POSTWEANING MULTISYSTEMIC WASTING SYNDROME (PMWS) IN PIGS: AN UP-DATE WITH STILL QUESTIONS

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Introduction

An unknown health problem was described first in Canada in 1996 (Harding 1996, Clark 1996) and soon after it was recognized in other countries throughout the world (Daft et al., 1996, Le Cann et al., 1997, Segales et al., 1997, Choi and Chae 1999).

The well targeted age of the affected pigs, the clinical signs and the lesions induced lead the veterinarians to name it "Postweaning Multisystemic Wasting Syndrome" (PMWS). Until 1998 the situation was rather confusing although the role of a porcine circovirus was rapidly pointed out (Daft et al., 1996, Allan et al., 1998, Ellis et al., 1998). Confusion came from the detection of two types of circovirus (PCV1 and PCV2) and also from the involvement of other pathogens in most of the concerned herds, PRRS virus in particular. This paper is intended to briefly recall the description of the syndrome but above all the emphasis will be placed on the current knowledge that could help in finding solutions for prevention.

Description of the syndrome

The postweaned-growing pig is the only real target for clinical signs of PMWS. The critical period varies from farm to farm within the range of 8-13 weeks of age. The first signals are unthriftiness, low feed intake and sometimes prostration. In the latter case, rectal temperature can be high (up to 41°C). Some of those affected pigs look pale. The situation evolves rapidly. Digestive as well as respiratory manifestations (diarrhoea, dyspnoea or laboured breathing, cough …) are common. Within 3-5 days those severely affected pigs have lost considerable weight and become backbone-showing.

Death can occur whereas most of the remaining wasting pigs have to be euthanized. The individual-pig expression of PMWS is noteworthy. In a room or a pen where contemporary pigs are accommodated, only a proportion of them will exhibit the disease, whilst the others will appear healthy.

The first signs of illness can be detected either at the end of post-weaning phase or at the beginning of fattening phase soon after transfer (week 11 or 12). In addition to the pigs showing wasting "*per se*", other individuals can show skin problems, irregular, red-to-purple macules or papules appear on the hind limbs and perineal area. They tend to coalesce and can

cover an important part of the body including the ears. With time, the skin becomes crusty. Most of those individuals are nice pigs suddenly affected and case fatality is high and rapid (usually within 3 days). The survivors usually turn into poor-doing pigs. Due to the simultaneous damage to the kidneys this condition was named PDNS (Porcine Dermatitis and Nephropathy Syndrome). In all the herds where we had to intervene in France for PMWS, PDNS was also present. The prevalence of PDNS pigs was low on average (0.2%) but its clear and typical expression makes the condition easily detectable. In one of the followed groups, 8% of pigs died from PDNS, sometimes at an older stage than the critical period for classical PMWS outbreaks but the cases were seldom. A huge recrudescence was observed after PMWS started and a similar scenario was seen in all the countries. Therefore it can be hypothesized that the conditions leading-predisposing to PMWS also enhance PDNS expression. When PMWS occurs in the herd, mortality rate suddenly increases. In a group of 12 severely affected farms, 14.6% mortality (from weaning to slaughter) was the average during the 3 month period following the outbreak. Mortality was only 4.6% on the year prior to the outbreak in the same herds (Madec et al., 2000).

In the recent years in France whereas the clinical signs of wasting had dramatically declined, ear necrosis became more prevalent. The tip of the two ears is concerned in the affected pigs. The condition in a second step can evolve into more damage due to ear biting. This issue of ear necrosis was also pointed out in other countries (Busch et al., 2002). The wide range of clinical signs and lesions is the rule in PMWS. In addition most of them can find an explanation with other infections that PCV2. Finally the disease can be more or less severely expressed depending on the farm of on the subsequent batches in a given farm and as said earlier the expression is more an individual pig one than a collective one. In an attempt to clarify the situation regarding the diagnosis of PMWS, Sorden in the US has proposed the following requirements (Sorden 2000) which have all to be exhibited in a pig or in a group of pigs.

