Research Report

Reproductive and health outcomes of horses affected by focal mucoid placentitis

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Abstract

Focal mucoid (nocardioform) placentitis occurs sporadically worldwide and occasionally has been associated with local epidemics of disease in central Kentucky. Objective was to quantify the effects of focal mucoid placentitis on a farm during spring 2020 outbreak. Outcomes were prospectively identified early in the spring and data were collected in a single cohort of mares during 2020-2021 and on their foals during 2020-2022. Focal mucoid placentitis was diagnosed in 36 of 162 mares; 6 foals died at birth and 30 foals (83%) were viable compared to 119 of 126 viable foals (94%) from normal mares. Foals born to mares with placentitis weighed 10 lb less compared to those from healthy mares, received colostrum that was slightly lower in quality and had ~ 30% lower blood IgG concentrations. However, postnatal foal survival, incidence of infectious or orthopedic foal diseases, sale values, and racing performances were not different between these 2 groups. Focal mucoid placentitis did not recur in subsequent years and the reproductive performance of mares with this form of placentitis was not affected in the subsequent breeding season. Study suggested that although the disease may be underdiagnosed via farm-submitted samples, surviving foals and affected mares were able to overcome the effects of this condition and their performance was comparable to their peers in the absence of additional treatment.

Keywords: Focal mucoid placentitis, nocardioform, mare, pregnancy loss, foal health

Introduction

Focal mucoid, or nocardioform placentitis is a well-recognized cause of equine perinatal disease that has been most often described in central Kentucky and has occurred sporadically worldwide.[1,2] Focal mucoid placentitis is characterized by acute abortion or birth of small, thin foals that may be precociously developed, but can also go undetected with normal pregnancy length and the delivery of healthy foals.[3] Gross examination of the chorioallantois frequently reveals a thick mucoid discharge on the chorionic surface that is characteristically at the base of the gravid uterine horn or occasionally extending into the gravid or nongravid uterine horns.[4] 'Nocardioform' organisms, including *Crossiella equi*, *Amycolatopsis* spp., and *Streptomyces* spp. are frequently detected on cytologic evaluation of a touch prep from the lesion margin or identified by lesion culture and/or PCR.[5] The condition has been reported in the US, Europe, and South Africa and several 'outbreaks' have been documented in the equine population of central Kentucky.[1-10]

The Objective was to monitor all pregnant mares in a farm in central Kentucky for clinical signs of focal mucoid placentitis, neonatal health, and gross and microscopic/microbiological changes to fetal membranes during a recognized regional outbreak in 2020 spring. Subsequently, breeding performance of mares, incidence of infectious and orthopedic diseases of foals, sale values, and racing performance as 2-years old were compared between animals affected by this form of placentitis and those that were not affected.

Materials and methods

Pregnancy monitoring and treatment

In a Thoroughbred farm in central Kentucky, 167 pregnant mares were managed for foaling. Mares ranged from 3-23 years (median 15 years) in age and all mares had been bred by natural cover in the preceding breeding season (February 15-July 4, 2019). For the purposes of this study, data were

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Table 1. Parameters for comparison between groups

Mares	Foals
Incidence of postpartum reproductive disease	Incidence of neonatal disease
Number of breeding attempts per pregnancy	Incidence of hernias
Incidence of pregnancy loss	Incidence of surgical developmental joint disease (osteochondritis dissecans)
Number of mares foaling in subsequent season	Sale value (highest numerical bid recorded by sales agency, independent of reserve)
Incidence of placentitis in subsequent season	Racing performance during first 3 months in 2-year-old foals

collected from routine clinical procedures on a private commercial farm and no experimental treatments or procedures were performed. Institutional animal care and use committee approval is not required, and the study is exempt.

Mares were monitored for evidence of impending parturition and brought to a designated foaling barn when parturition was deemed imminent. At the foaling barn, mares were observed throughout the day and night by an experienced foaling team. At the onset of parturition, the Caslick vulvoplasty (if present) was incised with Metzenbaum scissors and normal presentation and positioning of the foal were confirmed by palpation. In normal foaling, minimal intervention was provided other than amnion removal from the foal's nostrils and prophylactic application of iodine on the umbilical stump after umbilical rupture. In instances of dystocia, a veterinarian was called and the team provided immediate assistance to the mare. If delivery of the foal was not accomplished in 30-45 minutes, mares were transported to a referral hospital for further care. Only mares that foaled successfully on-site were included in this analysis (n = 162).

