spp. contamination can also be found. Pyometra could either be closed cervix or open cervix (Romagnoli, 2003). Clinical signs of pyometra in bitches will depend on the patency of the cervix. Treatment of choice for pyometra is ovariohysterectomy (Kustritz, 2005; Angulo, 2009). The aim of this article is to report an incidence of cystic endometrial hyperplasia-pyometra complex in a bitch treated with medroxyprogesterone acetate.

CASE REPORT

A four year-old Nigerian local breed bitch was presented to the Small Animal Unit of the Ahmadu Bello University Veterinary Teaching Hospital (ABUVTH) Zaria, with the chief complaint of vomiting, distended abdomen despite decreased appetite and persistent yellowish vaginal discharge. She had been given an injection of MPA at a dose rate of 1.5 mg/kg every 3 months to prevent estrous cycle. A month after the second dose of medroxyprogesterone acetate (MPA), the bitch developed those signs mentioned above. The reproductive history of the bitch was that she cycles twice a year. She usually gives birth to 4 to 6 puppies, hence MPA was administered. The contraceptive was administered about 2 months after her last whelping. The dosage of the contraceptive administered was 150 mg/ml (Depo-Provera[®] Pharmacia and Upjohn Company Kalamazoo, MI 49001, USA).

On physical examination, rectal temperature was 40.1°C and the mucus membrane was pale. Blood sample (5 mls) was collected from the cephalic vein- 3 mls for complete blood count and 2 mls for serum progesterone assay using ELISA 90 test kit (Fortress Diagnostic Ltd BT41 IQS USA). A swab sample of the

vaginal discharge was taken for bacterial culture. Vaginal swab was also taken for exfoliative vaginal cytology. The smear made from the vaginal swab was fixed in 95% ethanol, and then stained with Papanicolaou stain.

Ovariohysterectomy was performed, which revealed an enlarged uterus with thickened wall. The lumen of the uterus was filled with gray to tan sticky material trimmed sections of the surgically removed uterus were fixed in 10% formalin and stained with H&E stain for histopathological examination. Blood sample taken revealed anaemia (PCV 11%), leucocyte count was ($6.0 \times 10^9/L$), neutrophils (75%), lymphocytes (19%) total protein (7.0 g/dl), eosinophils (4%) serum progesterone concentration (8 ng/ml). *Streptococcus* spp was isolated on bacterial culture. The predominant cells on exfoliative vaginal cytology were abundant neutrophils and few intermediate cells. Histopathologically, there was hyperplasia of endometrium, proliferation of inflammatory cells in the endometrial stroma and fibrosis of the myometrium. The bitch made complete recovery following ovariohysterectomy.

DISCUSSION

Progestins are widely used in small animal medicine, with indications ranging from dermatological to behavioral problems, but the main use involves the control of the reproductive cycle. Exogenous progestin commonly used in dogs and cats are medroxyprogesterone acetate (MPA), proligestone (PR), chlomidione acetate (CMA), megestrol acetate (MA), delmadione acetate (DMA), norethisterone acetate (NTA) and melengestrol acetate (MGA) (Romagnoli, 2006). The use of these compounds are associated with side effects such as mammary tumor, decreased adrenocorticosteroid, increased prolactin and growth hormone, insulin resistance, increased appetite, weight gain, polydipsia, slight depression, decreased libido in males.

Progestin can cause masculinization of female fetuses when administered in the last trimester of pregnancy (Romagnoli and Concannon, 2003; Concannon, 2004; Romagnoli 2006). Clinical considerations for safe use of progestins are that a treatment period of 6 to 12 months is safe in healthy individuals. Treatment periods of over 12 months may worsen some subclinical conditions such as diabetes, microscopic mammary lesions or cystic endometrial hyperplasia. Progestin treatment should be restricted to bitches in anoestrus or early proestrus (Romagnoli and Concannon, 2003, Concannon, 2004). Bitches in late prooestrus, oestrus, or dioestrus if treated may result in abnormal stimulation of the reproductive tract and uterine pathology due to the presence of increased progesterone (Romagnoli and Concannon 2003). MPA is an exogenous progestin commonly used in temporal estrous prevention in dogs and cats in which future breeding are desired. However, proliferation of

