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SHORT PAPER

Cardiovascular Lesions in Pigs Naturally or Experimentally Infected with Porcine Circovirus Type 2

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Summary

Abundant intracytoplasmic porcine circovirus type 2 (PCV2) was associated with myocardiocyte swelling or necrosis, or myocardial fibrosis (or both) in three naturally infected pigs aged 4–7 weeks from three different farms. One 6 week old pig from a fourth farm had severe diffuse segmental to circumferential lymphohistiocytic and plasmacytic periarteritis and endarteritis in several organs, PCV2 antigen was demonstrated in endothelial cells, and inflammatory cells in the arterial walls. In three pigs experimentally infected with PCV2, viral antigen was also associated with obliterated blood vessels in areas of granulomatous and necrotizing lymphadenitis. Together these findings suggest that the cardiovascular system in general and endothelial cells in particular play an important role in the pathogenesis of PCV2–associated diseases.

Keywords: arteritis; myocarditis; porcine circovirus type 2; viral infection

Porcine circovirus type 2 (PCV2) infection of growing pigs is characterized by depletion of lymphoid follicles and histiocytic-to-granulomatous inflammation of varying degrees in lymphoid tissues and certain organs (Sorden, 2000). If the lymphoid lesions are severe and accompanied by high amounts of intralesional PCV2 antigen or nucleic acids a diagnosis of PCV2-associated postweaning multisystemic wasting syndrome (PMWS) (Sorden, 2000) can be confirmed.

The pathogenesis of PCV2 infection and the major cell types that support PCV2 replication are poorly understood. High amounts of PCV2 antigen or nucleic acids are often detected in the cytoplasm of macrophages and dendritic cells by immunohistochemistry (IHC) or in-situ-hybridization (ISH). To a lesser extent, PCV2 antigen is also found in epithelial cells in lungs and kidneys, in smooth muscle cells, and in endothelial cells in several tissues in pigs experimentally infected with PCV2 (Kennedy *et al.*, 2000) as well as in pigs with naturally occurring PCV2-associated PMWS (McNeilly *et al.*, 1999; Rosell *et al.*, 1999). This report describes field and experimental cases in which PCV2 was associated with severe cardiovascular lesions in growing pigs.

Pig 1. A previously healthy pig aged 4 weeks was found dead and submitted to the laboratory. On initial examination nutritional myocardiopathy was suspected. Histopathological changes included severe myocardial fibrosis and mixed leucocytic infiltration throughout the myocardium (Fig. 1a), mild multifocal chronic suppurative and histiocytic pericarditis, mild suppurative and lymphohistiocytic interstitial nephritis and hepatitis, and mild suppurative and lymphohistiocytic interstitial pneumonia. Routine immunohistochemistry (IHC) for porcine reproductive and respiratory syndrome virus (PRRSV), as described by Halbur *et al.* (1995), gave negative results on sections of heart and lung tissue. Similar IHC results were given by examination of these tissues with a

