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Porcine dermatitis and nephropathy syndrome (PDNS): An overview of the disease

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Summary

This report presents an overview of the current information available on the porcine dermatitis and nephropathy syndrome (PDNS). This disease has been recently described under various names and is characterized by a systemic vasculitis with marked tropism for the skin and kidney. There is strong evidence that the condition is immune-mediated, although the precise etiology is still undetermined. Several infectious agents have been suggested as being potentially responsible for the development of the disease but to date none of these have been confirmed to be causal. The possibility that a variety of etiologic factors could provoke the disease cannot be ruled out, especially in view of the nature of the lesions and their likely pathogenesis.

Keywords: swine, dermatitis, nephropathy, glomerulonephritis, vasculitis

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The purpose of this report is to summarize current knowledge on the porcine dermatitis and nephropathy syndrome (PDNS), a newly described disease of swine. Emphasis is given to the etiopathogenesis of the condition based on the more recent observations.

Nomenclature and geographic distribution of the disease

Porcine dermatitis and nephropathy syndrome was first described in the United Kingdom in 1993.[1,2] Since its original descriptions, the condition has been recognized in most pig producing countries. A variety of terms have been used to describe the disease, including porcine dermatitis/nephropathy syndrome[1] (the original name given to the condition), systemic necrotizing vasculitis of swine,[3,4] and porcine immune complex glomerulonephritis-dermatitis syndrome.[5]

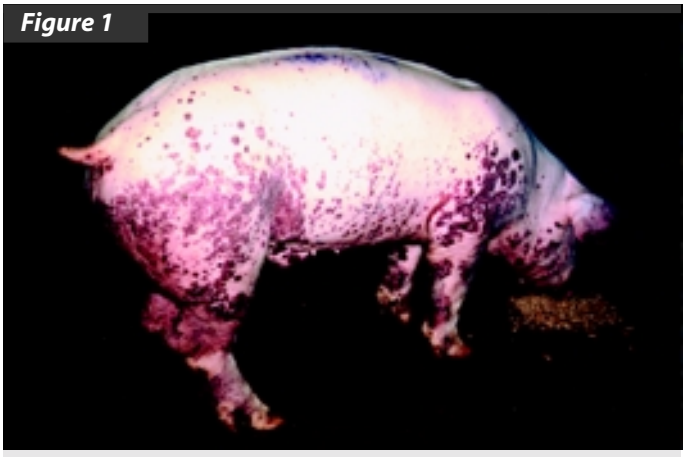
Clinical signs

PDNS is a vascular disease affecting weaners and growing-finishing pigs and, less commonly, breeding animals. It is observed in herds of various genetic origin and health status.[5] The prevalence of the disease in affected herds is usually low (<1%).[1,4,6] Several reports describing the clinical signs have appeared in the literature (Segales, et al. *Proc IPVS Cong.* 1996;14:709)[1,3,4,6,7] and are summarized here.

The most obvious sign, particularly in the acute phase of the disease, is the development of skin lesions that are characterized by round to irregular, red to purple macules and papules that occasionally coalesce to form large, irregular patches and plaques (Figure 1). With time, the lesions become covered by dark crusts and fade gradually (usually in 2–3 weeks), sometimes leaving scars. Typical distribution includes the perineal area of the hindquarters, limbs, dependent parts of the abdomen and thorax, and the ears. In severe cases, the flank and lateral thoracic wall may also be involved. On rare occasions, multifocal lesions are observed randomly over the entire body.

Mildly affected pigs may only show skin lesions and be afebrile and alert. A good proportion of these animals eventually recover without treatment. Severely affected pigs show a variety of other clinical signs including anorexia, depression, hyperthermia, stiff gait or reluctance to move, weight loss, dyspnea or tachypnea, and dependent subcutaneous edema. Many of these animals die within a few days after onset of clinical signs. The prognosis for affected pigs is probably dependent on the extent and the severity of the vascular lesions found in internal organs, particularly within the kidneys, in which a severe and fatal glomerulonephritis (GN) may develop (see pathological findings). Pigs with severe GN are usually uremic and have high blood urea and creatinine levels.

Figure 1



Skin lesions characteristic of porcine dermatitis and nephropathy syndrome

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The main clinical differential diagnoses include localized exudative epidermitis and septicemia, especially *Erysipelothrix rhusiopathiae* and *Actinobacillus suis* infections. The sporadic incidence of the disease and the nonresponsiveness to antimicrobial therapy are puzzling to producers, who will often turn to swine practitioners for an explanation.

