

Anoestrus Treated with Bromocriptine 2.5 mg (Parlodel®) in Atlas Shepherd Bitch: A Case-Control Study

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Rec date: October 26, 2017; Acc date: November 15, 2017; Pub date: November 16, 2017

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Abstract

This study reports the clinical, ultrasonographic and endocrinological findings of a bitch treated with bromocriptine (Parlodel® 2.5 mg Breakable tablet box of 30 tablets) for a heat induction. The dosage adapted for the dog was 1.25 mg per day. A atlas shepherd dog five years old, which had a heat back delay of more than 8 months, was presented to the canine clinical pathology of Tiaret veterinary science institute for consultation. The vaginal smears and ultrasound of the ovaries were combined with the proportioning of progesterone. Vaginal cytology detected a phase of anoestrus. the estimated ovarian volume measured with abdominal ultrasound was 9+/-1.04 mm. The ovaries were of small oval shape with homogeneous echogenicity, similar to that of the renal cortex, with the presence of a few very small, slightly hyperechoic structures on the two ovaries. The progesterone level was 3 nmol/l. No structural anomaly of ovaries and no genital infection were observed on clinical examination.

Keywords: Atlas shepherd dog; Ovary; Anoestrus; Ultrasonography; Cytology

Introduction

In the canine species, the induction of estrus has two major applications, in the case of impuberism for 24 months or in the absence of heat for more than 10 months. The use of dopaminergic substances is recommended as a first-line treatment for pathological anoestrus (more than 7 months of interestrus) [1]. The efficacy of these molecules in the onset of estrus depends on the dose, the duration of treatment and the anoestrus phase. The main diagnostic techniques for the monitoring of heat are physical and laboratory examinations. Vaginal cytology, Ultrasound and hormonal analyzes are the methods of choice for the diagnosis of estrous cycle disorder in bitch [2,3]. The present case was anoestrus treated with Bromocriptine 2.5 mg (Parlodel®) in Atlas Shepherd bitch.

Case Presentation

A Five year old intact female Atlas Shepherd Dog, weighing 16 kg was presented to canine clinical Pathology, Institute of Veterinary Science, University Ibn Khaldoun, with a history of no return to estrus more than 8 months. Vaginal cytology examination showed a clean smear; poor in cells with a few clusters of parabasal cells indicating an anoestrus on smear colored colored then with the trichrome of Harris-Shorr (Kits Diaagnoestrus-RAL A and B). The appearance and the measurement of the diameter of the ovaries in our case were made at the base of the echographic images obtained by longitudinal and transverse sections following the use of an electronic sectoral probe with a frequency of 5 MHz and a DRAMENSKI 4VET MINI transportable echograph. The hormonal analyzes showed a very low blood level of the progesterone in the serum analyzed using the Elecsys1010 Roche® analyzer. An oral bromocriptine treatment was administered at a dosage of 1.25 mg per day; our dog had vulvar loss

(proestrus) after 45 days of treatment. This research work is approved and validated by the Scientific Committee of the Faculty of Sciences of Nature and Life University Mustapha Stambouli of Mascara, Algeria. And recorded under the number: 12 / FSNV / 2014.

Results and Discussion

Vaginal cytology (Figure 1) revealed small clusters of parabasal cells with absences of red blood cells and leukocyte cells which indicated an anoestrus on smear read using a magnification of x40 (Figure 2) and x100 (Figure 3).



Figure 1: Vaginal swab for the realization of a cytological smear.

