Pferdeheilkunde 15 (1999) 6 (November/Dezember) 630–632

Placentitis in Central Kentucky broodmares

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Summary

Feto-placental infection caused by microorganisms was the most common cause of death of fetuses, stillborn foals, and foals that died within 24 hrs after birth in central Kentucky. Pathologically, three types of placentitis were seen: ascending, diffuse, and focal mucoid. The pathogenesis in each form is believed to be different and each is associated with certain types of causative bacteria or fungi. Ascending placentitis was the most common type of placentitis prior to the 1998 foaling season in Kentucky. This form is thought to be the result of microorganisms gaining access to the cervical portion of the placenta during gestation by spread from the lower reproductive tract through the cervix. Streptococci and E. coli were the most commonly isolated bacteria. Diffuse or multifocal placentitis was less commonly diagnosed and is associated with hematogenous spread of microorganisms to the uterus of the mare with subsequent infection of the placenta. This form was associated with infection by bacteria in the genera Leptospira, Salmonella, Histoplasma, and Candida. Focal mucoid placentitis is also known as nocardioform placentitis. Nocardioform placentitis has emerged as the most commonly diagnosed type of placentitis over the last two foaling seasons and is characterized by unique pathology and distinct bacteria. At present the pathogenesis of this form is unknown.
Diagnosis of placentitis during gestation is often difficult. Most mares show no outward signs of infection. Some mares will undergo premature mammary development with lactation and, occasionally, a vaginal discharge is present. Transrectal and transabdominal ultrasound examinations are useful in arriving at a diagnosis if placentitis is suspected. Various treatment modalities have been utilized in an attempt to maintain gestation for as long as possible to enhance foal viability.
Placentitis results in several outcomes. In addition to abortions and stillbirths, the mare may produce small weak foals or normal foals. The small, weak neonates represent a special management and medical challenge. These individuals have an increased risk of sepsis and orthopedic problems requiring extensive care.

Keywords: Placentitis, abortion, bacterial placentitis, bacterial abortion, equine abortion

Plazentitis bei Zuchtstuten in Zentral-Kentucky

Mikrobiell bedingte feto-plazentare Infektionen waren die hauptsächliche Ursache von Fruchttot, Totgeburten und neonatem Frühtod bei Zuchtpferden in Zentral-Kentucky. Es konnten drei Typen der Plazentitis beobachtet werden: aufsteigende, diffuse und fokal-mukoide Plazentitis. Die Pathogenese dieser drei Erkrankungsformen wird als voneinander unterschieden erachtet und jede steht in ursächlicher Verbindung mit bestimmten Bakterien oder Pilzen. Bis zur Abfohlsaison 1998 war die aufsteigende Plazentitis die am häufigsten vorkommende Variante. Es wird angenommen, dass diese Plazentitisform das Resultat einer aufsteigenden Kontamination des Genitaltraktes mit den verursachenden Mikroorganismen ist, von denen vorwiegend Streptokokken und E. coli nachgewiesen wurden. Diffuse oder multifokale Plazentitis wurde weniger häufig diagnostiziert und ist offensichtlich die Folge einer hämatogenen, absteigenden Kontamination des Uterus, die zur Infektion der Eihäute führt. Diese Form der Entzündung wurde in Zusammenhang mit Bakterien der Genera Leptospira, Salmonella, Histoplasma und der Pilzbesiedlung mit Candida diagnostiziert. Die fokal-mukoide Plazentitis ist auch als nocardioforme Plazentitis bekannt, die als die am meisten diagnostizierte Form der Plazentitis während der letzten zwei Abfohlsaisons vorgekommen ist und durch ein einheitliches pathologisches Erscheinungsbild und einem einheitlichen Bakteriennachweis charakterisiert ist. Die Pathogenese der Erkrankung ist zur Zeit noch nicht geklärt.
Die Diagnose der Plazentitis während der Trächtigkeit ist oft schwierig. Meist verläuft die Erkrankung zunächst klinisch inapparent. Einige der erkrankten Stuten zeigen Euteranbildung mit Laktation, gelegentlich erscheint Genitalausfluss. Die transrektale und transabdominale ultrasonographische Untersuchung sind brauchbare diagnostische Hilfen wenn Verdacht auf eine Plazentitis besteht. Verschiedene Behandlungsversuche sind unternommen worden mit dem Ziel, die Gravidität so lange wie möglich zu erhalten um die Vitalität des Neugeborenen zu verbessern.
Die Plazentitis führt zu verschiedenen Verlaufsformen. Neben Aborten und Totgeburten können lebensschwache aber auch normale Fohlen geboren werden. Lebensschwache neugeborene Fohlen bergen ein erhöhtes Risiko für septische und orthopädische Probleme und sind eine Herausforderung an die medizinische Intensivbetreuung.

