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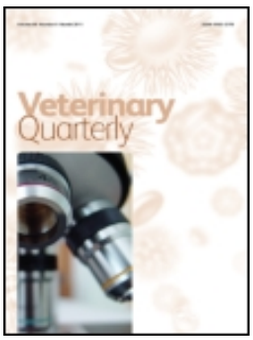

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RENAL DYSPLASIA IN THREE YOUNG ADULT DUTCH KOOIKER DOGS

C. Schulze[1], H.P. Meyer[2], A.L. Blok[3], K. Schipper[4], and T.S.G.A.M. van den Ingh[1]

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Short Communications

SUMMARY

Chronic renal failure as consequence of renal dysplasia was diagnosed in three young adult Dutch kooiker dogs (Dutch decoy dogs). Two animals were anorectic from an early age and were thinner than healthy dogs of the same breed. All three were presented because of apathy and weakness. Laboratory examination revealed anaemia and uraemia. One dog was presented with severe dehydration and died during emergency treatment. One dog was euthanatised because of a poor prognosis, and one was given a low-protein diet. This dog survived for 7 months after the diagnosis of chronic renal failure. At necropsy all three animals had shrunken, pale, and firm kidneys that showed microscopical lesions characteristic of canine renal dysplasia, such as asynchronous differentiation of nephrons, persistent immature mesenchyme, persistent metanephric ducts, and adenomatoid proliferation of the tubular epithelium. Secondary degenerative and inflammatory changes consisted of interstitial fibrosis and predominantly lymphocytic/plasmacytic inflammation. This is the first report of renal dysplasia in the Dutch kooiker dog. The disease should be included in the differential diagnosis in young Dutch kooiker dogs with signs of chronic renal failure. The presentation of three cases of this rare disease in this breed, which is based on a rather small gene pool, suggests that it is a familial or hereditary nephropathy.

INTRODUCTION

Chronic renal failure is common in old dogs but is uncommon in juvenile, adolescent, or young adult dogs, in which it is often the consequence of a hereditary nephropathy (16). Several breeds are known to be affected by hereditary nephropathy, including the Alaskan malamute, border terrier, Brie sheepdog, English bulldog, chow chow, golden retriever, Great Dane, King Charles spaniel, lhasa apso, Rhodesian ridgeback, miniature schnauzer, samoyed, shih tzu, soft-coated wheaten terrier, and standard poodle (2,4,6,9,13-18). Hereditary nephropathies can be subdivided into different disease entities, including agenesis, hypoplasia, dysplasia, primary cystic diseases, glomerulopathies, tubulo-interstitial nephropathies, and tubular transport dysfunctions (16). Renal dysplasia is defined as a disorganized renal development due to an abnormal differentiation of the parenchyma (12,19). The disease is characterised by the presence of structures that are inappropriate for the stage of development of the animal (5). In human medicine the term is used very restrictively and the diagnosis is based on the presence of two microscopic lesions, namely primitive metanephric ducts encompassed by collars of mesenchyme, and the formation of dysontogenic tissues such as cartilage or bone (19). In veterinary medicine the term renal dysplasia has been used in a broader sense and includes a wider range of lesions (12,17). Lesions which are characteristic of renal dysplasia in the dog include asynchronous differentiation of nephrons, persistent immature mesenchyme, persistent metanephric ducts, atypical tubular epithelial proliferation, and dysontogenic (cartilaginous or osseous) metaplasia (17).

We describe here the clinical and morphological findings in three young adult Dutch kooiker dogs with chronic renal failure due to renal dysplasia.

