HISTOPATHOLOGICAL OBSERVATIONS ON PIGS WITH PORCINE DERMATITIS AND NEPHROPATHY SYNDROME

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Summary

Porcine dermatitis and nephropathy syndrome (PDNS) is broadly discussed as a porcine circovirus type 2 (PCV2)-associated disease, although PCV2, in contrast to postweaning multisystemic wasting syndrome (PMWS), has to date not been proven to be the aetiologic agent. The clinical signs, gross post-mortem and histopathological changes observed in affected pigs, were similar to those previously described for PDNS. As in previous reports, the lesions were associated with PCV2 infection, which was demonstrated by in situ hybridization method.

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Introduction

Whereas porcine circovirus type 2 (PCV2) has been identified as the causal agent of the postweaning multisystemic wasting syndrome (PMWS) (Allan et al., 1998; Ellis et al., 1998), the implication of PCV2 in the pathogenesis of the porcine dermatitis and nephropathy syndrome (PDNS) is assumed, but not proven. This is of importance, as the simple presence of PCV2 in most PDNS animals is not inevitably a proof of this virus being the aetiologic agent of this syndrome as PCV2 is widespread also among clinically healthy pigs. In PDNS, pathomorphology reveals severe changes predominantly in the skin and kidneys characterized by multifocal erythematous skin lesions associated with dermal necrotizing vasculitis as well as renal enlargement with cortical petechiae. Histologically, renal lesions are due to vasculitis and acute necrotizing glomerulitis to chronic glomerular sclerosis with interstitial inflammation and fibrosis (Thomson et al., 2002). Although PCV2 nucleic acid or antigen could be detected in antigen presenting cells (APCs) and, to a lesser extent, in lymphocytes (Chianini et al., 2003).

Material and methods

In this study six 14-18-week-old pigs were included. All these animals showed the PDNS compatible clinical signs (weight loss, haemorrhagic skin lesions and oedema of the limbs). The animals had been euthanasied and the sections from lungs, lymph nodes, liver, kidney, were collected in the form of slices of about 5 mm thick. The collected pieces were fixed for 48 hours in a Stieve mixture, included in paraffin and cut at 5 µm thick slices. The sections were colored employing the Goldner’s Trichrome method. For detection of PCV2 specific antigen and nucleic acid were used immunohistochemistry and in situ hybridization.
Results and discussion

Skin lesions were represented by dermatitis associated with haemorrhagic necrotic vasculitis in the superficial derma; fibrinoid necrosis of vessels from the deep dermal layers, and sometimes of subcutis. Polimorph inflammatory infiltration in the derma were present and was predominantly composed of lymphocytes, plasma cells and neutrophyles. (Fig.1,2).

