Anovulatory Cycles

Lisa Metcalf, MS, DVM, DACT

Take Home Message: In the mare, the prediction of an ovulatory follicles is often challenging. Although their etiology remains largely unknown, appropriate management of mares predisposed to anovulatory cycles may decrease their incidence.

Author’s address—Honahlee, PC, 14005 S.W. Tooze Road, Sherwood, OR 97140; e-mail: honahlee@imagina.com

I. INTRODUCTION

Anovulatory cycles in the mare present a source of substantial reproductive inefficiency and economic loss to the equine breeding industry. These nonproductive cycles are enormously frustrating to both breeders and veterinarians. Not only are time and mare management costs lost when a mare fails to ovulate, but valuable semen and the expense associated with its attainment, processing and handling may also be incurred as well. Thus, prediction, prevention and treatment for anovulatory cycles would be of great benefit to the horse breeding industry.

II. PREDISPOSITION

Anovulatory follicles are commonly encountered in mares that are undergoing transitional cycles in both the spring and fall, at which time they are considered to be a normal physiological event. Additionally, the development of anovulatory follicles may occur occasionally during the breeding season, but are more commonly seen in older mares. The author has also found anovulatory cycles to be common in mares with pituitary dysfunction as well as in mares that are in high levels of competition. Overall, the incidence of an ovulatory cycles has been reported to range between 5-25%. Anovulatory follicles appear to be unresponsive to available ovulation induction agents, and their persistence may increase in estrous interval. It is in teresting to note that, in a given breeding season, affect ed mares te nd to ovulate significantly different between mares with normal ovulations and those with anovulatory cycles.

III. DIAGNOSIS

The ultrasonographic appearance of anovulatory follicles suggests that they have different forms and perhaps develop from different etiologies. Anovulatory follicles may appear as hemorrhagic anovulatory follicles (HAFs), wherein the antrum of the preovulatory follicle fills with blood and fails to reorganize appropriately. Hyperchoic flecks of fibrin or webs of fibrin strands often become visible as the follicle remodels. In these anovulatory follicles, the follicular wall also appears hyperchoic on ultrasound examination, as it lu teinizes and is capable of prostoglandin secretion. Especially in mid-late diestrus (8-14 days post formation), this type of HAF may ultimately undergo luteolysis in response to prostaglandin (PG) administration, or serial PG injections over several days, or it may regress spontaneously, but an increased interestrus interval is not uncommon. Interestingly, the use of PG analogues early in diestrus has also been reported to be associated with development of this type of HAF, possibly due to a premature increase in LH levels during a follicular wave.

Anovulatory follicles may also appear as cyst-like preovulatory follicles that grow to disproportionate size and persist for subsequent estrous cycles, hence termed persistent anovulatory follicles (PAF). Lastly, similar to developments occurring during the vernal transition period, dominant anovulatory follicles may simply regress instead of proceeding to ovulation.

Endocrine profiles, ovarian and follicular blood flow, as well as the expression of ovarian angiogenic factors have been examined to determine their potential relationship, if any, with anovulatory cycles. Gint her et al examined progestrone, estradiol, luteinizing hormone and follicle stimulating hormone and reported that the only difference between mares with ovulatory vs anovulatory cycles, was an elevation in estradiol levels 3 days prior to ovulation in anovulatory cycles compared to ovulatory cycles. Ex amining an additional periovulatory hormones associated with ovulation regulation, Metcalf and Roser concluded that estradiol levels were found to be significantly different between mares with normal ovulations and those with anovulatory cycles.
Ovarian anovulatory follicles have also been compared. Ginther et al. found that at the follicular wall of anovulatory follicles demonstrated a lesser degree of vascularization 1 day prior to ovulation in comparison to follicles undergoing successful ovulation. In another study, ovarian cell populations were examined with immunohistochemistry for expression of vascular endothelial factor. The researchers concluded that, despite the apparent expression of sufficient VEGF-A in the anovulatory follicles to allow ovulation and corpus luteum formation, there was a lack of the receptor, Flk-1, which affects the pro-angiogenic activity of VEGF-A, which could be a reason for ovulation failure associated with HAF formation.

Researchers have also compared follicular fluid components of equine ovulatory and anovulatory follicles during the physiological breeding season to anovulatory follicles in seasonally anestrous mares in attempt to further understand mechanisms in anovulation. Donadeu and Watson reported reduced vascular endothelial factor levels of progestins, testosterone and IGF-1 in anestrous follicles in comparison to estrous follicles, which are likely a result of reduced gonadotropin stimulation at that time of year. In a more recent study, Donadeu and Schauer further disclosed that microRNA expression differed significantly between follicular fluid obtained during the ovulatory and anovulatory seasons; although the significance of this finding is not yet understood, the results may be used to further elucidate the mechanisms involved in follicle maturation and ovulation.

IV. PREVENTION

To date, there are no proven treatments for the prevention of anovulatory cycles. However, one may perhaps lessen the chance of their occurrence in mares with a history of anovulation by:

1. Avoid breeding during seasonal transition periods.
2. Limit the use of PG in early diestrus.
3. Limit the use of drugs that inhibit secretion of PG in the periovulatory period.
4. Treat underlying metabolic and endocrine disease.
5. Track follicular perfusion of the dominant follicle in the periovulatory period.
6. Consider the use of dopamine agonists, a dopaminergic antagonist, during estrus.

V. CONCLUSION

Despite the results of the studies presented, the exact cause of anovulatory follicles is still unknown and reliable prediction remains elusive. Furthermore, not only do the underlying follicular processes that generate maturation of the follicle differ between ovulatory and anovulatory follicles, the mechanisms that generate different forms of a follicle may not be the same. An interesting area of research may lie with a potent GnRH secretagogue, kisspeptin, and its effect on follicle maturation, although current research does not support its direct effect in ovulation induction.

VI. REFERENCES

7. Metcalf ES, Roser JF. The relationships between prolactin and cortisol levels and the formation of an ovulatory follicle in the mare. Anim Reprod Sci 2010;121s:54.