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Factors affecting the prognosis for uterine torsion: the effect of treatment based on measurements of serum progesterone and estradiol concentrations after surgery

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This is a retrospective study of uterine torsion (UT) in seven mares. In two cases, serum progesterone and estradiol concentrations were also investigated. The mare and foal/fetus survival rate was 57% (4/7). Four cases presented with clockwise torsion, and two cases presented with counterclockwise torsion. The direction was undetermined in one case. The degree of torsion varied. Correction of torsion was performed by ventral midline celiotomy in all cases. In the two cases with measured hormone levels, elevated levels of P_4 were decreased through medication. All mares discharged from the hospital with a live fetus were able to carry a live fetus. Early diagnosis and treatment of UT increases the possibility of helping mares and foals in cases with acute UT.

Key words: *estradiol, mare, progesterone, uterine torsion*

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Uterine torsion (UT) in the mare is an uncommon but life- threatening event for both the pregnant mare and the fetus. Most cases occur in the last 60 days of gestation but before the onset of labor. The underlying cause of UT is unknown; however, vigorous fetal movement, sudden falls, and a large fetus in a small volume of fetal fluid have been proposed as causative factors [13]. Most mares with UT generally present with mild to moderate colic [2, 3, 5, 6]. Rectal palpation is the only way to confirm UT [8]. A variety of nonsurgical and surgical techniques for correcting UT have been described [3–6, 9]. It has been reported that the survival rates of mares and foals/fetuses were 60–90.5 and 30–82.3%, respectively [2, 8, 12, 16].

These reports suggested that the survival rates at <320 days gestation are higher than those at ≥320 days [2, 12]. On the other hand, Shikichi *et al.* suggested that measurements of serum progesterone (P_4) and estradiol (E_2) were useful indicators in management of pregnant mares during late-term gestation [11]. We have also previously suggested that using serum P_4 and E_2 measurements can be useful for pregnancy management after colic surgery. In this report, some high-risk cases were observed in which the P_4 level increased post surgery and then later decreased with medication [10]. There are no reports on the management of pregnant mares using measurement of serum P_4 and E_2 after correction of UT. The purpose of this study was to perform a retrospective study of diagnosis and correction of UT, including 2 cases in which the results of serum P_4 and E_2 measurements were used to manage pregnancy until foaling after correction of UT.

Seven Thoroughbred mares were diagnosed and treated for UT at Hokkaido South Agricultural Mutual Aid Association Mitsuishi Animal Medical Center between 2004 and 2017 (Table 1). The data available included age, fetal age, time from colic, packed cell volume (PCV) and lactic acid at the time of arrival at the hospital, direction of torsion, degree of torsion, survival of the mare, and survival of the

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Table 1. Ages of mares and fetuses, time from the occurrence of colic, packed cell volume (PCV), serum lactic acid concentration (Lac), direction and degree of torsion, and outcome of the treatment

Case No.	Age	Fetal age	Time from colic	PCV (%)	Lac (mmol/*l*)	*Direction of torsion	Degree of torsion	Survival of mare	Survival of foal/fetus
1	6	321	5 days	Not examined	Not examined	Unknown	Unknown	Died	Died
2	15	258	6 hr	40.8	Low	CC	540	Died	Died
3	14	323	2.5 hr	52.7	2.4	C	720	Died	Died
4	12	336	1 days	46.6	1.6	CC	180	Survived	Survived
5	8	253	1 days	51.2	1.2	C	360	Survived	Survived
6	11	329	7 hr	49.2	1	C	180	Survived	Survived
7	5	294	18 hr	36.5	1.3	C	180	Survived	Survived

*: C, clockwise; CC, counterclockwise. Unknown=not record. PCV and LAC represent the values at admission to the referral hospital. Direction and degree were confirmed during celiotomy. Survival of mares and foals/fetuses is indicated as of time of discharge.