Schlüsselwörter: Plazentitis, Abort, bakterielle Plazentitis, bakterieller Abort, Stutenabort

Abortions, stillbirths, and weak foals at birth represent significant causes of mortality in horses and result in a substantial economic loss to the equine industry *(Platt, 1973; Roberts, 1986)*. Placentitis is a major disease process causing these types of losses. In one study, feto-placental infection caused approximately one third of all abortions or deaths of neonates less that 24 hrs old. A bacterial infection was responsible for approximately three fourths of the abortions or deaths in cases where a specific etiologic agent was found *(Giles et al., 1993)*. In another study of causes of abortion, placentitis was the most common cause and resulted in 12.7% of the cases *(Tengelsen et al., 1997)*.

In the central Kentucky Bluegrass region placentitis represents a consistent and significant problem. Over a six-year period from 1993 through 1998, 941 cases of placentitis were diagnosed. This represented an average of 157 cases of placentitis per year and was the diagnosis in 30% of all submitted fetuses.

Placentitis in horses can be subdivided into several different forms based on pathological changes. In general, each type is associated with certain causative microorganisms and the pathogenesis is believed to involve different mechanisms. Equine placentitis includes two widely recognized types of placentitis that are commonly reported and

an atypical type that has recently been described. The two common forms of placentitis are ascending and diffuse placentitis *(Platt, 1975; Prickett, 1967)*.

Ascending placentitis is characterized by infection in the area of the cervical star that extends a variable distance up the body of the placenta. The affected area is thickened and is often discolored a brownish-tan color. The pathogenesis is believed to involve spread of infectious agents through the cervix during the second half of gestation *(Platt, 1975; Prickett, 1967)*. Since the bacteria and fungi associated with this type of placentitis are common isolates from the lower reproductive tract of the mare, it is believed that these organisms are opportunistic *(Hinrichs et al., 1988)*. In Kentucky, microorganisms associated with this form of placentitis in decreasing order included Streptococcus zooepidemicus, Escherichia coli, Pseudomonas aeruginosa, Streptococcus equisimilis, Enterobacter agglomerans, Klebsiella pneumoniae, and alpha-hemolytic Streptococcus *(Hong et al., 1993)*. Any one of several different fungi accounted for 6.7% of the cases. Ascending placentitis often spreads via the fetal circulation and fluids to infect the fetal organs. Bacteria were cultured from both the placenta and fetal tissues in approximately 60% of cases *(Hong et al., 1993)*.

Diffuse placentitis is much less common than ascending placentitis and is associated with extensive, randomly distributed lesions on the chorionic surface *(Hong, 1993; Prickett, 1967)*. Diffuse placentitis is sometimes referred to as hematogenous placentitis since the proposed pathogenesis involves septicemia in the mare with spread of infection to the uterus and infection of the placenta. This form of placentitis is associated with infection by certain bacteria and fungi. Microorganisms causing diffuse placentitis include Leptospira sp., Salmonella sp., Candida sp., and Histoplasma sp..

