CASE REPORT

Familial Glomerulonephritis in Doberman Pinscher Dogs

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Summary

Progressive renal disease in 13 related Doberman pinscher dogs had the histological criteria of membranoproliferative glomerulonephritis. Polyuria, polydipsia and weight loss were the usual initial abnormalities and were observed at one year of age or less in seven of 11 dogs diagnosed antemortem as having renal disease. There was no sex predilection. All dogs were traced to a common male dog no more than four generations previously.

Résumé

Glomérulo-néphrite familiale, chez des chiens Doberman

Une maladie rénale progressive, qui affectait 13 chiens Doberman apparentés, présentait les critères histologiques d'une glomérulonéphrite membraneuse. Les signes cliniques initiaux usuels se caractérisaient par de la polyurie, de la polydipsie et une perte de poids; ils se manifestèrent vers l'âge d'un an, ou même plus tôt, chez sept des 11 sujets chez lesquels on avait diagnostiqué, de leur vivant, une maladie rénale. Cette condition affectait indifféremment des mâles et des femelles. Tous ces chiens appartenaient à la quatrième génération d'un même géniteur.

Introduction

Breed predisposition to renal disease in dogs has been documented for cocker spaniels (7), Norwegian elkhounds (2) and Samoyeds (1). The disease in spaniels was originally termed renal cortical hypoplasia, but using current criteria of classification the lesion was that of nonspecific end-stage kidney (2). The disease in elkhounds and Samoyeds was similar, with variable age at clinical onset and generalized glomerular and interstitial disease at necropsy. In elkhounds the earliest change was periglomerular fibrosis followed by interstitial fibrosis, proliferative glomerular changes and interstitial mononuclear leucocyte accumulation. An immunological basis for the glomerular lesion was not demonstrated (2). In Samoyeds the advanced renal lesion in each case precluded a more specific diagnosis other than chronic generalized renal disease. Glomerular proliferative and sclerotic changes were more prominent than in the elkhound disease and the age of onset of clinical renal failure was younger (nine to 11 mo) than in elkhounds (up to four yrs). Medullary and cortical interstitial fibrosis, vascular lesions and interstitial inflammation were considered nonspecific changes in both diseases.

Breed or line predisposition to renal disease of young dogs has been proposed for German shepherds, dachshunds, Lhasa apsos, Shih Tzus and miniature schnauzers (10), but data to support this impression have not been published. This report describes generalized renal disease in 13 related Doberman pinschers from the Toronto area.

Clinical Data

Between February 1976 and July 1978, 11 Doberman pinschers were admitted to the Small Animal Clinic, Ontario Veterinary College with histories suggestive of acute or chronic renal disease. Five were males, six were females and most had long histories of polyuria, polydipsia, nocturia and weight loss. In seven of the dogs the age at onset of clinical signs was less than one year. The significant features of each medical history are presented in Table I. In most cases subsequent clinical and laboratory findings supported the diagnosis of severe glomerular disease (Table II).

Features common to all dogs with renal failure were marked proteinuria, mild nonregenerative anemia, and elevated serum concentrations of urea nitrogen, creatinine and, when measured, cholesterol. Most cases had received intensive antibiotic and steroid therapy, but renal function continued to

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TABLE I
CLINICAL HISTORIES OF DOBERMAN PINSCHERS WITH GLOMERULONEPHRITIS

Dog	Sex	Age at Onset of Clinical Signs	Initial Signs	Age at Euthanasia
1	F	6 wk	PU/PD,[a] poor growth	6 mo
2	F	1 yr	PU/PD	18 mo
3	F	1 yr	PU/PD, poor growth	18 mo
4	M	10 mo	PU/PD, ascites; edema	14 mo
5	F	6 mo	PU/PD, nocturia	3 yr
6	F	6 wk	PU/PD	9 yr
7	M	1 yr	PU/PD	5 yr
8	F	2, 5 yr	Vomiting	2, 5 yr
9	M	4, 5 yr	Wt. loss, bleeding	4, 5 yr
10	M	8 yr	PU/PD, weight loss	
11	F		No signs of renal disease	4 yr
12	M		No signs of renal disease	
13	M	2, 5 yr	PU/PD	4 yr

[a]Polyuria, polydipsia

deteriorate. Two dogs (No. 8, 10) had no biochemical alterations suggesting advanced renal disease but did have persistent proteinuria and, in one dog, neutrophils in the urinary sediment. One dog (No. 9) died from liver failure associated with portosystemic venous shunts. Glomerular disease was found at necropsy although antemortem routine urinalysis and blood chemistry had detected no renal dysfunction. Tissues from two other Doberman pinschers which died with renal disease were submitted to the Veterinary Services Laboratory, Guelph for histological examination.