foal/fetus. Hormones (P_4 and E_2) were measured by dissociation-enhanced lanthanide fluoroimmunoassay (DELFIA) or chemiluminescent enzyme immunoassay (CLEIA). In the DELFIA method, serum P_4 and E_2 concentrations were directly measured by time-resolved fluoroimmunoassay (TR-FIA) using anti-progesterone and anti-estradiol antibodies. A Progesterone and Estradiol Reagents Kit (Wallac Oy, Turku, Finland) was used according to the manufacturer's protocol with a minor modification as described previously [4, 7]. The antibody against progesterone cross-reacts with 5-dihydroprogesterone (6.5%) and shows <1% cross-reactivity with other progestogens. The antibody against 17β-estradiol cross-reacts with ethinyl estradiol (1%) and estrone (0.75%) and ahoes <1% cross-reactivity with other estrogens; however, it was not possible to test cross-reactivity with equilin and equilenin. P_4 was determined to be abnormal when exceeding 5ng/m*l* until Day 300 according to cutoff values reported by Shikichi *et al*. [11]. In the CLEIA method, serum P_4 and E_2 concentrations in case 7 were directly measured by end-point assay using anti-progesterone and anti-estradiol antibodies. Samples were measured using a PATHFAST kit (LSI Medience Corp., Tokyo, Japan) for progesterone and estradiol as described previously [14, 15]. For progesterone, the assay range of CLEIA was 0.2–40 ng/m*l*. The intra-assay coefficients of variance were 3.61–10.23% for serum samples. For estradiol, the assay range of CLEIA was 20–2,000 pg/m*l*. The intra-assay coefficients of variance were 6.3–12.9% for serum samples. The standard ranges for progesterone and estradiol in CLEIA were calculated as means ± standard deviation (SD) from 21 normal pregnant mares with weekly sampling (unpublished data).

The method used for correcting UT in all seven mares was ventral midline celiotomy. The mares were premedicated with medetomidine, and anesthesia was induced with ketamine and midazolam. The mares were then intubated and positioned in dorsal recumbency. Anesthesia was maintained with isoflurane in oxygen. A routine ventral midline approach into the abdomen was used. The direction and degree of the UT were confirmed by palpation of the uterus and broad ligaments (Fig. 1). Cesarean section was performed after correction of UT in four mares (cases 1, 3, 4, and 6). The mares received ampicillin (3 g/head intravenous [IV] twice daily) and kanamycin (5 g/head IV once daily) for 7 days after surgery. Management of pregnancy using hormone measurements collected several times after correction of UT was utilized in case 5 and case 7. For hormone measurement, the DELFIA method was used in case 5, and the CLEIA method was used in case 7. In both cases, ritodorine hydrochloride (0.1 mg/kg bis in die [BID], per os [PO]), medroxyprogesterone acetate (400 mg/day, PO) and sulphamethoxazole/trimethoprime (ST) (30 mg/kg BID, PO) were administered for maintenance of pregnancy after surgery.

The mean age was 10.1 (5–15) years, and the mean gestational age was 302 (253–336) days. All horses had an episode of colic from 2.5 hr to 5 days before treatment (Table 1). Two mares (cases 1 and 2) died after surgery, and one mare (case 3) was euthanized during surgery due to necrosis of the uterus. Case 1 appeared to have died from hemorrhage at the site of uterine torsion. Case 2 presented postanesthetic myopathy after general anesthesia. The mare recovered from anesthesia and was able to walk to the hospital stable. However, she was not able to remain standing and died 2 days after surgery. Four mares survived. Two foals were delivered and survived following cesarean section (cases 4 and 6). Two foals were delivered with fetal death following cesarean section (cases 1 and 3). Two foals were born alive at farms after the mares underwent correction of UT and were discharged from the hospital (cases 5 and 7). In both cases, hormones were measured before and after surgery, and P_4 was increased compared with the values of normal pregnant mares at the same gestational age. In case 5, the mare was diagnosed and treated for UT at Day 253, and medication for maintenance of pregnancy was administered for 80 days, from Day 255 to parturition.

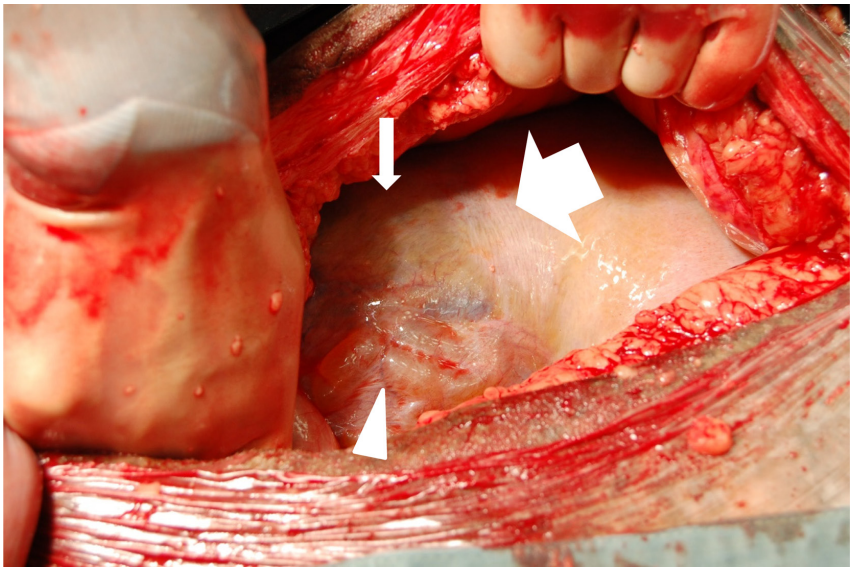

Fig. 1. Distorted uterus at ventral celiotomy in case 7. Gelatinous infiltration (arrowhead), distention of lymphatic vessels (small arrow), and partial cyanosis (large arrow) are seen.