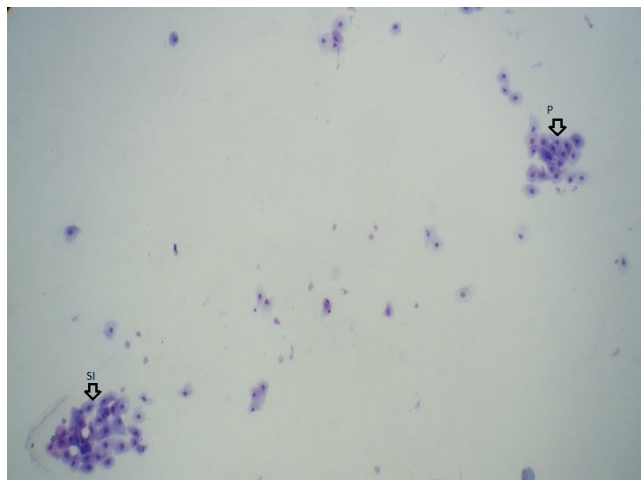


Figure 2: A view of a vaginal smear of anoestrus at magnification x40 which shows a cluster composed of parabasal cells colored by May-Grünwald Giemsa and a few small intermediate cells with a slightly clean background. Leukocytes are absent. Eosinophilic index is less than 10%. P: parabasal cells; SI: small intermediate cells.

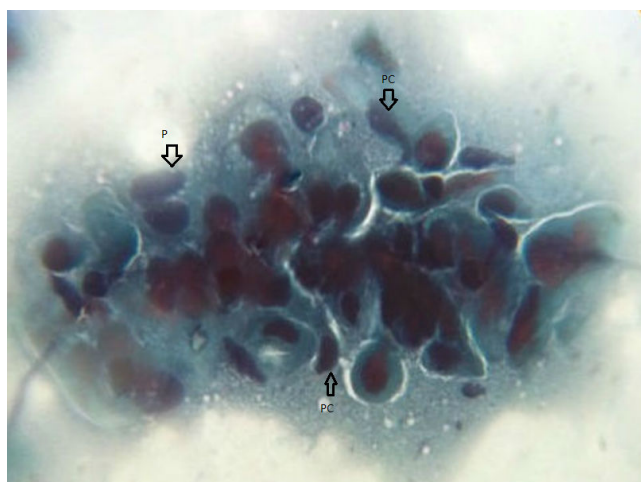


Figure 3: A view of a vaginal smear of anoestrus at magnification x100 which shows a cluster composed of parabasal basophilic cells round with large nucleus and some parabasal cells "in column" colored with by harris shorr with a slightly clean background. Leukocytes are absent. Eosinophilic index is less than 10%. PC: parabasal cells "in column"; P: parabasal cells.

However the clinical examination showed that the dog was in good health.

The smear of an anoestrus is poor in cells [4]. Parabasal cells and small intermediate cells are predominant [3,5].

The diameter of the ovaries estimated according to ultrasound measurement was equal to 9 ± 1.04 mm on average. Ultrasound examination of the ovaries (Figure 4) showed a small size of the ovaries

and small oval shape with homogeneous echogenicity, similar to that of then renal cortex, with the presence of a few very small, slightly hyperechoic structures on the two ovaries. No particular abnormality was detected on the ovaries. No anomalies in the uterus were detected.

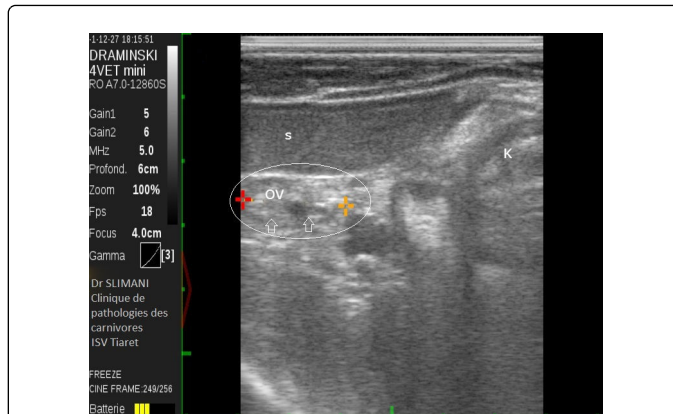


Figure 4: Longitudinal echo graphic view of the ovary showing parenchyma of a heterogeneous texture dominated by hyperechoic ovarian stroma and presence of a small hypoechoic cavity. This echo graphic aspect indicates the absence of a follicular activity related to an anoestrus. OV: ovary; S: spleen; K: kidney.

