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Precocious Udder In A Pre-Weaned Jersey Calf: A Novel Paradigm

Ankit Ahuja[1], Amit Sharma[2], Deepti Sharma[3], Surender Kumar[1], Pankaj Sood[2]

[1]Department of Veterinary Clinical Complex, Dr. G. C. Negi College of Veterinary and Animal Sciences, C. S. K. Himachal Pradesh Agriculture University, Palampur, Himachal Pradesh, India

[2]Department of Veterinary Gynaecology and Obstetrics, Dr. G. C. Negi College of Veterinary and Animal Sciences, C. S. K. Himachal Pradesh Agriculture University, Palampur, Himachal Pradesh, India

[3]Department of Veterinary Surgery and Radiology, Dr. G. C. Negi College of Veterinary and Animal Sciences, C. S. K. Himachal Pradesh Agriculture University, Palampur, Himachal Pradesh, India

ABSTRACT

Precocious udder implies galactopoietic mammogenesis in pre-pubertal heifers that is not associated with the process of calving. A pre-weaned Jersey female calf was presented with complaints of udder development and milk secretion. Calf was primarily fed dam's milk along with a few chunks of mulberry leaves (Morusalba) as fed to the mother. The udder was distended on palpation. A 6.8 cm vaginal length with a thin dorso-ventral muscular band (hymen) cranial to urinary meatus was unveiled in vaginoscopy. Trans-rectal ultrasonography revealed a normal tubular genital tract with non-palpable ovaries. Multiple anechoic pockets with the lower gland cistern containing a largely dispersed central anechoic cavity indicating a developed mammary gland were revealed during udder ultrasonography. The plasma progesterone level in calf was below 1 ng/ml indicating no luteal activity. Considering the steroidogenic activity of mulberry due to the presence of flavonoids, the owner was advised to discontinue its feeding to dam as well as the calf together with complete milking-out of the calf's udder. On reappraisal after four weeks, the udder showed atrophy with no secretion. Since a negligible amount of mulberry leaves was consumed by the calf, it is more likely that the estrogenic effects were indirectly delivered through the dam's milk. Mulberry leaves flavonoids present in the dam's milk have probably triggered the cascade of udder development in the calf. This is the first report of precocious lactation in a pre-weaned Jersey calf with estrogenic diet supplementation to the dam as the most plausible explanation for its development. Additionally, a primer bonafide review on the subject has also been comprehensively signed.

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CORRESPONDING AUTHOR:
Ankit Ahuja

E-MAIL ID:
ankit.ahuja1947@gmail.com

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INTRODUCTION

Early/premature/spontaneous are often used synonymously in conjunction with lactation / udder development to represent precocious udder, which denotes atypical udder transformation. Precisely, precocious udder implies galactopoietic mammogenesis in pre-pubertal heifers which is not associated with the process of calving [1]. Structural and endocrinal development of the mammary gland begins around puberty. Interplay of steroid hormones like estrogen and progesterone causes alveolar and ductal growth. Lactogenesis which marks the process of mammary alveolar cell differentiation, owing to which they gain the capacity to secrete milk, is physiologically driven by pregnancy. However incessant suckling or milk removal sustains the galactopoietic pathway that is the production of milk by the mammary glands [2].

Chronic treatment with estrogen alone, in conjunction with progesterone or estrogen after progesterone also induces lactation to some extent [3]. Hormonal disparities especially estrogen plus vague impetuses like suckling or milking also triggers udder development [1].Estrogen secreting ovarian tumor preferably granulosa cell tumor (GCT) and supplementation of feed contaminated with the mycotoxin zearalenone, a non-steroidal estrogenic mycotoxin produced by Fusarium fungi, are the main causes of precocious udder. However in the literature there is no report of precocious mammary development in heifers due to estrogenic diet supplementation moreover in majority of reported cases granulosa cell tumor was the main aetiology [4, 5, 6, 7]. The present article puts forth a novel case of the precocious udder in 40-day old Jersey crossbred calf along with a literary review of the subject in bovines.

CASE DESCRIPTION AND EXAMINATION

A Jersey female calf was presented in Advanced Multispecialty Veterinary Centre, CSK HPKV, Palampur, India with complaints of udder development and milk secretion. The calf was 40 days old, weighed 43 kg, and measured 103 cm tall at the withers (Figure 1). The calf was primarily fed dam's milk along with few chunks of mulberry leaves (Morusalba) as fed to the mother and ad libitum access to water and minerals. The owner noticed the firm mammary gland in calf after birth which started growing and now thin chalky excretion oozes out on milking. Physical examination of the udder revealed distended mammae (Figure 1a; inset) having a consistency similar to that of the lactating gland which was 12.7 cm deep with the teats measuring 1.9 cm in length. The physiological parameters mainly heart rate (58 beats/min), respiratory rate (36 breaths/min), and rectal temperature (100.5 °F) were within the normal range. Upon hand-stripping, a pale-white colored secretion with a skim milk-like consistency was readily expressed from all four teats. The secretion was collected aseptically with no preservatives and the composition of milk constituents was assessed using a mid-infrared analyzer (Automatic milk analyser, Milko Zonic-Rapid-S20, India). Various constituents present in the secretion (%) were fat 4.0, protein 3.0, lactose 4.5, solid not fat 8.2, density 27.9 and salt 0.7. There was no difference between the composition of secretion and milk; rather it fell in the same range.

