Virus Research 164 (2012) 10–19

Contents lists available at SciVerse ScienceDirect

Virus Research

journal homepage: www.elsevier.com/locate/virusres

Review

Porcine circovirus type 2 (PCV2) infections: Clinical signs, pathology and laboratory diagnosis

Joaquim Segalés[a,b,*]

[a] Centre de Recerca en Sanitat Animal (CReSA), UAB-IRTA, 08193 Bellaterra, Barcelona, Spain
[b] Departament de Sanitat i Anatomia Animals, Universitat Autònoma de Barcelona, 08193 Bellaterra, Barcelona, Spain

ARTICLE INFO

Article history:
Available online 17 October 2011

Keywords:
Porcine circovirus type 2 (PCV2)
Clinical signs
Pathology
Diagnosis

ABSTRACT

Clinical signs and pathological features are still the corner-stones to suspect and diagnose overt disease associated with PCV2 infection. The clinico-pathological scope of this viral infection has been expanded over time. From the initial description of postweaning multisystemic wasting syndrome, some enteric, respiratory and reproductive disorders have been subsequently linked with PCV2. Porcine dermatitis and nephropathy syndrome, an immunocomplex disease, has also been associated with infection by this virus. All together, these conditions have been grouped under the name of porcine circovirus diseases (PCVD) or porcine circovirus associated diseases (PCVAD). The precise mechanisms by which a PCV2 infected pig develops a PCV2 subclinical infection or a clinical PCVD/PCVAD are still to be fully elucidated, but inferences based upon clinical, gross and histologic findings from field cases of disease have been useful to suggest the pathogenesis of this viral infection. The objective of the present review is to update the current knowledge on the clinical and pathological scope of PCV2 infections, as well as on their diagnosis. Moreover, a proposal on a unified PCVD/PCVAD terminology and clearly defined diagnostic criteria for these conditions are also given.

Contents

1. Introduction

Postweaning multisystemic wasting syndrome (PMWS) was initially described in 1991 in Saskatchewan (Canada) as a sporadic disease characterized by wasting and jaundice (Clark, 1996; Harding, 1996). This condition was further observed from 1994 onwards by its discoverers (Dr. John Harding as clinician and Dr. Edward G. Clark as pathologist) and it was soon described in all continents, including Oceania (Grau-Roma et al., 2011). The new disease defined a clinical picture characterized by wasting, paleness of the skin, respiratory distress and, occasionally, diarrhea and jaundice in late nursery and fattening pigs (Segalés et al., 2005a). Affected animals displayed characteristic lesions in multiple tissues (multisystemic), mainly in lymphoid organs (Clark, 1997; Rosell et al., 1999).

Soon after initial descriptions of PMWS, a massive presence of porcine circovirus (PCV) antigen was demonstrated within lesions of affected animals (Clark, 1997; Segalés et al., 1997). Since PCV was considered non-pathogenic for swine (Allan et al., 1995; Tischer et al., 1986), an immediate reaction against the causality of PMWS by PCV occurred in the swine scientist and veterinarian communities worldwide. The following year, nucleotide sequence analysis of the PCV associated to PMWS revealed important

* Correspondence address: Centre de Recerca en Sanitat Animal (CReSA), UAB-IRTA, 08193 Bellaterra, Barcelona, Spain. Tel.: +34 935814563; fax: +34 935814490.
E-mail addresses: joaquim.segales@cresa.uab.cat, joaquim.segales@uab.cat

0168-1702/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.virusres.2011.10.007

differences compared to the previously known PCV derived from PK-15 cells (ATCC CCL-33) (Hamel et al., 1998; Meehan et al., 1998). Therefore these viruses were named PCV type 1 (PCV1) for the cell culture-derived virus, and PCV type 2 (PCV2) for the disease associated virus (Allan et al., 1999b).

After 1998, experimental studies with PCV2 were mainly focused on PMWS reproduction (Allan et al., 2004). It was soon realized that reproduction of the disease was rarely achieved by means of using only PCV2 in the inoculum (Bolin et al., 2001; Harms et al., 2001; Okuda et al., 2003). In most cases clinical disease was reproduced when PCV2 was inoculated together with another infectious or non-infectious agent (Allan et al., 1999a; Krakowka et al., 2000, 2001; Opriessnig et al., 2004; Rovira et al., 2002). Therefore, PCV2 was considered a necessary but not sufficient factor to develop the clinical disease (Ellis, 2003; Tomás et al., 2008).

The clinical and pathological scope of PCV2 infection has been expanded since 1991. Besides PMWS, PCV2 has also been implicated in other conditions. PCV2 has been suggested to play a role in reproductive disorders, the so-called porcine respiratory disease complex (PRDC), enteritis, porcine dermatitis and nephropathy syndrome (PDNS) and proliferative and necrotizing pneumonia (PNP) (Opriessnig et al., 2007; Segalés et al., 2005a). In addition, congenital tremor type A2 was initially linked to PCV2 infection (Stevenson et al., 2001), but subsequent studies suggested no association between the virus and the condition (Ha et al., 2005; Kennedy et al., 2003). It is worthy to remark that the role of PCV2 in all these conditions, as well as an unequivocal interpretation of what means to find the virus in a given lesion, has been a matter of controversy over the years. Such complicated scenario has caused that a number of terminologies have been used to name diseases linked to PCV2, being in some cases rather confusing. Confusion extended also to the establishment of unequivocal diagnostic criteria for PCV2 associated conditions.