CLINICAL HISTORY

Case 1

A Dutch kooiker dog (male, 9 months) was presented with signs of decreased endurance and apathy for 1 week. From an early age, the animal had a poor appetite and had always been too thin. Physical examination revealed no remarkable abnormalities except that the mucous membranes were pale. Laboratory examination revealed uraemia (creatinine 438 µM, reference values <75 µM; urea 57 mM, reference values 6-12 mM), severe hyperphosphataemia (4.07 mM, reference values 1.57-2.45 mM), and non-regenerative anaemia (haematocrit 0.20 L/L, reference values 0.42-0.59 L/L, reticulocytes 0.2%, reference values 0.1-2%). Because of the signs of uraemia a low-protein diet was given. During the next 7 months, creatinine, urea, and haematocrit were measured repeatedly. Creatinine concentration was relatively stable during the first 3 months after diagnosis, but it increased to 647 µM 2 weeks before the dog was euthanized. Urea and haematocrit values remained relatively stable. Because of the dog's deterioration, it was euthanatised on request of the owner at 16 month of age.

Case 2

The second Dutch kooiker dog (female, 21 months) had a history of frequent vomiting (1-2x/day), poor appetite, polyuria, and polydipsia, all beginning at an early age and increasing with age. The dog had always been underweight. In the preceding 3 months it had fainted four times and it had been apathic for three days. When presented, the dog was very apathic and had a rectal temperature of 35.5°C; its mucous membranes were pale and the capillary refill time was prolonged. The elasticity of the skin was poor and the extremities were cold. The dog was uraemic (urea > 50 mM) and anaemic (haematocrit 0.20 L/L). Intravenous administration of 0.9% NaCl solution (100 ml/kg body weight/24 hours) was started but the dog died within 3 hours.

[1] Department of Pathology, Faculty of Veterinary Medicine, Utrecht University, P.O. Box 80.158, 3508 TD Utrecht, the Netherlands.
[2] Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University, P.O. Box 80.154, 3508 TD Utrecht, the Netherlands.
[3] Gezelschapsdierenpraktijk, Enggraaf 22, 4175 ER Haaften, the Netherlands.
[4] Dierenkliniek, Ringweg Kruiskamp 68, 3814 TE Amersfoort, the Netherlands.

Case 3
The third dog (male, 15 months) was presented because of decreased endurance. The physical examination revealed pale mucous membranes. Laboratory examination revealed uraemia (creatinine 581 μM; urea >50 mM) and anaemia (haematocrit 0.08 L/L). Because of the presumptive diagnosis of chronic renal failure and the poor prognosis, the dog was euthanatised later.

PATHOLOGY

Macroscopic examination
The renal lesions were similar in all dogs. The kidneys were moderately reduced in size. The capsule could easily be removed from the renal surface, which was irregular and had many, sometimes large, indentations. The kidneys were firm and light brown. On the cut surface, white radial streaks were visible throughout the renal cortex and extended into the renal medulla, which was diffusely white and firm. There were numerous small cysts in the renal cortex. In the third dog one kidney was similar in appearance to those in the other dogs but the other kidney was severely shrunken, irregular, and firm.

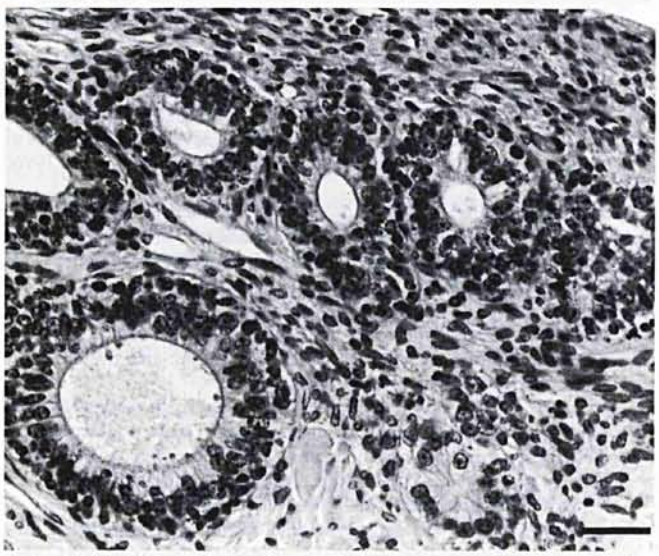

Figure 1. Renal cortex, dog 1: area of immature renal tissue containing persistent metanephric ducts lined by a tall, pseudostatified, columnar epithelium and surrounded by immature mesenchyme. HE, bar = 18 μm.