Preparturient milk production, placental weight and colostrum quality (via refractometer) were recorded at foaling. Complete examination of the neonate and fetal membranes was performed within 12-24 hours after foaling. On the morning after foaling, blood was collected from foals (> 2 hours old) for white blood cell count (WBC) and IgG assay and foals were given 1.5 liters of plasma for prevention of Rhodococcus pneumonia. Examination and plasma infusion of foals that were born between 4 and 6 AM was delayed until 2-4 PM of the same day. Foal and fetal membrane abnormalities and foal weight were recorded. At fetal membranes examination, samples were collected from any suspicious lesions for cytologic examination of a touch prep, PCR for nocardioform organisms, and aerobic culture. Cytologic examination of the touch prep was performed on-site by an experienced practitioner, blood samples were submitted to the diagnostic laboratory of the Rood and Riddle Equine Hospital, Lexington, KY, and samples of the fetal membranes were refrigerated and sent to University of Kentucky Veterinary Diagnostic Laboratory (UKVDL), Lexington, KY within 24 hours after collection.

A diagnosis of focal mucoid placentitis was made if any of the following occurred: evidence of branching, chain-forming bacteria on cytologic examination; histologic diagnosis of focal placentitis on necropsy; positive diagnosis of *Crossiella equi*, *Amycolatopsis* spp. or *Streptomyces* spp. on PCR; or culture of gram-positive branching bacilli on aerobic culture.

In the absence of additional clinical disease, mares and foals with diagnoses of focal mucoid placentitis received no additional treatment based on this diagnosis.

Comparisons were made between mares and foals with a diagnosis of focal mucoid placentitis and those which had no detectable periparturient disease (normal mares), for the parameters outlined in Table 1.

Data analysis

Data were analyzed using publicly available free software (www.socscistatistics.com). Duration of pregnancy at foaling, foal weight, placental weight, IgG, WBC, sale value, and racing income were analyzed using a Student's t-test and nonparametric data were analyzed using a Pearson's Chi-square test.

Results

During 2020 breeding season, 167 pregnant mares were maintained on the farm for foaling management. Of those, 5 mares experienced dystocia or delivered a severely compromised foal that was immediately transferred to a referral hospital without further diagnostics. Six mares with focal mucoid placentitis experienced abortion or stillbirth. Three mares delivered foals with traumatic injuries that necessitated immediate euthanasia, and 2 foals were medically compromised at birth and immediately transferred to a referral hospital without further diagnostics. Mares (n = 162) and foals born to them were included in the analysis; 151 (93%) mares delivered live foals that stood and nursed. Examination of fetal membranes revealed 36 cases (22% of foaling mares) with gross abnormalities of placental chorionic surface, characterized by a thickened chorioallantois with blunted or denuded villi and variable amounts of mucoid exudate adhered to chorion and were diagnosed with focal mucoid (nocardioform) placentitis. No cases of ascending placentitis were diagnosed, and focal mucoid placentitis was diagnosed more commonly earlier in the year than later during the same foaling season (Figure).

Thirty of 36 grossly abnormal fetal membranes were also examined on farm cytologically, whereas 22 of 36 were submitted to the UKVDL for aerobic culture and PCR assay (Table 2). Characteristic chain-forming branching bacteria were observed in 23 of 30 (76%) of examined smears and culture or PCR revealed the presence of nocardioform placentitis in 17 of 22 (77%) of submitted samples. Two of 22 (9%) cases that were grossly consistent with focal mucoid placentitis had no detectable organisms on microscopic examination of a touch prep slide, but were PCR positive for nocardioform organisms. In 5 of 22 (23%) cases, chain-forming organisms were observed cytologically, but PCR was negative. However, in 3 of those cases, culture and histology were most consistent with focal mucoid placentitis. In total, onsite cytologic findings matched advanced diagnostic results from the diagnostic laboratory in 16 of 22 (73%),

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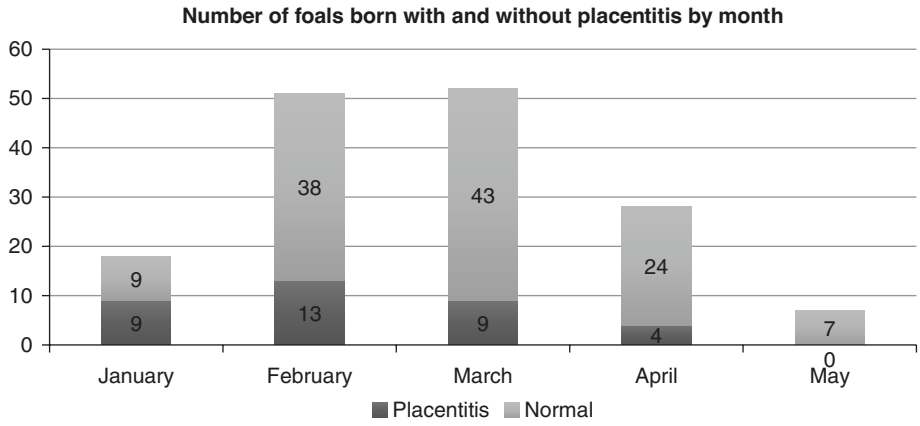