- Clinical signs: wasting/weight loss/ill thrift/failure to thrive, with of without dyspnea or icterus
- Histological lesions: depletion of lymphoid organs/tissues and/or lymphohistiocytic to granulomatous inflammation in any organ (typically lungs and/or lymphoid tissues and less often liver, kidney, pancreas, intestine).
- PCV2 infection within characteristic lesion

The author mentions the implication of this definition:

- Clinical signs are not diagnostic
- Gross lesions are not diagnostic
- PCV2 infection does not mean PMWS

Different methods are now available for PCV2 infection. Unfortunately the sensitivity and specificity of most of these methods have not been rigorously established or compared. Immunohistochemistry for PCV2 antigen or *in-situ* hybridisation for PCV2 nucleic acid are frequently used but several polymerase chain reaction assays (PCR) have also been developed taking advantage of their help in typing the isolates. It remains that the diagnosis of PMWS is still a challenge when the expression is mild.

Experiments

Soon after Porcine Circovirus type 2 (PCV2) was found in the lymphoid tissues of affected pigs, experimental reproductions of the syndrome were attempted. A severe wasting disease was obtained in young colostrum-deprived piglets which were inoculated with both PCV2 and Porcine parvovirus (Allan et al., 1999). In the trial, the pigs receiving PCV2 alone showed mild disease and lesions. Another experiment with several replications used SPF pigs of 6-7 weeks of age from a PCV2-negative herd (Albina et al., 2001). On the second and third weeks post-inoculation, clinical signs were regularly obtained (prostration, dypnea, reduced feed intake). At necropsy typical pathological lesions consisting in enlarged lymph nodes, mononuclear cell depletion and multinucleated giant cells were found. The PCV2 was recovered from the damaged tissues and no trace of other pathogens was detected in the sera. In the experiment, sentinel non-inoculated pigs, also fell ill but the clinical signs were delayed by 2 weeks, suggesting the need for a high infection pressure in the pens before the disease was launched in the latter pigs. Hence the disease was horizontally transmitted. In Canada PMWS lesions were obtained (without obvious clinical signs) in weaned piglets after inoculation of PCV2 alone (Magar et al., 2000). Other experiments were performed with conventional pigs co-infected by PCV2 and PRRSV (Porcine Reproductive and Respiratory Syndrome Virus). In five-week-old pigs, co-infection was found to induce much more severe disease than PCV2 alone (Rovira et al., 2002). The results supported the hypothesis that PRRSV could enhance PCV2 replication. PMWS was also reproduced in newborn pigs inoculated with a 1993 PCV2 isolate from Sweden (Allan et al., 2002). This isolate was obtained from a lymph node from a seropositive pig far before the disease was recognized and described in Sweden. From detailed microscopic observations it was shown that immune activation was a key component of the pathogenesis of PCV2-associated PMWS in pigs

(Krakowka et al., 2001). The immune system activation was suggested to result from an "*in vivo*" interaction of PCV2 and other pathogenic agents (Krakowka et al., 1999). Vaccination was also investigated as immune system activator. M. *hyopneumoniae* vaccination in young piglets was associated to more severe PMWS in PCV2 infected animals when compared to non-vaccinated ones (Allan et al., 2001).