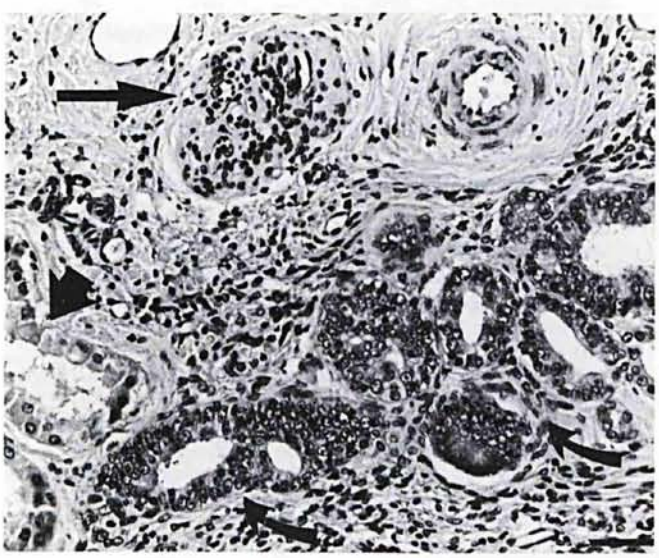

Figure 2. Renal medulla, dog 1: multiple persistent metanephric ducts (curved arrows) surrounded by undifferentiated mesenchyme adjacent to proliferated arteriolar structures (long arrow) and mature tubules with hypertrophied epithelium (short arrow). HE, bar = 72 μm.

Microscopic examination
For histological examination samples from both kidneys were fixed in 10% neutral-buffered formalin, embedded in paraffin wax, and cut into 4-μm sections. These sections were stained with haematoxylin-eosin, Van Gieson, alcian blue, and periodic acid-Schiff (PAS).

Case 1
The dysplastic lesions in this dog included persistent metanephric ducts, foetal nephrons, and undifferentiated immature mesenchyme. The renal medulla contained multiple metanephric ducts lined by tall pseudostratified columnar epithelium and surrounded by loose mesenchyme (Figures 1, and 2). These ducts extended multifocally to the inner cortex. Foetal nephrons were mostly located in radial cortical connective tissue bands and consisted of small immature tubules and small immature glomeruli with prominent visceral epithelium but without capillary lumina. Foetal glomeruli were also present in the adjacent cortical tissue and were multifocally accompanied by proliferative vascular structures and immature tubules. Undifferentiated immature stroma was present in the cortex and medulla and stained negatively with Van Gieson stain and positively with alcian blue. Secondary degenerative and inflammatory lesions consisted of interstitial fibrosis and a predominantly lymphocytic/plasmacytic infiltration. The renal medulla and papilla were diffusely fibrotic, whereas the cortical fibrosis was restricted to areas with foetal nephrons or secondary interstitial nephritis. Secondary to the fibrosis there was cystic dilatation of glomeruli and tubules accompanied by atrophy of the glomerular tufts and tubular epithelial cells. Some tubules contained PAS-positive hyaline casts as well as intraluminal and intraepithelial crystals of oxalates. There was mineralization of the basement membrane in a few areas. Compensatory changes consisted of hyperplasia and hypertrophy of glomeruli and tubules.

Case 2
The degenerative, inflammatory, and compensatory changes in this dog were identical to those in the first case but there was more extensive mineralization of the basement membranes. However, the dysplastic lesions in this case consisted only of foetal nephrons and persistent immature mesenchyme.

Case 3
The interstitial fibrosis in both kidneys of this dog was more pronounced than in the other cases and extended diffusely into the renal cortex, particularly in the smaller kidney. Metanephric ducts were present within the fibrotic areas in the medulla. Focally adenomatoid proliferation of tubular epithelium was surrounded by immature mesenchyme (Figure 3). The fibrotic cortical areas contained hypertrophic, proliferated arteriolar structures and primitive glomer ular structures. Inflammatory and compensatory changes were similar to those in the other cases.

DISCUSSION

The clinical signs in these cases were characteristic of chronic renal failure and can be explained by the renal lesions.

