New, More Affordable Drug Therapy for Perianal Fistula

A chronic, progressive, inflammatory condition found almost exclusively in middle-aged and older German shepherds, perianal fistula (anal furunculosis), is characterized by ulcerated sinus tracts involving the perianal skin and subcutaneous tissues. Treatment can include antibiotics, tail splintage, improved hygiene, and surgery. Success rates vary, and complications and recurrence can be intractable. Recent histologic investigations suggest an immune-mediated cause, similar to Crohn’s disease in humans, which often occurs with fistulous tracts. Histologic evaluation does not support a primary infectious cause, but indicates that the anal sacs are secondarily involved. Treatment with cyclosporine has been successful, if costly, in these cases. In this study, cyclosporine A was combined with ketoconazole, an antifungal that extends its half-life, and assessed for safety, effectiveness, and cost benefits. Fistula patients with varying severity of the condition included 15 German shepherds (3 female, 12 male), 3 German shepherd crossbreeds, and 1 Australian cattle dog. The otherwise-healthy dogs received amoxicillin (15 mg/kg PO Q 12 H) and clavulanic acid (12.5 mg/kg PO Q 12 H) for 7 days before the study. Dogs were then given ketoconazole (5.3 to 8.9 mg/kg PO Q 12 H) and cyclosporine A (0.5, 0.75, 1 or 2 mg/kg in 10 mg/ml corn oil PO Q 12 H). The cyclosporine dose rate was adjusted based on analyzed serum levels to achieve a target range of 400 to 600 ng/ml. Routine hematologic and biochemical examination was performed every 14 days. Signs resolved completely in 3 to 10 weeks, and therapy was continued for 2 more weeks. Seven of the 19 dogs (38.8%) experienced recurrence after 1 to 6 months and were retreated. None of the adverse reactions was considered serious (hair loss, lethargy, vomiting, or decreased appetite), and all resolved with treatment. Results were similar or better than surgical alternatives and were about 70% less expensive than the use of cyclosporine without ketoconazole.

COMMENTARY: Perianal fistula (or anal furunculosis) is almost breed specific for German shepherds and until recently was treated with a variety of surgical techniques, none of which were particularly successful. With the realization that the disorder may be associated with this breed’s abnormal mucosal immune system came more successful attempts to treat it with varying combinations of cyclosporine, diet, and prednisone. However, the cost of cyclosporine has precluded widespread application. Ketoconazole extends the half-life of cyclosporine, and the efficacy of combined therapy was evaluated in this prospective clinical study. The results are impressive, not only in the overall clinical improvement but also in cost. This combined treatment may set the new standard for treatment of perianal fistula.—Colin F. Burrows, BVetMed, PhD, MRCVS, Diplomate ACVIM