Bromocriptine Treatment for Inappropriate Lactation in Mares: A Case Report

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1. Introduction

Galactorrhea may be defined as secretion of milk or milk-like secretion that occurs in the absence of parturition or after weaning. Two conditions may be defined: premature lactation, when the lactation occurs precociously during pregnancy, or inappropriate lactation, when lactation occurs in the absence of gestation [1].

In humans, galactorrhea occurs as a result of increased plasma levels of prolactin, a hormone secreted by the adenohypophysis. Hyperprolactinemia is a common disorder of the hypothalamic-pituitary axis, which usually presents with reproductive abnormalities [2,3]; it may be caused by pituitary tumors, hypothyroidism, or secondary effects of drugs [1,4].

A transient mammary gland development and lactation can occur eventually in weanling foals, yearlings, and adult mares without previous or recent history of pregnancy. The etiology of this condition has not been well documented, and there is limited information on the occurrence, frequency of episodes, composition, and treatment of galactorrhea secretion. This article reports a case of Brazilian Sport Horse mare, aged 10 years, with persistent lactation during 5 months. The treatment consisted of bromocriptine 0.04 mg/kg, b.i.d., orally, for 10 days, associated with hydrotherapy for 20 minutes, twice daily. After 20 days of the treatment onset, the mare was reevaluated, and a significant decrease in the volume of the udder and the amount of secretion produced was noted, and its aspect was clearer (serous) and consisted of more fluid compared with the one collected before treatment. No other clinical alterations or associated diseases were identified. Based on these findings, we suggest the diagnosis of idiopathic inappropriate lactation. Although there is no information about pharmacokinetics and description of the oral bromocriptine use in horses, being a therapeutic option for inappropriate lactation treatment in mares, it was effective at the recommended dosage.
mares were reported having these clinical signs [9]. Thus, this report aims to describe galactorrhea in an animal without clinical signs of Cushing disease and proposes a new treatment option with the use of bromocriptine.

2. Case Report

A Brazilian Sport Horse mare, aged 10 years and weighing 570 kg, kept in a stable and fed coast cross hay and commercial concentrate (12% crude protein [CP]), was presented at the Veterinary Hospital of the College of Veterinary Medicine of the University of São Paulo, São Paulo, Brazil, with a 5-month history of persistent lactation, associated with discomfort caused by the swelling of the udder and spontaneous ejection of milk (Fig. 1).

The mare was nulliparous, and it was never inseminated or given any hormone treatment. The animal had no contact with foals, and there were no data available from previous reproductive examinations. Throughout the period, no drug therapy was performed, and the only procedure was milking daily, resulting in a total volume of approximately 1 L of milk per day.

The inspection of the mare revealed a body condition score equivalent to 5 (scale of 1-6) [10]. There were no alterations in vital parameters during physical examination.

In gynecological evaluation, the uterus had normal wall thickness and absence of free fluid, the left ovary had multiple follicles with diameters smaller than 15 mm, and the right ovary showed presence of corpus luteum. A firm enlargement of the mammary gland was identified, and there was no sensibility or hyperthermia. There was spontaneous secretion and ejection by sphincters on both teats. The collected secretion had milk-like appearance and odor.

The treatment started before obtaining the laboratory tests results. Bromocriptine was prescribed at a dose of 0.04 mg/kg, b.i.d., orally, for 10 days. Local hydrotherapy was also recommended for 20 minutes, twice daily. Milking was only allowed in situations where the mare was in extreme discomfort due to swelling of the mammary gland, without completely draining the secretion.

Samples of mammary gland secretion of both teats were sent to the Laboratory of Milk Production, University of São Paulo, for fat content analyses by the Gerber method, and CP content by the Kjeldahl method, calculated by multiplying the total nitrogen by a factor of 6.38.

Sample of blood plasma was sent to B.E.T. Laboratories for analyses of cortisol, triiodothyronine (T3), and total and free thyroxine (T4) levels. The level of prolactin, which would be interesting for this case, could not be measured due to an absence of laboratories that perform this analysis in the country.

Twenty days after treatment onset, the mare was reevaluated and a significant decrease in the volume of the udder and the amount of secretion produced was found, and its aspect was clearer (serous) and consisted of more fluid compared with the one collected before treatment.

3. Discussion

The results of the assessment of mammary secretion were fat content between 0.8% and 0.9% and CP content between 1.5% and 1.6%. These results are similar to the values reported for equine milk obtained from Brazilian breeds animals during the lactation period, in which the amount of fat ranged from 0.86% to 1.70% and CP content between 1.48% and 2.40% [11,12].

In hormonal evaluations, the results were 46.0 ng/dL for cortisol, 1.15 ng/dL for total T3, 16.1 ng/dL for total T4, and 0.55 ng/dL for free T4. The value of free T4 (0.55 ng/dL) appeared below the normal range considered for the equine species (1.76 ng/dL until 4 ng/dL) [13-15]. However, hypothyroidism in horses cannot be diagnosed by a single measurement of T3 and T4 and must be based on one of the thyroid gland stimulation tests [16].

The concentration of circulating iodothyronine can be influenced by many factors not related to the thyroid, including food deprivation [16-18], phenylbutazone administration [16,19,20], circadian rhythm [14,16], and dietary composition [16,21,22]. As women [23,24], rats [25], cows, and sheep [26,27] have a state of relative hypothyroidism during lactation, with levels of circulating T3 and T4 significantly lower [28], this condition may explain the decrease in circulating T4 in the mare of this case report.