During the anoestrus the ovaries have an echogenicity similar to that of the neighboring structures and the follicular structures are small, often less than 1 mm [6]. The ovaries are small and not very visible. They have a homogeneous echogenicity similar to that of the renal cortex. However, at the end of the anoestrus, at 30 days or more from the beginning of the pro-estrus, the hypoechoic ovaries tend to increase and small follicular cavities of one to two millimeters in diameter can be detected [7].

Blood level of the progesterone in the serum was 3 nmol/l which confirmed the presence of an anoestrus.

The induction of heat in a bitch is realized in the case of impubérisme for 24 months or in the case of absence of heat for more than 10 months. The use of dopaminergic substances is recommended as a first-line treatment for pathological anoestrus (>7 months interoestrus) [1]

An oral Bromocriptine (Parlodel 2.5 mg) treatment was administered at a dosage of 1.25 mg per day; the dog had an estrus at 45 days of treatment.

Antiprolactinics are dopaminergic agonists that inhibit the secretion of prolactin via dopamine secretion or suppression of serotonin secretion. The use of certain antiprolactinics during pseudo-lactation decreases the inter-estral interval of the treated bitches [1,8,9]. The use of dopaminergic agonists in anticipation of estrus (less than 7 months after the last heat) is very disappointing [10].

During the treatment period the bitch was presented for clinical control every 15 days; this control included the realization of vaginal smears in order to detect any change in the cellular structure of the vaginal mucosa.

In the last 15 days before the onset of the heats of cell clusters of small intermediate and large intermediate cells appeared gradually on the smear, indicating clear changes in the vaginal mucosa that are

evidence of the existence of ovarian rearrangement induced by the administered molecule (Figures 5 and 6).

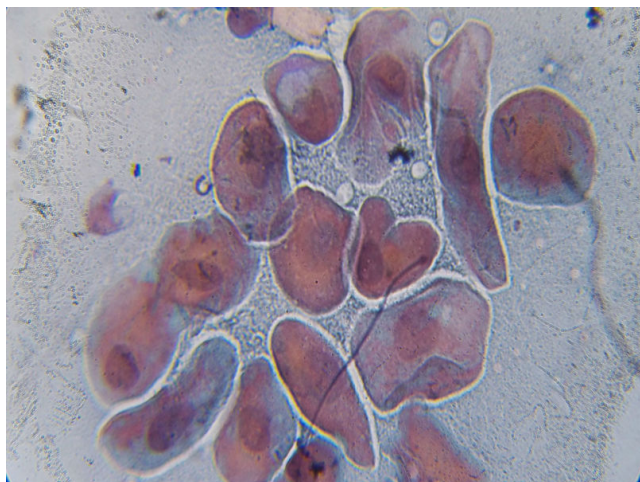


Figure 5: A view of a vaginal smear of proestrus (beginning) at magnification x100 which shows of the majority intermediate acidophilic cells in the course of keratinization colored by harris shorr. Eosinophilic index is less than 40%.

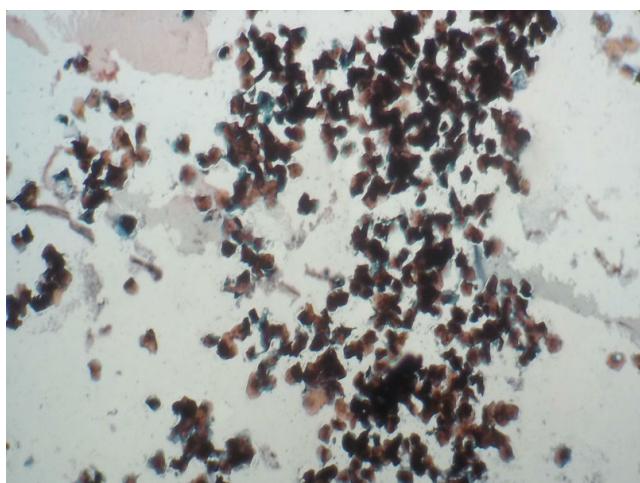


Figure 6: A view of a vaginal smear of proestrus (end) at magnification x40 which shows smear rich in acidophilic cells, dirty bottom, presence of red blood cells, keratinized superficial cells and large majority intermediate cells colored by harris shorr. Eosinophilic index is greater than 80%.

