Porcine abortions: Overview of PRRSV, PCV2, PPV and other causes

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Abstract

Reproductive failure in pregnant sows continues to present challenges for practitioners and diagnosticians. The diagnostic success rate on abortion cases is lower in comparison to many other disease syndromes and is estimated to be around 30-40% for pigs. Increased numbers of abortions in breeding facilities can often be linked to viral pathogens with the economically most important virus to date being porcine reproductive and respiratory syndrome virus (PRRSV). Besides PRRSV, other viruses such as porcine circovirus type 2 (PCV2), porcine parvovirus (PPV), swine influenza virus (SIV) and others continue to contribute to abortion outbreaks. Pseudorabies virus (PRV) and Hog Cholera Virus (Classical Swine Fever) may also play a significant role in reproductive disease in countries where these diseases have not yet been eradicated. Identification of a cause depends largely on correct sample collection strategies and use of appropriate diagnostic tests and accurate interpretation of test results.

Keywords: Abortion, porcine, viruses

Introduction

Reproductive failure in a pregnant sow may be associated with acute systemic illness of the dam, abortion, increased numbers of non-viable fetuses at parturition or increased numbers of weakborn piglets. Abortion is defined as termination of pregnancy after or accompanied by fetal death. Reproductive failure and abortions in pigs are often of great economic importance and can be caused by infectious pathogens, hormonal processes, nutritional or genetic events, toxicoses, traumatic reasons or other causes. In modern swine production, different production stages (breeding-gestation, farrowing, nursery, grow-finishing) are typically separated on distant sites. Breeding herds are usually comprised of a large population of mature females that are synchronized so that at any time point there are mature females in estrus, gestation or in the process of farrowing. There are also a small number of boars in these facilities that are used to make heat detection and artificial insemination easier. Although modern production facilities often have superior biosecurity barriers and protocols, the dense population of animals in these facilities may facilitate rapid dissemination of reproductive pathogens that are introduced potentially causing great loses in naïve populations.

Investigations should be conducted when any of the following conditions are met: the abortion rate exceeds 3% or when there are clusters of abortions over a short time period or if they are concentrated in one area of the facility. Early detection of reproductive pathogens in breeding herds is therefore crucial to prevent economic losses. Diagnostic challenges especially with viral infection are related to the fact that (1) not all fetuses in a litter are typically infected and (2) sows can abort due to maternal illness and thus, the virus may not be detected in fetal material. Therefore, collecting the appropriate number and types of samples is important to an accurate diagnosis in a timely fashion. We have attempted to provide a more detailed description of the most important viruses associated with porcine reproductive failure below.

Porcine reproductive and respiratory syndrome virus (PRRSV)

Etiology. PRRSV is an enveloped, positive-sense, single-stranded RNA virus in the family *Arteriviridae.*[1,2] PRRSV can infect pigs of any age resulting in reproductive failure in breeding animals, respiratory disease in growing pigs, and diarrhea in neonates. Clinical disease can occur in previously seropositive or vaccinated herds.[3]

Clinical signs in the breeding herd. Clinical signs are variable and in general sows will exhibit mild clinical illness when initially exposed to the virus. Clinical signs include slight depression, anorexia, and a mild fever for one to two days.[4] Sows will occasionally abort during this initial febrile phase of the illness.[1] More typically, animals abort two to four weeks following the initial illness. PRRSV classically

causes late gestation reproductive disease manifest as abortions, stillbirths, premature farrowing, and the birth of weakborn piglets.[1,2] Exposure of naïve sows to a virulent strain early in gestation (less than 45 days) often fails to result in fetal infection while exposure late in gestation (more than 70 days) leads to abortion.[5,6]

Gross and microscopic lesions. A typical PRRSV litter will have one to two, dark, autolyzed fetuses with abundant fluid in the body cavities and several fetuses with meconium staining of fetal skin.[1,2,7] The remainder of the litter may appear essentially normal. Additional gross changes reported with PRRSV abortion include umbilical cord edema with segmental umbilical cord hemorrhage, perirenal edema, mesocolonic edema and increased amounts of clear to serosanguinous fluid in the body cavities.[7] Microscopic lesions appear to be less common than gross changes. Umbilical cords that are grossly edematous with segmental hemorrhage will typically have necrotizing arteritis with periarterial hemorrhage.[7] Arteritis is occasionally observed in a variety of tissues. Additional microscopic lesions reported in fetuses include nonsuppurative encephalitis, myocarditis and interstitial pneumonia.[2,8,9]