Pathology

Significant gross extrarenal lesions in each of 10 dogs necropsied are listed in Table III. In every dog the most significant lesion was in the kidneys and varied little among the 10 animals. Both kidneys were firm and slightly smaller than normal. The surface was finely and diffusely pitted. The cortex was light brown and often had numerous small (1-2 mm) spherical cysts. There were miliary small white dots in a pattern suggesting abnormally-conspicuous glomeruli. The capsule was easily removed. Medulla was either normal or it was pale and rubbery. In three bitches the right ureter and kidney were absent. One of these bitches also had agenesis of right uterine horn. Only one of the three had compensatory hypertrophy of the remaining kidney (87 g).

Changes in other organs were those associated with advanced renal disease (3, 5) and will not be further described (Table III).

Microscopic renal lesions were consistently found in glomeruli. Specimens with severe glomerular changes also had tubular and interstitial disease. The mildest glomerular

TABLE II
LABORATORY FINDINGS IN DOBERMAN PINSCHER DOGS WITH GLOMERULONEPHRITIS

Dog Number	BUN (mg/dl) Initial	BUN (mg/dl) Final	Creatinine (mg/dl) Initial	Creatinine (mg/dl) Final	Serum Phosphorous (mg/dl) Initial	Serum Phosphorous (mg/dl) Final	Serum Cholesterol (mg/dl) Initial	Serum Cholesterol (mg/dl) Final	Urinary Protein (mg/dl) Initial	Urinary Protein (mg/dl) Final	Urine Specific Gravity Initial	Urine Specific Gravity Final
1		94	3,3	6,4			337	75			1,013	
2	35	125	ND	ND			ND	ND			ND	
3	140	117	7,8	6,0			273	+++[a]			1,017	
4	35	125	7,1	6,5	18		526	500	800		1,039	1,016
5	30	40	ND	ND			267	100	150		1,023	1,018
6		128	6,2	9,7			ND	75			1,012	
7	73	220	10,8	10	22		ND	375	200		1,018	1,010
8	294	290	13	22			ND	500	200		1,014	1,013
9		285	9	23			ND	500			1,016	
10		11	ND	4,2			ND	500			1,004	1,023
11		7	ND	ND			ND	0			1,023	
12		13	ND	ND			ND	600	750		1,058	1,020
13		100	23	ND			ND	+++[a]			1,020	

[a]Corresponds to about 300 mg/dl

TABLE III
EXTRARENAL GROSS LESIONS IN DOBERMAN PINSCHERS WITH RENAL DISEASE

Dog	Stunting Emaciation	Oral Ulcers	Gastric Ulcers	Gastric Mineralization	Hyperparathyroidism	Right Renal Aplasia
1	+	–	–	–	–	–
2	+	NR	NR	NR	+	–
3	+	–	–	–	–	+
4	+	–	–	–	–	–
5	+	–	–	–	–	–
6	+	–	–	+	+	+
7	+	–	+	–	+	–
8	+	–	+	–	+	+
9	+	+	+	+	–	–
11[b]	–	–	–	–	–	–
12[c]	–	–	NR	NR	NR	–
13[a]	+	NR	NR	NR	NR	–

[a]Selected tissues received for histological examination. NR = not reported.
[b]Euthanized because of hepatic encephalopathy. Cirrhosis was found at necropsy.
[c]Dog died with lymphosarcoma two years after discharge from O.V.C. Findings listed are from O.V.C. data.

lesion was in dogs 5 and 11, consisting of focal segmental mesangial thickening and accentuation of glomerular lobulation. Hyaline thickening of the mesangium was most obvious adjacent to the afferent arteriole (Figure 1).

In dogs killed in advanced renal disease, it was usual to see a wide spectrum of glomerular lesions in the same kidney. Common findings were mesangial cell proliferation, increased mesangial matrix and glomerular sclerosis. Mesangial cell proliferation was either segmental or diffuse and severely affected glomeruli often had adhesions between peripheral capillary loops and hypertrophic parietal epithelium (Figure 2).

