

CIRCOVIROSIS IS NOT A DISEASE: REVIEW OF PMWS

MARINA ŠTUKELJ, IRENA GOLINAR OVEN¹

SUMMARY: Postweaning multisystemic wasting syndrome (PMWS) is one of the disease among the porcine circovirus diseases (PCVD). PMWS has a significant economic impact on global pig industry. Porcine circovirus type 2 has been circulating in pigs for many years before being linked to disease. PMWS has been reported from all major pig-producing countries. Infection with porcine circovirus type 2 (PCV2) is necessary for PMWS to develop, but most research has shown that PCV2 needs one or more co-factors for PMWS to develop into severe and even fatal disease. The confirmation of PMWS should be based on certain criteria such are clinical signs (growth retardation and wasting, frequently with dyspnea and enlargement of inguinal lymph nodes and occasionally with jaundice), moderate to severe characteristic histopathological lesions in lymphoid tissues, moderate to high amounts of PCV2 within the lesions in lymphoid and other tissues and mortality in excess of expected or/and historical level for the farm. Introduction of PCV2 vaccines significantly changed the impact of PCV2 on the pig production globally.

Key words: PCV2, PMWS, risk factors, control, pig.

INTRODUCTION

Porcine circovirus diseases (PCVD) or porcine circovirus associated diseases (PCVAD) were proposed to group diseases or conditions linked to porcine circovirus type 2 (PCV2) (Baekbo et al., 2012). PCV2 infection is associated with postweaning multisystemic wasting syndrome (PMWS) (Clark, 1996), porcine dermatitis and nephropathy syndrome (PDNS) (Rosell et al., 2000), porcine respiratory disease complex (PRDC) (Kim et al., 2003), and reproductive diseases (Sanchez et al., 2001). PMWS is the most important PCVD and has a significant economic impact on global pig industry (Baekbo et al., 2012).

PMWS in pigs was first identified in western Canada in 1991 (Walker et al., 2000), in Europe was first described in France in 1996. PMWS has been reported from all pig-producing countries, most recently in Australia (Baekbo et al., 2012).

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PORCINE CIRCOVIRUS TYPE 2

Porcine circovirus (PCV) belongs to the genus *Circovirus* in the family *Circoviridae* (Chae, 2005). PCV, a small, nonenveloped, single-stranded DNA virus was first recognised as a contaminant of the continuous porcine kidney cell line PK-15 in 1974 (Opriessnig et al., 2007). Under experimental conditions, the PK-15–derived PCV isolate did not produce diseases in pigs (Allan et al., 1995). Sequence analyses of the PMWS-associated PCV revealed significant genetic differences compared with the PK15–derived PCV. The pathogenic PMWS-associated PCV was designated as porcine circovirus type 2 (PCV2) and non-pathogenic PCV as porcine circovirus type 1 (PCV1) (Opriessnig et al., 2007).

Analysis of PCV2 viruses from around the world showed close phylogenetic relationships and nucleotide sequence identity greater than 93% (Larochelle et al., 2002). Until now, five genotypes have been described. Most PCV2 genomic sequences fit into two major groups: PCV2 genotypes a and b and seem to have worldwide distribution (Segalés et al., 2008).

PCV2 is regarded as a ubiquitous virus and is present in most pig herds. Domestic and feral swine appear to be the natural host (Segalés and Domingo, 2002).

PCV2 has been found in nasal, tonsillar, bronchial, ocular secretion, faces, saliva, urine, colostrum, milk and semen but oronasal exposure is considered the primary route of transmission (Krakowska et al., 2000). Transmission of PCV2 among pigs can occur by mixing naïve with infected animals by direct contact. Most pigs became infected at 4-11 weeks of age, depending on the farm (Segalés et al., 2012).