Diagnosis. On an individual animal basis, examination of fetuses alone may be insufficient to establish a diagnosis of PRRSV abortion. The percentage of infected fetuses is reported to vary from 18.8% to 73.8%, with an overall rate of approximately 50% reported in two large studies.[7,9,10] Assuming a 50% fetal infection rate, material from four to six fetuses should be pooled to achieve 90-95% confidence that at least one infected fetus is represented in a submission.[10] If sows are exhibiting a mild febrile illness at the time of abortion, they may be aborting due to maternal illness. In these cases, fetal infection will generally not be demonstrated. Sow serum should be submitted for PRRSV PCR as these animals are typically viremic. The diagnostic test of choice for demonstration of PRRSV-associated abortion is PCR which is extremely sensitive and is impacted little by autolysis. Since all fetuses in a litter are typically not infected, it is critical to test multiple fetuses. With PCR, material from one positive fetus can be pooled with several negative fetuses without apparent loss of sensitivity.[4] Typically, pooled fetal thoracic fluid or lung tissues are used. It needs to be considered that marked strain variation can result in substantial genetic and antigenic differences between isolates[11-15] and therefore false negative results if the PCR does not detect all known PRRSV strains. Other diagnostic tools with less sensitivity include immunohistochemistry (IHC) stains on formalin fixed tissue or indirect immunofluorescence assay **(**IFA) on frozen tissue to demonstrate PRRSV antigen in fetal tissues; however, the sensitivity of this test is not great. If abortion due to maternal illness is suspected, seroconversion (by PRRSV ELISA) can be demonstrated on paired serum samples taken at the time of abortion and two weeks later. However, in the vast majority of PRRSV abortions, the sow will have seroconverted at the time of abortion and a single sample, collected at the time of abortion, will demonstrate high PRRSV titers. Results can be difficult to interpret in vaccinated or known seropositive herds. If a sow is seronegative at the time of abortion and remains seronegative, PRRSV can be ruled out with relative certainty.

Prevention and treatment. In order to prevent PRRSV-associated abortions, the establishment of naïve herds and implementation of biosecurity barriers and protocols to keep those herds negative is the best solution. Should this not be possible or economically feasible, practitioners may chose to do planned exposure of the population to PRRSV on a routine basis in order to develop immunity. Commercially available live PRRSV vaccines and autogenous farm-specific PRRSV isolates are commonly used for this purpose.

Porcine circovirus type 2 (PCV2)

Etiology. Porcine circovirus (PCV) is a small circular single-stranded, non-enveloped DNA virus of approximately 1.7 kb. There are two recognized types of PCV: PCV type 1 (PCV1) and PCV type 2 (PCV2). PCV1 was first discovered as a contaminate of a porcine kidney cell line (PK-15) in 1974, but has since been determined to be non-pathogenic in pigs.[16,17] In contrast, PCV2 is pathogenic and has been linked to many disease entities in growing swine as well as to reproductive failure in mature animals. Two main genotypes of PCV2 are currently recognized: PCV2a and PCV2b. Globally, most swine herds have evidence of exposure to PCV2 based on the presence of antibodies.

Clinical signs in the breeding herd. Clinical signs of PCV2 infection in the dam are generally absent. Dams may abort following infection due to systemic illness and abortions are often seen in a low percentage of females with the exception of rare cases of PCV2-infection of naïve populations. Pyrexia and anorexia are frequently observed in aborting dams.[18,19] Delayed farrowing (more than118 days of gestation)[20] or pseudopregnancy[21] may be additional clinical features in affected dams.

Gross and microscopic lesions. Gross lesions in dams are usually absent. Individual fetuses may have lesions of heart failure characterized by dilated and hypertrophied myocardium, plural effusion, ascites, and enlarged, congested livers.[22-24] Gross heart lesions are infrequently present and are typically seen in stillborns or late gestational mummified fetuses. Late gestational fetuses may exhibit generalized anasarca. Perirenal and mesocolonic edema may be evident in some stillborn pigs. PCV2-associated microscopic lesions commonly seen in affected growing pigs (lymphoid depletion; granulomatous inflammation of organ systems) have not typically been reported in dams with PCV2-associated reproductive failure. Fetal microscopic lesions can be absent or vary depending on stage of development in which the fetuses was infected. The most consistent microscopic lesions associated with PCV2-infection include myocardial degeneration and necrosis, nonsuppurative myocarditis, fibrosis and mineralization with occasional amphophilic to basophilic intranuclear inclusion bodies.[22,24] Liver congestion with heptocellular atrophy may also be present along with nonsuppurative pneumonia.[19,24] Follicular hyperplasia and lymphocyte depletion with macrophagic replacement and rare multinucleated giant cells has been reported in lymphoid tissues.[25,26]

