False pregnancy in bitch

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Abstract

False pregnancy is the most frequent term used to describe this clinical condition in bitches and simply refers to the prolonged luteal phase of non-fertile induced ovulatory cycles. Moreover, in the bitches, the signs of clinical false pregnancy are comparable not so much to those of pregnancy but to those of the peripartum and postpartum periods and lactation. False pregnancy is easy to diagnose and easy to treat using dopamine agonists. Although some of the agonists have side effects. The patho-physiology of the condition is not fully understood but a central etiologic role for prolactin is widely accepted. A short luteal phase with an abrupt decline in progesterone, which would be expected to stimulate prolactin release, has been proposed as the cause of false pregnancy.

Keywords: False pregnancy, Bitch, estrogen, progesterone, sex steroid, patho-physiology.

False pregnancy is a clinical phenomenon in which the non-pregnant female exhibits maternal behaviour and physical signs of pregnancy at the end of diestrus (luteal phase). The terms false pregnancy and psudopregnancy are often used interchangeably but they may not always refer to the same hormonal situations. The term psudopregnancy refers specifically to the non pregnant luteal phase, usually in reference to an animal that is induced to ovulate by coitus, when serum concentrations of progesterone are high. Progesterone causes mammary gland development and weight gain but not the other behavioral and physical changes of false pregnancy.

In contrast to Pseudopregnancy, false pregnancy is thought to be caused by the declining serum progesterone concentrations associated with the end of the luteal phase, which in turn causes an increase in serum prolactin concentrations. Prolactin causes lactation and the maternal; behavior of false pregnancy. Because the bitch ovulates spontaneously and always enters a long luteal phase, false pregnancy is a common phenomenon in cycling bitches. It is uncommon in queens because they must first have induced to ovulate but not conceive (i.e. pseudopregnancy) and they have a decline in the progesterone concentration appropriate to stimulate the prolactin release. False pregnancy also occurs after the withdrawal of exogenous progestin's and after oophorectomy performed during diestrus.

False pregnancy is considered a normal phenomenon in bitches. It is not associated with any reproductive abnormalities, including pyometra or infertility. Quite the contrary, the occurrence of the False pregnancy provides the evidence that ovulation took place during preceding cycle and that the hypothalamic-pituitary- gonadal axis is intact. Why some bitches are more prone to developing clinical signs and why the severity of clinical signs varies from cycle to cycle are not known. False pregnancy is frequently observed in bitches owing to the fact that the met estrus, luteal or proestrus phase of the cycle is approximately of the same duration as pregnancy i.e. 8 to 9 weeks long and is characterized by clinical signs such as nesting, weight gain, mammary enlargement and lactation. It typically occurs in non-pregnant bitches about 6 to 12 weeks after estrus. When the changes result in extreme behavior or atypical mammary activity, or are presented as clinical problems involving changes similar to those seen in late pregnancy or the early post-partum period (Allen, 1986; Arbieter *et al.,* 1988; Jochle *et al.,* 1987). The exact incidence of clinical false pregnancy or its distribution among breeds is not known, although it has been estimated

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to be as high as 50 - 75% (Johnston, 1980). The pituitary hormone prolactin plays a central role in the patho-physiology of overt false pregnancy, but its exact role is not completely understood. The incidence of clinical false pregnancy may be influenced by age, breed, parity and environmental factors. Nutritional practices may also have an influence on the occurrence of false pregnancy (Lawler *et al.,* 1999). The purpose of the present review is to examine the most relevant aspects of the physiology, clinical signs, diagnosis, treatment and prevention of clinical false pregnancy.

Clinical Signs

All non-pregnant bitches in mid and late met estrus (i.e., diestrus) and between 6 to 20 weeks after estrus, have mammary development much greater than at any other stage of the cycle and peak mammary size is seen at about 14 weeks (Concannon,1986).

The false pregnancy-syndrome usually begins with behavioral signs such as restlessness, decreased activity, nesting, aggression, licking of the abdomen and mothering inanimate objects. Later, pseudopregnant bitches show physical signs such us weight gain, mammary enlargement, even milk secretion and let-down and sometimes abdominal contractions that mimic those of parturition (Jochle *et al.,* 1987; Lawler *et al.,* 1999; Concannon, 1986). Mammary hypertrophy is usually more evident in the most caudal pair of glands although the entire mammary chain can be involved. Milk production during false pregnancy apparently results from the development of not only intra-acinar but also intra-canalicular mammary secretion in predisposed bitches. Lactation is often encouraged by self-nursing or by adoption of unrelated neonates. Vomiting, anorexia, diarrhea, polyuria, polydipsia, and polyphagia have also been reported by Johnston (1980).