2.1.Gross and UltrasonographicExamination

Gross vaginal examination using vaginal speculum revealed vaginal length of 6.8 cm with a thin dorso-ventral band in the cranial vagina suggestive of a hymen. Trans-rectal ultrasonography was done by adapting the transducer to a stainless steel bovine cervical dilator (diameter 15 mm and length-24 cm) to favor its manipulation inside the rectum (ImaGo, IMV, France). It revealed normal tubular genitalia with non-palpable ovaries, which cuts the chances of suspecting granulosa cell tumor. Ultrasonography of the mammary gland was performed using a real-time ultrasound scanner equipped with a 7.5 MHz linear array transducer (Fujifilm, Sonosite, USA). The lobular mammary parenchyma at the base of the udder was fully developed containing multiple anechoic trabecular pockets whereas the lower gland cistern enclosed a large dispersed central anechoic cavity (Figure 2a). Udder ultrasonography revealed a developed canal and lobular system (Figure 2b).

2.2. Progesterone Analysis

Blood was aseptically collected via jugular venepuncture in a sterile heparinized vacutainer for plasma progesterone analysis. Plasma was separated by centrifugation and stored at -200C till analysis. Progesterone was estimated by Chemi-luminescence analyzer using Acculite Progesterone kit (Tosoh India Pvt. Ltd.) with sensitivity of 0.105ng/ml. The level of plasma progesterone is <0.5ng /ml, indicative of no luteal activity. This confirms the absence of any functional luteal tissue and hence no cyclicity.

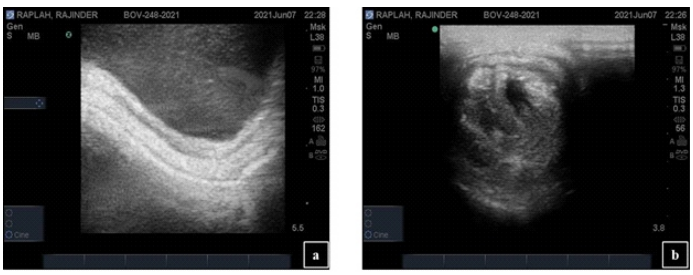
2.3 Case Moderation

Green fodder being fed to the dam and a portion of that being taken by calf are the leaves of the mulberry plant (Morus alba). Considering the steroidogenic activity of the plant, the owner was advised to discontinue the mulberry leaves feeding to the dam as well as the calf. Further, he was advised to completely milk out the calf's udder. On reappraisal, after four weeks the udder showed atrophy with no excretion. The udder seems tenderer in palpation than the firm initially, with no distension. Probably cessation of mulberry leaves supplementation along with milking out the udder has broken off the development cascade for mammary tissue (Figure 1b: inset). At the age of 14 months, the animal behaviorally expressed their first estrus (age at puberty-14 months), and in the third heat, the animal was conceived successfully (confirmed by rectal palpation 60 days later) to artificial insemination. During the third month of gestation, the animal was diagnosed with milder form of Lumpy Skin disease (LSD). Accordingly, she received an intramuscular dosage of 2000mg of amoxicillin plus 1000 mg of sulbactum (Amoxyrum forte; Virbac, India), a combination of 25 lakh IU of Vitamin A, 2.5 lakh IU of Vitamin D3 and 1000 IU of vitamin E (Vitade; Zenex, India), and 50 ml of oral supplementation of liver tonic (Livphoria; Zenex, India). The antibiotic therapy is provided once a day for five days where as the multivitamins are provided once a day at alternate days for four times. The liver tonic is supplemented to the animal for 15 days. The animal has been cured of LSD two weeks after the therapeutics and is now in its second trimester with a healthy and viable fetus. Additionally, there is no udder development and secretion as of now.

