“Sumner’s Potentially Problematic (Cyst)uation”

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Introduction

Equine endometrial cysts, also called uterine cysts, are fluid-filled structures that arise from the endometrial layer and can occur anywhere within the uterus[1,2]. Endometrial cysts are classified as glandular or lymphatic in origin[1]. Glandular cysts are a common incidental finding during pregnancy or hysteroscopic examination and can range from 1 millimeter to 1 centimeter in diameter but tend to be relatively small[2,3]. They are of little concern at this time as their relationship to infertility has yet to be investigated[2]. Research has shown that despite these two categories, clinically identified and relevant endometrial cysts are lymphatic in nature[1]. Lymphatic cysts are, most commonly but not always, a collection of lymphatic fluid that arises from the endometrium or myometrium[1]. They can have many different appearances including unilocular, multilocular, pedunculated, sessile, round, elongated and be associated with both normal and or chronically inflamed tissues[3,4]. It is thought that they are a result of impaired lymphatic drainage or due to the gravitational effects of a pendulous reproductive tract[5]. These structures begin small but can reach up to 20 centimeters or larger in diameter, often projecting into the lumen and causing greater clinical significance[1].

History & Presentation

Sumner, an approximately 15-year-old Thoroughbred mare, was presented to the Mississippi State University College of Veterinary Medicine Theriogenology Service on March 22nd, 2021 for breeding soundness evaluation, management and subsequent artificial insemination. Sumner is a multiparous mare with a history of two uncomplicated conceptions and foalings. Sumner has a chronic-active diagnosis of cellulitis of her right hind leg from 2008. For this reason, she is no longer used in hunter jumper competition but as a brood mare.

On presentation, Sumner was bright, alert and responsive. Her general physical exam and vital parameters were within normal limits. She had a heart rate of 40 beats per minute, respiratory rate of 20 breaths per minute and rectal temperature of 99 degrees Fahrenheit. A reproductive exam including transrectal palpation and transrectal ultrasonography was performed. Two follicles were observed on the left ovary measuring 40 mm and 39 mm respectively. A 37 mm follicle was seen on the right ovary. There was trace edema noted in her uterus and a previously diagnosed endometrial cyst present in the uterine body measuring 1.1 cm. Sumner was kept overnight and reassessed the next day with similar ovarian measurements obtained. It was determined that Sumner was in a transitional period and recommended she establish a regular estrous cycle with reevaluation in 1 month.

Pathophysiology

Horses are seasonally polyestrous, long-day breeders[6]. In short, this means they only cycle and ovulate during the time of year when there is >14 hours of daylight[4]. This corresponds to mid-April to early May in North America. When daylight hours are shortened, such as in winter months, mares remain in anestrus with inactive ovaries, no significant follicular development and low estrogen and progesterone plasma levels. During the transition from short to long days, the mare undergoes a vernal transition or transitional period. This is when she enters an extended estrus, demonstrating sexual receptivity without ovulation[6]. This transitional period is erratic and can last upwards of 2-3 weeks[4]. A surge of luteinizing hormone marks the end of vernal transition, triggering ovulation and a regular 21-day estrous cycle begins[6].

Maternal recognition of early pregnancy is species specific. While the exact chemical signaling pathway is still not fully understood, it has been proven that prolonged conceptus

mobility is essential for establishing pregnancy in the mare[7,8]. McDowell *et al.* (1988) demonstrated that "restricted conceptus mobility results in luteolysis in the mare, and that the subsequent decline in [progesterone] leads to embryonic death"[8]. This is of importance because anything that might hinder the vesicle from traversing >66% of the endometrial surface can lead to pregnancy failure[7,8].

Many studies have investigated the prevalence of equine endometrial cysts with a wide discrepancy in results ranging from 5% to 55.5%[9,10]. However, more recent investigations indicate an overall prevalence of 26.8% with mares ≥11 years old experiencing a 4.2 times higher prevalence[1,2]. Incidence of cysts in the mare has been seen to increase with parity, age and higher uterine biopsy score[2]. Commonly, those affected are typically greater than 10 years of age with those over 14 years of age being significantly affected with a prevalence reaching 73.1%[1,2,11].

Clinical implications of endometrial cysts can occur at any time but appear to be influenced by the size, number present and location within the uterus. A negative correlation has been identified between endometrial cyst formation and foaling rates when the number of cysts in an individual exceeds five[12]. Though cysts can form anywhere within the uterus, they are more commonly found within the uterine body at or near the bifurcation of the uterine horns[2]. This has a clinical significance, as it is the location of embryonic vesicle fixation in the mare. With one or more cysts present, embryonic vesicle fixation on day 16 post ovulation, conceptus mobility and placentation can be impeded with the potential of early embryonic loss[2, 13].