DEFINITION OF PMWS

PCV2 needs one or more co-factors for PMWS to develop into severe and even fatal disease (Lohse et al., 2008). Without co-factors PCV2 does not cause any disease, consequently circovirus is not a disease. Data from different European countries showed almost 100% herd seroprevalence to PCV2 in both PMWS affected and non-affected farms (Rose et al., 2002). The confirmation of PMWS should be based on certain criteria: 1. relevant clinical symptoms (growth retardation and wasting, frequently with dyspnea and enlargement of inguinal lymph nodes and occasionally with jaundice), 2. presence of PCV2-associated microscopic lesions and 3. detection of PCV2 within the lesions in lymphoid tissue of affected pigs (Sorden, 2000). According to Segales (2012) these diagnostic criteria should be: weight loss and paleness of skin (respiratory and/or digestive clinical signs may be present well), moderate to severe lymphocyte depletion with granulomatous inflammation of lymphoid tissues and moderate to high amount of PCV2 in damage tissue. Opriessnig et al. (2007) proposed that in order to put PMWS diagnosis, PCV2 antigen must be revealed in more than one lymphoid tissue (lymph node, tonsil, spleen) and at least one other organ system (lung, liver, kidney, intestines). It is generally accepted that the PMWS diagnosis at herd level should be based on two conditions: 1. a significant increase in mortality associated with clinical signs compatible with PMWS, and 2. an individual diagnosis in at least one of the three to five necropsied pigs (Grau-Roma et al., 2011; Grau-Roma et al., 2012).

DIAGNOSIS

PMWS most commonly affects pigs at 2-4 months of age (Grau-Roma et al., 2009). Morbidity in affected farms is commonly 4-30% (occasionally 50-60%) and mortality ranges from 4% to 20% (Segales and Domingo, 2002). PMWS is characterized clinically by wasting, pallor of the skin, respiratory distress, diarrhea and occasionally icterus. Enlarged subcutaneous lymph nodes are common finding in the early clinical phases of PMWS (Segales et al, 2004).

At necropsy, the typical macroscopic findings are wasting, non-collapsed lungs, pulmonary consolidation and enlargement of at least one lymph node. Microscopic findings in lymphatic tissue include lymphatic depletion, histiocytic infiltration, inclusion bodies and giant cells (Segales et al., 2004). Porcine circovirus type 2 antigens should be present in moderate-to-massive quantity in lymphoid tissues with typical lesions. Based on necropsy of three unthrifty pigs from all herds in a case-control study, pigs with PMWS were found in 78% of case herds and in 26% control herd with no obvious clinical signs of PMWS (Nielsen et al., 2008). Serological assays for the detection of antibodies to PCV2 have been developed, but diagnosis of PMWS using serological techniques is problematic because PCV2 is ubiquitous and seroconversion patterns are relatively similar in PMWS-affected and non-affected farms. PCV2 dynamic are interest because of their potential role in monitoring PCV2 vaccination (Opriessnig et al., 2008). Thus, to be able to classify a herd as PMWS-affected, the clinical appearance (wasting and excess mortality) must be combined with the laboratory findings. Several studies have assessed the diagnostic value of using serology (antibodies) and PCV2 DNA detection (qPCR) for the diagnosis of PMWS (Grau-Roma et al., 2009; Turner et al., 2009; Woodbine et al., 2010). Even though all studies found significantly higher viral load in PMWS pigs compared with non-PMWS pigs, they can currently conclude that neither viral load nor antibodies can be used for diagnosing pigs or herds as PMWS- affected because the diagnostic sensitivity and specificity are too low (Grau-Roma et al., 2009).

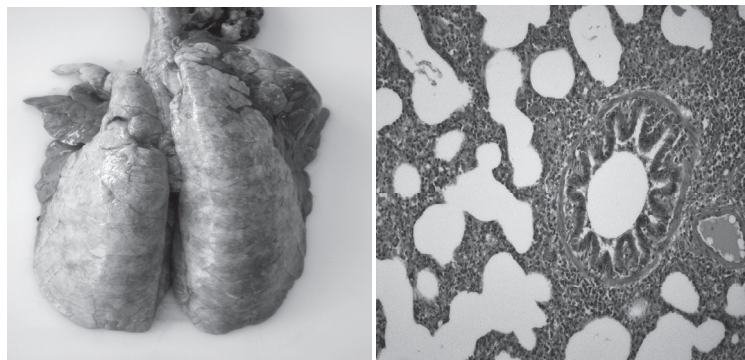


Fig 1. Interstitial pneumonia (Photo: Švara T). Fig 2. Histopathological examination; Interstitial pneumonia (Photo: Švara T).