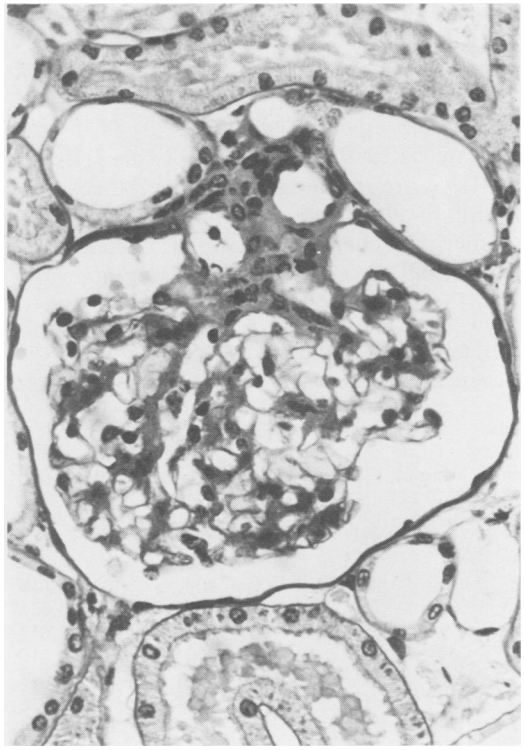

FIGURE 1. Increased mesangial prominence in a glomerulus of a six month old Doberman pinscher bitch with poor growth and persistent polyuria. Three micrometers. PAS. X116.

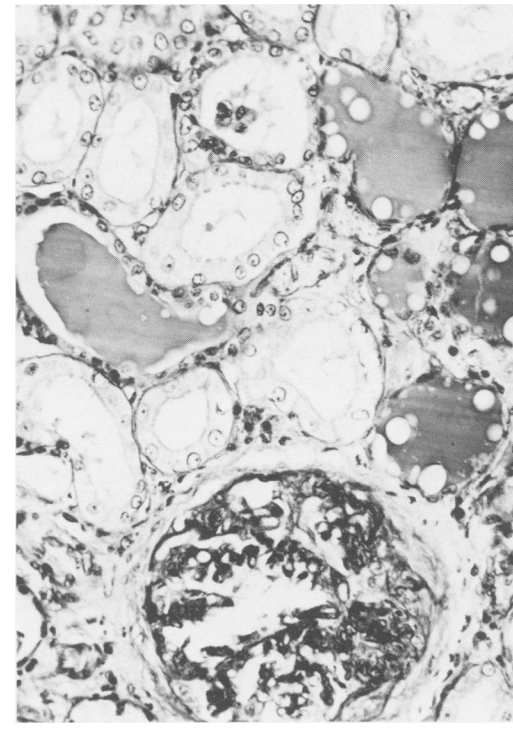

FIGURE 2. Glomerular tuft adhesions and intratubular protein casts in the kidney from a four year old Doberman pinscher. There is slight interstitial fibrosis and patchy flattening of tubular epithelium. Three micrometers. PAS. X40.

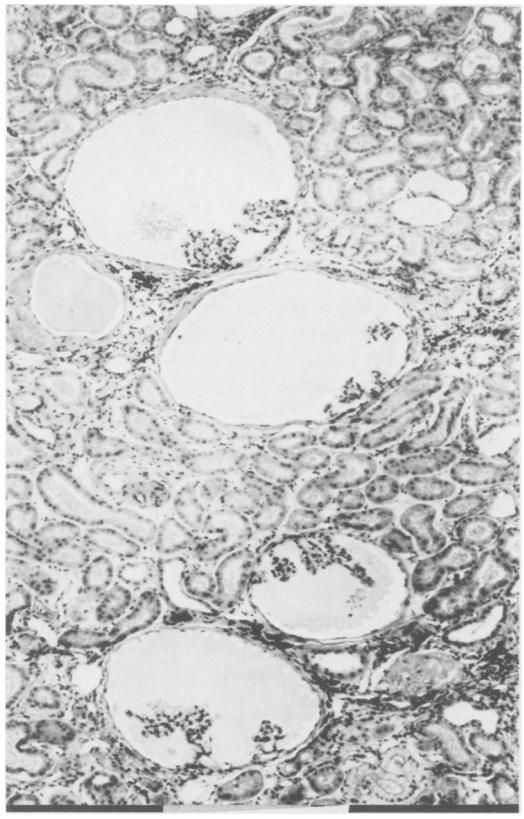

FIGURE 3. Shrunken glomerular tufts in fluid-filled, dilated Bowman's spaces. Interstitial and tubular changes are scant. Three micrometers. H & E. X24.

