Diagnosis and management of canine idiopathic renal haematuria

Idiopathic renal haematuria is a relatively rare disease associated with unilateral or bilateral renal bleeding for which a causal condition has not been identified. The aims of this review are to describe the epidemiology and clinical signs of affected dogs, to summarise the diagnostic work-up leading to the diagnosis of idiopathic renal haematuria and review the evidence regarding treatment.

**Key words:** Idiopathic renal haematuria, haematuria, uro-nephrology, dog

**Introduction**

Idiopathic renal haematuria is a relatively rare condition in the dog. Owners report macroscopic haematuria, which is either persistent or intermittent. Diagnostic investigations, centred on imaging and clinicopathological testing, do not reveal the source of bleeding (Holt et al. 1987). Idiopathic renal haematuria can also occur in cats (Berent et al. 2013b) but this will not be discussed here.

In human patients, the terms ‘benign essential haematuria’, ‘familial renal haematuria’, ‘lateralising essential haematuria’ or ‘chronic unilateral haematuria’ are also used (Rogers et al. 1973; Kupor et al. 1975; Tanimoto et al. 2017). The condition in human patients is considered to be a clinical syndrome rather than a single disease. Immunohistochemistry has identified frequent occurrence of IgA nephropathy (20% to 49% of patients with asymptomatic isolated haematuria) and only 17% to 22% of patients have no or minimal changes on their renal biopsy (Kupor et al. 1975; Copley et al. 1987).

Similarly, advances in ureteroscopy have allowed clinicians to identify discrete or diffuse vascular lesions, such as renal haemangioma or minute venous rupture (Tanimoto et al. 2017). A condition known as “nutcracker syndrome” in which left renal vein hypertension occurs secondary to entrapment between the aorta and the superior mesenteric artery, has also been detected in some cases (Russo et al. 1998).

Management of the asymptomatic haematuria therefore depends on the underlying diagnosis with the most benign conditions mainly requiring monitoring.

Idiopathic renal haematuria is a diagnosis of exclusion in the dog. Initially haematuria must be differentiated from other causes of pigmenturia, such as haemoglobinuria, myoglobinuria and food pigments. Investigations must then rule out systemic causes of bleeding (e.g. coagulopathies, thrombocytopenia, thrombocytopenia, angiostrongylosis) versus haemorrhage due to pathology in the upper urinary tract (e.g. nephrolithiasis, pyelonephritis, leptospirosis, neoplasia, telangiectasia in the Pembroke Welsh Corgi (Moore et al. 1983), or lower urinary tract (e.g. urinary tract infections, neoplasia, cystoliths, cystitis).

**Pathophysiology**

By definition, idiopathic renal haematuria has no known underlying cause. However, the extent of the investigations performed is often limited in the cases described in the literature. It is probable that canine patients with asymptomatic renal haematuria are affected by a variety of conditions.

In the study by Holt et al. (1987) of nine dogs with idiopathic renal haematuria, cystotomy and catheterisation of the left and right ureters allowed a diagnosis of renal haematuria to be made. Where unilateral bleeding was found (seven cases), these dogs were treated by nephrectomy of the affected kidney. Renal histopathology and electron microscopy were performed in all nine cases, however a potential cause was only found in one dog, where a haemangiomatous malformation associated with bleeding was observed on histology. The authors commented that similar lesions may have been missed if they were too small to be noted, not associated with bleeding (another dog in this study had a similar vascular malformation with no apparent bleeding) or if the lesion had collapsed following nephrectomy. In the same study, electron microscopy only revealed scanty electron dense deposits in the mesangium (Figure 1) in five out of nine dogs. This was considered unlikely to be of significance, suggesting that, in contrast to humans, IgA nephropathy is not a prevalent cause of idiopathic haematuria in the dog. However, immunofluorescence testing was not performed and the renal
histopathology was undertaken prior to the development of standardised protocols so the results of this study should be interpreted with caution.

Although the left kidney appears to be affected more frequently in dogs with unilateral renal bleeding (around two thirds of the cases in this study), there was no evidence of “nut-cracker syndrome” on imaging. However, whilst intravenous urography and retrograde contrast radiographic studies of the lower urinary tract were performed in all the dogs in the Holt et al. (1987) study, and two dogs also had renal angiography, abdominal ultrasonography and computed tomography (CT) were not readily available at the time and were therefore not performed. Subtle changes may, therefore, have been overlooked, although subsequent clinical reports have also not identified major ultrasonographic changes (Hawthorne et al. 1998; Bazelle et al. 2011; Di Cicco et al. 2013; Berent et al. 2013; Pineda et al. 2015; Adelman et al. 2017a).