The kidney lesions were always bilateral and severe, with considerable different degrees of progression from acute glomerulonephritis (with hyalinization of tubules) to chronic glomerular sclerosis (with interstitial fibrosis and inflammation) (Fig.3,4,5). Frequently occurring degenerative and inflammatory injuries translated by acute and chronic nephropathy. Were reported haemorrhagic glomerulonephritis lesions, plasmocitary and interstitial nephritis (Fig.3,4). Acute cases had severe glomerulities infiltrated with neutrophil groups, glomerular necrosis, the presence of fibrinous exudates which is in the hialinized Bowman’s spaces (Fig.3); vascular clews were obsolete due to expansion Bowman space by accumulating hyalin material (Fig.3,4,5). Almost all glomeruli were affected, but some damages were segmented. The medullary and cortically renal tubules were invaded by protein material (fibrin) with tubular epithelium necrosis, sometimes hyperplasia of tubules were reported with interstitial infiltrate dominated by plasmocytes (Fig.3). In lamina propria of proximal tubules the presence of erythrocytes have been reported. Vasculities and haemorrhages have affected many of vessels of cortex (Fig.6). Diffuse sclerosis, atrophy of glomerules, tubular atrophy, loss of nephrones, chronic inflammation and interstitial fibrosis were described. Early interstitial inflammatory cells were associated with damages of glomerules. In chronic cases, infiltration was extended throughout corticales and accompanied with interstitial fibrosis. Also in the chronic form characteristic PCV2 induce nephropathy with hyaline distrophy, tubular epithelium necrosis (Fig.), fibrosis with glomerular atrophy, interstitial nephritis with fibrosis (Fig. 4,5). In the renal vessels were also marked by injuries and granulomatous vasculitis with necrotic lympho-plasmocytic perivascularities (Fig.6). Regarding the presence of PCV2 in kidney by in situ hybridization were detected positive signals for PCV2 DNA in the macrophages and interstitial lympho-plasmocytic, and around renal tubules (Fig.7,8).
Lung lesions were reported by limpho-histiocytic multifocal or diffuse interstitial pneumonia. Subacute interstitial pneumonia was characterized by the presence necrosis of cell in the alveolar lumen with partial epitelization of alveolas (proliferation of type II epithelial cells) (Fig.9). In the alveola were present neutrophiles, eozinophiles, macrophages, lymphocytes and cell detrituses. The main cells affected by type 2 porcine circovires were macrophages and epithelial like cells, these results were supported by positive hybridization signals of PCV2 DNA in cytoplasm of these cell types.
The main lymphoid lesions were characterized by lymphocyte depletion and infiltrations with epyteloid and multinucleate giant cells. In the lymph nodes have been reported granulomas in the center composed of cells in necrosis, cellular proliferation surrounded by macrophages and giant epiteloides (Fig.11,12) cell types. Granulomatous and epiteloid reaction were evident (Fig.11) accompanied by the destruction of lymphocytes foliculles.

In a small proportion were observed giant cells which sometimes contained inside basophyl inclusion bodies. All these lesions contribute to formation of diffuse granulomatous lymphadenytis (Fig.11).

Our PDNS cases had completely specific PDNS skin lesions. It was issued on the assumption that the renal PDNS are more involved than skin lesions, although numerous cases were observed absence of renal lesions (Ségalès et al., 1998; Thibault et al., 1998). Non-specific skin lesions particularly traumatic lesions were sometimes difficult to differentiated from
macroscopic vascular dermatities. The starting point of pathological processes that still seems to be at corpuscles renal changes in the permeability barrier of filtering up to the level where they no longer work, the kidney filter is practically abolished. Pronounced alteration of the filtration barrier is illustrated by the high content of protein material that accumulates in the capsular and especially the presence of red blood whose passage demonstrating virtually dissolved barrier filter. The vascular changes are observed which are accompanied by sero-haemorrhagic swelling and even necrosis. Vascular disorders are amplified by of intravascular coagulation with blocking movement of vessels and small necrosis areas served by them. It is clear that the virus (PCV2) acting on blood vessels whereas such issues were both vessels at the skin and at the level of parenchymal organs (kidney) and the lymphoides (lymph nodes, spleen). The vasculities associated with this syndrome suppose the involvement of an immune mediated mechanism (Rosell et al., 2000; Thibault et al., 1998). Presumed mechanisms of viral infection on the vascular changes are many and varied, many of which may be operating simultaneously in this syndrome.

Figure 12. Positive hybridization signals for PCV2 DNA in cytoplasm of renal multinucleate giant cells and macrophages from lymphoid follicles. In situ hybridization ×200.

Two of these mechanisms of viral infection associated vasculities are action/changes in virus-induced lesions respectively humoral and/or cell mediated on the blood vessels (Lie, 1996). Therefore, these findings suggest that PCV2 induces vascular lesions may indirectly via immune complexes. The significance of natural infection by PCV2 has undoubtedly been expanded since its initial association with PMWS. However, the relationship between PCV2 and other non-PMWS conditions have only been established by means of retrospective studies (PDNS, PNP) and clinical cases (reproductive disease, PRDC, CT), and no experimental background is supporting this putative association at present. Further studies are needed to confirm or extend the knowledge on the cause–effect relationship of PCV2 with conditions other than PMWS.

References