FIGURES

Figure 1. *Jersey calf with precocious udder development (a; inset). Udder atrophy after cessation of mulberry leaves feeding, 4 weeks later (b; inset).*

Figure 2. *Lower gland cistern contains a dispersed large central anechoic cavity (Figure 2a). Udder ultrasonography revealed developed canal system (Figure 2b).*



DISCUSSION

The author's literary review suggested scarce reports of the precocious udder in bovines. Most of them were associated with granulosa cell tumor (four out of seven) [4, 5, 6, 7]. Single case studies with sex chord stromal tumor [8]and squamous cell carcinoma [9] were also reported. A single unique report of precocious udder development with idiopathic cause has also been reported [10]. The minimum age in which precocious udder was reported was 8 months however in the present case the age of calf was 40 days (1.3 months). Preliminary report by Short et al [6] depicted GCT along with normal lactation in 2 years 9 months old maiden heifer with left ovarian diameter fanning around 15 cmand elevated hormonal levels in cystic fluids. Likewise, Palmer et al [5] and Tautenhahn et al [7] reported precocious/inappropriate lactation in 11 months and 15-month-old unbred Holstein-Friesian heifer contemporaneously occurring with GCT in right ovary. Follicular activity resumed four weeks post right oophorectomy and the heifer became pregnant to insemination four months later in the former case study. However, Gunn and Reader [4] reported spontaneous lactogenesis and galactopoiesis with evidence of GCT in 15 month old unmated heifer. The animal was having a right ovarian diameter of 8 cm with heterogeneous ultrasonographic echogenicity including the presence of a few small (less than 5 mm) cyst-like structures. They also reported a slightly higher values of testosterone (0.1 ng/mL) and drastically higher (more than 55 times the normal value) concentration of anti-Müllerianhormone (AMH; >20 ng/mL). AMH has been reported to be a reliable and sensitive biomarker of GCT in cattle when concentrations are >0.36 ng/mL[11]. Similar findings were reported by Ambrose et al [10] in an 8 month old heifer having left ovarian diameter around 8 cm with normal blood hormonal concentration ruling out GCT (Table 1). Whitacre et al [8] reported premature lactation in a heifer with the sex-cord-stromal tumor showing granulosa cell like pattern. The animal was having large mass in the abdomen with markedly high concentrations of estrogen and progesterone.

Jha et al [9] also reported a case of squamous cell carcinoma in a heifer associated with persistent lactation, cystic ovaries and mucometra. Ambrose et al [10] reported a unique case of precocious mammary development in an 8-month-old Holstein heifer suspected to be due to GCT initially. However they reported that mammary development and secretion occurred in the absence of neoplasia or toxicosis and the heifer turn out to be cyclic and eventually became pregnant following artificial insemination. In the present case also, precocious lactation occurs in the absence of neoplasia or toxicosis. However, we propose mulberry leaf feeding is the most likely cause. Mulberry leaves are rich in a flavonoid named astragalin, which possesses a unique structural homology with steroid hormones [12]. Mulberry leaves flavonoid (MLF) has been proven to increase the endogenous estrogen and progesterone by inhibiting ovarian granulosa cell apoptosis [13]. They also confer unique antioxidant and antimicrobial properties owing to which it is considered a potential resource for livestock feeding [14]. Traditional Chinese medicines used in the majority of countries for the management of menopausal symptoms also constituteMorusalba leaves and they have proven to increase the levels of endogenous estrogen and progesterone [15]. Considering a negligible amount of Morusalba leaves consumption by the calf (2-3 leaves per day for 15 days), it is more likely that the estrogenic effects were indirectly delivered through the dam's milk (because the dam would have consumed large quantities of the Morus alba leaves). The MLF present in the dam's milk has probably triggered the cascade of udder development in the calf. Hence, the cessation of mulberry leaves supplementation along with no udder massage has broken off the development cascade for mammary tissue in the calf, in the current investigation. A present case study is the only report of precocious lactation in 40 days old Jersey calf, youngest of the all previously reported, with supplementation of estrogenic diet (not reported previously) as the most plausible explanation for its udder development. The low plasma progesterone levels are indicative of no luteal tissue functionality and hence it strongly justifies our hypothesis.

TABLE 1- PRECOCIOUS UDDER IN BOVINE-REPORTS IN VETERINARY LITERATURE

S. No.	Age (months)	Breed	Cause	Outcome	Hormone Profile	Reference
1	45	Holstein Friesian	GCT	Slaughter	Not known	Short et al 1963
2	Unknown	Unknown	Squamous cell carcinoma	Unknown	Not known	Jha et al 1973
3	Unknown	Unknown	Sex chord stromal tumor	Unknown	Markedly high	Whitacre et al 1988
4	8	Holstein Friesian	Idiopathic	Conception and slaughter	Estradiol- 1.0 pg/mL, Progesterone- 1.6 ng/mL, Prolactin- 2.1 ng/mL	Ambrose et al 2008
5	11	Holstein Friesian	GCT	Conception	Estradiol-17β- 9.1 pg/mL, Progesterone- 0.2 ng/mL, Testosterone - 0.01 ng/mL, Prolactin -5.8 ng/mL, LH- 0.14 ng/mL, FSH- 0.32 ng/mL	Palmer et al 2008
6	15	Unknown	GCT	Slaughter	Progesterone- 0.56 ng/mL Testosterone- 0.1 ng/mL AMH- >20 ng/mL	Gunn et al 2015
7	15	Holstein Friesian	GCT	Slaughter	Estradiol- 21.4 pg / ml Progesterone- 0.52 ng / ml Testosterone- 0.01 ng / ml	Tautenhahn et al 2018

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