History

An 8.5-year-old neutered male Norwegian Elkhound was referred for evaluation because of sudden onset of pododermatitis and lameness 6 weeks earlier. The dog had a 6-year history of epilepsy that was controlled with phenobarbital treatment. Staphylococcus organisms had been cultured from swabs of the cutaneous lesions, but response to antimicrobial treatment was minimal. Some response to glucocorticoid administration was reported, but signs of pain and lameness recurred when that treatment was discontinued.

Clinical and Gross Findings

The skin lesions were most severe on the paw pads and adjacent skin (Figure 1) with less involvement of truncal skin and general sparing of the face. Paw pads were generally thickened with fissures and crusts, and the adjacent haired skin was reddened. Lameness was attributed to the painful cutaneous lesions on the paws. Histologic examination of multiple 6-mm-diameter punch biopsy specimens of affected haired skin adjacent to the paw pads was recommended.

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

Figure 1—Photograph of the paw and distal portion of the left forelimb of a dog that was evaluated because of sudden onset of pododermatitis and lameness 6 weeks earlier. All 4 limbs were affected. Cutaneous lesions are most severe on the pads (digital, metacarpal, and carpal) and adjacent haired skin. The pads are thickened with fissures and crusts, and the adjacent haired skin is reddened.
**Histopathologic Findings**

In all H&E-stained sections of biopsy specimens of haired skin of the paws, a distinctive epidermal stratification (red, white, and blue coloration) was observed microscopically with formation of clefts and bullae in the laminar lytic zone of the stratum spinosum (Figure 2). Hyperkeratotic, parakeratotic stratum corneum formed the most superficial eosinophilic layer. Hydropic swelling and lysis of keratinocytes in the superficial stratum spinosum comprised the white laminar pallor between the eosinophilic stratum corneum and basophilic hyperplastic basilar keratinocytes (Figure 3). Inflammation was concentrated around superficial dermal venules and composed of neutrophils and lymphoid cells.

**Morphologic Diagnosis**

Superficial necrolytic dermatitis (SND [hepato-cutaneous syndrome secondary to phenobarbital toxicosis]).

**Comments**

In the dog of this report, the thickened paw pads with crusts, fissures, erythema, and ulcers were consistent with findings in dogs with SND and prompted the clinical diagnosis of hepato-cutaneous syndrome secondary to phenobarbital toxicosis. Histologic changes in the epidermis (parakeratotic hyperkeratosis, hydropic swelling and lysis of superficial keratinocytes, and hyperplasia of basilar keratinocytes) were the basis for the diagnosis of SND. The signalment, history, distinctive histologic changes in the paw pad epidermis, and sparing of facial skin provided supportive evidence to rule out other potential causes of paw pad hyperkeratosis, such as generic dog food dermatosis, zinc-responsive dermatosis, or pemphigus foliaceus.

The histologic lesions of SND are almost identical to those associated with necrolytic migratory erythema in humans. The human syndrome is most often associated with glucagonoma, whereas in dogs, SND is more commonly associated with hepatic disease with or without diabetes mellitus than with glucagonoma or other pancreatic neoplasia. The hepatic disease is usually idiopathic but has been associated with phenobarbital administration in several dogs. On the other hand, hepatic disease secondary to phenobarbital treatment is not inevitably associated with SND.

Further diagnostic testing in the dog of this report included abdominal ultrasonography and biopsies of the liver, gallbladder, and pancreas. Ultrasonographic examination revealed variably sized, multifocal hypoechoic hepatic nodules surrounded by an echogenic border (typical of the ultrasonographic findings in dogs with SND) and gallbladder mucocele. The only histologic change identified in a 1-mm-diameter core biopsy specimen of liver tissue was diffuse hepatocellular swelling with a pale ground-glass appearance to the cytoplasm. This was attributed to phenobarbital treatment. Histologic examination of a wedge-biopsy specimen of liver that was obtained subsequently revealed lesions similar to those detected in phenobarbital-treated dogs that developed SND. In those tissue sections, nodules of hepatocytes were surrounded by collapsed parenchyma in which hepatocytes...
were either vacuolated or lost (Figure 4). Cystic mucinous hyperplasia was evident in the gallbladder, but lesions were not detected in a biopsy specimen of the pancreas.

The prognosis for dogs with SND is poor; in 1 study, most affected dogs survived < 6 months from the time of diagnosis (based on histologic examination of a skin biopsy specimen). Hypoaminoacidemia is a consistent abnormality in dogs with SND and is the basis for IV treatment with amino acid infusions. The dog of this report responded partially to amino acid infusions but recovered poorly after cholecystectomy (performed as treatment for the mucocele) and was euthanatized 2 months after the diagnosis of SND.

Figure 4—Photomicrograph of a section of a wedge biopsy specimen of liver obtained from the dog in Figure 1. Nodules of relatively normal hepatic parenchyma are separated by collapsed stroma with vacuolated or absent hepatocytes. H&E stain; bar = 50 μm.

References