Guerin et al. [11] report that vaginal smears are good indicators in the monitoring of the heats but are insufficient for the determination of the ovulatory period. Similarly Van Haaften et al. [12] points out that the eosinophilic index allows estrus to be well detected but not for ovulation.

In contrast to bromocriptine (Parlodel®, dopaminergic molecule) or cabergoline (Galastop®, an anti-serotonergic and dopaminergic molecule), metterolol (Contralac®, an anti-serotonergic molecule) does not induce estrus. The central dopaminergic effect of antiprolactinics

that seems to act favorably during this heat-inducing effect. Their efficacy in the onset of estrus depends on dose, duration of treatment [1,8,9].

The bitch presented a vulvar losses and vulval hypertrophy as of the 45 th day of treatment, proestrus and estrus were confirmed by vaginal cytology and the increase in the eosinophilic index measured during heat monitoring was consistent with the manifestation of the heat.

Dumon [13] reports that heat is obtained after 30 to 40 days of treatment with bromocriptine (Parlodel®) 20 µg/kg twice day. Their effectiveness in the onset of estrus depends on the dose, the duration of the treatment and the anoestrus stage.

According to Audrey and Samuel [1]. The two most widely used anti-prolactinic are cabergoline at the dose of 5 µg/kg/day until proestrus is obtained (usually for 3 weeks) and bromocriptine 20- 50 µg/kg twice daily until porestrus was obtained (usually for 4 weeks) [8,13].

A chronological correlation between the eosinophilic index and the increase in the diameter of the ovaries during the period located between the 5 th day of the proestrus and the middle of the estrus was observed. The diameter of the ovaries was equal to 19+/-2.07 mm and corresponded to an eosinophilic index equal to or higher than 80% at the time of ovulation.

A positive correlation was observed between the progesterone level and the eosinophilic index (EI) during the period between the 5 th day of proestrus and the middle of the estrus. The progesterone level increased from 9 nmol /l at the beginning of proestrus to 21.04 nmol/l at the time of ovulation (Figure 7).

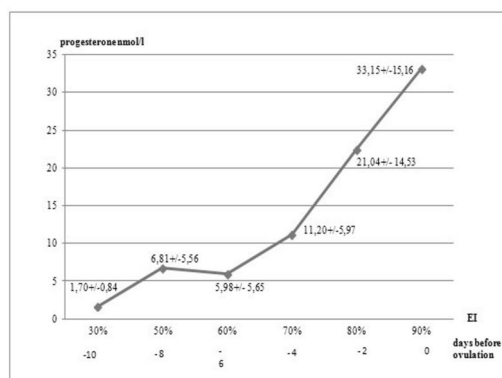


Figure 7: A positive correlation was observed between the progesterone level and the eosinophilic index (EI) during the period between the 5th day of proestrus and the middle of the estrus.

England and Concannon [14] report that ovulation can occur between the 5 th and 30 th day after the beginning of the heat. The use of the vaginal smears must be supplemented by the determination of the level of progesterone [3,15].

Fontbonne and Malandin [16] show that the echo graphic examination on the ovaries increases only 10% the precision of detection of ovulation compared to the proportioning of progesterone. They also estimate that the detection of ovulation can be realized with an echograph of standard quality by practicing daily examination for the bitches of weight lower than 25 kg. On the other hand for the large

or the obese bitches, it seems necessary to use an echograph of higher quality.

Marseloo et al. [17] reports that there is a good correlation between the values of progesterone and the echo graphic aspect of the ovaries during the follow-up of heats. Vomiting was the only treatment-related side effect observed in our case.

