A 14-year-old multiparous Saddlebred broodmare was presented at 304 days of gestation for evaluation of abortion and dystocia. Manual vaginal examination on the farm revealed the fetus to be in cranial longitudinal presentation and right dorsoiliac position, with the head and neck ventroflexed and neither forelimb extended. Mutations repositioned the head and neck into full extension. However, the front legs were not within reach in the standing mare, so the mare was transferred to the Widener Hospital at New Bolton Center for a controlled vaginal delivery under general anesthesia. The mare had an abortion of unknown etiology at 9 months of gestation the previous year. No information regarding this pregnancy’s management was provided.

Formulate differential diagnoses, then continue reading.

Diagnosis

Umbilical cord torsion is a noninfectious cause of abortion in the mare. Dystocia was due to abnormal posture of the fetus. An abnormality of fetal presentation, position, or posture is the most common cause of dystocia in the mare. Bilateral shoulder flexion of the forelimbs is a common reason the front legs are not within reach during dystocia. This fetus aborted due to umbilical cord torsion and had ventral flexion of the neck and head and bilateral, symmetrical limb deficiency amelia of the forelimbs or an absence of all parts of the front legs derived from the limb bud.

Treatment and Outcome

Upon presentation at the Widener Hospital, the mare was anxious and alert. The perineum and vulva were slightly swollen and edematous. The mucous membranes were pink with a prolonged capillary refill time of 3 seconds. Body temperature (37 °C), heart rate (44 beats/min), and respiratory rate (20 breaths/min) were all within normal parameters. The mare’s PCV (50%), total solids (6.4 g/dL), and peripheral lactose (4.4 mmol/L) indicated dehydration and decreased perfusion.

The mare’s tail was wrapped with brown gauze and secured to the mare’s neck, and the perineum was cleansed with povidone iodine surgical scrub and water. Manual vaginal examination revealed a fetus in cranial longitudinal presentation and right dorsoiliac position with the head and neck extended and that had no evidence of fetal viability (no suckle and no palpebral reflex). Fetal forelimbs were not within reach. General anesthesia was induced using IV xylazine (0.8 mg/kg), midazolam (0.02 mg/kg), guaifenesin (55 mg/kg), and ketamine (3 mg/kg) and maintained by administration of desflurane gas after intubation. The mare was positioned in dorsal recumbency with the hind limbs slightly elevated for a controlled vaginal delivery. A sterile nasogastric tube was passed into the uterus, and methyl cellulose obstetric lubricant was pumped into the uterus and around the fetus to ease mutations and passage of the fetus through the pelvic canal. At this time, a more thorough evaluation of the fetus was possible, and it was apparent that the fetus did not have front legs. This diagnosis was based on the presence of a left and right scapula but no distal limb. An obstetrical chain was positioned around the head of the fetus, and moderate traction was applied manually, allowing the fetus to pass through the pelvic canal.
All fetal membranes were passed within 15 minutes after the expulsion of the fetus. Postmortem examination of the fetus revealed it to be in good nutritional status and postpartum condition with a crown-rump length of 110 cm. There was bilateral, symmetrical limb deficiency amelia of the front legs (Figure 1), characterized by vestigial scapulae, each with a rounded distal neck, absent glenoid tubercle, and miniaturized spine. Both kidneys were discreetly surrounded by approximately 30 mL of dark-red blood; the stomach was relatively empty with scant amounts of light-yellow, viscous fluid. The lungs were diffusely dark pink with innumerable pleural gas bubbles. Sections from all lung lobes sank in neutral-buffered 10% formalin. The allantoic portion of the umbilical cord had > 10 complete twists with surface ecchymoses, edema, and constriction of the vessels (Figure 2).

Discussion

The umbilical cord torsion most likely caused the fetal compromise that prompted preterm delivery and subsequent dystocia at 304 days of gestation. A diagnosis of umbilical cord torsion requires that the twisting of the cord is excessive and interferes with the integrity of the umbilical vessels and urachus. The specific number of twists in an umbilical cord is not diagnostic. Criteria for a diagnosis of umbilical cord torsion has been thoroughly described and includes ballooning and constriction of the umbilical vessels, surface ecchymoses, thrombosis, and local edema of the stroma and vessel walls. Excessively long (> 84-cm) cords may be associated with torsion. Previous estimates that 35.7% to 46.2% of abortions in the UK were due to umbilical cord torsion when the diagnoses were based on late gestation abortus submissions to diagnostic laboratories. A 2021 study looking at pregnancy loss after day 70 of gestation on 3,586 pregnancies reported an incidence of umbilical cord-related pregnancy loss at 1.5%, most of which were due to umbilical cord torsion. In a California diagnostic laboratory study, noninfectious causes of abortion accounted for 10.5% of case submissions and umbilical cord torsion was the most common noninfectious abnormality reported.