Thyroid hormones modulate the secretion of other hormones that regulate the mammary function and milk ejection, thus exerting an indirect regulation of the mammary gland. Hypothyroidism is often associated with galactorrhea in nonpregnant women, and in female virgin rats under experimentally induced hypothyroidism, it is known to be related to mammary development. All these phenomena are associated with hyperprolactinemia because of the hypothalamic secretion of thyrotropin-releasing hormone (TRH) induced by hypothyroidism. In addition to stimulating the secretion of pituitary thyroid stimulating hormone, TRH is a potent stimulator of prolactin secretion [25,28].

Prolactin is a single chain peptide hormone secreted by lactotrophs cells located in the adenohypophysis [29,30]. It is essential for all stages of mammary gland development and regulates the production and secretion of milk, including protein synthesis, as casein and α-lactalalbumin [1,4,31]. Its secretion is regulated by dopamine, the main prolactin inhibitor factor produced by hypothalamus [1,31]. The stimulatory signal for prolactin secretion may be

![Fig. 1. Swelling of the udder and spontaneous milk ejection.](image-url)
mediated by TRH, vasoactive intestinal peptide, and prolactin-releasing peptide [30]. The connections between the hypothalamus and pituitary are critical in maintaining the physiological secretion of prolactin, and any malfunction of the pituitary leads to the loss of inhibition by dopamine and consequent hyperprolactinemia [3,32].

In women, increased prolactin levels present in cases of pathological hyperprolactinemia result in effects equivalent to those observed during the postpartum period, with inhibition of gonadotropin-releasing hormone from the hypothalamus and subsequent inhibition of follicle-stimulating hormone and luteinizing hormones. This results in suppressed gonadal function and promotion of lactation, which explains why hyperprolactinemia is one of the most common causes of anovulation. In severe cases of hyperprolactinemia, galactorrhea and abnormal cycles are often observed, whereas mild cases may be associated with a short luteal phase, decreased libido, and anovulatory infertility [30].

In the present study, the reproductive examination of the mare showed no signs of dysfunction of the reproductive tract. The presence of a corpus luteum indicates cyclicity. However, because there was no possibility of the follow-up of two consecutive reproductive cycles, we cannot exclude that the mare did not have reproductive disorders.

Hyperprolactinemia, secondary to Cushing disease, was ruled out by the absence of clinical features of this syndrome, such as hirsutism, hyperhidrosis, lameness, lethargy, polyuria, polydipsia, weight loss, or redistribution of adipose tissue [33]. Regardless of its low sensitivity, a serum cortisol evaluation was performed in this study, and the values were considered normal for adult horses [15].

In approximately 30%-40% of women with hyperprolactinemia and galactorrhea, no tumors in the hypothalamic-pituitary axis were detected. In such cases, the disease was classified as idiopathic [30]. Similar to this statement, we did not identify other clinical alterations or diseases associated in this mare. Therefore, we propose the diagnosis of idiopathic inappropriate lactation.

In the literature, there are few reports of therapeutic options for the treatment of inappropriate lactation in mares. The drugs mentioned are dopaminergic agonists used to treat hyperprolactinemia in humans, such as bromocriptine, cabergoline, and quinagolide [30]. In this study, we chose oral bromocriptine because of its lower cost.

Bromocriptine was the first dopamine agonist to be widely used in the treatment of hyperprolactinemia in humans [32]. This ergot alkaloid is also used for the treatment of prolactinomas or other micro- or macroadenomas of the pituitary gland, in cases of menstrual disorders, and in Parkinson disease. In equine medicine, it is used for treating Cushing disease [34]. The mechanism of action is by its binding to dopaminergic receptors (D2) on the surface of the lactotrophic cells in adenohypophysis, reducing the activity of adenylyl cyclase and inhibiting prolactin secretion [30,32,34].

Bromocriptine is well established as a safe and effective therapy [30,35,36]. However, its dosage, efficacy, and side effects are not well defined in the mare [1,37]. There is no basic information on pharmacokinetics of bromocriptine in horses, and the use of oral formulation in this species has not been reported yet [34]. The administration of bromocriptine at a dose of 0.08 mg/kg, b.i.d, intramuscularly, in ponies during the final third of gestation period caused a reduction in plasma levels of prolactin and progesterone and induced clinical signs similar to those observed in pregnant mares intoxicated by the fungus Acremonium coenophialum in fescue pastures [1,37].

Bromocriptine in this case report provided a rapid remission of clinical signs. However, the milking interruption may have contributed to the early resolution of this case, with consequent inhibition of the reflex that leads to the release of oxytocin by the posterior lobe of the pituitary gland [1,31].

4. Conclusions

In this case, no apparent clinical disorders or associated diseases were identified; therefore, we suggest the diagnosis of idiopathic inappropriate lactation for the mentioned animal. The treatment with bromocriptine at a dose of 0.04 mg/kg, b.i.d, orally, for 10 days, associated with local hydrotherapy and not milking provided rapid improvement of clinical signs and resolution of the inappropriate lactation, without the occurrence of side effects. The protocol proposed was effective in the case reported and can be considered as a therapeutic option for the treatment of idiopathic inappropriate lactation in mares.

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References

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