Complications of false pregnancy, like mastitis and mammary dermatitis, are not common and, unless these complications appear, signs of false pregnancy normally cease after 2 to 4 weeks. Susceptible bitches have a high recurrence rate in successive estrous cycles (Johnston, 1986). Overt false pregnancy has also been observed to be induced under the following circumstances: during prolonged progestin treatment; after termination of progestin treatment; in response to antiprogestin treatments; and at 3 or 4 days after spaying during the luteal phase (Johnston, 1980 & 1986; Gobello *et al.,* 2001). These instances of progesterone exposure and subsequent reduction or withdrawal of progesterone presumably have the same effects as occur in response to the decline in progesterone that normally occurs in pregnant bitches immediately before parturition. Whether prolactin plays a role in mammary tumor development is unclear however 30% of malignant tumors have prolactin receptors.

Patho-physiology

Role of Progesterone - False pregnancy appears to be related to and dependent on exposure to elevated levels of progesterone. False pregnancy may occur as a result of increased concentrations of prolactin or an increased sensitivity to prolactin induced by a more rapid than normal decline of progesterone levels in the late luteal phase (Concannon and Lein, 1989; Gerres *et al.,* 1988; Graf *et al.,* 1977; Smith and Mc Donald, 1974). Spaying or ovariectomy during the luteal phase induces false pregnancy in some bitches (Gobello *et al.,* 2001).

Role of Prolactin, Estrogen and Growth hormone - Prolactin concentrations normally increase slightly above basal values between days 60 and 90 of the non-pregnant estrous cycle (Onclin and Verstegen, 1997) with increases often seen as early as day 40. There is also an inverse relationship between progesterone and prolactin concentrations in the normal non-pregnant cycle between days 40 and 90 (De Coster *et al.,* 1983). In bitches with false pregnancy higher serum concentrations of prolactin had been reported (Okkens *et al.,* 1997), whereas prolactin during false pregnancy is variable or not elevated (Lawler *et al.,* 1999; Gobello *et al.,* 2001; Harvey *et al.,* 1997; Hoffman *et al.,*1992). Prolactin appears to be the most important endocrine factor in the development of the symptoms of false pregnancy; other hormones including estrogen might also play a role (Brugere,1998). A positive correlation between prolactin and estrogens has been found in some bitches (Hadley, 1975). The role of growth hormone, which is deeply implicated in the process of mammogenesis in many mammalian species (Brugere, 1998) is not clear in canine false pregnancy.

Diagnosis

Diagnosis of false pregnancy is based on the presence and extent of the more commonly reported clinical signs. Because unscheduled mating may be overlooked by owners, pregnancy should always be considered. In case of doubt, ultrasound or

radiography should be used. Other conditions of the luteal phase, such as pyometra or recent pregnancy and abortion, should be ruled out by abdominal ultrasonography or radiography, a complete blood cell count including vulvar and vaginal examination is helpful for diagnosis. It is also important to keep in mind that false pregnancy can coexist with other reproductive or non-reproductive clinical problems, sometimes making diagnosis more difficult.

Treatment

Considering that false pregnancy is typically a self-limiting state, mild cases are usually considered to need no treatment other than discouraging maternal behavior. Sometimes placing Elizabethan collars to prevent licking of the mammary glands is recommended. Licking, milking, or use of compresses are potential stimuli for lactation and need to be avoided. Water removal overnight for 5 to 7 nights promotes fluid conservation and also helps to terminate lactation. When behavioral signs are significant, light tranquilization with non-phenothiazine drugs can be useful. However phenothiazines are not recommended in pseudopregnant bitches because they stimulate prolactin secretion.

Sex Steroid Therapy

Sex steroids are necessary for mammary development but high doses appear to exert a negative effect, either by suppressing pituitary prolactin or decreasing sensitivity to prolactin (Allen, 1986; Johnston, 1980).

Estrogens - Estrogens such as diethylstilbestrol, estradiol benzoate or estradiol cipionate have been used. They may cause signs of proestrus or estrus, uterine disease such as pyometra, and bone marrow depression resulting in anemia.