Analytic epidemiology

A limited number of surveys were performed about PMWS and most of them took place in the recent years. A cross-sectional study with a limited number of farms (n = 25) undertaken in Canada was focused on the risk factors of PCV2 infection detected on poor-doing pigs (Cottrell et al., 1999). The level of health at the early stage (nursery) and biosecurity were found as possible risk factors. More recently a case-control study was carried out in The Netherlands taking co-infections as main target (Wellenberg et al., 2004). A concurrent infection of PCV2 and PRRS virus was found at a higher prevalence in pigs showing clinical PMWS. Co-infections of European and American-type of PRRS virus were detected in PMWS herds. In France a considerable research effort was directed at epidemiological aspects of PMWS. A case-control study involving 149 farrow-to-finish farms pointed out a combination of risk factors (Rose et al., 2003a). They mainly related to herd management and husbandry (intense cross-fostering). In a second step a follow-up observation was performed (Rose et al., 2003b) and revealed sharper risk factors like those related to vaccination. The combined results are recapitulated Table 1. Events occurring early in life like Porcine Parvovirus and PCV2 in the pregnant sow were found to be involved. By the way, studies focused on PCV2 isolates showed that PMWS were most likely not due to the emergence of a new genotype of circovirus (Boisséson et al., 2004). Therefore, unless new findings comes in from laboratory investigations, and since PCV2 was present in the pig herd far before PMWS stroke, it can be hypothesized that our way of raising pigs has changed and some practices might massively trigger PCV2 replication at a certain time in life in predisposed piglets. Whereas all the pigs get seropositive at the end of fattening phase, those which seroconvert early in life are more at-risk to develop disease. The dynamics of PCV2 in the herd is suspected to be a key determinant of PMWS expression (Rodriguez-Arrioja et al., 2002).

In Spain an exploratory case-control study was carried out in 2002-2003 (Lopez-Soria et al., 2005). Three variables were found significant in the final model: two related to sow vaccination scheme and one to PCV2 seroprevalence in growing pigs.

Conclusion

In spite the considerable research efforts, PMWS remains a puzzling problem. The immune system is pivotal in the pathogenic process. PCV2 massive replication is believed to be enhanced when certain circumstances are met in the pigs and in their environment, some of them taking place early in life. Preventive measures can be proposed, based on risk factors where animal hygiene at large has a place of choice.

Table 1: The risk factors involved in PMWS (Rose et al., 2003, adapted)

1- At the herd level (farrow-to-finish farms)	***less risky value***
• Porcine parvovirus (PPV) status of fattening pigs (at the end of finishing phase)	negative
• PRRSV status of fattening pigs (end of finishing phase)	negative
• Source of semen used	PCV2 negative
• Vaccination scheme/PPV + Erysipelas	Grouped
• Cross-fostering	limited (<15% piglets)
• Pen size at the nursery-postweaning stage	small pens
• Hygiene in weaning facilities	perfect
• Hygiene in farrowing facilities	perfect
• Type of housing for pregnant sows	group-housing
• Hygiene *vs.* parasites (sow herd)	perfect
2- At the sow (litter) level	
• PPV seroconversion during pregnancy	no seroconversion
• Abcesses/injuries at the injection zone (neck)	no abcess
• PCV2 serol. status at farrowing	positive

References

1- *Allan G., Meehan B., Todd D., Kennedy S., Mc Neilly F., Ellis J., Clark E.G., Harding J.C., Espuno E., Botner A., Charreyre C. 1998. Novel porcine circoviruses from pigs with wasting disease syndromes. The Vet. Rec., 142: 467-468*

2- *Allan G.M., Kennedy S., Mc Neilly F., Foster J.C., Ellis J.A., Krakowka S.J., Meehan B.M., Adair B.M. 1999. Experimental reproduction of severe wasting disease by co-infection of pigs with porcine circovirus and porcine parvovirus. J. Comp. Pathol., 121: 1-11*

3- *Allan G.M., Mc Neilly F., Mc Nair F., O'Connor M., Meehan B., Gilpin D., Ellis J., Townsend H., Lasagna C., Boriosi G., Krakowka S. 2001. Neonatal vaccination for Mycoplasma hyopneumoniae and Postweaning Multisystemic Wasting Syndrome: a field trial. The Pig Journal, 48: 34-41*

4- *Allan G.M., Mc Neilly F., Meehan B., Kennedy S., Johnston D., Ellis J., Krakowka S., Fossum C., Wattrang E., Wallgren P. 2002. Reproduction of PMWS with a 1993 Swedish isolate of PCV2. The Vet Record Feb. 23, 255-256*

5- *Boisséson C. de, Béven V., Bigarré L., Thiery R., Rose N., Eveno E., Madec F., Jestin A. 2004. Molecular characterization of porcine circovirus type 2 isolates from PMWS-affected and non affected pigs. J. of General Virology, 85: 293-304*

