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SIVE

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Next SIVE Meeting:

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Case histories and partial workups for 4 cases are included below. Additional information concerning each case will be provided within text.

**CASE 1**

Signalment: 10 year old Thoroughbred mare. In the last 5 years, the mare has become pregnant twice but lost the pregnancy both times by 60 days of gestation. It was presumed that both pregnancy losses were due to Mare Reproductive Loss Syndrome as Kentucky experienced many losses both of those years and the timing of the pregnancy loss occurred at the typical gestational age for the disease. In the last 2 breeding seasons, the mare has been bred many times but has never been found to be pregnant. Seven culture swabs obtained before breeding were negative for bacteria while cytology specimens always had > 5 neutrophils/400x field. The mare was bred in the face of uterine inflammation. Following breeding the mare consistently had 4 or more cm of cloudy intra-uterine fluid. She was treated post mating with uterine lavage and intra-uterine infusion of an antibiotic. Antibiotics infused on various cycles included Timentin, ceftiofur and Gentamicin. Intra-uterine fluid was never noted at the 14 day pregnancy examinations. We examined the mare in June. Findings were:

**External exam:** Perineal body and dorsal aspect of vulva 60 degree cranial-ventral slope; 8 cm of vulva open above pelvic brim; aspiration of air into the vagina when the vulvar lips are parted.

**Rectal exam:** Uterus located 10 cm below the pelvic brim; LH 60 mm; RH 65 mm. No free intra-uterine fluid. Edema score 2 out of 4 with 4 being excessive. Uterus was thick walled and meaty in consistency. 40 mm follicle L ovary; 30 mm follicles (x2) on the R ovary

**Vaginal exam:** Hyperemic, wet vaginal walls; cervix edematous, lying on floor

**Cervical exam:** 5 cm in length. Patent, no adhesions or tears noted

**Uterine swab culture:** No growth by 72 h on blood or McConkey agars

**Uterine cytology:** > 5 neutrophils/400x field (severe inflammation)

**Management plan?**

Mare was re-bred in late June, developed 4 cm of intra-uterine fluid. She was treated post mating with uterine lavage and ecbolics. Mare was re-evaluated in December. On rectal exam the uterus was flaccid, small and there was no intra-uterine fluid. Both ovaries contained 20 mm follicles. Vaginal exam revealed a dry, pale mucosa with a cervix partially relaxed and approximately 4 cm off the vaginal floor. Culture swab revealed no growth, cytology had > 5 pmn/field. We returned 72 h later to obtain an endometrial

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biopsy. The biopsy was a Kenney Category IIa with the findings of subacute, focal, mild endometritis.

Management plan?

Endoscopic exam: see video

Management plan?

How to perform a small volume uterine flush

A low-volume uterine flush can be performed during estrus or diestrus. Performing the flush during diestrus frequently results in recovery of a larger amount of fluid as the infused fluid can be trapped among the prominent, edematous endometrial folds during estrus. If the sample is collected during diestrus, it is recommended that the mare be given prostaglandin so that she returns to estrus within a few days. Before the procedure, the rectum should be evacuated, the tail wrapped and deviated laterally and the perineum scrubbed, rinsed and dried. Ten to twenty cm of a sterile uterine catheter is passed per vaginum into the uterus and up into a uterine horn by an examiner whose arm is covered by a sterile sleeve. Commercially obtained uterine lavage tubes or medical grade silicone tubing can be used. If the latter is used catheters should be cut to 60 to 80 cm lengths. Two to three holes should be made about 3 cm from the end of the catheter with a scalpel blade and the end beveled to smooth the roughened edges. Medical grade silicone tubing can be autoclaved. Sterile saline is infused into the uterus by attaching either a 60 ml catheter-tip syringe containing 60 ml of saline or a 150 ml bag of sterile saline to the end of the catheter. The uterus is then manipulated by transrectal palpation for a minimum of 30 seconds to distribute the sterile saline throughout the uterine lumen. The uterine horn containing the catheter tip is cradled transrectally by the veterinarian’s hand and the saline is either drained into a sterile 50 ml conical tube by gravity flow or the fluid is allowed to drain back into the 150 ml bag. If one is working without an assistant extension tubing can be attached between the uterine lavage catheter and 150 ml saline bag for easier manipulation. However, the extra length of the tubing creates negative pressure impeding fluid recovery. The efflux recovered in the bag is transferred into a 50 ml conical tube. The volume of fluid recovered is recorded. It needs to exceed the fluid volume held within the uterine catheter for the sample to be considered an accurate representation of the uterine lumenal contents. Clarity of the fluid is recorded as being cloudy, clear or containing mucus strains. Degree of opacity or thickness and amount of mucus strains can also be noted using a numerical system from 0-3 with 0 being clear. Mucus strains are best viewed by rotating the tube while holding it up to the light. The precipitant is allowed to settle or the sample can be centrifuged at 400 g for 10 minutes and all but 5 ml of supernatant is poured off. Two sterile cotton tipped swabs are placed into the pellet at the bottom of the tube. One is used for uterine culture while the second is used for a cytological specimen. Samples need to be processed within 8 hours as the saline does not preserve the bacteria.