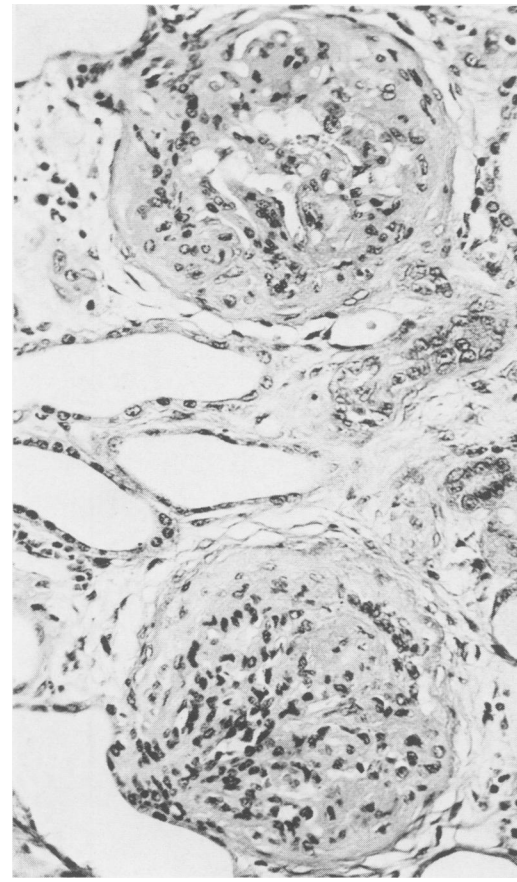

FIGURE 4. Glomerular sclerosis, interstitial fibrosis and tubular loss in a Doberman pinscher with advanced renal disease. Three micrometers. H & E. X96.

Glomerular sclerosis was seen as shrunken glomerular tufts at the vascular pole of cystic Bowman's spaces which corresponded to the cortical cysts seen grossly (Figure 3). Particularly in areas of interstitial fibrosis the glomeruli were sclerotic and tightly surrounded by a thick fibrous capsule (Figure 4).

Tubular and interstitial lesions paralleled glomerular changes. Kidneys with mild glomerular disease had no tubular or interstitial lesions. In kidneys with severe glomerulonephritis the distribution of tubular loss, fibrosis and mononuclear leucocyte infiltration corresponded to the distribution of nephrons served by severely altered glomeruli (Figure 5). There was compensatory hypertrophy and hyperplasia of tubules associated with mildly affected glomeruli in otherwise severely affected kidneys. In the medulla there was usually fibrosis with tubular loss and occasional accumulations of mononuclear leucocytes. The histological diagnosis was membranoproliferative glomerulonephritis.

Pedigree Analysis

Pedigrees were obtained from nine affected dogs. All were related and could be traced, usually through both sire and dam, to a common male (dog A) no more than four generations previously. His son, dog B, appeared in all pedigrees except that of dog C, a litter brother (Figure 6).

Discussion

The diagnosis of membranoproliferative (mesangiocapillary) glomerulonephritis was based upon the observation of bilateral, generalized and predominantly glomerular disease characterized by segmental or diffuse mesangial thickening and lobular accentuation (4, 6). Exudative lesions were absent and capillary thickening was seen only in kidneys with advanced disease. In three cases extraglomerular renal lesions were minor or

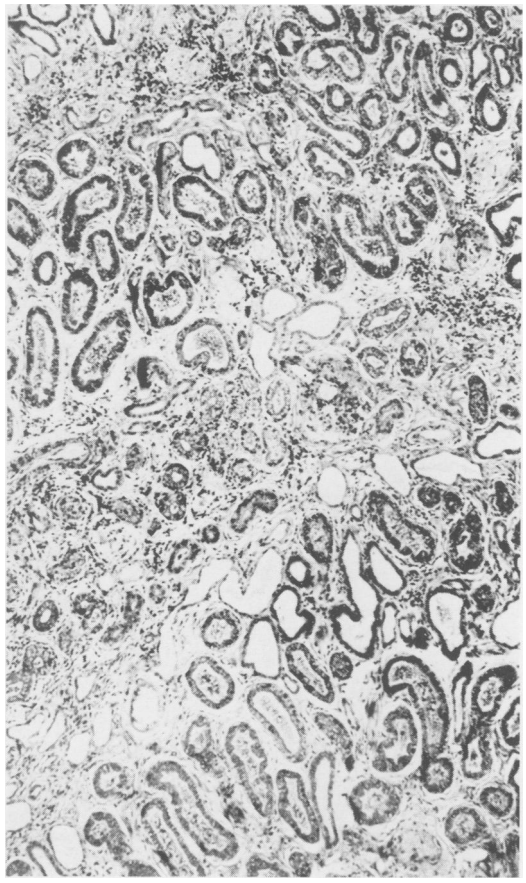

FIGURE 5. Alternating bands of scarring and tubular hyperplasia in a severely affected kidney. Three micrometers. H & E. X24.

