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Porcine Circovirus Type 2 (PCV-2) Coinfections in US Field Cases of Postweaning Multisystemic Wasting Syndrome (PMWS)


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described in other species with lipid mobilization disorders. As with the affected bison in the present study, fatal hepatic lipidosis has been recently described in obese bison in late gestation; therefore, obesity during late gestation should also be included as a key factor in the development of fatal hepatic lipidosis in bison (Berezowski J, Simko E, Feist M, Haigh J, Woodbury M: 2001, Fat bison syndrome: a report of fatal hepatic lipidosis in obese, late pregnant bison (Bison bison) cows. Proc Am Assoc Vet Lab Diagn: 17.)

A disease syndrome associated with excessive lipid mobilization and hepatic lipidosis has not been previously identified in bison. These findings suggest that pregnant bison are susceptible to such a syndrome. Although the bison in the current report were exposed to various unique stressors that are not present in commercial bison captive herds, bison producers and veterinarians should be aware of the potential for such changes and monitor feeding of pregnant bison as well as potential stressors that could initiate anorexia and negative energy balance situations.

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Sources and manufacturers
a. Colorado Serum Co., Denver, CO.

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of the cesarean-derived, colostrum-deprived pigs,\textsuperscript{7,16} the gnotobiotic pigs,\textsuperscript{11} the colostrum-deprived conventional pigs,\textsuperscript{2,18} or the conventional pigs\textsuperscript{6} inoculated with PCV-2. All the gnotobiotic pigs infected with PCV-2 and injected with keyhole limpet hemocyanin in incomplete Freund’s adjuvant developed lesions characteristic of PMWS, whereas those given only PCV-2 did not develop any lesions.\textsuperscript{20} Commonly used vaccines such as bacterins for \textit{Mycoplasma hyopneumoniae} and \textit{Actinobacillus pleuropneumoniae} also showed evidence of enhancement of PCV-2 associated disease and lesions.\textsuperscript{5,22} Most recently, characteristic lymphoid and lung lesions of PMWS were reproduced in specific pathogen-free pigs inoculated with an infectious DNA clone of PCV-2; but the pigs did not exhibit wasting.\textsuperscript{12} Several studies have demonstrated enhanced disease and lesions with experimental coinfection of PCV-2 and other infectious agents. Clinical signs of disease were more severe when pigs were coinfected with PCV-2 and porcine reproductive and respiratory syndrome virus (PRRSV).\textsuperscript{3,16} and PCV-2 replication was potentiated by PRRSV.\textsuperscript{3,28} PMWS has also been reproduced by coinfection of PCV-2 and porcine parvovirus (PPV) in colostrum-deprived pigs\textsuperscript{2} and gnotobiotic pigs.\textsuperscript{21} The objective of this retrospective survey was to examine which coinfecting agents are most commonly diagnosed with PCV-2 in field cases of PMWS submitted to a US diagnostic laboratory that receives swine cases from all over North America.

The presence of PCV-2 antigen in lymphoid tissues and/or lung, demonstrated by immunohistochemistry (IHC),\textsuperscript{32} together with moderate to severe lymphoid depletion and/or granulomatous lymphadenitis, was used as the criteria for the diagnosis of PMWS. PMWS was not diagnosed if lymphoid tissues were not submitted with the case. The presence of PRRSV and swine influenza virus (SIV) was confirmed by IHC, polymerase chain reaction (PCR), and/or virus isolation (VI). \textit{Mycoplasma hyopneumoniae} was detected by fluorescent antibody (FA) or IHC, but characteristic microscopic lesions of moderate to severe peribronchial and perivascular lymphoid hyperplasia were considered diagnostic of \textit{M. hyopneumoniae}–induced pneumonia despite a negative FA or IHC test for \textit{M. hyopneumoniae}. The isolation of bacterial agents was performed by routine culture procedures. A Kolmogorov–Smirnov test\textsuperscript{a} was used to determine if the age of the animals affected with PMWS followed a normal distribution.