Androgens - Androgens including testosterone and synthetic androgens can suppress lactation. Side effects can include clitoral hypertrophy, other forms of virilization, and epiphora. The synthetic androgen milbolerone has been shown to reduce the duration of false pregnancy.

Progestin - Progestin such as megestrol acetate and medroxyprogesterone acetate, administered orally, have been used to suppress the symptoms of overt false pregnancy. This involves suppression of prolactin secretion or reduction of tissue sensitivity to prolactin. However progestins can cause cystic endometrial hyperplasia-pyometra complex and insulin resistance, as well as mammary gland nodules, mammary tumors, and acromegaly (Feldmen and Nelson, 1987).

Prolactin-Suppression Therapy

Dopamine Agonists - Inhibition of prolactin secretion by ergot alkaloid drugs has produced a revolution in the treatment of canine false pregnancy. This inhibition can be modulated indirectly by serotonin, which suppresses dopamine release and increases prolactin (Thorner *et al.,* 1998). The most common ergot compounds used clinically to inhibit prolactin secretion are the dopamine agonists bromocriptine and cabergoline. Another ergot alkaloid, is a serotonin antagonist, and thus has a dopaminergic effect and thus reduces prolactin secretion when administered at high doses (Janssens, 1986; Jochle *et al.,* 1989; Hammon *et al.,* 1981).

Bromocriptine - A large number of therapeutic protocols have been proposed, using oral doses of bromocriptine ranging from 10 to 100 mg/kg/day for 10 to 14 days (Jenssens, 1986). Due to short half-life it should be administered at least twice a day for greatest efficacy. To prevent the incidence of emesis, bromocriptine can be administered along with atropine. Bromocriptine 2.5 mg tablets fractionation is necessary to achieve dosages of 10 to 30 mg/kg typically administered to pseudopregnant bitches (Voith, 1980).

Cabergoline - It can be effectively administered once a day. Cabergoline crosses the blood brain barrier only slightly and consequently has much less central emetic effects than some other dopamine agonists (Arbieter *et al.,* 1998; Jochle *et al.,* 1987 ; Harvey *et al.,* 1997). Cabergoline is marketed with an indication for use in pseudopregnant bitches at a dose of 5 mg/kg/day for 5 to 10 days, orally

Metergoline - Metergoline is an anti-serotonergic veterinary drug marketed for the treatment of false pregnancy in bitches. It has a short half-life so it has to be administered twice a day. The recommended dose is 0.1 mg/kg, orally, twice a day, for 8 to 10 days. Anxiety, aggressiveness, hyper excitation and whining are the most frequent side effects of metergoline, which are due to its central anti-serotonergic effect (Hamon *et al*., 1981).

Ovariectomy - Predisposed bitches not intended for breeding should be spayed. Ovariectomy is the only permanent preventive measure (Johnston, 1980; Jochle *et al.,* 1989). This should preferably be done during anestrus. Ovariectomy during lactation can lead to an extended false pregnancy (Allen,

1986). In bitches with a history of overt false pregnancy, spaying during metestrus (diestrus) may provoke an episode of false pregnancy 3 to 7 days after surgery (Gobello *et al.,* 2001).

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* 28/02/2008: Equine influenza, Japan, (Follow-up report No. 6)
* 27/02/2008: Classical swine fever, Hungary, (Follow-up report No. 31)
* 27/02/2008: Highly pathogenic avian influenza, Benin, (Follow-up report No. 5)
* 27/02/2008: Aujeszky's disease, Romania, (Follow-up report No. 2)
* 27/02/2008: Newcastle disease, Romania, (Follow-up report No. 1)
* 27/02/2008: Rabies, France, (Immediate notification)
* 26/02/2008: Highly pathogenic avian influenza, Pakistan, (Follow-up report No. 11)
* 26/02/2008: Highly pathogenic avian influenza, Turkey, (Follow-up report No. 5)
* 26/02/2008: Classical swine fever, El Salvador, (Immediate notification)
* 25/02/2008: Highly pathogenic avian influenza, China (People's Rep. of), (Follow-up report No. 11)
* 25/02/2008: Highly pathogenic avian influenza, Ukraine, (Follow-up report No. 3)
* 23/02/2008: Highly pathogenic avian influenza, Vietnam, (Follow-up report No. 16)