Obtaining 9,200 litres of milk from an unmated heifer: the effects of an ovarian granulosa thecal cell tumour diagnosed using an anti-Mullerian Hormone (AMH) assay

A. GUNN1,2, J. READER2

1 SAVS, and the Graham Centre for Agricultural Innovation, Charles Sturt University, Wagga Wagga, NSW, Australia. (Corresponding author algunn@csu.edu.au)
2 Synergy Farm Health, Evershot, Dorset, UK.

INTRODUCTION

Typically, lactogenesis occurs as a result of the endocrinological status associated with pregnancy and parturition in the cow1. The reproductive steroid hormones induce allometric mammary growth: oestrogen for ductal growth, and progesterone for lobulo-alveolar growth. Lactogenesis requires the factors, growth hormone (GH) and prolactin (PRL), as it does not occur when animals are hypophysecomised. Other growth factors such as thyroid hormone, insulin-like growth factor one (IGF-1), transforming growth factor alpha (TGFalpha) and epidermal growth factor (EGF) play undetermined roles in lactogenesis and galactopoeisis. TGF beta was found to be both inhibitory and stimulatory in cattle mammary cells in vitro depending on dose. 2 Galactopoeisis is the maintenance of milk production which is a poorly understood phenomenon. A combination of factors including growth factors, lack of inhibition (feedback inhibitor of lactation (FIL)), and the effects of apoptosis on mammary secretory cells 3 contribute to the maintenance of lactation. Pregnancy and suckling, or milk removal, are the physiological drivers of lactogenesis and galactopoeisis.

Although rare, ovarian granulosa thecal cell tumours (GTCT) are the most commonly reported tumour in the reproductive tract of the cow4-6. Definitive diagnosis of a GTCT is via histopathology, with varying histological patterns of GTCT’s reported6. Ante-mortem signs rely on a combination of history, clinical signs, and hormonal assays to diagnose the tumour. In mares, testosterone and inhibin assays 7 have been utilised to enhance ante-mortem diagnosis. More recently anti-mullerian hormone (AMH) has been used as a highly sensitive and specific assay in both the mare8, 9 and the bovine10, 11. 

Lactogenesis in the absence of pregnancy is not commonly reported. It has been anecdotaly reported in fillies, and in a ewe with GTCT12. There are several reports of transient lactogenesis associated with GTCT in dairy cattle13-15, and in dairy cows transported by boat16. Induction of lactation has also been reported in cattle using various hormonal protocols17-19. To the authors’ knowledge, this is the first report of lactogenesis and galactopoeisis in an unmated heifer that was not iatrogenically induced to lactate. A GTCT was diagnosed in the heifer based on her history, clinical signs and AMH assay results. The hormonal status of the putative GTCT is likely to have been the cause of lactation, with galactopoeisis occurring as result of continued harvesting of milk.

CASE REPORT

History

A 15 month old Friesian/Holstein heifer was presented with an enlarged udder at a routine herd health visit. She had not previously shown signs of oestrus, and had not been inseminated.

Clinical Examination

The animal was in a body condition, and size expected for her age and breed; and was bright, alert and responsive. Remarkable aspects of the clinical examination were a distended udder, with milk-like fluid being ejected from all of the teats. There was no sign of mastitis. There were no vulval or perineal signs consistent with recent parturition, or structural abnormalities of the external genitalia. Per rectum palpation and ultrasonogrophy of the reproductive tract revealed a uterus consistent with not having been gravid, a large right ovary approximately 6 cm in diameter, with variable ultrasonographic echogenicity. The left ovary was small, less than 2cm diameter with no follicular or luteal activity detected.

Based on the clinical examination and history, a putative diagnosis of a GTCT was made. The owners were offered further (endocrinological profile, biopsy) options to confirm the diagnosis, which was declined at the time. As the heifer was lactating, it was suggested they milk her to determine the success of lactation. Initially her daily milk yield was approximately 5-8 L. With continued twice daily milking this increased, and she was reported to have produced approximately 9,200 L up to January 2014 (approximately 13.5 L milk/day over a 665 day lactation). From late 2013 she started showing frequent and intermittent signs of oestrus, and had become intractably lame probably as a result of the continual oestrus activity. Her milk yield decreased to 12 L/day, and the owner decided to cull her.
Endocrinological Assay

In January 2014, prior to culling, the animal was re-examined. She was in good body condition, and had signs consistent with oestrus. A per rectum ultrasonogram confirmed an enlarged (approximately 8cm diameter) and irregularly echogenic right ovary. A blood sample taken at the time was assayed for Progesterone (P4): 1.8 nmol/l (0.56 ng/ml); Testosterone (T4): 0.35 nmol/l (0.1 ng/ml), and Anti-Müllerian Hormone (AMH): >20ng/ml. Based on these results assaying for Inhibin and Oestradiol was deemed unnecessary.

AMH is reported to be a reliable and sensitive biomarker of GTCT when the level is greater than 0.36 ng/ml\[^{11}\]. Histopathology is the definitive diagnostic means for diagnosing GTCT, but the ovaries were not able to be recovered after slaughter. A blood AMH value of >20ng/ml, in association with her clinical findings, supports a diagnosis of GTCT in this heifer.

**DISCUSSION AND CONCLUSION**

Based on previous reports of heifers with lactogenesis and the presence of a GTCT\[^{13, 15}\], it is a reasonable assumption that this heifer’s lactation was a result of the clinically and endocrinologically diagnosed GTCT. The continued lactation, galactopoeisis, is likely to be as a result of the continued harvesting of milk from the mammary gland, thereby removing feedback inhibitors of lactation present within the intramammary milk.

Lactogenesis is speculatively due to the hormonal milieu induced by the steroidogenically active tumour, probably due to secreted oestrogens. A similar reason was proposed by experts consulted on the likelihood of pregnant animals lactating whilst being transported by boat from Australia to Asia\[^{16}\], where oestrogenic compounds such as zearalenone were present in the feed. A similar high oestrogen scenario occurs during iatrogenic lactation induction\[^{17-19}\]. It is interesting to speculate as to the effect that TGF’s, of which AMH is one, may have in lactogenesis in cattle with a GTCT.

There are reports of pregnancy occurring after removal of GTCT’s, resulting in galactopoeisis post calving.\[^{20-24}\] However, this is the first reported case of a virgin heifer, in the genus *Bos*, that has undergone galactopoeisis without being iatrogenically induced to lactate.

**REFERENCES**


Palmer CW, Clark EG, Carruthers TD. Monitoring Return to Cyclicity Following Removal of...


