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Changes in Peripheral Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Inhibin, Estradiol-17β, Progesterone and Testosterone Levels Before and After the Administration of Equine Chorionic Gonadotropin (eCG), Human Chorionic Gonadotropin (hCG) and Gonadotropin Releasing Hormone Analogue (GnRH-A) in Three Cases of Bovine Gonadal Hypoplasia (XY female)

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Abstract. To clarify the endocrinological characteristics of bovine gonadal hypoplasia (XY female), peripheral FSH, LH, inhibin, estradiol-17β (E2), progesterone (P) and testosterone (T) levels were measured before and after the administration of eCG, hCG and GnRH-A in the 3 bovine XY females without the Sry gene. Before the administration of hormonal drugs, the concentrations of FSH and LH were higher than in adult bulls, cows in the luteal phase and castrated bulls. On the other hand, the concentrations of inhibin and E2 were lower than those observed in the follicular phase during the estrous cycle. Concentrations of P and T were much lower than those observed in the luteal phase during the estrous cycle and in bulls. Gonads of our XY females did not respond to eCG or hCG stimulation, whereas the pituitary was highly responsive to GnRH-A in LH secretion.

Key words: Sex hormone profiles, XY female, Bovine.

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levels before and after the administration of equine chorionic gonadotropin (eCG), human chorionic gonadotropin (hCG) and gonadotropin releasing hormone analogue (GnRH-A) in the 3 cases of bovine XY female.

Materials and Methods

Three cases of bovine gonadal hypoplasia (XY female) which were reported previously [13, 14] were used in this study. They were heifer in appearance, and had streak gonads and underdeveloped uteri, and showed no sign of estrus during observations.

Prior to the hormone administration, blood samples were collected and gonadal changes were investigated by transrectal palpation for 23 days. Blood samples were also collected from 5 cows in the luteal phase, 5 bulls and 5 castrated bulls as controls. In all blood samples, the concentrations of FSH, LH, inhibin, E2, P and T were determined by radioimmunoassay (RIA) [11, 22].

Concentrations of immunoreactive (ir-) inhibin in plasma were measured with a rabbit antiserum to purified bovine inhibin (TNDH 1) and 125I-labeled 32 kDa bovine inhibin, as described previously [8]. The intra- and interassay coefficients of variations were 15.5% and 11.4%, respectively. Plasma concentrations of FSH were measured by RIA with anti-bovine FSHβ-subunit serum (UCB bioproduct, S.A. Brainel Alleud, Belgium) and USDA-FSH-BP3 for radioiodination. Results are expressed in terms of USDA-FSH-B1. Plasma concentrations of LH were measured by RIA with anti-ovine-LH (YM18), USDA-bLH-11 for radioiodination and USDA-bLH-B-5 as the reference standard. The intra- and interassay coefficients of variations were 5.5% and 7.6% for FSH and 6.9% and 8.7% for LH, respectively. Plasma concentrations of T, E2 and P were determined by a double-antibody RIA systems with 125I-labeled radioligands as described previously [22]. Antisera to T (GDN#250), E2 (GDN#244) and P (GDN#337) were used in each RIA. The intra- and interassay coefficients of variations were 5.0% and 9.1% for T, 2.7% for E2 and 11.2% and 7.1% for P, respectively.

To determine gonadal response in gonadotropin, 3,000 IU eCG (Serarumon®, Denka Seiyaku Co. Ltd., Kawasaki, Japan) and 5,000 IU hCG (Gonatropin®, Teikoku Hormone MFG Co. Ltd., Tokyo, Japan) were administrated. GnRH-A (Conceral®, Takeda Chemical Industries Ltd., Osaka, Japan) was also administrated to determine the pituitary responsiveness to LHRH. After i.v. administration of 3,000 IU of eCG, blood samples were collected every day for 14 days to determine the concentration of E2. After i.v. administration of 5,000 IU of hCG, blood samples were collected every hour for 12 hours and every day for 8 days to determine the concentrations of P and T. After i.v. administration of 100 µg of GnRH-A, blood samples were collected every 30 minutes for 8 hours to determine the concentration of LH.

Results

Gonadal activity

It was recognized that follicles and corpus lutea did not develop in 23 days by transrectal palpation and ultrasonographic diagnosis.