Diagnosis. Sow serology is difficult to interpret because PCV2 is ubiquitous and most dams have been previously exposed to PCV2 and will have a positive anti-PCV2-antibody titer. PCV2 viremia in the sow at parturition is also not diagnostic for PCV2-associated reproductive failure due the ubiquitous nature of PCV2. IHC[27,28] and *in situ* hybridization (ISH)[29] are considered to be the gold standard diagnostic assay for confirmation of PCV2-associated abortion by detection of PCV2 antigen or DNA in formalin fixed, paraffin embedded tissues from affected fetuses. Myocardium readily stains if PCV2 is present and the antigen can be seen in the cytoplasm as well as the nucleus of infected cells. PCV2 antigen or DNA can also be present in thymus, spleen, tonsil, and lung. Demonstrating the presence of PCV2 in presuckle live-born piglet sera, aborted, mummified or stillborn fetuses can also be accomplished by other techniques including PCR,[30,31] virus isolation,[27,32] ELISA,[33] IFA,[34] and immunoperoxidase monolayer assay (IPMA).[35]

Prevention and treatment. PCV2-associated abortion is usually an individual sow problem and treatment of the herd is usually not necessary. Incoming gilts can be exposed to PCV2 prior to breeding to guarantee exposure prior to breeding. This can be done by using commercially available killed vaccines or by comingling animals from different sources.

Porcine parvovirus (PPV)

Etiology. Porcine parvovirus is a non-enveloped, single-stranded DNA virus.[36] All PPV isolates appear to be antigenically similar, if not identical.[36,37] PPV is endemic in most swine herds.[38,39] The virus is shed in secretions for several weeks and then survives for four months in the environment.[40] Contaminated premises are likely the major reservoir of the virus.

Clinical signs in the breeding herd. PPV infection of naïve dams is characterized by increased numbers of mummified fetuses, increased numbers of sows that return to estrus, small litters, and decreased farrowing rates. Abortions are not typically observed following *in utero* PPV infection.

Gross and microscopic lesions. In natural infections the primary gross lesion is fetal mummification. Fetuses are dark in color, markedly dehydrated and the skin is dry and leathery. Mummified fetuses are typically 3 to 16 cm in crown to rump length. Due to *in utero* spread of the virus, fetuses are often mummified at different stages of gestation resulting in mummies of varying sizes. Fetal infection during the first 35 days of gestation causes death and reabsorption of embryos, resulting in irregular return to estrus or reduced litter size. Infection between 35 and 70 days of gestation results in fetal death and mummification. Fetuses infected after 70 days of gestation develop an antibody response and may successfully resist infection and are born normal. Microscopic lesions in fetuses are rarely

observed but most commonly consist of perivascular accumulations of mononuclear inflammatory cells in both grey and white matter of the cerebrum and meninges, necrotizing and nonsuppurative hepatitis, interstitial nephritis and placentitis with calcification.[41,42]

Diagnosis. PPV antigen can be easily demonstrated in heart or lung tissues of affected fetuses either by IFA or IHC. PCR can also be used to demonstrate PPV DNA in these tissues. Hemagglutination inhibition (HI) is done to confirm if antibodies against PPV in pre-suckle blood are present which is indicative of intrauterine exposure to the virus. Unlike several reproductive diseases of swine, serology is typically of little value. Interpretation of antibody titers is difficult because a majority of farms vaccinate against PPV, the virus is ubiquitous and natural exposure is common prior to introduction into the breeding herd, there is evidence for an anamnestic response in sows that do not develop reproductive disease, and high HI titers can occur in a herd without any PPV-related symptoms.[38] Serology on stillborn pigs or neonates can provide useful information. The presence of PPV antibodies in the presuckle serum or thoracic fluid of stillborn pigs indicates *in utero* exposure to the virus.