Figure. Number of foalings with and without gross or histologic evidence of focal mucoid placentitis during each month of the 2020 foaling season.

whereas 6 cases with gross lesions consistent with focal placentitis but which were cytologically negative were confirmed to have focal mucoid placentitis by the diagnostic lab (27%). In 7 cases (32%), culture and PCR did not identify nocardioform organisms, whereas cytologic or histologic examination of grossly abnormal tissues confirmed a diagnosis of focal mucoid placentitis.

Retrospective comparison of pregnancy outcomes

Mares diagnosed with focal mucoid placentitis after foaling had a slightly shorter ($p = 0.0009$) pregnancy length on average than mares with normal uncomplicated pregnancies (325.4 ± 15 versus 331.9 ± 9 days). Thirty of 36 mares (83%) with focal mucoid placentitis produced live foals ($p = 0.0015$) compared to 119 of 126 (94%) mares without placentitis. Mares that foaled with gross lesions of mucoid placentitis were not more likely to drip milk ($p = 0.18$) during prefoaling (20 versus 11%). However, colostrum quality was assayed in 117 foaling mares and was lower ($p = 0.0015$) in foaling mares with a diagnosis of placentitis than normal mares (25 ± 6.3 versus 28 ± 3.3%). Duration of pregnancy at foaling for mares with focal mucoid placentitis that produced live foals was similar ($p = 0.054$) to normal mares (328.8 ± 10 versus 331.9 ± 9 days). Birthweights of 30 live foals born to mares with placentitis were ~ 10 lb lower ($p = 0.001$) on average than those of 113 live foals from normal mares (112.7 ± 19.7l versus 123 ± 14.9 lbs). Fetal membrane weights were not different (18.9 ± 3.5 versus 18.5 ± 3.6 lbs; $p = 0.29$). However, the relative fetal membrane weight in relation to foal weight was greater ($p = 0.002$) in cases of focal mucoid placentitis (16.7 ± 3.1 versus 15 ± 2.6%). Immunoglobulin G of foals born to mares with placentitis was lower ($p = 0.0003$) at the first examination than that of normal mares (1,498 ± 1,005 mg/dl versus 2,295 ± 1,134 mg/dl); however, this did not translate to a difference in the incidence of failure of passive transfer (IgG < 400: 4 and 8 respectively) or partial failure of passive transfer (IgG 400-800: 2 and 7 respectively in foals born to mares with placentitis compared to normal mares; $p > 0.1$). Foals' WBC at the first examination was not different ($p > 0.1$) between groups (11 ± 2.9e^3/ml versus 11.2 ± 2.5e^3/ml).

Subsequent mare reproductive performance

None of the 36 mares with placentitis experienced peripartu-rient complications (e.g. retained fetal membranes or metritis) or significant vaginal or vulvar trauma that required intervention. Consequently, in accordance with our protocols, mares diagnosed with focal mucoid placentitis did not receive any systemic or local treatment at foaling. During 2020 breeding season, 156 foaling mares were bred again. There were no differences ($p > 0.1$) between foaling outcomes of mares that had experienced focal mucoid placentitis in the previous year and those that had not; 33 of 35 mares (94%) that had experienced focal mucoid placentitis were bred again and became pregnant with an average of 1.5 cycles/pregnancy, and 113 of 121 mares (93%) that had foaled normally and were bred back became pregnant ($p > 0.1$) with an average of 1.5 cycles/pregnancy. No mares in either group were diagnosed with focal mucoid placentitis in 2021. Three mares that had experienced placentitis and 8 normal foaling mares experienced embryonic loss ($p > 0.1$) before 45 days of pregnancy. In these groups, 128 mares were maintained on the farm until foaling in 2021. Of those, 1 pregnant mare that had experienced placentitis and 9 normal mares aborted in the 2021 foaling season ($p > 0.1$; Table 3).

Neonatal and developmental disease

Incidences of broken ribs, neonatal developmental limb contracture and infectious disease broadly were not different ($p > 0.1$) in foals born to mares with focal mucoid placentitis than normal mares; however, foals born to mares with placentitis had a slightly higher risk ($p = 0.04$) of developing umbilical hernias that required surgical repair (Table 4).

