

Case Report Rapport de cas

Precocious mammary development in an 8-month-old Holstein heifer

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Abstract – An 8-month-old, virgin Holstein heifer with precocious mammary development was presented for examination. Protein, fat, and lactose in the mammary secretion were 14.90%, 0.12%, and 0.20%, respectively; somatic cell count was $3.9 \times 10^6/\text{mL}$, with no bacterial infection. The heifer was inseminated at 15 months of age, confirmed pregnant, and subsequently slaughtered.

Résumé – Développement mammaire précoce chez une génisse Holstein âgée de 8 mois. Une génisse Holstein vierge, âgée de 8 mois, a été présentée pour développement mammaire précoce. La sécrétion mammaire contenant 14,90 % de protéine, 0,12 % de graisse et 0,20 % de lactose. Le compte des cellules somatiques était de $3,9 \times 10^6/\text{ml}$ et il n'y avait pas d'infection bactérienne. La génisse a été inséminée à l'âge de 15 mois et abattue après confirmation de gestation.

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A virgin Holstein heifer, first observed to have precocious mammary development at 8 mo of age, was presented for examination at 10 mo of age. The heifer weighed 305 kg, measured 119 cm tall at the shoulder (Figure 1), and was receiving a ration of Timothy grass silage + 4 lb grain mix, with ad libitum access to alfalfa hay, water, and minerals.

Case description

Physical examination revealed normal rectal temperature (38.1°C), heart (58 beats/min) and respiratory (36 breaths/min) rates. The udder appeared distended (Figure 1; inset), had a consistency similar to that of a lactating gland, and was 23-cm deep, with the teats measuring 5 cm in length. Upon hand-stripping, a pale yellow secretion with skim milk-like consistency was readily expressed from all 4 teats. The secretion was collected aseptically with no preservatives, chilled on ice, and delivered to the Central Milk Testing Laboratory in Edmonton, within 3 h of collection, for compositional and bacteriological analyses. The concentrations of protein, fat, and lactose, and the somatic cell count were determined by using a midinfrared analyzer (MilkoScan 605; A/S N Foss Electric, Hillerod, Denmark).

A granulosa cell tumor was suspected, and the reproductive organs of the heifer were examined by transrectal palpation. The left ovary was easily palpable and enlarged, with an estimated diameter of 8 to 9 cm. The surface of the left ovary was smooth with no distinct palpable follicles or corpus luteum.

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Figure 1. The 10-month-old nonpregnant Holstein heifer with precocious mammary development. The size of the mammary gland and teats resemble that of an adult lactating gland (inset).

The right ovary was very small (1 cm in diameter) and smooth with no palpable structures. The uterus was of normal size for a 10-month-old heifer, and remained flaccid at palpation. Transrectal ultrasonography was performed 4 wk after the 1st transrectal examination with a real-time ultrasound scanner equipped with a 7.5 MHz linear array transducer (Aloka 500V; Aloka, Tokyo, Japan). At this time, the size of the left ovary was determined to be 3.5×5.0 cm, with a highly echogenic structure resembling that of luteal tissue and containing multiple fluid-filled pockets. This tissue mass appeared distinctly different from that of a normal corpus luteum in that multiple small pockets of anechogenic areas were dispersed throughout alongside a large multi-lobular central cavity. The right ovary measured 2.0×1.0 cm. The uterine horns measured 1.5 cm in

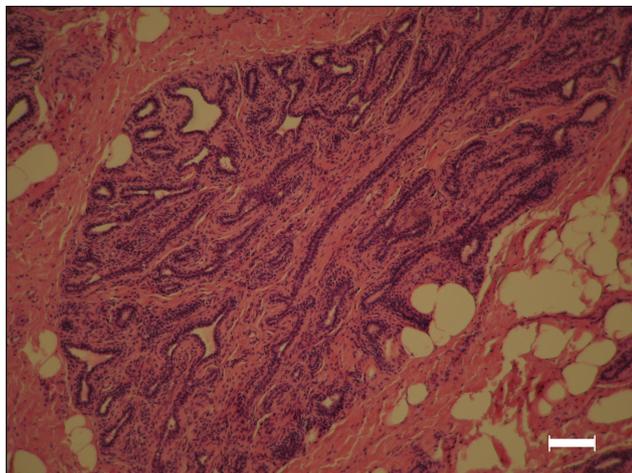


Figure 2. Microscopic section of the mammary gland from the heifer with precocious mammary development. Tissues were collected at slaughter (17 months of age). Alveoli resembled that of a nonlactating gland. Bar = 0.10 mm.