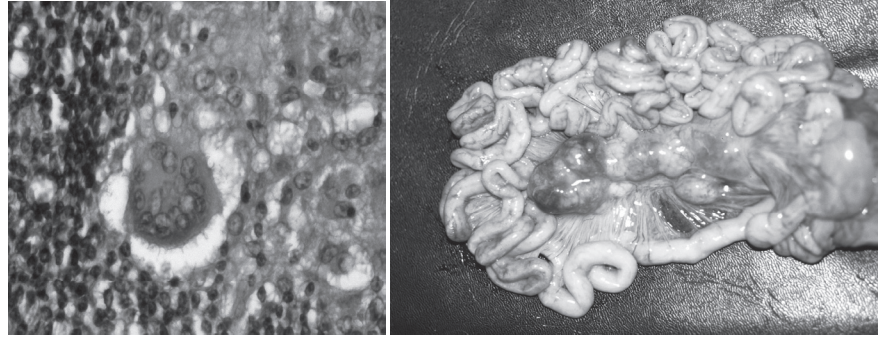


Fig 3. Multinucleate giant cell and macrophages (Photo: Černe M) Fig. 4: Swollen mesenterial lymph nodes. in a medulla of the lymph node (Photo: Švara T).

RISK FACTORS FOR PMWS

Epidemiological studies comparing affected herds with non-affected herds have been carried out in the UK, France, the Netherlands, Spain and Denmark with the objective of identifying factors that either increased or decreased the risk for a herd to be affected by PMWS (Rose et al., 2003; Enoe et al., 2006; Vigre et al., 2006; Woodbine et al., 2007). The most significant factors identified in these studies are summarized in Table 1. Several studies have focused on risk factors for PMWS at the individual pig level. Pigs with low PCV2 antibody titers at 7 weeks of age (and no subsequent seroconversion) and piglets born by seronegative sows were at higher risk of being affected by PMWS (HR = 7.0 and 2.8, resp.) (Rose et al., 2005). Likewise, active infection of the pregnant sows with parvovirus increased the risk (HR = 2.3). It has also been shown that more piglets died from viremic sows than from non-viremic sows (OR = 2.1) and from sows with low antibody titres (OR = 3.0) (Calsamiglia et al., 2007). A longitudinal study in seven PMWS farms showed an increased risk of PMWS if piglets were infected early (before 7 week of age), whereas reduced risk was found if piglets were weaned after 21 days and if they were born of seropositive sows (Rose et al., 2009). The significance of maternal immunity as protective for disease development, as indicated in these studies, was supported by a longitudinal cohort study in 13 Spanish/Danish PMWS farms (Grau-Roma et al., 2011; Grau-Roma et al., 2012).

Table 1. Risk factors for PMWS (Grau-Roma et al., 2011; Baekbo et al., 2012).

	Factors increasing the risk of PMWS	Factors decreasing the risk of PMWS
Animals	<ul style="list-style-type: none"> ● Gender (male) ● Litter of origin ● Low birth weight ● Low weaning weight ● Low weight at the beginning of fattening period 	<ul style="list-style-type: none"> ● Gender (female)
Facilities	<ul style="list-style-type: none"> ● Large number of sows ● Large pens at nursery and growing ages ● Proximity to other pig farms 	<ul style="list-style-type: none"> ● Separation pit for adjacent fattening rooms ● Shower facilities ● High level of external biosecurity ● Quarantine for purchased pigs and gilts ● Change of boots/clothes in entrance room of the farm
Management practice	<ul style="list-style-type: none"> ● High level of cross-fostering ● Short empty periods at weaning and fattening ● Large range in age and weight entering the nursery ● Continuous flow nursery ● Purchase of replacement gilts (>500 per year) ● Sows with neck injuries due to poor injection technique ● Early weaning (<21 days of age) ● Herd size >400 sows 	<ul style="list-style-type: none"> ● Sorting pigs by sex at nursery stage ● Greater minimum weight at weaning ● Group housing sows during pregnancy ● Long empty period (weaners and sows) ● Dry sows in collective pens ● Visitors with no pig contact for several days before visiting farm ● Use of semen from an insemination centre
Vaccination/ treatment/ nutrition	<ul style="list-style-type: none"> ● Vaccination of gilts against porcine reproductive and respiratory syndrome (PRRS) ● Vaccination of sows against <i>E. coli</i> ● Use of separate vaccines against erysipelas and porcine parvovirus (PPV) on gilts ● PPV antibodies among finishers ● Active PPV infection in pregnant dams ● On-farm semen collection 	<ul style="list-style-type: none"> ● Vaccination of sows against atrophic rhinitis ● Regular treatment for ectoparasites ● Use of oxytocin during farrowing ● Use of spray-dried plasma in initial nursery ration

PREVENTION AND CONTROL

PMWS is considered a multifactorial disease (Segalés et al., 2012). Before the introduction of commercially PCV2 vaccines, the focus was on good production practice and on control of other diseases (Baekbo et al., 2012). The implementation of „Madec’s 20-point plan“, a list of management practices lowered the impact of the disease and decreased the mortality in severely affected farms (Madec et al., 2008). These factors still have relevance in the control of PMWS.