This side effect observed only during the first week of treatment. Audrey and Samuel [1] report that the most observed side effects are vomiting occur in 3 to 25% following treatment with anti-prolactinics.

On the other hand, we did not observe cases of hair discoloration related to the use of bromocriptine, in contrast to cabergoline, which induces transient skin discoloration in 25% of bitches that receive this molecule for 14 to 45 days [1,9].

Conclusion

Any disturbance of the estrous cycle in the dog inducing a delay in the appearance of the estrus requires a complete physical exam which must be complemented by cytological exam, ovarian ultrasound and hormone dosage in order to arrive at a diagnosis of certainty that is required before initiating estrus-inducing therapy. This study, carried out at the Veterinary Science Institute, will allow us to use this protocol for induction of estrus by using the bromocriptine of the Future to treat pathological anoestrus in bitches, which is an alternative to the use of hormones.

Acknowledgement

The authors thank the staff of the Canine Clinical Pathology, Institute of Veterinary Sciences service for their assistance.

References

1. Pierson A, Buff S (2009) Induction of estrus in dogs and pussies: which molecule and which molecule and which protocol to use?. Colloquium AERA- house-Alfort.
2. Concannon PW (2000) Canine pregnancy: predicting parturition and timing events of gestation. In: Recent advances in Small Animal Reproduction. International Veterinary Information Service, Ithaca, NY.
3. Concannon PW (2011) Breeding cycles of the domestic bitch. *Anim Repro Sci* 124: 200-210.
4. Neveux M (1999) The vaginal smears in the bitch. *Item Vet* 30: 557-564.
5. Concannon PW, Digregorio GB (1987) Canine vaginal cytology. In Burke editor. Small animal reproduction and infertility, Philadelphia, pp: 96-111.
6. Concannon PW, England G, Verstegen J, Linde Forsberg C (2002) Recent advances in small animal reproduction. International Veterinary Service, Ithaca, New York.
7. England G, Yeager A, Concannon PW (2003) Ultrasound imaging of the reproductive tract in the bitch.
8. Beijerink NJ, Dieleman SJ, Kooistra HS, Okkens AC (2003) Low doses of bromocryptine shorten the interestrus interval in the bitch without lowering plasma prolactin concentration. *Theriogenology* 60: 1379-1386.
9. De Gier J, Beijerink NJ, Kooistra HS, Okkens AC (2008) Physiology of the canine anoestrus and methods for manipulation of this length. *Reprod Dom Anim* 43: 157-164.
10. Fontbonne A, Levy X, Fontaine E, Gilson C (2008) Guide practice of canine and feline clinical reproduction, pp: 41-43.
11. Guerin C, Petit C, Badinand F (1996) Fecundity in dog after protrusion or artificial insemination: study on 202 bitches. *Item* 28: 51-56.
12. Van Haafte B, Dieleman SJ, Okkens AC (1989) Timing the mating of dogs on the basis of blood progesterone concentration. *Vet Rec* 125: 524-526.
13. Dumon C (1992) Vaginal smears in the bitch. In *Indispensable Reproduction*, (ed. PMAC), 7508 Paris, pp: 47-52.
14. England G, Concannon PW (2000) Determination of the optimal breeding time in the bitch: basic considerations. In: *Recent Advances in Small Animal Reproduction*.
15. Wright PJ (1990) Application of vaginal cytology and plasma progesterone determinations to the management of reproduction in the bitch. *J Small Anim Pract* 31: 335-340.
16. Fontbonne A, Malandain E (2006) Ovarian ultrasonography and follow-up of estrus in the bitch and queen. *Waltham Focus* 16: 22.
17. Marseloo N, Fontbonne A, Bassu G (2004) Comparison of ovarian ultrasonography with hormonal parameters for the determination of the time of ovulation in bitches. In: *Proceedings of the 5 th International Symposium on Canine and Feline Reproduction*, pp: 75-77.