diameter and no fluid was present. The cervix appeared to be normal and was 4.0 cm long. At this time, a blood sample was collected from the coccygeal vein into an evacuated tube containing sodium heparin; plasma was harvested by centrifugation ($1500 \times g$, 20 min) for estradiol, progesterone, and prolactin analysis. Changes in the ovarian structures of the heifer were monitored by repeated transrectal ultrasonography, performed at approximately 2-wk intervals. Progressive regression of the structure was observed at each examination and the abnormal ovarian structure eventually disappeared over a period of 8 wk. However, the size of the mammary gland remained unchanged during this period. Approximately 5 mo after the precocious mammary development was 1st observed, the heifer was reported to be in estrus, following which ovulation and the development of an apparently normal corpus luteum on the right ovary were confirmed. At 15 mo of age, the heifer was placed on a controlled breeding protocol consisting of gonadorelin acetate (Fertiline; Vetoquinol Canada, Lavaltrie, Quebec), 100 μ g, dinoprost tromethamine (Lutalyse; Pfizer Animal Health, Orangeville, Ontario), 25 mg, and gonadorelin acetate, 100 μ g, given IM on Days 0, 7, and 9, respectively, and artificially inseminated 18 h after the 2nd gonadorelin treatment. Pregnancy was confirmed by transrectal ultrasonography 32 d after insemination. At this time, the herd manager did not wish to retain the heifer, fearing poor milk production; therefore, she was removed from the herd and sent for slaughter at 17 mo of age.

At slaughter, the reproductive organs were examined for any abnormalities. The ovaries were apparently normal. The left ovary, where the large cystic structure had been present, contained a corpus luteum and a large follicle; whereas, the right ovary had only very small follicles. The fetus was removed and examined macroscopically. No visible fetal anomalies were evident. The mammary gland did not appear to have changed in size. Ovarian and mammary tissue samples were sent to a veterinary pathology laboratory for histological examination. Sections of the ovary ipsilateral to the pregnant uterine horn revealed 1 large corpus luteum and several follicles. Mammary tissue

Table 1. Composition of the mammary secretion and plasma hormone concentration of the virgin Holstein heifer with precocious udder development

Composition of mammary secretion	Concentration	Normal range
Protein (%)	14.92	3.1 to 3.5
Fat (%)	0.12	3.3 to 4.0
Lactose (%)	0.20	4.6 to 4.9
Somatic cell count ($\times 10^6$ /mL)	3.9	0.1 to 0.4
Plasma hormone		
Progesterone (ng/mL)	1.6	0.5 to 14.0
Estradiol (pg/mL)	1.0 ^a	2.0 to 16.0
Prolactin (ng/mL)	2.1	20 to 40

^a This value is lower than the detection limit (2.0 pg/mL) of the assay

had mild multifocal interstitial infiltration by lymphocytes and plasma cells, and the gland appeared inactive with little secretory tissue (Figure 2). Based on the initial description of the enlarged udder, the condition was suspected to be fibroadenomatous hyperplasia of the mammary gland, which occurs most commonly in cats (1,2) and, occasionally in humans (3). In those species, the condition may involve 1 or more mammary glands, and enlargement occurs due to rapid proliferation of mammary duct epithelium and stroma (4). In the present case, however, the microscopic findings were not consistent with fibroadenomatous hyperplasia, as sections of the mammary gland revealed the normal microscopic anatomy of a nonlactating gland.