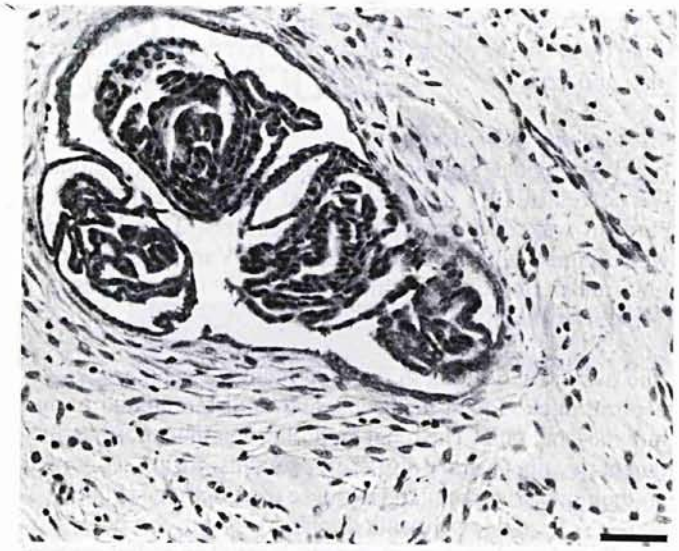

Figure 3. Renal medulla, dog 3: extensive adenomatoid proliferation of tubular epithelium surrounded by loosely arranged immature stroma. HE, bar = 36 μm.

Chronic renal failure is a common consequence of renal disease in older dogs, in which it may be caused by several disorders including interstitial nephritis, glomerulonephritis, pyelonephritis, and amyloidosis (10). However, in young dogs chronic renal failure occurs less frequently and is often the consequence of a hereditary disease (16). In veterinary medicine, there is some confusion with respect to the appropriate terminology for juvenile renal diseases. A general term to describe disorganized renal development that gives rise to renal failure in young dogs is juvenile nephropathy (12). When the disease is suspected to have a familial background the term familial nephropathy can be used (8). Only when the mode of inheritance has been determined may the disease be diagnosed as a hereditary nephropathy (8). The juvenile nephropathies include a variety of morphological disease entities, including renal dysplasia (16). Helpful diagnostic information may be gained from clinical investigations but the final diagnosis is based on histological examination of a renal biopsy or post mortem-material (14). In contrast to renal dysplasia in humans, where, except for rare cases of segmental renal dysplasia (7), dysplastic lesions are diffusely present in the kidney (19), lesions in canine renal dysplasia are in general segmentally distributed (17). Therefore, renal biopsies may be non-diagnostic. Of the five primary lesions characteristic of renal dysplasia in the dog, i.e., asynchronous differentiation of nephrons, persistent immature mesenchyme, persistent metanephric ducts, atypical tubular epithelium, and dysontogenic metaplasia (17), only three were found in case 1, two in case 2, and three in case 3. Thus, not all dysplastic lesions occur in each case, and especially dysontogenic metaplasia is rare (12,17). Asynchronous differentiation of nephrons, persistent immature mesenchyme, atypical tubular epithelium, and persistent metanephric ducts are the most common lesions (4,17) and were present in the dogs described here, which led to the diagnosis of renal dysplasia. An explanation for the individual variation in dysplastic lesions may be the presence of pronounced secondary degenerative changes, since these dogs were in a chronic stage of the disease. It is known that in the chronic stage of the disease dysplastic changes can be obscured by advanced interstitial inflammation and fibrosis (17). The aetiology of renal dysplasia in dogs is uncertain (12,16). Various possible causes have been proposed, including familial disease, urethral valves, canine herpesvirus infection, and teratogenic agents that damage the developing renal parenchyma during the intrauterine or early neonatal period when an active subcapsular nephrogenic zone is still present in carnivores (1,12). Since very little anamnestic information was available for our patients, the cause of dysplasia remains uncertain. However, since common environmental factors causing renal dysplasia were unlikely and since the Dutch kooiker dog population is based on a rather small gene pool with high levels of inbreeding (11), renal dysplasia may be a familial or hereditary nephropathy in this breed.

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