absent. Glomerular changes were invariably more severe than the interstitial and tubular lesions. The preponderance of young animals, slow but inexorable clinical course and resistance to corticosteroid therapy are similar to membranoproliferative glomerulonephritis in man (4, 6). Lesions meeting the pathological criteria of membranoproliferative glomerulonephritis are reported to be common in dogs with glomerular disease but no familial predisposition has hitherto been reported (8, 11, 14). Familial renal disease in cocker spaniels and in Samoyeds may be glomerulonephritis but advanced lesions in the kidneys examined in these studies preclude interpretation as to the initial classification of the renal disease. In Norwegian elkhounds the early lesions are clearly different from those described in this paper in that periglomerular fibrosis and hyperplasia of parietal epithelial cells are the prominent early changes (2). In interesting parallel to

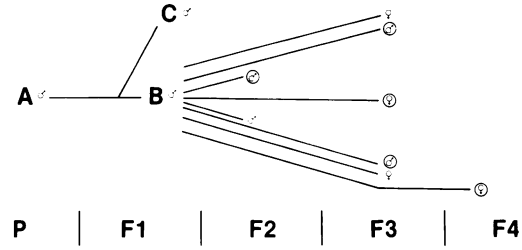

FIGURE 6. Schematic representation of familial pattern of glomerulonephritis in Doberman pinschers. Dogs A and B (both dead) were of unknown renal status. Dogs encircled are descended from B through both dam and sire, others through sire only. Each line represents separate litter.

the findings in Doberman pinschers, membranoproliferative glomerulonephritis (13) and renal agenesis (9, 12, 14) have been reported in beagle dogs raised in pharmaceutical research colonies in Canada and in the United States. Glomerulonephritis and renal agenesis were not reported in the same dog.

The frequency of this form of renal disease among Doberman pinschers is unknown, but the affected line of dogs is very prominent among show dogs and, presumably, among the pet population of Doberman pinschers as well. The strong familial association evident in our pedigree data suggests that siblings and offspring of affected dogs have a high risk of renal disease. Until the breeders of the known affected dogs are prepared to disclose complete breeding information for the purpose of medical follow-up of related dogs, the frequency and mode of transmission will remain unknown. For the individual affected dog the clinical course is usually prolonged but refractory to drug therapy and eventually fatal.

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LETTER TO THE EDITOR

"For not Looking than not Knowing"

DEAR SIR:

Most practitioners have been aware of the above phrase either from training at veterinary colleges or from seminars, etc. . .

A four year old German shepherd male cross was presented after being hit by a car twelve hours previously. The dog favoured the left hind leg and ambulated on three legs. A pain killer,[1] had been administered the previous night by a pharmacist. The owner had noted that the dog would occasionally hyperventilate when given tranquilizers prior to presentation but had showed no adverse drug reactions.

On examination, several superficial lacerations were present on the medial left thigh, colour of mucosa and capillary refill were normal, and the animal appeared bright and alert. Auscultation revealed slight muffled heart sounds on the right thorax, but abdominal palpation revealed no abnormalities. Twelve milligrams of xylazine[2] were administered intravenously and lateral and ventral/dorsal radiographs of the pelvis were taken. The diagnosis was established as a dislocated left hip, and the animal was given 125 mg thiopental sodium[3] to facilitate manipulations of the hip joint. The hip was reduced and a light flexion bandage applied. The animal appeared to make a smooth recovery from anesthesia then went into respiratory distress, and collapsed. Supportive treatment had no effect, and the animal died one hour later.

At necropsy, a 5 cm tear was discovered on the right lateral muscular portion of the diaphragm, with stomach and approximately one metre of small intestine projecting into the thoracic cavity. On further questioning, the owner mentioned that the animal had always shown poor exercise tolerance. It was theorized that the herniation was either congenital or had occurred prior to the car accident. The combined effects of shock, herniated intestinal contents and barbiturates had compromised the respiratory system to the point where cardiovascular collapse was nonreversible.

This case demonstrates the importance of a thorough history taking and physical examination in any victims of automobile accidents.

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[1]Talwin, Winthrop Laboratories, Division of Sterling Drug, Aurora, Ontario.
[2]Rompun, Haver-Lockhart Laboratories, Division of Bayvet Corp., Shawnee Mission, Kansas.
[3]Pentothal sodium, Abbott Laboratories Ltd., Montreal, Quebec.