Small Intestinal Diarrhea in a Wheaten Terrier

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Skipper, an 8-year-old, castrated soft-coated wheaten terrier (SCWT), presented for marked weight loss, poor appetite, and distended abdomen.

History

Skipper had a history of recurrent mild GI upset consistent with small intestinal diarrhea characterized by large, voluminous stool with decreased appetite, weight loss, and occasional vomiting. The referring veterinarian's management included a novel protein diet, prednisone at 0.5 mg/kg PO q48h, and metronidazole at 12.5 mg/kg PO q12h with minimal resolution of clinical signs.

Physical Examination

Skipper was quiet, alert, and responsive with normal vital parameters. Abnormal findings included distended abdomen, poor coat, generalized weakness, and decreased BCS (2/9).

Diagnostics

CBC, serum biochemistry profile, and abdominal ultrasonography were completed. Serum biochemical abnormalities included panhypoproteinemia, hypocholesterolemia, and hypocalcemia (**Table**). CBC and urinalysis were within reference ranges. Abdominal ultrasonography revealed diffusely thickened small intestine with hyperechoic mucosal layer and preservation of wall layering. A moderate amount of aspirated anechoic peritoneal fluid was evident. The remainder of the abdomen was unremarkable.

BCS = body condition score, SCWT = soft-coated wheaten terrier

Table **Abnormal Serum Biochemistry Results**

Variable	*Result*	*Reference Range*
Albumin (g/dL)	1.1	3–4
Calcium (mg/dL)	7.1	8.2–12.4
Cholesterol (mg/dL)	67	112–328
Globulin (g/dL)	1.3	2.1–4.5
Total protein (g/dL)	2.4	5.1–7.8
Total protein–effusion (g/dL)	1	

Ask Yourself

1. What are the differentials for abdominal effusion characterized as a pure transudate, and how can biochemistry profile findings narrow the differentials?
2. What diagnostic and screening procedures should be used to evaluate a SCWT with suspected protein-losing disease?
3. What treatments are available to manage potential protein-losing nephropathy differentials in a SCWT?

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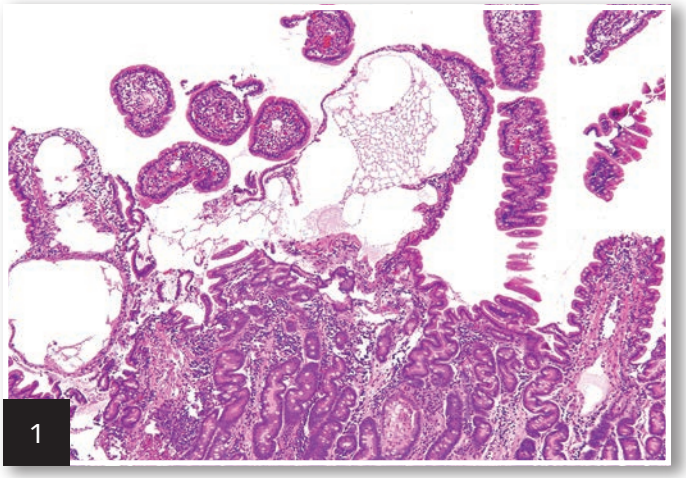
Diagnosis
Protein-losing enteropathy (PLE)

Preliminary Diagnosis
Preliminary diagnosis of PLE is based on GI signs and free abdominal fluid that is a direct result of the significant panhypoproteinuria. Common causes include lymphatic abnormalities, inflammatory bowel disease (IBD), and neoplastic conditions. Breed-specific enteropathies have been identified. Protein-losing nephropathy (PLN), meanwhile, refers to any glomerular disease of the kidney that results in excessive protein loss.

SCWTs are predisposed to familial PLE and PLN; middle-aged bitches are most frequently affected. Mode of inheritance is complex and unclear. Concurrent PLE–PLN is occasionally (ie, uncommonly) seen in other breeds. Affected patients can have PLE or PLN in isolation. Both conditions may affect 5% to 15% of the breed and have many more suspected carriers.