The mammary secretion had a freezing point of -0.568°C , was high in protein, low in fat and lactose, and had a very high somatic cell count (Table 1). The standard plate bacterial count was fewer than 3000 cfu/mL. No evidence of mastitis due to bacterial infection was present. Estradiol was undetectable in plasma; whereas, the concentrations of progesterone and prolactin were within normal ranges (Table 1).

Discussion

Precocious mammary development in heifers has been associated with neoplasms of the ovary (5,6) and zearaleone toxicosis (7). To our knowledge, there are only 2 reported cases of precocious lactation in heifers and both were associated with granulosa cell tumors (5,6). In this case, a granulosa cell tumor was suspected initially, based on the history of udder development and enlarged size of the left ovary on palpation per rectum.

In cattle, estrogen stimulates mammary duct growth, and a combination of estrogen and progesterone synergistically stimulates lobulo-alveolar development of the mammary gland (8). Estrogen and progesterone can also induce lactation in nonpregnant cattle (9). In 1 of the previously reported cases in which precocious mammary development and lactation were associated with granulosa cell tumor, serum concentrations of estrogen and progesterone were 1446 pg/mL and 5.6 ng/mL, respectively, prior to tumor removal (5). Hormone concentrations were unremarkable in the other study (6). Although clinical signs similar to those reported previously (5,6) were observed in the present case, granulosa cell tumor was ruled out, as the ovarian structure regressed spontaneously over time. There is no report of spontaneous regression of a granulosa cell tumor in cattle, making it highly unlikely that this was a case of granulosa

cell tumor. Estrogen concentrations are usually elevated in active follicular cysts (10), whereas serum progesterone concentrations are in the range of 0.1 to 2.0 ng/mL (11). In the present case, the serum concentration of estrogen was lower than the detectable limit of 2.0 pg/mL for the assay used, but the progesterone concentration was within the reported range for cows with follicular cysts. Considering the large amount of what appeared to be luteal tissue in the ovary, the measured progesterone was lower than expected. It is suspected that the abnormal structure in the ovary may have started as a persistent follicle, developed into a follicular cyst with active production of estradiol, and then luteinized progressively. This led to a decline in estrogen concentrations by the time the only blood sample was taken, approximately 12 wk after the increased mammary development had been observed by the farmer. Although normal variations in estrogen and progesterone concentrations associated with estrus cycles do not usually induce mammary gland growth in heifers (12), high concentrations of estrogen and progesterone over a sustained period can induce mammary development (13). Follicular cysts are relatively less frequent in heifers than in lactating dairy cows; in the present case, it is speculated that estrogen produced at an early stage and progesterone produced by subsequent luteinization of the cyst likely induced mammary gland growth and associated secretions.

In 1 of the other cases of precocious mammary development and lactation in a heifer (6), fat and protein content of the mammary secretion was normal for milk. Prolactin acts synergistically with insulin and cortisol to induce secretion of milk proteins (14). Even in the absence of insulin and cortisol, prolactin can induce the expression of milk protein mRNA (15). The heifer in this case may have been producing large amounts of prolactin accounting for the high protein content in the mammary secretion (Table 1), but this is unlikely, as the concentration of prolactin was lower than the 20 to 40 ng/mL range reported for normal cycling heifers (16). So, it is not clear as to what contributed to the unusually high protein content of the mammary secretion. The somatic cell count was almost 10 times greater than the accepted limit (Table 1), which is similar to what was observed in the case reported by Palmer et al (6). The cause of this increase in somatic cell count is unknown, as it was not associated with a mammary infection.

The present case is unique in that the mammary development and secretion occurred in the absence of neoplasia or toxicosis. The heifer became cyclic after spontaneous regression of the abnormal ovarian structure and eventually became pregnant following artificial insemination. Though we could neither confirm the present case as an ovarian cyst nor find any literature associating ovarian cysts with precocious mammary development

in cattle, this etiology cannot be ruled out. We conclude, based on the observations in the present case and that available in literature (6) that pregnancy establishment is not necessarily impaired in heifers with precocious mammary development. Whether such heifers will have a normal lactation following a full-term gestation and calving is not known.

Authors' contributions

Both authors were involved in the case study and the manuscript preparation.

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