6- *BPEX 2004: finishing pigs systems research production trials 1 and 2: British pig executive, Milton Keynes, UK*

7- *Busch M.E., Nielsen E.O., Hassing A.G., Wachmann H. 2002. Risk factors for each necrosis in growing-finishing pigs. Proceedings IPVS congress, Ames, P 345*

8- *Choi C., Chae C. 1999. In-situ hybridization for the detection of porcine circovirus in pigs with Postweaning Multisystemic Wasting Syndrome. J. Comp. Pathol., 121: 265-270*

9- *Clark E.G. 1996. Postweaning Multisystemic Wasting Syndrome: preliminary epidemiology and clinical findings. Proceedings. Western Can. Assoc. Swine Pract., PP 22-25*

10- *Cottrell T.S., Friendship R.M., Dewey C.E., Jesephson G., Allan G., Walka I., Mc Neilly F. 1999. A study investigating epidemiological risk factors for porcine circovirus type II in Ontario. The Pig Journal; 44: 10-17*
11- *Daft B., Nordhausen R.W., Latiner K.S., Niagro F.D. 1996. Interstitial pneumonia and lymphadenopathy associated with circoviral infection in a six week-old pig. Proceedings. Am. Assoc. Vet. Lab. Diag., 39: 32*
12- *Ellis J., Hassard L., Clark E., Harding J., Allan G., Willson P., Strohappe J., Martin K., Mc Neilly F., Meehan B., Todd D., Haines D. 1998. Isolation of circovirus from lesions of pigs with PMWS. Can. Vet. J., 39: 44-51*
13- *Harding J.C. 1996. Postweaning Multisystemic Syndrome: preliminary epidemiology and clinical findings. Proceedings. Western Can. Assoc. Swine Pract., P 21*
14- *Krakowka S., Ellis J.A., Mc Neilly F., Ringler S., Rings D.M., Allan G.M. 2001. Activation of the immune system is the pivotal event in the production of wasting disease in pigs infected with porcine circovirus-2 (PCV2). Vet. Pathol., 38: 31-42*
15- *Krakowka S., Ellis J.A., Rings M., Allan G.M., Mc Neilly F., Meehan B. 1999. Porcine circovirus infection: reproduction of Postweaning Multisystemic Wasting Syndrome (PMWS) in gnotobiotic swine. Proceedings Am. Assoc. of Swine Practioners, PP 417-422*
16- *Lopez-Soria S., Segalès J., Rose N., Vinas M.J., Blanchard P., Madec F., Jestin A., Casal J., Domingo M. 2005. An exploratory study on risk factors for Postweaning Multisystemic Wasting Syndrome (PMWS) in Spain. Prev. Vet. Med. in press.*
17- *Mager R., Larochelle R., Thibault S., Lamontagne L. 2000. Experimental transmission of porcine circovirus type 2 (PCV2) in weaned pigs: a sequential study. J. of Comp. Pathol. 123: 258-269*
18- *Rose N., Abhervé-Guéguen A., Le Diguerher G., Eveno E., Jolly J.P., Blanchard P., Oger A., Houdayer C., Jestin A., Madec F. 2003b). A cohort study about clinical Postweaning Multisystemic Wasting Syndrome (PMWS) in pigs of different genetic background. Proceedings ISVEE Congress, Viña del Mar, Chile*
19- *Rose N., Larour G., Le Diguerher G., Eveno E., Jolly J.P., Blanchard P., Oger A., Le dimna M., Jestin A., Madec F. 2003a). Risk factors for porcine Postweaning Multisystemic Wasting Syndrome (PMWS) in 149 French farrow-to-finish herds. Prev. Vet. Med., 61: 209-225*
20- *Wellenberg G.J., Stokhofe-Zurwieden N., Boersma W.J.A., Jong M.F. de, Elbers A.R.W. 2004. The presence of co-infections in pigs with clinical signs of PMWS in The Netherlands: a case-control study. Research in Vet. Sci., 77: 177-184*