History

A 7-year-old 24-kg (52.8-lb) spayed female mixed-breed dog was referred to the Louisiana State University Veterinary Teaching Hospital and Clinic with a 3-week history of licking its feet and extensive ulceration of the paw pads. The dog had developed extensive oral inflammation and ulceration, was salivating excessively, and had signs of extreme pain. The dog had received imidacloprida and ivermectinb regularly for flea and heartworm control, although there was no obvious temporal association between the administration of these medications and the development of disease. Prior to referral, the dog received injections of methylprednisolone acetate, dexamethasone, and a lime sulfur dip, with no clinical improvement.

Clinical and Clinicopathologic Findings

On initial evaluation, there was a focally extensive plaque with multifocal cutaneous erosions on the ventral aspect of the muzzle and chin. The dorsal aspect of the planum nasale was extensively thickened by hyperkeratosis, with ulceration of the cranial aspect of the nasal planum and philtrum. There were multifocal perioral depigmentations and erosions. The gums, hard palate, and tongue had multifocal ulcerations (Figure 1). All 4 feet were swollen and erythematous, with ulcerated paw pads and hemopurulent exudates. There were minor multifocal perivulvar erosions. The ocular and anal mucocutaneous junctions were spared from similar changes.

Impression smears of the plaque on the ventral aspect of the muzzle revealed neutrophilic and eosinophilic inflammation with cocci too numerous to count (septic neutrophilic inflammation). A CBC revealed mild hypoproteinemia (5.7 g/dL; reference range, 6.0 to 7.8 g/dL), mild to moderate neutrophilia (19.7 X 10³ neutrophils/µL; reference range, 3 X 10³ neutrophils/µL to 11.5 X 10³ neutrophils/µL), and mild monocytosis (2.0 X 10³ monocytes/µL; reference range, 0.1 X 10³ monocytes/µL to 1.4 X 10³ monocytes/µL). Serum biochemical analysis revealed mild hyperglycemia (159 mg/dL; reference range, 80 to 115 mg/dL), hypoalbuminemia (1.6 g/dL; reference range, 2.6 to 4.2 g/dL), mildly low BUN concentration (6 mg/dL; reference range, 8 to 22 mg/dL) and creatinine concentration (0.45 mg/dL; reference range, 0.50 to 1.70 mg/dL), mild hyponatremia (138 mmol/L; reference range, 140 to 133 mmol/L), and mild hypochloremia (100 mmol/L; reference range, 107 to 115 mmol/L). Moderate hypocalcemia (7.7 mg/dL; reference range, 9.4 to 11.4 mg/dL) was also noted, although the calcium concentration was within reference limits after correcting for hypoalbuminemia (9.6 mg/dL).

Biopsy specimens from the plaque on the ventral aspect of the muzzle, tongue, buccal mucosa, nasal planum, paw pads, and perioral erosions were obtained for bacterial culture and histologic examination. Aerobic bacterial culture of skin samples yielded a heavy growth of β-hemolytic Streptococcus spp, a light growth of Pseudomonas aeruginosa, and a light growth of Proteus spp.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →
Histopathologic Findings

Biopsy specimens were processed for histologic examination. All sections of skin had similar changes. There was extensive epidermal ulceration with multifocal to coalescing suprabasilar clefting of the epidermis and hair follicles (Figure 2). Basal cells lining the floor and deep margin of vesicles were rounded (tombstone cells). The dermis underlying the ulcerated areas was infiltrated by large numbers of neutrophils, macrophages, and eosinophils with hemorrhage, edema, and fibrin exudation. Neutrophils multifocally infiltrated clefs, forming pustules, with low numbers of intrapustular acantholytic cells. Less affected areas had moderate epidermal hyperplasia and mild to moderate intercellular edema. The superficial dermis in the less affected areas was moderately edematous.

Findings for sections of the tongue and oral mucosa were similar, with locally extensive mucosal ulceration with replacement by a large mat of fibrin admixed with degenerate neutrophils and rare acantholytic cells. The submucosa was infiltrated by large numbers of neutrophils, macrophages, lymphocytes, and plasma cells. At the margin of the ulcer, there was suprabasilar clefting of the mucosal epithelium with rounding of basal epithelial cells. There was multifocal mucosal hyperplasia of less affected areas.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: severe, multifocal to coalescing, acantholytic and ulcerative dermatitis, pododermatitis, stomatitis, and glossitis with suprabasilar clefting.

Case summary: pemphigus vulgaris in a dog.

Figure 2—Photomicrograph of sections of cutaneous biopsy specimens obtained from the margin of the perioral erosions and ulcers in the dog in Figure 1. Extensive epidermal erosion and ulceration with suprabasilar clefting of the epidermis and hair follicles is evident. The superficial dermis is infiltrated by large numbers of neutrophils and macrophages with fibrin and hemorrhage. H&E stain; bar = 300 µm. Inset—Higher-magnification image of a hair follicle illustrating suprabasilar clefting with rounded basal (tombstone) cells (arrows). H&E stain; bar = 50 µm.