The serum P_4 concentration in case 5 was 8.11 ng/m*l* on Day 253, and it progressively decreased with medication (Fig 2). The serum E_2 concentration in case 5 was 737 pg/m*l* on Day 253, and it generally remained in the normal range (Fig. 2). The mare delivered a normal foal on Day 335.

In case 7, the mare was diagnosed and treated for UT at gestational age 295, and medication for maintenance of pregnancy was administered for 10 days, from Day 299 to Day 309 of gestational ags. The serum P_4 concentration in case 7 was 13.5 ng/m*l* on Day 295, and it momentarily increased, as shown in Fig. 3. The P4 level then decreased with medication (Fig. 3). The serum E_2 concentration in case 7 was 608 pg/m*l* on Day 295, and it decreased on Day 302 (Fig. 3). In previous study, E_2 concentrations were significantly reduced a few day before abortion [1]. However, the mare in case 7 in the present study delivered a normal foal at gestational day 322. Furthermore, E_2 concentrations decrease before foaling in normal mares (Fig. 3). Therefore, the E2 concentration was considered to have decreased within the normal range in Case 7 because it experienced premature delivery.

In this study, the mare and foal/fetus survival rate was 57% (4/7). This result is comparable with those in previous reports [2, 7, 12, 16]. However, in the last four cases, all mares and foals survived, with the surviving mares having delivering live foals. There was no correlation between survival rate and gestational age of the mare in this study. These results showed that rapid diagnosis, rapid treatment, and experience in treating UT increased the survival rates of mares with UT. Because the method for correcting torsion was ventral midline celiotomy in all cases, no information on which UT correction method may be the most effective was available from this study. Previous reports have suggested that mare and foal/fetuses survival rates are higher with standing flank laparotomy than with other methods [2, 12]. However, because all mares and foals/fetus survived in our last four cases, ventral midline celiotomy was considered a good method for correcting UT. The degree of torsion did not affect the survival rate of the mare or foal/feuses in a previous study [2]. However, in cases 2 and 3, the degree of torsion was greater than in other cases, and the mares died. In this study, greater UT was considered to present severe vascular occlusion and uterine tissue damage compared with cases with a lower degree of torsion. Spoormakers *et al.* reported that the survival rates of mares and foals/fetuses were higher with torsion <360° than with more severe rotation [12]. There was no significant difference between the numbers of clockwise and counterclockwise torsion cases in this study. In a previous study, Pascoe *et al.* found that clockwise torsion is more common [8], whereas others reported that counterclockwise torsion is more common [2, 16]. This is similar to results from previous studies [13]. In case 5 and case 7, the P_4 levels were higher than normal values [11]. This was thought to be because the uterus under torsion had decreased blood supply and because the intrauterine environment became acutely worse as necrosis of the uterus progressed. However, elevated levels of P_4 could be decreased with medication for recovery of the uterine condition. The duration of medication was different between cases 5 and 7. Case 7 was treated for UT at gestational