Changes in plasma concentrations of FSH, LH, inhibin, E2, P and T before the administration of hormonal drugs

Before the administration of hormonal drugs, the plasma concentration of FSH (Fig. 1a) was much higher (111.5 ± 2.8 ng/ml: Mean ± SE) than those of 5 cows in the luteal phase (15.3 ± 1.0 ng/ml), 5 bulls (35.2 ± 4.3 ng/ml) and 5 castrated bulls (45.9 ± 10.0 ng/ml). The plasma concentration of LH (Fig. 1b) also changed to higher levels (1.7 ± 0.1 ng/ml) than those of 5 cows in the luteal phase (0.9 ± 0.2 ng/ml), 5 bulls (1.5 ± 0.4 ng/ml) and 5 castrated bulls (0.8 ± 0.1 ng/ml). The plasma concentration of E2 (Fig. 1c) changed irregularly, sometimes lower levels (1.4 ± 0.1 pg/ml), and sometimes higher (5.2 ± 0.3 pg/ml) than those of 5 cows in the luteal phase (2.5 ± 0.3 pg/ml) and 5 castrated bulls (0.7 ± 0.1 pg/ml). The plasma concentration of inhibin (Fig. 1d) became lower (317.4 ± 23.4 pg/ml) than those of 5 bulls (1062.9 ± 111.2 pg/ml), but sometimes higher than those of 5 cows in the luteal phase (263.8 ± 55.0 pg/ml) and 5 castrated bulls (183.0 ± 37.7 pg/ml). The plasma concentrations of P (Fig. 1e) and T (Fig. 1f) became very low (under 1 ng/ml in P level, under 23.3 pg/ml in T level).

Changes in plasma concentrations of LH, E2, P and T after the administration of hormonal drugs

The plasma concentrations of E2 (Fig. 2) after the
administration of eCG became low (1.5 ± 0.2 pg/ml) for 14 days. The plasma concentrations of P (Fig. 3a) and T (Fig. 3b) did not increase after the administration of hCG and remained very low for 8 days (under 109 pg/ml in P level, and under 18.4 pg/ml in T level). The plasma concentrations of LH (Fig. 4) increased rapidly within 30 minutes after the administration of GnRH-A (11.4–63.2 ng/ml), but had gradually decreased to the basal levels (0.9–1.9 ng/ml) 4.5 hours later.

Fig. 1. Changes in peripheral FSH (1a), LH (1b), E2 (1c), inhibin (1d), P (1e) and T (1f) levels. *not examined. The values obtained from cows in the luteal phase, bulls and castrated bulls are also shown (means S.E.M. for five animals). In the figures, –, –, – and – show the hormonal changes from Case 1, Case 2 and Case 3, respectively.
Discussion

It has been reported that chromosome abnormalities, especially in sex chromosomes are closely related to reproductive disorders in domestic animals [4]. This has been particularly well documented in the case of sex chromosomal chimerisms [17] with absolute sterility, cases of chromosomal translocation [7] with relative sterility and others [16]. As there are only a few papers [1, 6, 10, 20, 21] in which cases of chromosome abnormalities were studied with reference to the levels of gonadotropin and sex steroid hormones, the reasons for abnormal profiles of the hypothalamo-hypophysial-gonadal axis remain unclear. It is therefore very important to clarify the hormonal profiles of such individuals, because of the possible harmful effects of chromosome abnormalities on reproductive performance. Furthermore, these studies will help to understand the endocrinological characteristics of normal animal reproduction.

The present study clearly demonstrates that gonadal function of bovine XY females was in a silent state and did not respond to the administration of eCG, hCG or GnRH-A. Because of low levels of circulating inhibin and steroid hormones, it became also clear that an excess amount of gonadotropins was synthesized and secreted from the anterior pituitary gland in the bovine XY females. The results also suggest that abnormal hormonal control in the hypothalamo-hypophysial-gonadal axis in bovine XY females would affect the time required from the administration of GnRH-A to the peak of the LH surge. That is, the time from the administration of GnRH-A to the peak of LH was 30 minutes and was...
shorter than that of normal females (about 60–120 minutes later) [3]. Probably the reserve of LH in the anterior pituitary gland would be large, because of abnormal production and continuous secretion of LH.

Abdel Malak et al. [1] reported the case of a 61, XXY bull which was azoospermic with testicular hypoplasia and had a high level of circulating FSH. They suggested that the high circulating FSH concentration was probably due to a lack of a gonadal negative feedback which could be generated from the germ cells beyond the spermatogonia. The results of the present study suggest that a high level of circulating FSH in bovine XY females is probably due to the lack of inhibin as shown in man with azoospermia and oligospermia [2, 5, 9, 18]. It is now beyond question that inhibin is a major factor in the regulation of FSH secretion in females.

It was reported by Kaneko et al. [11, 12] that the peripheral E2 levels in bovine were 5–15 pg/ml in the follicular phase and 2–5 pg/ml in the luteal phase. The peripheral E2 levels in XY females in the present study were lower than that observed in the follicular phase during the estrous cycle, and the levels did not change after the administration of eCG. As it was shown that there were some primary follicles in ovarian-like gonads (unpublished data) of the XY females, it seems unlikely that these follicles put a large amount E2 into the circulation in bovine XY females.

In conclusion, the bovine XY females in this study are phenotypically expressed by an early arrest of folliculogenesis which seems to result in enhanced secretion of gonadotropin and decreased secretion of inhibin and steroid hormones. The present findings also demonstrate that gonadal responsiveness to gonadotropins is lacking, whereas the pituitary responsiveness to GnRH is extremely high.

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References