Differential Diagnoses, Diagnostic Approach & Considerations

If a previous diagnosis of endometrial cyst had not been made for Sumner, then several differential diagnoses would have to be considered and investigated before pursuing artificial insemination. The small fluid-filled structure appreciated on ultrasonographic examination demonstrates the same characteristics as that of a vesicle or early conceptus and can be difficult to differentiate. A stalk or broad-based attachment to the endometrium may or may not be appreciated in the case of a cyst and should not be relied upon for diagnosis or pregnancy confirmation. Even though, a cyst and vesicle diverge when considering movement, without cyst mapping or repeated, thorough ultrasonographic imaging and documentation a cyst may be misinterpreted for a vesicle. Lastly, in the case of two identical ultrasonographic structures, twins must be considered. In this situation, it is routine to isolate and manually crush the smaller vesicle to allow the larger to grow and be unimpeded by the twin. Given the appearance of cysts as discussed above, it is possible to mistakenly terminate the vesicle in the presence of an unidentified cyst.

Management

In Sumner's case, a single mild to moderately sized endometrial cyst present with no previous history of conception complications, intensive monitoring and medical management was elected.

Sumner was returned for several recheck visits as follows: April 5, 2021 (Diagnosis: Diestrus), April 12, 2021 (Diagnosis: Diestrus), and April 19, 2021 (Diagnosis: Transitional Period) with erratic results. On April 22, 2021 a diagnosis of abnormal cyclicity was made and Sumner was started on Altrenogest (Regu-Mate) at 0.044 mg/kg orally once daily for a total of

14 days with completion on May 5, 2021. Altrenogest is a synthetic progestin commonly used for suppression of behavioral estrus, maintenance of pregnancy and estrus synchronization as in Sumner's case[4].

On May 6, 2021, Sumner was presented to MSU-CVM Theriogenology service with the intent to breed. Serial transrectal ultrasonography was performed to track Sumner's estrous cycle during her stay. She was confirmed to be in estrus and a presumed dominant follicle on her right ovary was tracked for ovulation. Ovulation occurred the night of May 8, 2021 and Sumner was artificially inseminated using frozen thawed semen and a deep right horn insemination technique. A corpus luteum was documented on the right ovary the next morning. During this process, Sumner was given a dose of Buscopan (N-butylscopolammonium bromide) at 0.1 mg/kg and Dexamethasone at 0.38 mg/kg intravenously for smooth muscle relaxation to aid breeding and anti-inflammatory properties respectively. A routine series of three oxytocin injections at 0.02 IU/kg intravenously was also administered the following morning at 4-6 hour intervals to promote post-breeding uterine fluid expulsion.

Sumner returned on May 21, 2021 and May 24, 2021 for pregnancy evaluation where the previously identified corpus luteum was retained on the right ovary, her static endometrial cyst visualized and a small vesicle was monitored for growth and endometrial fixation. Sumner was officially diagnosed pregnant on June 7, 2021. A strong fetal heartbeat was seen at this time and a plasma progesterone level was measured at 5.12 ng/ml with 5-20 ng/ml being the target range for pregnancy. Progesterone is the hormone responsible for pregnancy maintenance in the equine species[6, 14]. During early pregnancy the corpus luteum on the ovary is responsible for progesterone production[6, 14]. By day 90-120 the placenta takes over production and produces sufficient levels to maintain pregnancy[4, 14]. Due to Sumner's somewhat challenging conception

combined with a very low normal plasma progesterone level early in pregnancy she was continued on Regu-Mate until day 90 of gestation.

Treatment Options

Various treatment options for endometrial cysts have been proposed in the mare including manual traction, puncture or lancing, curetting, aspiration via hysteroscopy, hypertonic saline infusions, electrocauterization, and laser photoablation[5, 15]. Treatment is selected on a case-by-case basis with breeding history, cyst location, number and size playing a role in selection. However, medical management as described above remains the mainstay of treatment at this time. For individuals significantly affected with numerous or large cysts laser photoablation is considered the treatment of choice. This technique requires sedation, aseptic preparation, endometrial visualization via videoendoscope, uterine insufflation, cyst localization and cauterization with a diode laser system[15, 16]. Each targeted cyst is ablated until complete reduction in size and voidance of fluid is achieved[16]. Uterine lavages using sterile solution are performed immediately post laser photoablation and at 1 and 2 days afterwards[16]. Several studies report no obvious deleterious effects observed with this procedure with some individuals achieving pregnancy the following breeding season[15, 16].

Case Outcome & Prognosis

To date, Sumner is doing great. Her owner reports she has had a quiet and uncomplicated gestation thus far. She is due April 11, 2022, which would place her at 320 days gestation. However, her owner reports her two previous pregnancies were prolonged at 366 and 360 days respectively. So no one is crossing fingers as of yet.

Sumner is expected to have no long term or lasting negative effects as a result of her endometrial cyst. As with other older mares, Sumner's current cyst will likely continue to slowly increase in size with additional cyst formation possible in the future, which may impede future conception. Similar intensive management is recommended for any future breeding as these structures have been documented to decrease conception and foaling rates[2, 13].

Conclusion

Overall, those mares with diagnosed endometrial cysts have lower conception rates due to uterine embryo migration impedance[1]. It is recommended to manage these mares more intensely during the breeding season as conception rates can be heavily influenced by the presences of multiple cystic structures and their locations within the uterus. As seen in Sumner's case, it is not impossible for these mares to conceive and many carry to term without any complications. However, this diagnosis requires detailed documentation, an attentive, invested practitioner and dedicated owner for success.

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