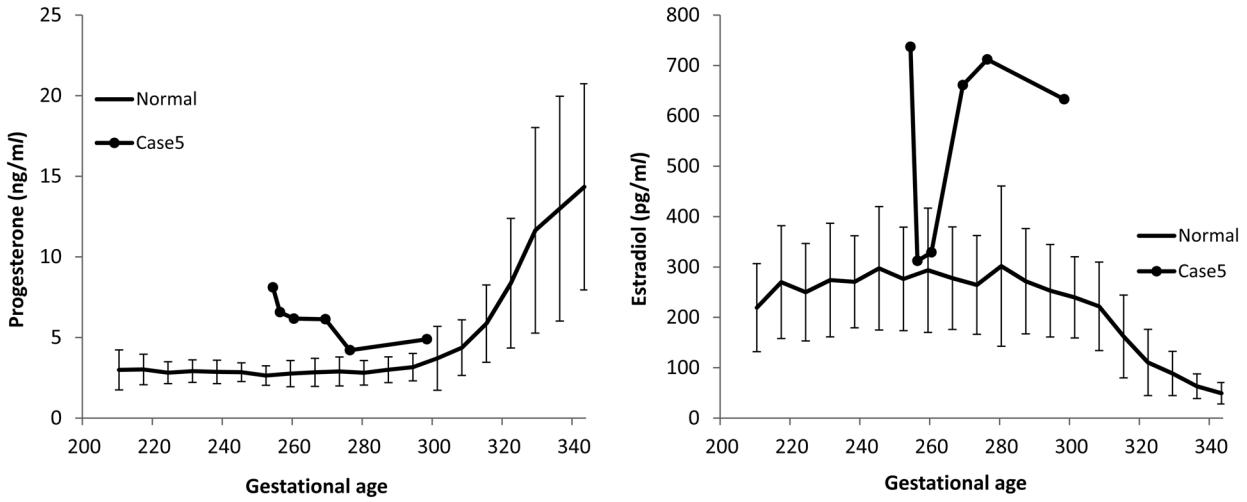

Fig. 2. Serum P_4 (left) and E_2 (right) concentrations following surgery in case 5. Standard values were calculated as the mean ± SD from 28 normal pregnant mares with weekly sampling (unpublished data). Hormone assays were carried out by DELFIA.

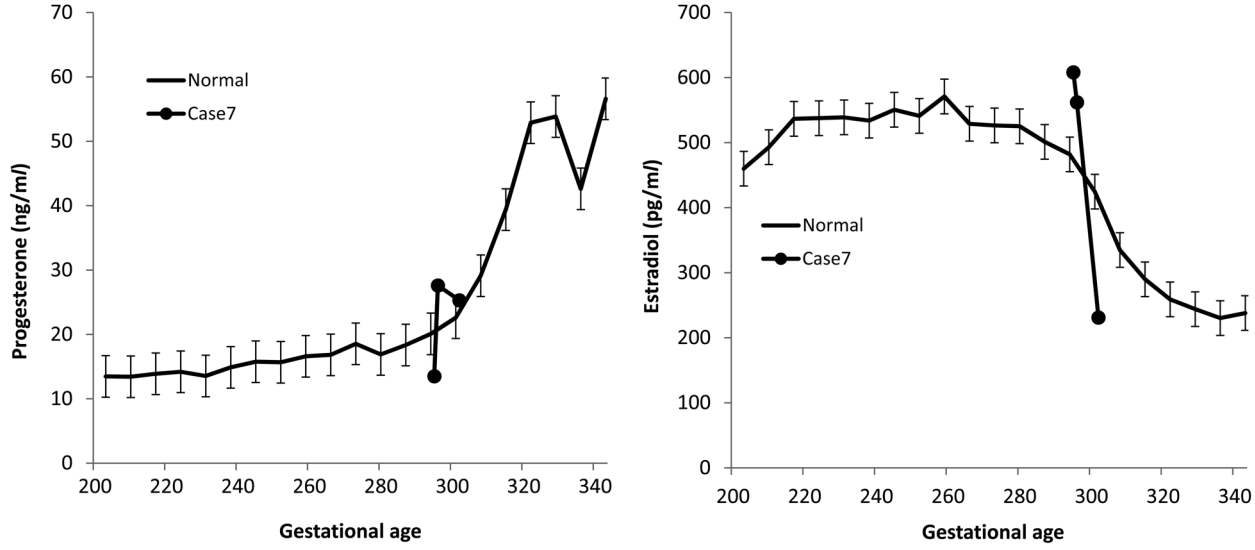

Fig. 3. Serum P_4 (left) and E_2 (right) concentrations following surgery in the case 7. Standard values were calculated as the mean ± SD from 21 normal pregnant mares with weekly sampling (unpublished data). Hormone assays were carried out by CLEIA.

day 295, and its P_4 level increased momentarily but was decreased by medication; therefore, medication was administered only 10 days. In this study, because P_4 and E_2 were measured by another method in case 5 and case 7, we were unable to compare results [4, 7]. Moreover, the normal data set used in this study was comprised of unpublished data from a CLEIA. However, when hormones were measured and compared using the same method in one case, the results were considered useful and meaningful.

In conclusion, the stage of gestation and degree of rotation when UT occurs should be considered. Veterinarians should advise clients accordingly regarding the prognosis for survival of mares and foals. This study involved only a small number of cases. However, because it is difficult to determine an accurate prognosis for mares and foals/fetuses in cases of UT and the only other study involved colic surgery [10], measuring hormones (P_4 and E_2) may be useful in pregnancy management post UT correction. On the other hand, because hormones were measured using two different methods in this study, the values were different for the two cases. Therefore, further studies are required. Nevertheless, this study suggests that hormone measure-

ments provide valuable indicators for the management of pregnancy post correction of UT. Early diagnosis and treatment of UT increases the possibility for helping mares and foals/fetuses in cases with acute UT. If the mare survives to be discharged from the hospital and is carrying a live fetus, measuring hormones (P_4 and E_2) is useful for pregnancy management post UT correction.

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