A total of 4,688 submissions in which PCV-2 IHC had been performed between January 2000, and September 2001, were reviewed. Of these, 1,751 (37.3\%) tested positive for PCV-2, and 484 (10.3\%) were diagnosed as PMWS. Approximately 80\% of the cases were received from Iowa. The rest, in decreasing order, were from North Carolina, Oklahoma, Minnesota, Indiana, Ohio, Colorado, Illinois, Michigan, Kansas, Missouri, Utah, Wisconsin, and Virginia. Of all the animals that tested positive for PCV-2 antigen by IHC, lymphoid lesions characteristics of PMWS were confirmed in only 484 out of 1,751 (27.6\%); but lymphoid tissues were not submitted from many of the cases, and thus PMWS could not be ruled out or confirmed in those cases. The number of cases having each of the different combinations of pathogens is illustrated in Fig. 1. Coinfection of PCV-2 + PRRSV was the most common combination with 164 cases. In decreasing order, other coinfections were PCV-2 + \textit{M. hyopneumoniae} (92 cases), PCV-2 + PRRSV + \textit{M. hyopneumoniae} (77 cases), PCV-2 + bacterial septicemia (68 cases), PCV-2 + bacterial pneumonia (37 cases), and PCV-2 + SIV (13 cases). There were only 9 cases in which singular PCV-2 infection was confirmed without any coinfecting pathogens. The total prevalence of coinfection with PCV-2 was 51.9\% for PRRSV, 35.5\% for \textit{M. hyopneumoniae}, 14.0\% for bacterial septicemia, 7.6\% for bacterial pneumonia, 5.4\% for SIV, and 1.9\% for PCV-2 alone.

The types of bacterial pathogens isolated for each of the combinations of PCV-2 + bacterial septicemia and PCV-2 + bacterial pneumonia are illustrated in Figs. 2, 3. The most common bacterial septicemia was \textit{Streptococcus suis} followed by \textit{Salmonella} sp. Bacterial pneumonias were primarily caused by \textit{Pasteurella multocida}.

Ages were provided in 369 of the 484 cases. Among these cases, PMWS primarily occurred between 8 and 18 weeks of age (294/369), with the highest number of cases occurring.
at 10 weeks of age. The corresponding histogram followed a normal distribution curve according to the Kolmogorov–Smirnov test ($P > 0.2$) (Fig. 4). Interestingly, there were 8 cases in which PMWS was diagnosed at $\leq 5$ weeks of age. Coinfection was with PRRSV was found in 6 of these 8 cases.

In some of the PCV-2–positive cases, PMWS confirmation was not possible if lymphoid tissue was not submitted; so the 27.6% is likely a low estimate of the percentage of PCV-2–infected pigs that develop PMWS. In the present survey the prevalence of PMWS was 10.3% (484 cases of PMWS out of 4,868 cases examined), which is very close to the 8.1% (133 cases of PMWS out of 1,634 cases examined) found in a South Korean study during 1999 and 2000, and the 12.9% (7 cases of PMWS out of 59 cases examined) reported in a Canadian study carried out in 1998.

The fact that many different infectious agents were isolated in cases of PMWS strongly supports the idea that a variety of pathogens may share a common mechanism in stimulating the immune system, with subsequent progression of PCV-2 infection to PMWS. Alternatively, PCV-2 may make pigs more susceptible to other pathogens. The pathogens commonly involved in porcine respiratory disease complex (PRDC), PRRSV, and M. hyopneumoniae were the most common agents that coexisted with PCV-2 in cases of PMWS. PRRSV + PCV-2 coinfection was found in 52% of the cases of PMWS, which is considerably higher than the 29.3% reported in South Korea, more than double the 20% reported in one Canadian field case study, and less than the 67% of the cases with PCV-2 + PRRSV coinfection reported in another Canadian study. European field studies also confirm that PRRSV is involved in many farms with PMWS.