The objective of the present review is to update the current knowledge on the clinical and pathological scope of PCV2 infections, as well as on their diagnosis. Moreover, a proposal on terminology and clearly defined diagnostic criteria for these conditions are given.

2. Clinical features associated to PCV2 infections

2.1. PCV2 subclinical infection

Based on PCV2 serological studies, it is assumed that PCV2 infection is ubiquitous all over the world (Segalés et al., 2005a), while prevalence of clinical disease is much lower. On the other hand, the first evidence of PCV2 infection was retrospectively found in Germany in 1962 (Jacobsen et al., 2009), while the first retrospectively established diagnoses of PMWS are from middle 80s (Jacobsen et al., 2009; Rodríguez-Arrioja et al., 2003). Therefore, the most common form of PCV2 manifestation is the subclinical infection. Even no overt clinical signs are seen, different field evidences indicate that PCV2 vaccination is able to improve productive parameters (average daily gain, percentage of runts, body condition and carcass weight) in PCV2 subclinical infection scenarios (Young et al., 2011). However, it must be emphasized that such effect of PCV2 vaccines on subclinical infection scenarios should be further studied.

It has also been demonstrated experimentally that subclinical PCV2 infection may be associated with decreased vaccine efficacy (Opriessnig et al., 2006c). In contrast, another experimental PCV2 subclinical infection was not able to establish detrimental effects upon pseudorabies vaccine immunological responses (Díaz et al., in press).

2.2. PCV2 clinical infection

A number of clinical syndromes have been linked to PCV2 infection. The most described one is PMWS, which has been referred with different names in the literature including porcine circovirosis (Rosell et al., 2000b), PCV2-associated systemic infection (Opriessnig et al., 2007) and porcine circovirus-associated disease (PCVAD) in some cases (Carman et al., 2008). Other pathological conditions linked to PCV2 have been porcine dermatitis and nephropathy syndrome (PDNS) (Allan et al., 2000; Rosell et al., 2000a; Wellenberg et al., 2004), reproductive failure (Madson et al., 2009a; Mateusen et al., 2007; O'Connor et al., 2001; West et al., 1999), proliferative and necrotizing pneumonia (Grau-Roma and Segalés, 2007; Szeredi and Szentirmai, 2008), respiratory disease (Cheng et al., 2011; Kim et al., 2003; Wellenberg et al., 2010) and enteritis (Kim et al., 2004; Opriessnig et al., 2007).

All these clinical conditions were initially referred as porcine circovirus diseases (PCVD) (Allan et al., 2002). This name was widely used in Europe, but in 2006, in North America, it was felt that any new term used in connection with PCV2 should include the word "associated", which led to the creation and introduction of the term (PCVAD) (http://www.aasv.org/). At the very end, and paraphrasing Dr. John Harding (University of Saskatchewan, Canada): "The use of PCVAD versus PVCD more clearly separates the Europeans, who collectively are the leaders in PCV research, from the North Americans, which except for a few individuals have lagged. Because we are dealing with a global disease with the same etiology, pathogenesis, and pathology, there must be one cohesive name for this syndrome." (Harding, 2007). In order to be cohesive, the author of this revision proposes the use of the first terminology proposed, porcine circovirus diseases – PCVD, to designate all the above mentioned conditions, including the PCV2 subclinical infection.

In addition, Table 1 configures a proposal on terminology of the different PCVDs described so far based on a number of publications, with special emphasis on the contribution of Opriessnig et al. (2007). These authors introduced a number of specific PCVD names, which have been used irregularly in the literature to date. The present review will use the proposed terminology (Table 1) from here onwards.

From a clinical point of view, PCVDs with overt clinical outcome may potentially include the following signs in broad sense:

PCV2 systemic disease (PCV2-SD): Morbidity in affected farms is commonly 4–30% (occasionally 50–60%) and mortality ranges from 4 to 20% (Segalés and Domingo, 2002). PCV2-SD is clinically characterized by wasting or weight loss, pallor of the skin, respiratory distress, diarrhea, and occasionally, icterus (Harding and Clark, 1997; Krakowka et al., 2004; Rosell et al., 1999). Enlarged subcutaneous lymph nodes are a common finding in the early clinical phases of the systemic disease (Clark, 1997; Rosell et al., 1999). More details on clinical signs of PCV2-SD have been described elsewhere (Chae, 2005; Harding, 2004; Harding and Clark, 1997; Madec et al., 2000; Segalés and Domingo, 2002).

PCV2 lung disease (PCV2-LD) and PCV2 enteric disease (PCV2-ED): Main clinical signs are respiratory distress (Harms et al., 2002; Kim et al., 2003) and diarrhea (Kim et al., 2004; Opriessnig et al., 2007), respectively. There is potential diagnostic overlapping between PCV2-SD and these two conditions (Opriessnig et al., 2007), since both clinical signs can be easily present in cases of the systemic disease. Their differentiation, even of limited interest by field veterinarians, must rely on histopathological findings and examination not only of lung and gut but also lymphoid tissues (which must not display microscopic lesions of PCV2-SD). Importantly, PCV2 is considered as one more pathogen potentially contributing to PRDC outcome (Hansen et al., 2010b; Kim et al., 2003). Taking into account that PRDC is diagnosed based on clinical signs (Dee, 1996), the involvement of PCV2 on it may lead to a