Intraperitoneal injection of piglets, five days before weaning with serum from 100 kg pigs, from the same farm (serum therapy) was reportedly successful in reducing losses in growing period (Valenčák and Martinjak, 2005).

Introduction of PCV2 vaccines significantly changed the impact of PCV2 on the pig production globally (Baekbo et al., 2012). In pigs, vaccination improved average daily gain (ADG) and feed conversion, decreased mortality rates, reduced medication costs, and reduced viral loads and PMWS lesions (Pejsak et al., 2009). Even in farms with a subclinical level of PCVD and acceptable low mortality rates, vaccination of piglets increased ADG among grower-finishers (Baekbo et al., 2012). In sows, vaccination increased fertility and reduced returns to service (Kekarainen et al., 2010).

The vaccine success is based on activated humoral and cellular immune responses against PCV2. PCV2 vaccine efficacy in pigs may rely on humoral immunity. Low antibody responses, as well as lack of antibody development after vaccination, do not necessarily correlate with lack of protection. Cell-mediated immunity is also assumed to be important (Segalés et al., 2012).

Four PCV2 vaccines are commercially available in most countries: one sow vaccine (Circovac^R, Merial) and three piglet vaccines (Ingelvac^R CircoFlex^R, Boeringer Ingelheim; Porcillis^R PCV/Circumvent^R PCV, Intervet/Merial & Circovac^R, Merial) (Baekbo et al., 2012). All current vaccines are based on PCV2a strains (Kekarainen et al., 2010).

High levels of maternal-derived antibodies were found to interfere with active seroconversion following vaccination (Fort et al., 2009), even though the vaccine significantly reduced viremia and shedding of virus. It is recommended to avoid vaccination of too young piglets.

CONCLUSIONS

PCV2 is ubiquitous and most PCV2 infections are sub-clinical. PCV2 needs one or more co-factors for PMWS to develop into severe and even fatal disease. Unfortunately no single viral co-factors have yet been identified. Post-weaning mortality is one of the most significant losses in PMWS affected herds, but reduction in growth and poor feed utilization as well as increased consumption of antibiotics add to the cost of the disease. Introduction of PCV2 vaccines significantly changed the impact of PCV2 on the pig production globally.

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CIRKOVIROZA NIJE BOLEST: PMWS

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Izvod

Post-weaning multisystemic wasting syndrome (PMWS) je jedan od oblika cirkovirusnih bolesti (PCVD). PMWS ima značajan ekonomski uticaj na globalnu proizvodnju svinja. Cirkovirus svinja tip 2 je cirkulirao u populaciji svinja mnogo pre nego što je bio povezan sa bolešću. PMWS je izveštavan iz svih zemalja koje su značajne kao proizvođači svinja. Infekcija sa cirkovirusom tipa 2 (SCV2) je potrebna za razvoj PMWS, ali većina od istraživanja pokazala su da SCV2 treba jedan ili više ko-faktora da se PMWS razvije u tešku, pa čak i smrtonosnu bolest. Potvrda PMWS treba da temelji na određenim kriterijumima kao što su klinički znakovi (zaostajanje u rastu i gubitak težine, često sa dispnejom i povećanjem ingvinalnih limfnih čvorova, a povremeno i sa žuticom), umerenim do teškim karakterističnim patohistološkim lezijama

u limfnim tkivima, umerenim do visokim količinama SCV2 unutar lezija u limfnim i drugim tkivima i smrtnost koja je veća od očekivane i/ili istorijske razine za pojedinu farmu. Uvođenje vakcinacije sa SCV2 cepivima značajno je promenilo uticaj SCV2 na svinjogojstvo na globalnoj razini.

Ključne reči: SCV2, PMWS, faktori rizikovanja, kontrola, svinja.

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