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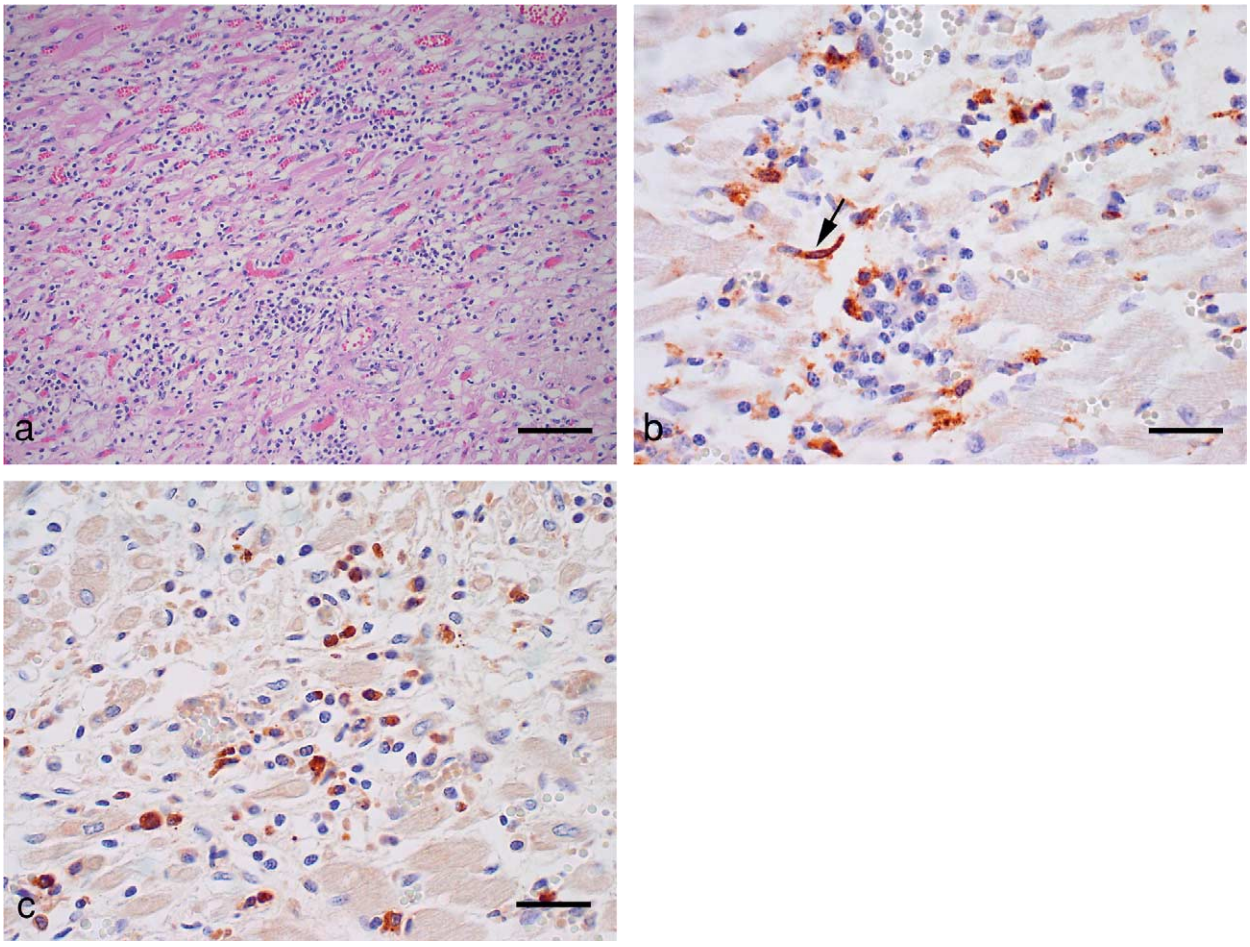

Fig. 1 a–c Section of ventricle (myocardium) from pig 1. (a) There is mild-to-moderate, multifocal fibrosis and necrosis and moderate lymphohistiocytic inflammation in the heart. HE. Bar, 100 µm. (b) PCV2-antigen positive cells include fibroblast-like cells (arrow) and inflammatory cells resembling macrophages or lymphocytes. IHC (streptavidin-biotin peroxidase complex method, haematoxylin counterstain). Bar, 40 µm. (c) There is abundant PPV labelling in many macrophage- and lymphocyte-like cells in areas of myocardial fibrosis. IHC (streptavidin-biotin peroxidase complex method, haematoxylin counterstain). Bar, 40 µm.

pseudorabies virus (PRV) monoclonal antibody (VMRD, Pullman, WA, USA), diluted 1 in 1000, overnight at 4 °C, with protease pretreatment. Abundant PCV2 antigen was detected by IHC with a polyclonal antibody (Sorden *et al.*, 1999) in the cytoplasm and nuclei of myocardiocytes, within vascular endothelial cells in the myocardium and in areas of myocardial fibrosis (Fig. 1b). IHC for porcine parvovirus (PPV), as described by Opriessnig *et al.* (2004), revealed strong labelling within inflammatory cells in areas of inflammation in the myocardium (Fig. 1c). IHC as carried out by Haines *et al.* (1992) gave negative results for bovine virus diarrhoea virus (BVDV) in the heart.

Although there was no bacterial growth in culture, the lesions in this pig were consistent with chronic bacterial septicaemia and with PCV2- and PPV-associated myocarditis and heart failure. Experimentally, PPV has been shown to enhance progression of PCV2-infection towards clinical PMWS (Allan *et al.*, 1999; Opriessnig *et al.*, 2004); however, this pig had no PCV2-associated lymphoid lesions and died from heart failure rather than from PMWS. PCV2-induced myocarditis is typically observed in fetuses and newborn piglets (West *et al.*, 1999). PPV has sporadically been associated with myocarditis in growing pigs (Bolt *et al.*, 1997).

Pigs 2 and 3. Both animals came from herds with a history of previously healthy animals being found dead. Pigs 2 (aged 5 weeks) and 3 (aged 7 weeks) came from herds of 1100 and 4000, respectively. Both animals had severe transmural cardiac haemorrhages and the lungs were inflamed and oedematous, and nutritional myocardiopathy was initially suspected. In addition, pig 2 had fibrin tags adherent to the liver, and pig 3 had an enlarged