Although an association between limb deficiency amelia and umbilical cord torsion was not found in the literature, one can surmise that the absence of 2 legs may have contributed to abnormal fetal movements. In early gestation (2 to 5 months), the relatively large amount of fetal fluid to fetal mass and fetal activity allows a fetus to alternate freely between a cranial and caudal longitudinal presentation. As pregnancy progresses, the relative amount of fetal fluid decreases, and by 8 months of gestation, both uterine horns close and reposition most of the fetal fluid into the uterine body. After the final cranial presentation, the fetus’s hind legs enter a closed horn and then the fetus normally remains in a cranial presentation until parturition. In a report describing 57 abortions due to umbilical cord torsion, 2 of the fetuses were presented in caudal longitudinal presentation and 3 had limb deformities. The absence of front limbs in the fetus described in the present report may have contributed to excessive alternation of its presentation or made the fetus prone to turning in 1 direction, resulting in excessive twisting of the umbilical cord.

The veterinarian initially examining the mare did not attempt extraction of the fetus, as the posture of the forelimbs could not be confirmed in the standing mare. Limb deficiency amelia is rare in the mare, and few veterinarians consider it when forelimbs are not extended during a dystocia.

The development of the limb has been extensively studied in vertebrates because the chicken

Figure 1—Equine fetus with bilateral, symmetrical fore-limb amelia.

Figure 2—Equine fetus with > 10 twists in the allantoic portion of the umbilical cord.
limb bud is easy to manipulate for gene expression experiments. Limb development is thought to be due to the simultaneous proliferation of active basal cells and the dermal mesenchyme cells. Organogenesis of the equine embryo and early fetus has been analyzed in multiple studies. The musculoskeletal system develops from the embryonic mesodermal blade. Bones of the appendicular skeleton are formed by a central nucleus of support from the limbs. The cartilage that forms is converted to bone by endochondral-type ossification. This is compared to the axial skeleton that covers the internal tissues and is induced to form bone from the mesenchyme. In 1 study that analyzed morphologic stages of the embryo between 17 to 40 days after ovulation, the forelimb buds began to develop around day 20. By day 28, the forelimb buds were paddle shaped, and a footpad was forming by day 30 of development. Ossification of the limbs was apparent by day 35. By days 37 to 40, the forelimbs were obviously formed with a footplate, forearm, elbow, and shoulder region. The hind limb buds began to project around day 22 and continued to develop behind the forelimbs, with footpads being evident around day 35 of gestation. Another study based on organogenesis of the musculoskeletal system in equine embryos showed limb bud differentiation in 25-day-old embryos. A study of equine embryo and fetal development between days 15 and 107 showed early limb bud formation around day 25 and complete formation of the limbs by day 34. These reports would suggest that if a teratogenic agent caused the lack of forelimb development, the agent would have to have been present between 3 and 5 weeks of gestation. Environmental exposure to teratogens has been associated with many malformations in humans and animal species. One teratogen that leads to limb defects in human fetuses is thalidomide. Thalidomide is an immunomodulatory drug that was previously used as a sedative and for treatment of morning sickness in pregnant women in the 1950s and 1960s. If the drug was used between 20 and 36 days after fertilization, lack of limb development through absent radii, ulna, or humerus—known as limb deficiency amelia—or hypoplasia or malformation of these long bones, phalanges, or scapula—known as an intercalary defect—were seen. Up to 50% of pregnancies resulted in birth defects after a single dose of thalidomide. Thalidomide exerts its teratogenic effects by increasing cereblon-mediated destruction of a zinc-finger transcription factor (SALL4), which is critical to limb bud development; thus, the mechanism is thought to be disruption of a regulated cascade of transcription factors patterning limb bud development, rather than an inhibition of angiogenesis. The absence of forelimbs in the fetus could stem from a genetic anomaly in the foal. Based on information from human genomics and gene manipulation studies performed in mice and chickens, Tbx5 has been identified as a key transcription factor in the formation of appropriate forelimbs. Tbx5 mutations in humans cause upper forelimb defects and heart abnormalities. The Tbx5 gene is detected in the mesenchyme that gives rise to forelimbs prior to limb bud development and is continually expressed through the limb development stages. It is currently the earliest known marker of the forelimb mesenchyme. Knockout studies of mice and chickens demonstrated that Tbx5 is required for early limb bud stage development in the forelimb and for later stage limb bud development and limb outgrowth. The mare of the present report had uneventful recovery from general anesthesia and postpartum management. An extensive history was taken from the farm manager to explore the possibility of environmental exposure to a teratogen that could have led to this malformation, but no exposures were discovered. Unfortunately, no additional information regarding management of the mare during this pregnancy or the etiology of the previous abortion was provided. Genetic material from the dam and fetus was submitted for genetic analysis. No definitive genetic mutations were found when the fetal genome was compared to a 260-cohort group to attempt to explain the abnormality. The fetal genome will be characterized in a whole genome sequencing database when the database is complete for proper analysis.

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