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Editors
W. Christopher Scruton
Stephen Claas

Layout
David Brown

Cover Design
Ruth Cronje, and Jan Swanson;
based on the original design by Dr. Robert Dunlop

The clinical expression of porcine circovirus

J.C.S. Harding,[1] DVM, MSc; E.G. Clark,[2] DVM, MVSc; J.A Ellis,[3] DVM, PhD
1Harding Swine Veterinary Service Inc, Humboldt, SK; 2Prairie Diagnostic Services Inc, Saskatoon, SK; 3Western College of Veterinary Medicine, Saskatoon, SK

Introduction

Although the complete pathogenesis of Post-weaning Multisystemic Wasting Syndrome (PMWS) has not yet been elucidated, several studies have clearly shown that type-2 porcine circovirus (PCV-2) is the primary viral pathogen of PMWS.[1-3] Other pathogens, particularly porcine parvovirus (PPV),[2] appear to contribute significantly to the disease expression, yet it remains to be determined the exact mechanism by which PCV-2 and PPV act synergistically and which other pathogens, if any, are able to result in the expression of clinical disease. With these uncertainties in mind, the objectives of this paper are to review the clinical, serologic, and most distinguishing features of PMWS/PCV-2.

Clinical features

There are six fundamental clinical signs of PMWS that form the basis of clinical diagnosis (**Table 1**).[4,5] While not all six clinical signs are generally noted in a single pig, affected farms will present with the majority, if not all, of these clinical signs over a period of time. When monitoring for PMWS on farm, without a doubt the most consistent clinical signs to note are unthriftiness/wasting and dyspnea; while not pathognomonic, these provide a substantial clinical suspicion that warrants further investigation.

Wasting/unthriftiness

Wasting/unthriftiness is by far the most consistent clinical feature of PMWS. It begins as a very subtle weight loss which progresses over a number of weeks. Affected pigs are typically of excellent weaning weight, but in our experience they tend to be of longer, lean (Landrace-type) confirmation. In end stage disease, severe wasting/unthriftiness becomes apparent.

Table 1: Relative frequency of clinical signs characteristic of PMWS

Clinical sign	Relative frequency
Wasting/unthriftiness	Very frequent
Dyspnea	Very frequent
Enlarged lymph nodes	Very frequent
Diarrhea (profuse/watery)	Frequent
Pallor	Frequent
Jaundice	Less frequent

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Lymph node enlargement

Lymph node enlargement is a consistent feature but rarely recognized by the producer. All lymph nodes may be enlarged, but the inguinal nodes are the most clinically obvious. On gross necropsy, enlargement of the mediastinal and mesenteric lymph nodes are consistently seen.

Dyspnea

Dyspnea (puffing) is also frequently observed but ranges in severity from mild to life threatening. Although it cannot be clinically differentiated from the dyspnea associated with other diseases, including PRRS, the presence of dyspnea in farms free of the major respiratory diseases is of particular concern. The dyspnea is the result of a patchy to diffuse interstitial pneumonia which is typically lymphohistiocytic in early or mild cases and granulomatous in late or severe cases.

Pallor/anemia

Although the pathogenesis of the anemia is not clearly understood, we suspect it involves the direct effect of the virus on bone marrow. The anemia is non-regenerative and may be associated with leukopenia.

Diarrhea

In some cases, the post-weaning diarrhea associated with PMWS is multifactorial in etiology, involving other pathogens such as *Salmonella* sp., *Brachyspira* sp., and enterotoxigenic *E. coli*. However, PCV-2 by itself directly affects all levels of the GIT, particularly the stomach, duodenum, and ileum. The resulting diarrhea is typically profuse and a homogenous brown in color and can be accompanied by marked dehydration. Intestinal lesions are characterized as a granulomatous enteritis with villous atrophy and infiltration of the lamina propria with multi-nucleated macrophages.

Jaundice/icterus

Although not one of the most frequent clinical signs, most farms report icteric or jaundice pigs at least on a sporadic basis. Jaundice may be noted with dyspnea or marked unthriftiness and is usually progressive and terminal. In the early stages, liver lesions consist of lymphocytic infiltration of portal zones, accompanied by single cell necrosis of hepatocytes. In end stage disease, complete obliteration of hepatocytes occurs in most lobules, leaving congested sinusoids, condensed portal areas, and remaining hepatocytes swollen with karyomegaly.

Herd presentation

The clinical signs of PMWS are restricted to the post-weaned aged groups but particularly the late nursery and grower stages, typically affecting pigs between 7 and 12 weeks of age. On occasion, new cases are reported in the late grower or finisher, but this appears to be most common in multiple-sourced grow-finish barns. At the time of writing, there is no evidence to suggest that PCV-2 affects adult animals or their fertility; however, the affect on perinatal piglets in sow herds remains unclear and presently under investigation. Two cases recently reported in western Canada are the first evidence of a possible link between PCV-2 and perinatal infection.

PMWS usually results in low-grade but persistent losses, but the severity of clinical signs in affected herds can vary. Although rare, severe epidemics resulting in a three- to four-fold increase in post-weaning mortality have occurred, but mild and transient elevations in post-weaning mortality are typical. The complete cessation of clinical signs, at least for short periods of time, is also possible. No information on long term cessation or complete eradication is available, although partial depopulation of clinically affected stages in combination with improved hygiene and the segregation of sick animals are critical control strategies.