Foals (n = 139) that were kept beyond 12 months of age received full radiographic examination for developmental orthopedic disease (survey radiographs) with evaluation by an experienced practitioner blinded to foals' status. There was no difference ($p > 0.1$) in the number of yearlings requiring arthroscopic surgery from mares with placentitis (8/29; 29%) compared to those from normal mares (39/110; 35%).

Sale and racing performance

Foals of mares with placentitis (n = 28) and 116 foals born to normal mares survived until December 2022 and were included in analysis of performance. There were no differences ($p > 0.1$) in either sales value or racing income of horses born to mares with focal mucoid placentitis compared to normal mares. Nine of 28 (32%) foals of mares with placentitis were sold for an average of $106,670 (range: 10,000-425,000; median

Table 2. Diagnostics performed and outcomes for mares diagnosed with focal mucoid placentitis

Mare #	Histologic diagnosis	Cytologic diagnosis	Culture results	PCR results	Outcome
1	placentitis	not performed	G+ branching bacillus	*Amycolatopsis* sp. And *Crosiella equi*	abortion
2	chronic focal placentitis	branching bacilli	nonpath	not performed	normal foal
3	placentitis	branching bacilli	not diagnostic	*Crosiella equi*	abortion
4	not performed	not performed	G+ branching bacillus	*Crosiella equi*	stillbirth
5	placentitis	branching bacilli	G+ branching bacillus	*Amycolatopsis* sp.	normal foal
6	placentitis	branching bacilli	G+ branching bacillus	*Amycolatopsis* sp.	normal foal
7	avillous placenta	normal	no growth	not performed	normal foal
8	placentitis	not performed	G+ branching bacillus	*Crosiella equi*	abortion
9	focal placentitis	normal	nonpath	not detected	normal foal
10	placentitis	branching bacilli	G+ branching bacillus	*Amycolatopsis* sp.	normal foal
11	placentitis	not performed	G+ branching bacillus	*Crosiella equi*	abortion
12	placentitis	branching bacilli	G+ branching bacillus	*Amycolatopsis* sp.	abortion
13	chronic focal placentitis	normal	nonpath	not performed	normal foal
14	not performed	branching bacilli	nonpath	*Amycolatopsis* sp.	normal foal
15	not performed	branching bacilli	G+ branching bacillus	*Crosiella equi*	normal foal
16	not performed	branching bacilli	nonpath	not detected	normal foal
17	not performed	branching bacilli	nonpath	not detected	normal foal
18	not performed	branching bacilli	G+ branching bacillus	*Crosiella equi*	normal foal
19	not performed	branching bacilli	not performed	not performed	normal foal
20	placentitis	normal	nonpath	not detected	normal foal
21	not performed	branching bacilli	G+ branching bacillus	not detected	normal foal
22	not performed	normal	not performed	not performed	normal foal
23	not performed	normal	nonpath	*Crosiella equi*	normal foal
24	not performed	branching bacilli	G+ branching bacillus	*Crosiella equi*	normal foal
25	not performed	branching bacilli	not performed	not performed	normal foal
26	not performed	branching bacilli	G+ branching bacillus	*Amycolatopsis* sp.	normal foal
27	not performed	branching bacilli	not performed	not performed	normal foal
28	not performed	normal	*Acinetobacter wolfii*	not performed	normal foal
29	not performed	branching bacilli	not performed	not performed	normal foal
30	not performed	branching bacilli	not performed	not performed	normal foal
31	not performed	branching bacilli	nonpath	*Crosiella equi*	normal foal
32	not performed	branching bacilli	*Rhizobium radiobacter*	not detected	normal foal
33	not performed	branching bacilli	nonpath	not detected	normal foal
34	not performed	branching bacilli	not performed	not performed	normal foal
35	not performed	branching bacilli	G+ branching bacillus	*Amycolatopsis* sp.	normal foal
36	not performed	normal	not performed	not performed	normal foal

Table 3. Pregnancy outcomes of mares with and without evidence of focal mucoid placentitis in the 2021 foaling season

	Foaled	Barren	Early embryonic death	Aborted	Sold
Normal (n = 121)	76 (63%)	8 (6.6%)	8 (6.6%)	9 (7.4%)	23
Focal mucoid placentitis (n = 35)	25 (71%)	2 (5.9%)	3 (8.6%)	1 (2.9%)	5

50,000) whereas 42 of 116 (36%) foals of healthy mares were sold for an average of $130,200 (range 1,000-950,000; median 75,000; p = 0.7). Fifteen of 28 (54%) foals with placentitis were started in races with an average of 1.67 starts per horse, whereas 39 of 124 (33%) foals of healthy mares started with an average of 0.84 starts per horse ($p < 0.05$). Foals of mares with placentitis (n = 28) produced $353,549 in earnings with an average of $12,626.75 for each surviving horse. Foals (n = 116) of

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Table 4. Incidence of neonatal disease in foals from mares with or without evidence of focal mucoid placentitis

	Placentitis (n = 30)	Normal (n = 119)
None	27	92
Infectious disease	1	15
Fractured ribs	2	4
Limb contracture	2	8
Hernia	6	9

healthy mares produced $886,073 with an average of $7,638.5 for each horse that survived to December 2022 (p = 0.26).

