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Pathology in Practice

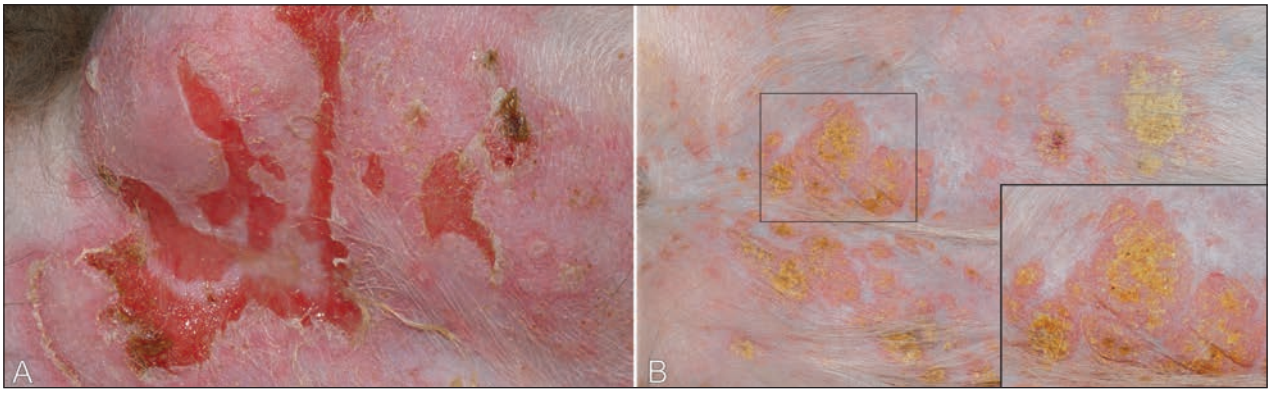

Figure 1—Photographs of the left inguinal region (A) and ventral aspect of the abdomen (B) of a 7.5-year-old spayed female Shetland Sheepdog. The dog had a several-year history of diffuse erythema with multifocal polycyclic to serpiginous oozing ulcerations (A), characteristic of vesicular cutaneous lupus erythematosus (VCLE). After receiving oral treatment with prednisolone and cyclosporine for 4 weeks, the VCLE was markedly improved but erythematous and scaly papules and plaques (atypical of VCLE) developed on the ventral aspect of the dog's abdomen (B). Inset—Higher-magnification view of the erythematous plaques with adherent yellow crusts in the rectangular outlined area.

History

A 7.5-year-old 20-kg (44-lb) spayed female Shetland Sheepdog with a several-year history of polycyclic to serpiginous ulcerations on the sparsely haired ventral aspect of the abdomen and inguinal region (**Figure 1**) was evaluated. Microscopic examination of routine biopsy specimens of the lesions revealed marked, lymphocytic interface dermatitis with focal dermal-epidermal separation. The signalment, history, and clinical and histopathologic findings led to a diagnosis of vesicular cutaneous lupus erythematosus (VCLE), and treatment with prednisolone[a] (1 mg/kg [0.45 mg/lb], PO, q 24 h) and cyclosporine[b] (10 mg/kg [4.5 mg/lb], PO, q 24 h) was initiated. Within 4 weeks, the lesions of VCLE markedly improved. However, the dog developed new lesions on the ventral aspect of the abdomen that were markedly different from the ulcerative lesions typical of VCLE.

This report was submitted by Frane Banovic, DVM; Thierry Olivry, DVM, PhD; Keith E. Linder, DVM, PhD; and Jeremy R. Tobias, DVM; from the Departments of Clinical Sciences (Banovic, Olivry) and Population Health and Pathobiology (Linder, Tobias), College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27607.

Address correspondence to Dr. Olivry (tolivry@ncsu.edu).

Clinical and Gross Findings

On physical examination, the dog was bright, alert, and in good body condition with abnormalities limited to the integument. The dog had numerous, multifocal to coalescing, 0.5- to 1.5-cm-wide, raised, erythematous, and scaly papules and plaques on the caudal ventral aspect of the abdomen (Figure 1) and bilaterally on the inner aspects of the pinnae. Superficially, adherent yellow crusts were present with underlying moist, erythematous erosions. Cytologic examination of the erosions revealed degenerative neutrophils and low to moderate numbers of cocci. The lesions were neither pruritic nor apparently causing pain. Three 8-mm-wide punch biopsy specimens were submitted for histologic examination. Two specimens were obtained from the center and 1 sample was obtained from the margin of erythematous plaques.