There is a high prevalence of food hypersensitivities in SCWTs with PLE, but whether these hypersensitivities have a primary or secondary role is unknown. Affected patients can have lymphangiectasia with or without concurrent IBD (**Figure 1**); both can be patchy and missed on biopsy sample analysis. A functional-structural change in glomerular permeability, specifically a podocytopathy, has been identified in SCWTs with PLN. Glomerular lesions are generally characterized by focal and segmental glomerulosclerosis (**Figure 2**) secondary to the podocytopathy, although immune-complex–mediated glomerulonephritis is sometimes reported.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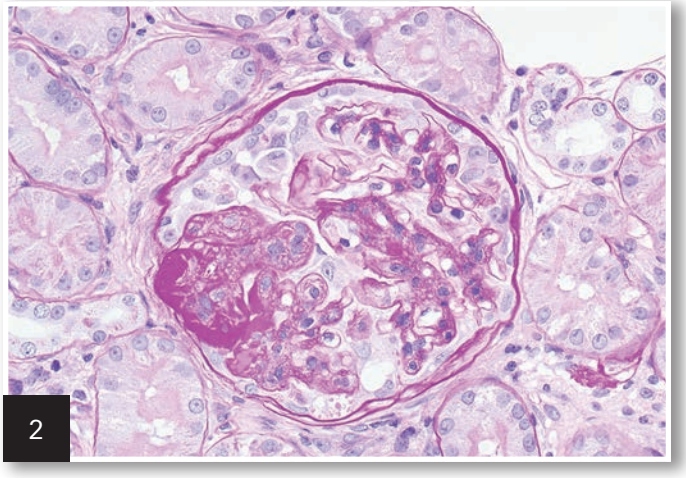
Intestinal lymphangiectasia with lacteal dilation.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Glomerular lesion of glomerulosclerosis.

Prognosis
PLE or PLN prognosis may be poor if either condition is detected late in disease course; however, detection before serum protein concentrations decrease offers the best chance that treatment may slow progression. Because of genetic predisposition, affected dogs should not be bred.

Treatment
Lymphoplasmacytic enteritis with lacteal dilation was diagnosed by endoscopic biopsy. Medical therapy before diagnostics does not affect obtaining a diagnosis. Immunosuppressive therapy was fortified (prednisone 2 mg/kg PO q24h; azathioprine 2 mg/kg PO q24h for 7 days, then transitioned to q48h long-term). Additional treatment included spironolactone (2 mg/kg PO q24h) and cromolyn sodium (100 mg q8h, off label), along with a hydrolyzed protein diet. Skipper's ascites resolved, but total serum protein levels remained low.

Outcome
Skipper's PLE was well controlled with this treatment, although recurrent urinary tract infections and an episode of sepsis occurred, likely secondary to prolonged immunosuppression. Skipper developed proteinuria after resolution of the urinary tract infections (urine protein:creatinine 0.85; range, <0.5) which was within 1 year of PLE diagnosis. The proteinuria was responsive to enalapril at 0.5 mg/kg q12h; however, Skipper was euthanized because of unrelated illness. ■ cb

See **Aids & Resources**, back page, for references & suggested reading.

IBD = inflammatory bowel disease, PLE = protein-losing enteropathy, PLN = protein-losing nephropathy, SCWT = soft-coated wheaten terrier

Did You Answer?

1. Pure transudate is a clear fluid with low protein level (<2.5 g/dL) and nucleated cell count (<1,000/µL); decreased oncotic pressure from hypoalbuminemia is the primary cause. Decreased serum albumin is most frequently caused by decreased production as occurs in synthetic liver failure (>70% loss of functional parenchyma) or protein loss via the GI tract or kidneys. Protein loss via the GI tract is nonselective and results in decreased albumin and globulin.

   Exceptions include some breed-specific (eg, Basenji) and infectious (eg, histoplasmosis) enteropathies, in which globulin is normal or increased. Other abnormalities associated with PLE include hypocholesterolemia, hypocalcemia, and hypomagnesemia. A definitive diagnosis of IBD, other infiltrative disease (eg, infectious, neoplasia), or lymphangiectasia requires intestinal biopsy. Ideally, a full-thickness biopsy specimen can be obtained; however, given the severity of disease and patient serum albumin, endoscopic biopsy may be safer. PLN and liver failure generally cause hypoalbuminemia only. If severe, PLN can progress to azotemia and/or nephrotic syndrome characterized by hypercholesterolemia and edema. Animals with synthetic liver failure often have additional markers of dysfunction (eg, reduced BUN, jaundice, hypoglycemia, hypocholesterolemia). Total serum bile acids should also be performed to assess liver function.

2. Annual screening to identify protein loss is recommended. An ideal protocol includes CBC, serum biochemistry profile, urinalysis, urine protein:creatinine ratio, and fecal α-1 proteinase inhibitor test on 3 naturally voided samples. A DNA test at University of Pennsylvania (scwtca.org/health/dnatest.htm) can identify dogs at risk for podocytopathy. Definitive diagnosis and characterization of intestinal and/or glomerular lesions require histopathology.

3. Therapy for PLE includes probiotics, antimicrobials (eg, metronidazole, tylosin), cobalamin supplementation, antiplatelet therapy (eg, low-dose aspirin, clopidogrel), immunosuppressive agents, and gluten-free hypoallergenic diet. Cromolyn sodium (cost restrictive) can be beneficial in refractory cases.

   PLN management involves inhibition of the renin–angiotensin–aldosterone system, control of systemic hypertension, diet therapy with protein restriction and omega-3 supplementation, and antiplatelet therapy. If immune complex deposition is confirmed via renal biopsy with electron microscopic analysis, immunosuppressive therapy may be indicated.