Pathological findings

The primary lesion in this condition is a systemic necrotizing vasculitis (Thomson, et al. *Proc IPVS Cong*. 1998;15(3):395).[1,3,4] The organs involved vary from case to case. Because of the frequent involvement of the skin and kidneys, the disease was originally called porcine dermatitis and nephropathy syndrome.[1] However, not all pigs presenting cutaneous lesions develop renal lesions, and vice versa.

In the acute phase of the disease, characteristic gross lesions may be found in the skin (see clinical signs) and kidneys. Both kidneys are enlarged and pale with petechial hemorrhages in the cortex. Other gross lesions commonly associated with the disease include serous effusions in body cavities, subcutaneous edema, enlarged peripheral and internal lymph nodes, pneumonia, gastric ulceration, and increased amount of synovial fluid (Thomson, et al; *Proc IPVS Cong*. 1998;15(3):395. Segales, et al; *Proc IPVS Cong*. 1996;14:709).[1–4,6–8]

Microscopic lesions consist of a systemic necrotizing vasculitis involving predominantly small-caliber blood vessels and occasionally medium-sized vessels (Thomson, et al; *Proc IPVS*. 1998;15(3):395. Segales, et al; *Proc IPVS Cong*. 1996;14:709).[1,3–6] In the skin, vascular lesions are often associated with focal dermal hemorrhages and epidermal necrosis. Suppurative dermatitis is observed in some animals. In acute cases, the kidneys may present a severe exudative and occasionally necrotizing glomerulonephritis (Segales, et al. *Proc IPVS Cong*. 1996;14:709).[1,3,5,6] Glomerular sclerosis (possibly with synechiae and crescent formation), interstitial inflammation and fibrosis, and tubular atrophy are found in chronically affected pigs (Thomson, et al; *Proc IPVS Cong*. 1998;15(3):395. Segales, et al; *Proc IPVS Cong*. 1996;14:709).[1,3,5,6]

Cases of PDNS, in which the kidney is the only organ involved, may be confused with other primary glomerular diseases of swine. One of these glomerular diseases, called porcine membranoproliferative glomerulonephritis type II, is a hereditary and often fatal condition of the Yorkshire breed and represents a nonimmune complex-mediated glomerular disease.[9] It is caused by an autosomal recessive deficiency of factor H, a plasma protein that regulates complement.[10] This deficiency is associated with extensive complement activation and its subsequent deposition within glomeruli. Another potentially fatal renal disease, characterized by an acute proliferative and exudative GN, but without systemic vasculitis, has been observed sporadically in pigs for more than 30 years.[11–13] In their retrospective study of 20 years (1973–1993), Bourgault and Drolet[13] did not find vascular lesions in organs other than kidneys in the 30 cases of proliferative and exudative GN they examined. This latter disease is believed to be immune-mediated although its precise cause remains unknown.[13] Until more is known about this latter condition and PDNS, it is prudent to consider them as two separate entities even though the renal pathology (glomerulonephritis) and the pathogenic mechanisms (probably immune mediated) involved in both diseases have some similarities.

It has been suggested that cutaneous and renal glomerular vasculopathy (CRGV) of greyhound dogs (also called Alabama rot) might represent a disease similar to PDNS. However there are several significant differences between these two diseases. The canine disease — characterized by well-demarcated cutaneous ulcers involving mainly the limbs and, in some cases, a potentially fatal glomerulopathy — is due to a vasculopathy.[14,15] In CRGV, microscopic lesions are limited to the skin and kidneys (unless the animal develops renal failure); whereas in PDNS, vascular lesions may be found in a variety of organs. Moreover, in CRVG the vascular lesions are mainly degenerative and characterized by fibrinoid necrosis of the arterioles without significant inflammation, whereas in PDNS, arterial and venous blood vessels present not only necrotizing changes in their walls but also an inflammatory infiltrate that may be intense, especially in the skin in which neutrophils often predominate. The cause of the disease in greyhounds is unknown but the condition does not appear to be immune complex mediated. Toxic endothelial damage (perhaps due to verotoxin?) has been speculated to be involved in the pathogenesis of this canine disease.[15]

Pathogenesis

The lesions in PDNS are strongly suggestive of an immune complex-mediated disorder, a suspicion already highlighted in the first report of the condition.[1] Immune complexes are composed of an antigenic component and of immunoreactants, namely immunoglobulins (IgG, IgM, or IgA) and complement factors. These complexes, once deposited (circulating soluble complexes) or formed (in situ) within the vascular or glomerular capillary walls, initiate an acute inflammatory process. Recent studies have demonstrated, using immunopathological techniques, the presence of such immunoreactants, namely complement and IgM, within affected vessel walls[3,4] and within renal glomeruli.[3,5] Electron microscopic examination of affected kidneys revealed dense deposits (presumably representing these immune complexes) at the inner aspect of the glomerular basement membrane.[5]

Etiology

The etiology of PDNS is undetermined. Although there are now strong suggestions that this condition represents an immune complex-mediated vascular disease, the responsible antigen(s) remain(s) unknown. Theoretically the condition could be triggered by a variety of factors including drugs, chemicals, food allergens, endogenous antigens, and infectious agents (Thomson, et al. *Proc IPVS Cong*. 1998;15(3):395).[4] Several recent studies have tried to determine the precipitating factors that could be linked to this disease.