Cytology findings post small volume uterine flush.

Diagnosis and treatment plan after endoscopy:

Returned 14 days later for 2nd endoscopy. Endometrial plaques submitted for culture and Sensitivity

Treatment plan

Outcome: The mare left the practice. However, she became pregnant off the first breeding and aborted twins at 9 months of gestation. She returned to the practice following the abortion. She was bred the following year, became pregnant on the 2nd cover and foaled.

a Silicon tubing 0.313D, 0.500D, Professional Plastics.com, Fullerton, CA 92831.

b Fifty milliliter Tube (Fischer Scientific; Hanover Park, IL).
She foaled for 2 additional years after which time she died from a uterine artery rupture in mid-gestation.

**CASE 2**

**Signalment:** 18 year old pluriparous Thoroughbred mare. She has been barren the last 2 seasons after repeated breedings. Referring veterinarian reported that bacteria were isolated before the latter breedings in the season and the mare was treated with the appropriate intra-uterine antibiotic for 3 days after each positive culture. The mare had a history of accumulating varying amounts of intra-uterine fluid after breeding. Examination was performed in September.

**External exam:** Long, weak back and loin. Lame right front 2/5. Body condition score 4 out of 10. Perineal body had a 20 degree cranial-ventral tilt. Caslick was placed in vulva and extended 4 cm below the pelvic brim.

**Rectal exam:** Uterus was located 18 cm below the pelvis. It was large (LH 80 mm; RH 65 mm), meaty and thick walled. There was an abnormal edema pattern; edema score: 1.5. The mare was in diestrus. CL on right ovary; multiple small follicles on both ovaries.

**Vaginal exam:** Vaginal walls were pale pink and dry. There was no discharge. Vestibulovaginal fold intact. Cervix was puckered, located off the vaginal floor. There was no adhesions attached to the external os.

**Cervical exam:** Cervix was 7 cm in length. Canal was intact with no palpable tears within the cervical canal.

**Diagnostics?**

**Diagnosis and treatment?**

**Outcome:** Mare foals. Dies 10 days later from uterine artery rupture. Is it possible that diagnostic findings could have provided information on her possible death?

**CASE 3**

**Signalment:** 10 year old Saddlebred mare imported from South Africa. Mare was a highly competitive performance horse until she importation into the USA. The mare foaled once in the USA. She developed Cushing’s Disease (EPD-Equine Pituitary Dysfunction or also known as PPID-Pars Pituitary Intermedia Dysfunction). Mare was started on Pergolide at 2 mg/day daily. She developed a yeast infection (Candida) that persisted for 3 breeding seasons. The mare had been treated with various intra-uterine anti-mycotics, ecbolics and uterine lavage. The owner wanted her to serve as an embryo donor.

**External exam:** Low in the back, no tilt to the perineal body. Vulvar lips intact and tightly closed; No air was aspirated when vulvar lips were parted.

**Rectal exam:** The uterus was located at the pelvic brim. It was small (LH 40 mm; RH 35 mm) and contained 1 cm of fluid in the left horn. Edema score was a 2. The cervix was 10 cm in length and narrow (1 cm wide). There was a 40 mm follicle on the right ovary.

**Vaginal exam:** Vaginal walls were splotchy, being red and white in color. Walls were moist. There was no discharge on floor. Cervix was puckered, located off the vaginal floor.

**Uterine culture obtained by small volume uterine flush and cytology:** Candida sp and E coli were isolated; There were > 5 neutrophils/400x field on cytology, heavy debris and some spores.