Serologic investigations

Several IgG antibody assays are presently in use that offer some degree of specificity to PCV-2.[1,6] In a recent study of 25 Canadian herds of a common genetic source, the PCV-2 IgG titer level, sero-prevalence, and variability (measured by coefficient of variation or CV) were compared in herds with and without evidence of clinical disease attributable to PMWS. PCV-2 titers were measured with the competitive ELISA antibody test, recently developed at the University of Saskatchewan (manuscript submitted). Preliminary results of the study confirm the circulation of PVC-2 in the nursery or grower of all herds, regardless of clinical status. The highest, most prevalent, and least variable titers were consistently noted in the finisher sections. Furthermore, there were no significant differences in the titer level, prevalence of sero-positivity, or the variability between PMWS-clinical and PMWS-negative herds (**Table 2**). On all farms, the typical pattern of sero-conversion reflects one of declining colostral antibodies in the suckling piglets, low and variable IgG titers in the nursery with active sero-conversion of virtually all animals during the grower period.

Table 2: Comparison of PCV-2 titers in PMWS clinical and non-clinical herds (mean ± S.D.) measured with the competitive ELISA

	PMWS Clinical	PMWS Non-clinical
Titer level (% inhibition)		
Suckling	67.2 (17.6)	63.3 (15.1)
Nursery	35.3 (12.3)	34.9 (14.7)
Grower	62.4 (24.1)	79.4 (20.6)
Finisher	89.8 (10.5)	93.6 (5.6)
HERD	63.7 (8.4)	67.8 (9.7)
*Prevalence of sero-positivity (%)**		
Suckling	84.2 (18.8)	77.5 (17.6)
Nursery	48.3 (20.4)	45.0 (22.4)
Grower	73.3 (23.9)	90.8 (19.8)
Finisher	97.5 (6.2)	100 (0.0)
HERD	78.5 (11.8)	78.6 (10.9)
Coefficient of variation (CV)		
Suckling	40.9 (24.9)	48.2 (19.0)
Nursery	65.5 (23.5)	65.5 (13.0)
Grower	45.8 (26.2)	29.0 (32.7)
Finisher	13.3 (13.7)	9.2 (8.4)
HERD	52.9 (11.8)	49.8 (13.5)

*cELISA titers with % inhibition >25% considered positive

Diagnostic rule-outs and distinguishing features

The most distinguishing feature of PMWS is the wide assortment of clinical signs and gross lesions associated with the syndrome and their appearance concurrently in affected herds. In contrast, there is a marked consistency in the type of histopathologic lesion noted in both grossly affected and unaffected tissue (**Table 3**). It is very clear that histologic examination is essential to any diagnostic work-up. Thus, a complete diagnostic submission would include normal and abnormal tissue from multiple organ systems and from multiple pigs. Proper due diligence is required to rule out each of the numerous pathogens or mycotoxins that could cause similar disease (**Table 4**). Those lesions considered pathognomonic for PMWS are the chronic destruction of airway epithelium and the PCV inclusion bodies, noted on H&E stained sections.

For the practicing veterinarian, the most distinguishing clinical features of PMWS that should result in further diagnostic work-up include:

- The presence of dyspnea in the absence of PRRS or other significant respiratory diseases
- The presence of icterus in more than a sporadic pig
- The presence of four to six clinical signs concurrently in one herd

Table 3: Relative frequency of observing lesions in gross versus histologic samples

	Gross lesions (%)	Histologic lesions (%)
Lung	90	100
Liver	30	90
Kidney	50	100
Lymph nodes	80	100
Spleen	10	100
Tonsil	0	100
Peyer's patches	0	100
Stomach	40	90
Duodenum	0	90
Ileum	10	90
Colon	0	50
Pancreas	0	40

Conclusion

In spite of the uncertainty surrounding the pathogenesis of PMWS, it is an emerging syndrome of growing prevalence worldwide in both PRRS-positive and PRRS-negative herds. Serologic investigation appears to be a potentially powerful tool for herd investigation, but better understanding of the sensitivity and specificity of the available tests would be useful. A presumptive diagnosis can be made on the basis of clinical presentation and gross necropsy lesions; however, detailed histologic examination of multiple tissues and carcasses is required for confirmation. A definitive diagnosis should be made on the basis of associating PCV-2 antigen or DNA at the lesional tissue with immunohistochemistry or in-situ hybridization. Polymerase chain reaction (PCR) tests specific for PCV-2 may be available in some labs, but care should be taken in interpreting the results in the absence of other evidence if PCV-2 infection.

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Table 4: PMWS differential diagnosis from gross lesions

Lung	PRRS, congestive heart failure, lesion obscurity due to secondary bacterial penumonias, bacteremia and septicemia, Fumonisin mycotoxicosis
Liver	Parasitic migration, mycotoxicosis, bacteremia
Kidney	Leptospirosis, bacteremia, lymphosarcoma
Lymph nodes	Bacteremia, PRRS, lymphosarcoma
Spleen	Bacteremia, PRRS, lymphosarcoma
Stomach	Other causes of gastric ulcers
Colon	Other causes of colitis
Ileum/jejunum	Other causes of villus atrophy