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

Histopathologic Findings

The epidermis and follicular infundibula were diffusely and irregularly hyperplastic and moderately hyperkeratotic and contained multifocal, small, discrete pustules of degenerate neutrophils, scant necrotic cellular debris, and cocci that were gram positive with special staining (**Figure 2**). Some pustules had progressed to thick neutrophilic crusts within foci of parakeratosis. A moderate, subepidermal band of inflammatory cells in the dermis was dominated by lymphocytes and plasma cells and contained fewer histiocytes, neutrophils, and eosinophils. Predominately lymphocytic exocytosis and mild basal vacuolation slightly blurred the dermal-epidermal junction; although apoptotic basal cells were rare, interface dermatitis was not substantially developed. Similar mixed inflammation and mild fibrosis were present around hair follicles.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: neutrophilic intraepidermal pustular dermatitis of the haired skin with intrapustular gram-positive cocci, moderate epidermal hyperplasia, and hyperkeratosis and lymphoplasmacytic lichenoid band infiltrate.

Case summary: psoriasiform lichenoid dermatitis (PLD) in a dog with VCLE.

Discussion

Taken together, the dog's treatment with cyclosporine at a high dosage, the clinically distinctive erythematous hyperkeratotic plaques with the presence of bacteria in the erosions, and the histopathologic findings led to the diagnosis of PLD, a rare adverse event associated with the administration of cyclosporine.

The term PLD is derived from the unusual histopathologic combination of some of the features of psoriasiform and lichenoid tissue reactions.[1] Unlike psoriasiform hyperplasia in humans, which is characterized by long and evenly developed rete ridges alternating with thin regions of suprapapillary epidermis, the condition in dogs frequently involves irregular epidermal hyperplasia.[1] A major histologic feature of the psoriasiform tissue reaction is the migration of neutrophils from dermal capillaries into the epidermis where they form microabscesses (known as Munro's microabscesses in human cases of psoriasis).[1] Neutrophils involved in the formation of microabscesses ultimately become associated with focal to locally extensive caps of parakeratotic hyperkeratosis.[1] Additionally, mild to moderate orthokeratotic hyperkeratosis can be present in dogs with PLD.[1]

A true lichenoid tissue reaction, also known as interface dermatitis in the veterinary medical literature, is characterized by a dense band of lymphocytes and plasma cells in the superficial dermis with epidermal basal