**Diagnosis and treatment plan?**

**Outcome:** Owner was advised to sexually rest the mare for a few months to allow residual inflammation to clear. She elected to breed the mare. See ultrasound video. Did the mare ovulate? No embryo was recovered.
Fungal endometritis

Development of fungal endometritis is a frequent consequence of repeated intra-uterine antibiotic treatments (Dascanio 2007; Hinrichs et al. 1992). Many of these cases resolve spontaneously if the mare has normal perineal anatomy and adequate uterine clearance. If the infection does not resolve in one to two estrous cycles, the uterus should be irrigated with a disinfectant for five to seven days. Disinfectant solutions used for fungal infections include 3% (v/v) hydrogen peroxide solution (30 ml hydrogen peroxide in 1 L of 0.9% saline), 2% (v/v) acetic acid (white vinegar-20 ml of vinegar in 1 L of 0.9% saline), 0.1-0.2% (v/v) povidone-iodine solution, or 20% DM-SO (Dascanio 2007; Ricketts 1999). If fungi are isolated after uterine irrigation with a disinfectant for 3 to 5 days, a uterine culture should be submitted for antibiotic sensitivity. Recalcitrant fungal infections require prolonged therapy which is costly and relapses are common. Both local and systemic treatments have been advocated and in some cases, mares are treated with both. Breaches in anatomical barriers must be repaired. Unfortunately, the most difficult fungal infections to resolve, in the author’s opinion, are those in mares with a fibrotic cervix and inadequate uterine clearance and in mares with insulin resistance or Cushings Disease (Equine Pituitary Dysfunction). In humans, a minimum of 10 to 14 days of treatment is recommended. In horses, intra-uterine treatment is usually limited to the duration of estrus or five to seven days. Mares may require two to three treatment sessions conducted during consecutive estrus periods to resolve an infection. The interval between treatments can be shortened by administration of prostaglandin. Two to three weeks after the second treatment session the uterus should be re-cultured. If fungi are isolated, the reproductive tract should be re-eval-

Table 1. Usual dosages of systemic and topical antifungal agents for use in equine reproduction.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Interval (h)</th>
<th>Spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphotericin B0.3</td>
<td>0.9 mg/kg</td>
<td>IV*</td>
<td>24-48</td>
<td>Broad spectrum</td>
</tr>
<tr>
<td>Ketoconazole20 mg</td>
<td>(in 0.2 N HCL) NGT</td>
<td>a</td>
<td>12</td>
<td>Yeast</td>
</tr>
<tr>
<td>FluconazoleLoading dose 14 mg/kg</td>
<td>PO, IV*</td>
<td>24</td>
<td>Yeast</td>
<td></td>
</tr>
<tr>
<td>Clotrimazole400 – 700 mg</td>
<td>IV24h x 7d</td>
<td>Broad spectrum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miconazole500 – 700 mg</td>
<td>IV24h x 7d</td>
<td>Broad spectrum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nystatin 0.5 – 2.5 million units</td>
<td>IU24h x 7d</td>
<td>Yeast</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphotericin B100 -200 mg</td>
<td>IU24h x 7d</td>
<td>Broad spectrum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole100 mg</td>
<td>IU24h x 7d</td>
<td>Yeast</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Topical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clotrimazole</td>
<td>400 – 700 mg</td>
<td>IU24h x 7d</td>
<td>Broad spectrum</td>
<td></td>
</tr>
<tr>
<td>Miconazole</td>
<td>500 – 700 mg</td>
<td>IU24h x 7d</td>
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<td>IU24h x 7d</td>
<td>Yeast</td>
<td></td>
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</tbody>
</table>

* Nasogastric intubation is require to avoid the irritant effect of HCL on the oral cavity and throat
* The bioavailability of the oral suspension is superior to that of the capsules
* Yeasts: *Candida* spp
* Broad spectrum: yeasts, *Aspergillus*, dimorphic fungi
* Diluted to 1 mg/ml in 5% dextrose and administered over 1-2 h
* Must be diluted in sterile water (100 to 200 ml) as it precipitates in saline

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uated for anatomical defects and cervical incompetence and testing should be performed for Equine Pituitary Dysfunction. Systemic therapy for a minimum of 21 days should be considered. Table 3 contains antifungal drugs and dosages for systemic and local infusion.