The other, less widely reported, form of placentitis is referred to as nocardioform placentitis or focal mucoid placentitis. Nocardioform placentitis was first recognized in the late 1980's and is characterized by a solitary focal area of placentitis located in the area of the junction of the horns with the body of the placenta *(Giles et al., 1993; Hong et al., 1993)*. The affected area usually is covered by thick brown or tan mucoid material with the underlying chorionic surface being thin and more transparent. There is a relatively sharp line of demarcation between the affected and normal areas of the placenta. The placentitis does not communicate with the cervical portion of the placenta, and it appears that the infection begins on the ventral surface of the chorion. Microscopically, the lesion is characterized by necrosis of the chorionic epithelium with blunting and necrosis of the villi. Inflammation consists of mononuclear cells and neutrophils infiltrating the deeper stroma and migrating into the villi. The chorionic surface and intervillous areas are covered by amorphous eosinophilic material consisting of secretions, sloughed degenerating trophoblasts, and leukocytes. Gram stains reveal variable numbers of gram-positive branching filamentous bacteria in the material and within the superficial trophoblastic epithelium. Sections from the interface of affected and normal placenta demonstrate active inflammation and bacteria; while in the central portion of the area of placentitis, the reaction is more chronic with the villi being blunted or absent. The leukocytic response is reduced and mononuclear in character and bacteria are rare. The pathogenesis of this form of placentitis is not known, however, the lesion location, pathology, and associated bacteria suggest that the pathogenesis is different from the other forms of placentitis. The nocardioform bacteria can be cultured on routine media, but grow slowly necessitating holding of culture plates up to five days. Nocardioform bacteria are not cultured from the fetal organs or fluids, and pathological changes indicating spread of infection to the organs are not observed. In approximately 50% of the cases, the foal was alive at the time of submission of the placenta.

The causative bacteria in nocardioform placentitis are unclassified gram-positive branching filamentous bacilli which places them in the broad informal group of nocardioform actinomycetes. Based on characterization of isolates, the bacteria appear to be a heterogeneous group of organisms with at least three species or sub-groups involved. Over the past two foaling seasons, nocardioform placentitis has emerged as the most common form of placentitis in central Kentucky. During the 1998 and 1999 foaling seasons there were over 200 cases of nocardioform placentitis diagnosed which represented a dramatic increase over previous years (Fig. 1).

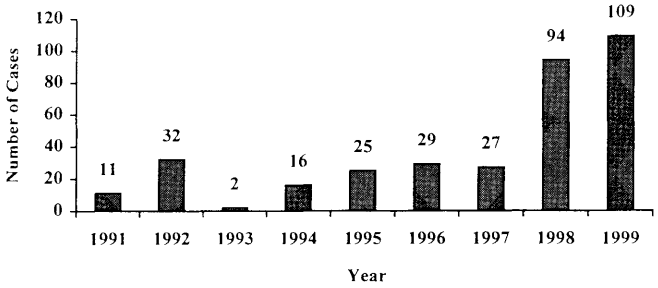

Fig.1: Cases of Nocardioform Placentitis in Central Kentucky by Foaling Year (1991–1999*). * Through 3/20/99
Fokal-mukoide Placentitis in Zentral-Kentucky während der Jahre (1991–1999)

Clinical diagnosis of placentitis has been enhanced through the use of ultrasonography. Prior to the utilization of ultrasound examinations, physical signs of placentitis had to be relied on in order to make the clinical diagnosis. Usually the first clinical sign of impending abortion from placentitis is premature udder development. Significant development of the udder earlier than three weeks before the calculated foaling date is cause of concern. In some mares this may be a normal occurrence but usually it indicates premature preparation for parturition. Although placentitis is the predominate cause of premature mammary development, it is not the only cause. Other common causes are twin pregnancies and dead or abnormal fetuses. When udder development is accompanied by a vaginal discharge and an open cervix is observed, a presumptive diagnosis of placentitis can be made. In most instances this would represent an ascending placentitis that progressed anteriorly from the cervix. If an open cervix and a vaginal discharge are not present, placentitis can not be ruled out, and ultrasonography may be helpful in arriving at a definitive diagnosis.