Viruses

In two studies, porcine reproductive and respiratory syndrome virus (PRRSV) has been suspected to be involved in the pathogenesis of PDNS.[4,7] A large proportion of the animals affected with PDNS in the Spanish study[7] and all pigs examined in the Canadian study[4] were infected with the PRRSV. This virus was thought to be a good candidate because it has been shown to cause necrotizing vasculitis in experimentally

infected pigs[16] and because it may cause viremia coexisting with antibodies,[17] a situation that may favor the development of immune complexes. However PRRS is a widespread disease in many countries and there is some evidence that PDNS can be observed in PRRSV-negative herds (SHD, personal observation) and in PRRSV-free geographical areas such as Australia.[18] These observations leave three possibilities as to the speculative role of the PRRSV in the pathogenesis of the disease:

- PRRSV only represents a coincidental infection,
- PRRSV may in some cases trigger another as-yet-unidentified factor responsible for the development of PDNS, or
- PRRSV may be one of the several potential causes of the disease.

To confirm this last hypothesis, PRRSV antigen would have to be demonstrated within the injured vascular walls. PRRSV antigens, although present within some macrophages around cutaneous and renal blood vessels, were not detected in vessel walls in these organs in any of the pigs examined in one study.[4] However, we can't exclude the possibility that another PRRSV antigen, not recognized by the antibodies used in that latter study, could be circulating and inducing vasculitis.

Porcine circovirus (PCV) has been associated with a condition recently described in Canada under the name "postweaning multisystemic wasting syndrome" (PMWS).[19] The presence of PCV in tissues of pigs affected with PDNS has been investigated in some studies. Using in situ hybridization and immunohistochemistry techniques, (Segales, et al. *Proc IPVS Cong*. 1998;15(2):215), investigators found porcine circovirus in 14 of 25 PDNS-affected pigs. However, viral genome and PCV antigen were not detected in vasculitis and GN lesions of these pigs. Porcine circovirus was detected by PCR in the tissues of two of 12 PDNS-affected pigs examined by Thibault, et al.,[4] (Thibault, et al., 1998, unpublished data). Concurrent lesions of PDNS and PMWS have also been reported on few occasions (Ramos-Vara et al; *Vet Pathol*. 1998;35:436 Abstr # 79. Clark; *Proc ISU Swine Dis Conf Swine Pract*.1997;5:15–18). More recently in France, Madec et al. (*Journées Rech Porcine en France*.1999;31:347–354) in a study of herds affected with PMWS, reported the presence of a cutaneous problem of low prevalence, similar to PDNS, on all 20 farms studied. The precise link between these two syndromes was not elucidated although it was recognized that the causal agent of PMWS could have predisposed to the emergence of other pathogens. The role of PCV in PDNS appears uncertain at this time and warrants further investigation.

Bacteria

An association with *Pasteurella multocida* and PDNS has been suggested in a series of Scottish PDNS cases (Thomson, et al., *Proc IPVS*. 1998;15(3):396) in which a high prevalence of a single electrophoretic type (01) of *Pasteurella multocida* was isolated from a range of tissue sites. These latter findings also warrant further investigations.

Streptococcus spp infections have also been suspected to be involved in the pathogenesis of PDNS[5] because immune complex-mediated GN is known to occur in humans following streptococcal infection. Others have speculated that the vascular damage may be induced by lipopolysaccharides (LPS) of gram-negative bacteria.[6]

Noninfectious causes

In the series of cases studied by Thibault, et al.,[4] part of a questionnaire concerning each case was specifically designed to identify potential precipitating factors such as vaccines, antimicrobials, and other biological or chemical products used on the farms. The results of this study were inconclusive, although a detailed examination of the feed and water constituents was not performed.

Conclusion

Although there is growing evidence that PDNS is an immune-mediated vascular disorder, the precise cause(s) of the disease remain(s) elusive at this time. If this condition indeed represents an immune complex vasculitis, the ultimate determination of the etiology would require the detection of the triggering antigen within the injured vessel walls. This may not prove to be an easy task, particularly if more than one factor is responsible for the development of the disease, as is the case in humans with similar vasculopathies.[20]

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