**CASE 4**

Signalment: 7 yr old Maiden Thoroughbred mare. The mare was bred in 2003 but lost her pregnancy by 60 days of gestation so she returned to racing for a year. In 2005, the mare was bred 5 times. Each time she accumulated intra-uterine fluid for 5 to 10 days post breeding. Referring veterinarian performed uterine lavages post breeding for 4 to 5 days and infused an antibiotic each time. We evaluated the mare the last week of May 2005, two days after ovulation.

**External exam:** Body condition score 6; Perineal body conformation satisfactory; Caslick in vulvar lips to the pelvis.

**Rectal exam:** Uterus soft, flaccid, small (LH 35 mm; RH 40 mm, located at pelvic brim. There was a newly developed CL on the right ovary. The cervix was approximately 10 cm in length. There was 2 cm of intra-uterine fluid and an abnormal edema pattern within the uterine wall. The mare had not been bred that estrous cycle.

**Vaginal exam:** The vaginal walls were pale pink and dry. The cervical os was small, puckered and located off the vaginal floor.

**Cervical exam:** It was difficult to pass one finger through the cervical canal.

**Diagnosis:**

The referring veterinarian bred the mare in June and sent her to the hospital within 2 h of mating. We treated her with intra-uterine lavage and ecbolics for 3 days. She continued to pool intra-uterine fluid (4cm) for 4 additional days. The mare did not become pregnant. She was re-evaluated on the 25th of June, her first day of estrus. There was 2 cm of intra-uterine fluid. The cervix was tightly closed and a Serratia Marcesens was isolated from the uterus.

**Additional diagnostics? Treatment plan?**

The following year (2006) the mare was sent to the hospital in February. She was in transition with multiple small follicles on each ovary. On rectal exam the uterus was small, had a mild amount of edema (grade 1) and no free intra-uterine fluid. Vaginal walls were pink, glistening and the cervical os was small and puckered. A culture swab was obtained and no bacteria were isolated. Uterine cytology had 0-2 neutrophils and moderate debris. The mare returned to the hospital 48 h later with a vaginal discharge. There was 3.5 cm of fluid in the uterus. Vaginal walls were inflamed and there was a cloudy discharge on the pelvic floor. A beta hemolytic Streptococcus equi subsp. zooepidemicus was isolated.

**Treatment? Breeding protocol?**

**Outcome**

**Immunomodulation of the uterine inflammatory response**

For the past 20 years, treatment of post mating induced endometritis has emphasized methods for improving physical drainage. However, modulation of the immune response with steroids given around the time of mating has been shown to increase pregnancy rates in mares with fluid accumulation or uterine inflammation (Bucca et al. 2008; Papa et al. 2008). Immunomodulation may help restore homeostatic local inflammatory mechanisms through reducing pro-inflammatory cytokines. Single dose dexamethasone administered within one hour of mating and daily prednisolone administration given before and after mating have improved pregnancy rates in mares with uterine fluid (Bucca et al. 2008; Papa et al. 2008). A single injection of dex-
amethasone administered within one hour of mating (50 mg, IV; approximately 0.1 mg/kg) combined with routine post breeding therapies (uterine irrigation, ecbolic drugs and in some cases intra-uterine antibiotics) resulted in increased pregnancy rates in mares with a history of fluid accumulation after ovulation and in mares with cervical incompetence (Bucca et al. 2008). Increased pregnancy rates were also observed in mares with a history of intra-uterine fluid accumulation following oral administration of acetate 9-alpha-predinisolone (0.1 mg/kg) given at 12 h intervals for 4 days beginning 48 hrs before breeding (Papa et al. 2008). In contrast, administration of dexamethasone (10 or 20 mg, IM) 6 to 12 h after insemination did not improve pregnancy rates of warmblood mares (n=783 cycles) with a history of intra-uterine fluid retention (Vandaele et al. 2008). A plausible cause for the different results is that steroids block both the cyclooxygenase and 5-lipoxygenase pathways of inflammation. The 5-lipoxygenase pathway includes leukotriene B, a potent neutrophil chemotactic factor found in uterine fluids of susceptible mares after mating (Watson et al. 1988a, b). Reducing neutrophil chemotaxis and the number of neutrophils recruited into the uterus post mating may diminish the severity and length of the inflammatory response. Candidates for steroid use should be chosen carefully as misuse in mares with bacterial endometritis may exacerbate the infection.

REFERENCES