Comments

Pemphigus vulgaris is one of a group of acantholytic dermatoses that includes pemphigus vulgaris, pemphigus foliaceous, and paraneoplastic pemphigus. This group of dermatoses is caused by a breakdown in keratinocyte-keratinocyte attachment, which results in the formation of detached keratinocytes, called acantholytic cells. The breakdown in keratinocyte attachment is usually a result of autoantibody-mediated disruption of desmosomal proteins, with each clinical form associated with a different constellation of targeted proteins. Histologic evaluation of skin biopsy specimens is often required to definitively diagnose acantholytic dermatoses, and cutaneous wedge biopsy specimens of intact vesicles or the epithelialized margin of a recently formed erosion or ulcer provide the most diagnostically useful samples.

If it is not practical to obtain wedge biopsy specimens, 8-mm punch biopsy specimens may be adequate for diagnosis. Punch biopsy specimens should be obtained by twisting the punch in a single direction because back and forth rotation can cause excessive shear and artifactual changes to the dermal-epidermal junction. Tissue samples should extend completely through the dermis and into the subcutis. Care should be taken to not scrub the biopsy site prior to sample acquisition (clipping the hair is permissible).

Pemphigus vulgaris is one of the rarest forms of pemphigus in dogs, and affected cats have been rarely described. It is distinguished clinically from pemphigus foliaceous by the involvement of mucous membranes and mucocutaneous junctions. Histopathologically, pemphigus vulgaris is characterized by the formation of suprabasilar epidermal clefs, vesicles, and bullae with acantholytic cells. These vesicles rupture easily, leading to the predominant clinical lesions of erosion and ulceration. Pemphigus vulgaris is caused by binding of circulating autoantibodies (typically IgG4) against desmoglein-3. Patients with lesions on haired skin may also have detectable antibodies against desmoglein-1.

Paraneoplastic pemphigus is another rare form of pemphigus in dogs, which is associated with neoplasia. Like pemphigus vulgaris, paraneoplastic pemphigus affects the oral mucosa and mucocutaneous junctions; thus, clinical differentiation between the 2 dermatoses is difficult. The desmosomal proteins targeted by the immune system in cases of paraneoplastic pemphigus are more diverse than those in cases of pemphigus vulgaris and have been reported to include envoplakin, perilakin, desmoglein-1, desmoglein-3, bullous pemphigoid antigen 1, and desmoplakin II. As such, the histologic changes associated with paraneoplastic pemphigus are heterogeneous and difficult to interpret because this dermatosis is often associated with a mixture of features consistent with pemphigus foliaceous (subcorneal...
Pemphigus foliaceous is the most common form of pemphigus in dogs, cats, and horses; it has rarely been reported to affect goats. The clinical signs of pemphigus foliaceous differ greatly from those of pemphigus vulgaris and paraneoplastic pemphigus. Pemphigus foliaceous causes bilaterally symmetric crusts and large pustules primarily on the face, pinnae, and paw pads in dogs and cats; on the face, neck, trunk, and distal portions of the extremities in horses; and on the face, ventral aspect of the abdomen, limbs, perineum, and tail in goats. Unlike pemphigus vulgaris and paraneoplastic pemphigus, pemphigus foliaceous rarely affects the oral mucosa; however, mucocutaneous involvement has been reported, albeit uncommonly. The classic histologic finding in cases of pemphigus foliaceous is the formation of subcorneal pustules that contain rafts of individualized acantholytic cells. Desmocollin-1, a calcium-dependant cadherin found predominately in the superficial epidermis, has recently been identified as a major target in pemphigus foliaceous.

Given the clinical signs of the dog of this report, several differential diagnoses had to be considered, including bullous pemphigoid, mucous membrane pemphigoid, epidermolysis bullosa acquisita, erythema multiforme, mycosis fungoides, and fungal dermatitis and stomatitis. Identification of suprabasilar clefting, pemphigus vulgaris (suprabasilar clefting), and erythema multiforme (keratinocyte apoptosis).

Pemphigoid, pemphigus vulgaris (suprabasilar clefting), and erythema multiforme (keratinocyte apoptosis).

The dog of the present report received prednisone (2 mg/kg [0.91 mg/lb], PO, twice daily, tapered to 2 mg/kg, PO, once daily), gastroprotectors (famotidine, omeprazole, and sucralfate administered PO), and pain medication (tramadol hydrochloride [4.88 mg/kg (2.22 mg/lb), PO]) with daily chlorhexidine footbaths and paw bandaging to prevent contamination with debris and facilitate healing of the paw pad ulcers. The dog was managed in hospital for 2 weeks, during which time its condition improved; the dog was discharged from the hospital for continued treatment at home. One week later, at a follow-up visit with the primary veterinarian, the dog was severely anemic, presumably secondary to gastrointestinal bleeding despite the use of gastric protectants. The owners elected euthanasia because of the dog’s poor prognosis. A necropsy was offered, but not permitted by the owners.

References