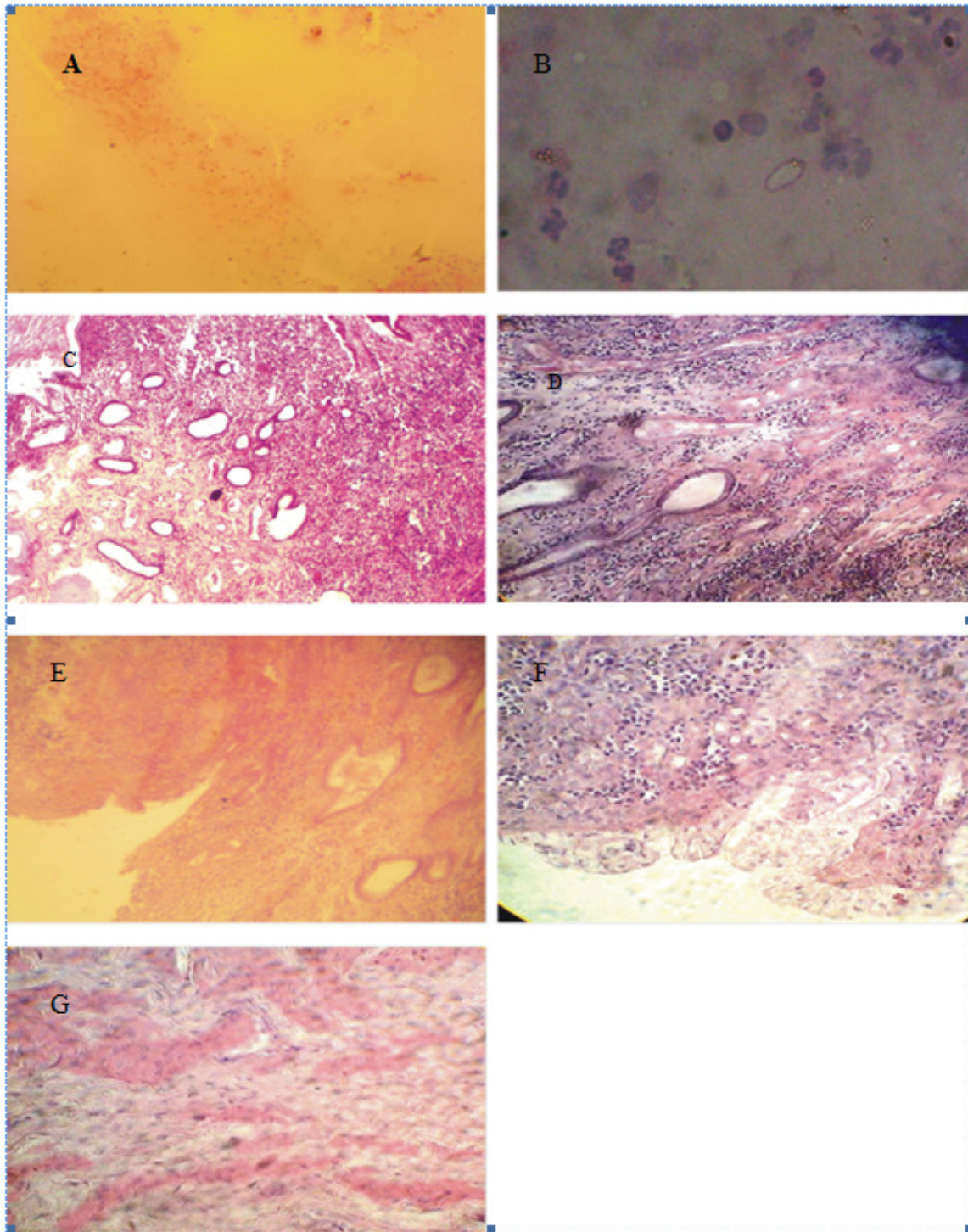


Figure 1. (A and B) Vaginal cytology showing neutrophils ($\times 10$ and $\times 100$ respectively). (C and D) showing endometrial glands ($\times 10$ and $\times 400$, respectively). (E and F) showing showing proliferation of the superficial layer of the endometrium and infiltration of the stroma with polymorphonuclear cells ($\times 10$ and $\times 400$ respectively). (G) showing fibrosis of the myometrium ($\times 400$).

endometrium and mammary hyperplasia are the side effects of the exogenous progestin (Chatdarong et al., 2008). CEH is difficult to diagnose because it is not

usually associated with clinical signs unless accompanied with pyometra (Feldman, 2000). Pyometra is the most common sequel to CEH (Feldman, 2000; Angulo, 2009).

Incidence of pyometra is thought to be greater in the bitch than the queen because dogs are more exposed to natural progesterone frequently than the cat (Davidson, 2000). Bitches older than 7 years of age are prone to CEH than pyometra due to repeated exposure to progesterone, thus it is unlikely that CEH is the cause of pyometra in bitches younger than 6 years of age (Feldman, 2000). Some breeds are more predisposed to the condition like the Rottweiler, Saint Bernard, Chow Chow, Golden Retriever, Miniature Schnauzer, Terriers, Collie, The Alsatian, Dachshund, and other hounds however are at lower risk (Angulo, 2009). Open cervix pyometra is easily recognized because it is associated with vaginal discharge which is usually purulent, creamy, reddish-brown to green in colour and foul smelling (Kustritz, 2005). Closed cervix pyometra is not easily recognized. It is usually associated with abdominal distension and when it is accompanied with septicemia and toxemia, can result in progressive dehydration, shock and death (Feldman, 2000). Some bitches may suffer uterine rupture (Davidson, 2000). Other common signs of pyometra include pyrexia, lethargy, depression, inappetance or anorexia, polyuria, polydipsia, vomiting and diarrhoea (Feldman, 2000; Kustritz, 2005).

This case report recorded slight distended abdomen due to uterine enlargement. Grossly the surgically operated uterus was enlarged with thickened walls. On complete blood count, the bitch was anaemic with PCV at 11% and leucocytic neutrophilia. Predominant cells on vaginal cytology were neutrophils (Figure 1A, B). There was enlargement of endometrial glands (Figure 1C, D), proliferation of the superficial layer of the endometrium and abundant polymorphonuclear cells in the stroma of the endometrium (Figure 1E, F) fibrosis of the myometrium (Figure 1G).

Conclusion

CEH–Pyometra complex can occur in normal and bitches undergoing contraceptive treatment. Despite administering the drug at a low dose and for a short period of time, the bitch came down with a uterine pathology. There is the likelihood of a pre-existing CEH.

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