In a recent survey the prevalence of PCV-2 and other pathogens in cases of PRDC received at the Iowa State University Veterinary Diagnostic Laboratory, Ames, Iowa, in the year 2000 was studied, and PCV-2 + PRRSV was demonstrated in 56% of the cases, PCV-2 + M. hyopneumoniae in 19%, and PCV-2 + SIV in 12%. PRRSV was the most prevalent coinfecting agent associated with PCV-2 in swine pneumonia cases, with a percentage very similar to that found in the cases of PMWS in this study. The percentage of PRDC cases with PCV-2 + M. hyopneumoniae coinfe-
tion was lower and the percentage of PRDC cases with PCV-
2 + SIV coinfection was higher than those observed in
PMWS cases in this study.
Porcine parvovirus has been used as a model coinfecting
agent with PCV-2 to induce PMWS in experimental stud-
ies.2,13,21 PPV was demonstrated by IHC and PCR in about
18% of the cases of PMWS in Canada1 and by in situ hy-
bridization in 25.6% of the cases of PMWS examined in
South Korea.19 Only one of the cases of PMWS in this sur-
vey was positive for PPV, but tests for PPV were conducted
in only 8 out of 484 cases (5 by FA and 3 by VI). Increased
testing of PMWS cases for PPV coinfection is warranted on
the basis of the experimental models that clearly demonstrate
enhanced clinical signs and lesions typical of PMWS in
PCV-2 + PPV–coinfected pigs.

The most prevalent bacterial coinfection with PCV-2 in
this survey was PCV-2 + S. suis in 5.5% of the cases. The
combination of PCV-2 + Haemophilus parasuis was diag-
nosed in only 1.6% of the cases; but in a recent South Ko-
rean study19 PCV-2 + H. parasuis was the most prevalent
bacterial coinfection and was found in 32.3% of the PMWS
cases.

It was not possible to determine the vaccination status of
the PMWS cases in this survey because the case histories
provided often did not include vaccination protocols. There
is experimental evidence that common vaccines may trigger
PCV-2 infection and cause it to progress toward PMWS and
that vaccination could potentiate PCV-2 replication.5,22 A re-
cent field trial supports the hypothesis that vaccine or drug-
induced immuno-modulation can potentiate the effects of
PCV-2 infection,22 but the risk of not using vaccines to min-
imize the effects of coinfections such as M. hyopneu-
moniae may be greater than the risk of vaccination-induced PMWS.

The age of presentation of PMWS followed a normal dis-
tribution and coincides with the data from other reports.10,14,19
It is uncommon in the US to find PMWS in animals less
than 5 weeks of age. In all the 8 cases of PMWS in pigs ≤5
weeks of age presented here, other coinfecting agents such
as PRRSV were present in addition to PCV-2. Such findings
suggest that these pigs have a lack or early loss of maternal
immunity against PCV-2 and/or that coinfecting agents such
as PRRSV induced increased replication of PCV-2 and ear-
lier development of PMWS.

Perhaps, the strongest argument for the necessity of a co-
infection or other cofactors25 for full development of the
pathogenic potential of PCV-2 (whether in PMWS or PRDC)
was the low percentage of cases in which PCV-2 is found alone
(only 1.9% in this study). In a similar South Korean study19
singular PCV-2 infection was found in 15% of the PMWS
cases. With other established pathogens such PRRSV33 or
SIV (Janke BH, et al.: 2000, Keeping pace with SIV . A. D.
Leman Swine Conference, pp. 6–16), the percentage of cases
in which they are the only agents found is much higher
(39.8% of the PRRSV cases and 36.9% of the SIV cases).

Proven protocols for management and prevention of
PMWS are not yet established. There is no PCV-2 vaccine
to date. At this point in time, veterinarians often recommend
thorough sanitation between groups with the use of disin-
fectants effective against PCV-2,29 all-in-all-out pig flow, and
controlling farm-specific coinfecting agents that may ac-
count for progression of PCV-2 infection to PMWS. This
survey confirms that in the US, PRRSV and M. hyopneu-
moniae are the most common coinfections in cases of PCV-
2–associated PMWS. At least 2 experimental reports3,28 sup-
port PRRSV-induced increased replication of PCV-2 and in-
creased incidence of PMWS in PCV-2 + PRRSV–coinfected pigs.
Because more than half the cases of PMWS in our
study were associated with PRRSV infection, an effective
PRRSV control or eradication program may be important in
reducing the incidence of PMWS in US herds.

Sources and manufacturers

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