It is also important to recognise that some patients who initially have unilateral ureteral bleeding subsequently develop contralateral bleeding (Bazelle et al. 2011; Di Cicco et al. 2013; Berent et al. 2013) whilst some patients have bilateral bleeding at the time of diagnosis (Holt et al. 1987; Berent et al. 2013). This is not supportive of an isolated small bleeding lesion and may rather represent more generalised vasculopathy.

**Epidemiology**

Around 30 dogs have been described in the literature at the time of writing. Although the numbers remain too low to draw meaningful conclusions, it is noticeable that many patients are large breed dogs. Whilst some breeds, including the Boxer (Chandler et al. 2007) and Dogue De Bordeaux (Lavoue et al. 2015) have been diagnosed with familial nephropathies, haematuria is not a typical feature of these conditions and renal failure is not a frequent outcome in patients affected by idiopathic renal haematuria.

Patients are frequently diagnosed as young adults but the reported age range varies between six months and 12 years. There does not appear to be a sex predisposition.

**Clinical signs**

Intermittent to persistent haematuria is the hallmark of the condition (Figure 2). Approximately 25% of patients present with signs of lower urinary tract disease including pollakiuria and stranguria, due to obstruction of the urinary tract by blood clots (Hawthorne et al. 1998; Bazelle et al. 2011; Berent et al. 2013; Pineda et al. 2015; Adelman et al. 2017a). This often leads to a delay in diagnosis of the renal origin of the bleeding. Some patients may also exhibit lethargy or vomiting (Bazelle et al. 2011; Adelman et al. 2017a) but many patients present with haematuria alone. It is the opinion of the author that the published studies may demonstrate selection bias towards more severe cases and mildly affected patients are, perhaps, more prevalent than described.

**Clinicopathology**

Anaemia was present in around half of the cases described (Stone et al. 1983; Holt et al. 1987; Di Cicco et al. 2013; Berent et al. 2013; Pineda et al. 2015). This may be attributed to acute blood loss or, in chronic haematuria, an iron-deficiency anaemia may develop. Other haematological changes are not generally noted. In the literature there is only one report of a dog in which anaemia was also associated with thrombocytopenia and marginal leucopenia (Holt et al. 1987). This study does not mention the severity of thrombocytopenia but bone marrow assessment demonstrated a normal megakaryocyte population and the thrombocytopenia was not considered the cause of the haematuria.

It is striking that, in the reported cases, there is no evidence of renal dysfunction, although an isolated elevation of urea is sometimes reported (Holt et al. 1987; Hawthorne et al. 1998; Bazelle et al. 2011). Hypoalbuminaemia, either due to blood loss or negative acute phase protein effect, has been reported in two patients (Di Cicco et al. 2013; Pineda et al. 2015).

A coagulation profile (particularly prothrombin time and activated partial thromboplastin time) was frequently performed in the reported cases and was unremarkable, apart from mild and clinically insignificant hypofibrinogenenaemia in two cases (Bazelle et al. 2011) and thrombocytopenia as previously described (Holt et al. 1987). *Angiostrongylus vasorum* testing, buccal mucosal bleeding time, von Willebrand factor measurement and blood pressure were not or infrequently performed in the available literature.

Urinalysis showed evidence of haematuria with no evidence of active urinary tract infections in any patient. A previous urinary tract infection had been noted in two dogs (Berent et al. 2013; Adelman et al. 2017a). Urine specific gravity has been reported to be variable. Urine culture is recommended to exclude occult urinary tract infections and antibiotic therapy should be avoided prior to culture to reduce the risk of false negative results.

**Abdominal imaging**

Plain abdominal radiographs are generally not informative but can be used to exclude other differential diagnoses (e.g. urolithiasis, renal mass) or concomitant conditions. Contrast studies including intravenous urography, double contrast cystography and retrograde urethrogram were more frequently used in earlier studies (Stone et al. 1983; Holt et al. 1987; Jennings et al. 1992; Hawthorne et al. 1998; Berent et al. 2013) but these procedures have been replaced by abdominal ultrasonography.