Transrectal ultrasound allows the examiner to visualize the placenta at the cervical star and forward though the body of the uterus. With this technique placental thickening and separation can be readily visualized and an ascending placentitis can be diagnosed. If there is no separation the combined uterine-placental thickness (CTUP) can be measured and any abnormal thickening noted. The normal thickness of this structure during various stages of gestation has been calculated and upper limits for CTUP established. A CTUP of >7 mm is considered to be abnormal up to 270 days of gestation. From 271 to 300 days a CTUP > 8 mm, from 301 to 330 a CTUP > 10 mm, and a CTUP > 12 mm from 331 to term are all considered abnormal *(Renaudin et al., 1997)*.

If transrectal ultrasound is normal or non-diagnostic then a transabdominal ultrasound can be performed and, depending on the sophistication of the ultrasound machine used, various parameters can be measured. With many of the ultrasound machines that are available today the fetus can be examined and the health of the fetus assessed *(Adams-Brendemuehl and Pipers, 1987)*. However with practice the ultrasound machine that is used for routine rectal examinations and a 5 MhZ probe can give the veterinarian a great deal of information. Careful examination of the ventral uterus might reveal the present of pockets of exudate that would allow a presumptive diagnosis of nocardioform placentitis to be made. After the diagnosis is made and fetal parameters measured, it can still be difficult to estimate the extent to which the placenta has been compromised, and consequently the prognosis for the pregnancy and fetal viability.

If treatment is attempted, several problems need to be addressed. Controlled experiments, that evaluate the effectiveness of treatment have not been done and would be difficult to design. Therapy is designed to arrest further placental damage by the infective agent and to improve the function of the remaining normal placenta. In an ascending placentitis with an open cervix, the organism causing the condition can often be cultured and treated locally by introducing antibiotics directly through the cervix. However, with the other forms of placentitis the treatment must be systemic and more empirical, based on probabilities rather than actual cultures and sensitivities of the organisms that may be involved. Over 100 isolates of nocardioform bacteria have been tested in vitro for inhibition of growth by various antibiotics. Cephalosporins, tetracyclines, sulfonamides, trimethoprim, carboxypenicillins, and penicillin plus beta-lactamase inhibitor combinations greatly inhibited the growth of over 90% of these isolates, indicating potential usefulness in a treatment regime for nocardioform placentitis. In addition to antibiotic and anti-inflammatory therapy, topolytic agents have been used in an attempt to prevent premature uterine contractions.

Pentoxyphiline is another drug that has been used to treat placentitis. This treatment is used in an attempt to improve capillary circulation which should help the antibiotics better penetrate the tissue and possibly limit the further spread of the placentitis. This drug may enhance function of the remaining placenta. It must be emphasized that, although many clinicians believe that these treatments are beneficial, there are no experimental data to validate these claims.

The outcome of placentitis can be quite variable and depends on several factors. The most important factor is the time in gestation that the placentitis occurs. If it is an ascending placentitis and the organism gains access late in gestation, it may have little effect on the fetus, unless the organism is very virulent. If the same organism infects the placenta earlier in gestation, however, the outcome could be very different and the mare may deliver a premature or dead fetus. Likewise, if the nocardioform placentitis destroys enough placenta, the fetus may die of starvation and be aborted. Since the bacteria causing nocardioform placentitis rarely infect the fetus, the chances of a live foal being born are much greater with this type of placentitis than in other forms of the disease. However, these foals are often weak and small. They may require significant nursing care and even then not grow up to be useful individuals. Additionally, in many cases of nocardioform placentitis perfectly normal healthy foals are produced.

Placentitis is a many faceted disease that can be caused by a variety of organisms and is often missed by the owner, farm manager, and veterinarian. Until we do a better job of recognizing this condition both prior to and after delivery, the true prevalence of the condition will not be known and its impact on the economics of the horse industry not fully appreciated.

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