

PAPER

Cutaneous and renal glomerular vasculopathy as a cause of acute kidney injury in dogs in the UK

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Context

Cutaneous and renal glomerular vasculopathy (CRGV) is a canine thrombotic microangiopathy (TMA) of unknown aetiology, which causes ulceration of the distal extremities and is variably associated with clinically relevant acute kidney injury (AKI). CRGV has previously been recognised in greyhounds in the USA but has only sporadically been reported in dogs elsewhere. This is the first case series describing CRGV in non-greyhound dogs and is the first series of dogs with CRGV in the UK.

Main conclusion

Thirty dogs from England were identified between November 2012 and March 2014 with clinicopathologic findings compatible with CRGV. These findings included: skin lesions predominantly affecting the distal extremities; AKI; histopathological evidence of renal TMA and, variably, anaemia, thrombocytopenia and hyperbilirubinaemia. Known causes of AKI were excluded. Shiga toxin and *Escherichia coli* genes encoding shiga toxin were not identified in the faeces or kidneys of affected dogs. All 30 dogs died or were euthanased. The authors identified six suspected cases that survived (not included in the dataset) for which renal histopathology was not available and thus the diagnosis of CRGV could not be confirmed. Highest case numbers were seen between November and April.

Approach

Cases were identified by searching computerised records at two referral practices, with further case submissions from two other referral practices and 49 first opinion practices. The medical records of suspected cases were reviewed. Dogs were included if they presented within the defined time period with skin lesions and AKI, with no known identifiable cause, and with histopathologically confirmed renal TMA.

Results

Seventy-one cases were identified for which there was clinical suspicion of CRGV. Forty-one cases were excluded due to limited investigation and/or incomplete medical records. Thirty cases met the inclusion criteria.

Numerous breeds were represented. Median age was 4.9 years. The main presenting signs were: skin lesions (30), anorexia (20), vomiting (20), lethargy (19), hypothermia (19), lameness (10), icterus (six) and pyrexia (six). Diarrhoea and clinical signs associated with thrombocytopenia were also occasionally observed. Management of skin lesions before the development of AKI was variable.

Lesions were painful, variably sized and affected the distal limbs, ventrum, oral cavity and/or muzzle. The lesions ranged from superficial erosions through to full thickness ulceration, often with erythema, oedema and exudation.

At presentation, the main clinicopathological findings were: azotaemia; hyperbilirubinaemia; thrombocytopenia; anaemia and proteinuria. Eleven dogs were oligoanuric.

Eight dogs were hypertensive. Investigations confirmed the azotaemia to be attributable to AKI. Leptospirosis microscopic agglutination titres were negative in 10 dogs and positive in five dogs. Faecal culture (performed in seven dogs) yielded *E. coli*. PCRs for *E. coli* virulence genes were negative. Urine toxicology was negative (five dogs). Ten cases were managed at referral centres and 20 in primary practice. Initial management consisted of intravenous fluid therapy and antibiotics. Three cases underwent continuous renal replacement therapy. All 30 dogs died or were euthanased. Causes of death/euthanasia included: oligoanuria, anaemia, thrombocytopenia, progressive azotaemia, dyspnoea, ascites and owners' request (six dogs). Dogs survived a median of seven days (range one to 16 days) after the onset of clinical signs.

The most prominent histopathological changes were noted in the kidneys and skin. Renal glomerular arterioles displayed fibrinoid necrosis with thrombosis. Warthin-Starry stains did not reveal leptospire. The epidermis was focally to diffusely ulcerated and fibrinoid necrosis and thrombosis was occasionally observed in the small dermal arterioles. Renal electron microscopy (three dogs) revealed distension of the glomerular capillary loops by erythrocytes, occasional schistocytes and rare polymorphonuclear cells. Endothelial cells were swollen and podocyte foot processes were globally effaced. Immune complexes were not identified.

PCR for verotoxin 1 and 2, and fluorescent in situ hybridisation for shiga toxin (performed on renal tissue) were negative. A proportion of dogs living in the same household as the reported cases developed skin lesions (six of 14 dogs, 43 per cent), with, or without, AKI (two of 14 dogs developed AKI, 14 per cent).

Interpretation

Known differential diagnoses for canine TMAs include CRGV and haemolytic uraemic syndrome (HUS). The most common form of HUS in humans is associated with shiga toxin-producing bacteria causing diarrhoea (STEC-HUS). However, *E. coli* shiga toxin has not previously been identified in dogs with HUS or CRGV and was not identified in the dogs in this case series. Management of human TMAs is dependent on the underlying cause. The optimal management for CRGV remains unknown.

Although renal histopathology was not available for the six surviving dogs with a presumptive diagnosis of CRGV, their survival may suggest that CRGV is not invariably fatal.

Significance of findings

CRGV appears to be a novel or emerging disease in the UK. The aetiology remains unknown and, when azotaemia develops, the prognosis appears to be poor. Continued clinical, clinicopathological and epidemiological evaluation will further enhance understanding of CRGV, aiding the identification of possible triggers, prognostic indicators and the most appropriate management strategies for these patients.