Discussion

Results of this observational field study on the incidence of focal mucoid (nocardioform) placentitis in a single farm during the 2020 outbreak in central KY suggested that subclinical focal mucoid placentitis may be more common than previously recognized during an outbreak. In the farm studied 36/162 (22%) of foaling mares examined had gross lesions consistent with this form of placentitis.

As reported,[3] most cases of focal mucoid placentitis were associated with the growth of nocardioform actinomycetes, most commonly *Crosiella equi*, *Amycolatopsis* spp., and *Streptomycetes* spp. However, as described,[3] nocardioform actinomycetes were not isolated on culture or PCR in all clinical cases with typical pathological lesions. When combined with results of prospective inoculation studies that failed to induce disease with intrauterine, oral, respiratory, and intravenous inoculation of these microorganisms,[11] raises the question whether nocardioform actinomycetes caused the disease or if their frequent identification merely represents an opportunistic consequence of the disease. Clinically, these findings underscore the importance of detailed gross and cytologic evaluations of fetal membranes on-site that may be more sensitive in detecting placentitis than laboratory results of submitted samples. Furthermore, it is unknown with what frequency positive PCR or culture results for nocardioform actinomycetes might be obtained from normal foaling mares.

Mares with focal placentitis had a slightly shorter duration of pregnancy than normal mares (325 days versus 331 days) and focal mucoid placentitis had substantial effects on foal survival and birthweight of affected foals, with a 17% mortality and 10 lb lower birthweight than foals from normal mares. This can likely be explained by a reduction in attachment of healthy chorion to the endometrium with consequences on prepartum nutritional fetal support; however, nocardioform placentitis was not associated with any detected clinical changes in these mares. Incidence of prepartum milk production was not different and there were no reports of vulvar discharge or precocious mammary development in this group. Routine transabdominal ultrasonographic examinations and endocrine monitoring were not performed in this farm and it is unknown whether such procedures could have accurately diagnosed focal mucoid placentitis or whether treatment of affected mares might have altered pregnancy outcomes. However, mares with focal mucoid placentitis had 83% foal survival rate and surviving foals from mares with focal mucoid placentitis were of normal age of pregnancy at parturition and did not experience neonatal health issues commonly observed in foals from mares with ascending placentitis. Furthermore, the risk of surgical osteoarthritis was not increased in foals born to mares with focal mucoid placentitis and they performed similar as yearlings and 2-year old race-horses. Statistical increase in umbilical hernias in this group of foals was surprising and should be confirmed with additional observations. However, hernial size was similar and all were repaired surgically with no clinical impact. It was interesting to observe that foals born to mares with focal mucoid placentitis were more likely to race and had more starts per horse than the cohort of foals that was unaffected by placentitis. These findings suggested that in foals surviving to term or born with precocious joint and gastrointestinal maturation sufficient to allow normal neonatal development, any effect of focal mucoid placentitis related to fetal starvation can successfully be compensated after birth.

Focal mucoid placentitis in the absence of other perinatal disease did not negatively affect the subsequent mare's reproductive performance or foal health and development. The per cycle and seasonal pregnancy rates in mares with placentitis were nearly identical to those of normal-foaling mares on the same farm in the absence of any treatment, and none of the affected mares developed placentitis during the subsequent pregnancy. This demonstrated that mares had the capacity for uterine clearance during postpartum and supported a conservative treatment approach in foaling mares with placentitis.

In conclusion, under the conditions of a regionally recognized outbreak, focal mucoid (nocardioform) placentitis occurred on this farm more frequently than has been reported elsewhere. Most cases were subtle, with relatively small placental lesions that would have gone undetected without close monitoring for typical focal mucoid lesions of the chorioallantois. Postpartum treatment was not necessary for mares with uncomplicated cases of this form of placentitis and their future reproductive performance was not affected by the condition. Although surviving foals were smaller, this disadvantage was effectively corrected during very early stages of their lives, and focal mucoid placentitis did not affect athletic performance or sale prices of these foals.

Conflict of interest

None to declare.

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