Prevention and treatment. In order to prevent PPV-associated abortions, many producers vaccinate gilts on a routine basis using commercially available killed products. Feedback of mummified fetuses to gilts in isolation and acclimatization has also shown to be beneficial in some situations.

Pseudorabies virus (PRV)

Etiology. Pseudorabies virus (PRV) (suid herpesvirus-1) is an alphaherpesvirus.[43] PRV has been eradicated from commercial swine operations in the US and throughout many intensive swine rearing regions worldwide; however, it is still present in the feral swine population and transmission to the commercial populations could potentially occur.

Clinical signs in the breeding herd. Sows may develop fever, become anorectic, and exhibit mild respiratory signs which may include sneezing and coughing.[44,45] A generalized pruritis is occasionally observed.[45] PRV-associated maternal illness may result in abortion or fetal mummification (depending on the stage of gestation) without evidence of fetal infection due to the non-specific effects of maternal pyrexia.[45] Similar to what is seen with PPV, fetal PRV infection during the later stages gestation leads to fetal mummification, abortion, stillborn, and weakborn pigs.[43] Pigs are usually weak, develop neurologic signs, and die within one to two days. Suckling piglets will develop a high fever, neurologic signs (trembling, incoordination, ataxia and seizures) and shortly after onset of clinical signs, mortality in suckling pigs born to naïve dams may reach 100%.[43]

Gross and microscopic lesions. Fetal PRV infection results in the development of 1-2 mm foci of necrosis.[44,46] Lesions are most readily visualized in liver and spleen, with occasional lesions observed in the lungs. It needs to be noted that fetal bacterial septicemia may occasionally cause similar gross changes. Microscopically, PRV infection causes multifocal random necrotizing lesions in many fetal organs including; liver, adrenal, spleen, lung, lymph node and placenta.[44,46] Eosinophilic to amphophilic intranuclear inclusions are occasionally observed in cells adjacent to foci of necrosis. Brain lesions typical of a viral encephalitis may be identified in weakborn pigs and include nonsuppurative perivascular cuffs, multiple foci of gliosis and neuronal necrosis.

Diagnosis. The most common methods for detecting PRV in aborted fetuses include FA, VI and PCR. Because of the regulatory implications, multiple tests should be undertaken to establish a definitive diagnosis. Fetal tissues of choice include lung, liver and spleen.[44] As commercial operations are considered to be free of PRV and are presently naïve (free of DNA and antibody), serology on sow or pig serum and fetal thoracic fluid can also be used to confirm PRV–associated abortions.

Prevention and treatment. Highly effective vaccines are available for PRV.

Additional viral causes of porcine abortion

Other potential viral causes of abortion are many and include viruses indigenous to the United States (SIV, enteroviruses, teschoviruses and others) and a variety of foreign animal diseases (Classical swine fever, African swine fever and other). Some of these pathogens (i.e. SIV) only induce disease in

the dam and rarely if ever cross the placental barrier. For these pathogens, diagnostics need to focus on demonstration of the pathogen in the dam.

Conclusion: suggested sampling protocol and testing if a viral agent is suspected

Sickness of the dam is present. Any sampling strategies and diagnostic tests must focus on the dam. If the animal is alive, nasal swabs can be tested by PCR for presence of SIV RNA and serum of the dam can be tested by PCR for the presence of PRRSV RNA. If the dam is dead, lung tissues can be tested for presence of SIV or PRRSV RNA. In addition, bacteriology on major organ systems should be conducted to rule out bacterial septicemia (*Salmonella* sp., *Actinobacillus suis* and others). Serum samples from affected and non-affected animals can be tested for seroconversion to PRRSV or SIV.

The dam appears normal. Sampling and diagnostics should focus on the fetuses and piglets. More than one pig per litter needs to be examined. Hearts (including hearts from mummies) should be collected in formalin to test for presence of PCV2 antigen by IHC or ISH. Fresh hearts can also be tested by FA or PCR for PPV. Pooled fetal thoracic fluid or pooled fetal lungs (five fetuses and more) should be tested for presence of PRRSV RNA. If presuckle serum from weakborn pigs is available it can be used to test for presence of antibodies against PPV, PRRSV or PCV2 to rule out or confirm intrauterine exposure. Alternatively, serology can also be conducted on fetal thoracic fluid. Fetal kidneys can be tested by PCR or FA for presence of *Leptospira* sp. Pooled fetal stomach contents, fetal livers and fetal lungs should be cultured for bacteria.

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