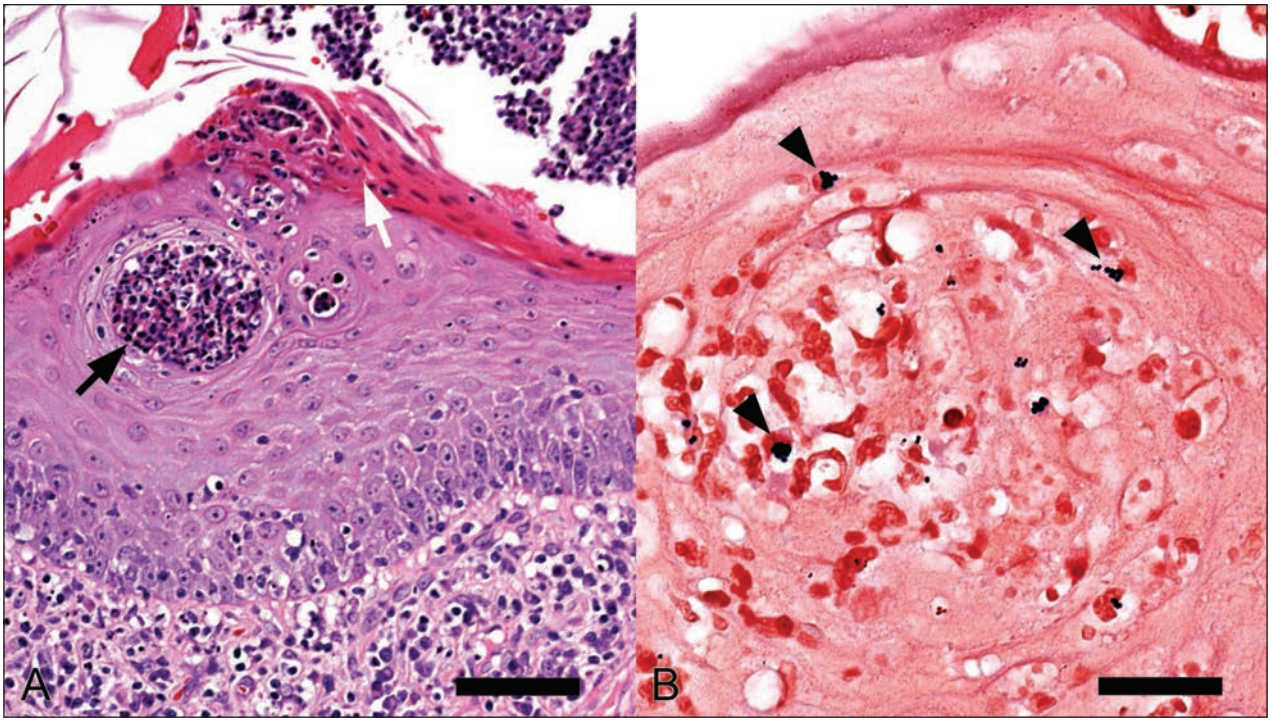

Figure 2—Photomicrographs of sections of skin biopsy specimens obtained from the dog in Figure 1 after treatment with prednisolone and cyclosporine for 4 weeks. The specimens were collected from areas on the ventral aspect of the abdomen affected with lesions that were markedly different from the ulcerative lesions typical of VCLE. A—In this section, the hyperplastic epidermis is bordered by a band of lymphocytes and plasma cells in the dermis and contains discrete neutrophilic pustules (black arrow), some of which have progressed to neutrophilic crusts and areas of parakeratosis (white arrow). The histopathologic findings are consistent with cyclosporine-induced psoriasiform lichenoid dermatitis. H&E stain; bar = 60 μm. B—In this section, several cocci (arrowheads) are visible within an epidermal pustule. Similar organisms were present within surface crusts (not shown). Tissue Gram stain; bar = 20 μm.

cell damage in the form of vacuolar change or apoptotic basal keratinocytes.[1] Psoriasiform lichenoid dermatosis also involves a moderate to severe band of lymphocytes and plasma cells within the superficial dermis (lichenoid band), but it lacks the consistent basal cell injury of interface dermatitis and the full lichenoid tissue reaction. Although the occasional presence of lymphocytic satellitosis with individual necrotic keratinocytes in the basal and spinous cell layers of affected dogs has been reported,[2] epidermal basal cell injury or degeneration is not a typical feature of this condition.[3] Rare individual apoptotic keratinocytes were detected in biopsy specimens obtained from the dog of the present report, but consistent basal cell injury was not evident.

Similar to the histopathologic findings in the case described in this report, hair follicle involvement is sometimes evident in dogs with this condition.[3,4] Lesions may resemble those associated with lichenoid keratosis in dogs, although lichenoid keratosis is not characterized by the presence of intraepidermal pustules.[5]

Psoriasiform lichenoid dermatosis develops spontaneously in several breeds, predominantly in young Springer Spaniels for which a genetic predisposition is suspected.[1,6,c] In addition, PLD has been reported to develop in various dog breeds following cyclosporine administration.[2–4] Initial cutaneous lesions are usually observed between 3 and 6 weeks after the start of cyclosporine administration but can develop even after years of treatment.[3,4] Cyclosporine-associated PLD is thought to develop most frequently in dogs treated with the drug at high dosages[4] or for an extended period of time.[2] In the case described in the present report, lesions developed 4 weeks after a high dosage of cyclosporine was started (10 mg/kg, PO, q 24 h) to treat skin lesions of VCLE.

The etiopathogenesis of PLD in dogs is not known, but an immunologic mechanism is suspected. A few authors attribute this reaction to an aberrant immunologic response to staphylococcal infection, given that cocci are frequently present in lesions and affected dogs sometimes respond rapidly to antimicrobial agents.[2,3] Research in humans with psoriasis has revealed the potential of bacterial superantigens to trigger the psoriasiform tissue reaction.[7] Psoriasiform lichenoid dermatosis is clinically characterized by erythematous waxy, crusted papules that, with time, coalesce to form multiple well-demarcated plaques. In chronic cases, adherent yellow keratinous debris covers the plaques. Lesions are usually limited to the concave portion of the pinnae, periocular skin, ventral aspect of the abdomen, and limbs.[5]

The prognosis for affected dogs depends on the type of PLD: spontaneous or cyclosporine-induced. The main emphasis of treatment for the spontaneous form, depending on the severity and distribution of lesions, is to resolve the bacterial infection with oral or topical administration of antimicrobial agents. Four Springer Spaniels with spontaneous PLD that were treated with cephalexin had an excellent response with complete resolution of lesions and no recurrence.[c] Notably, oral administration of glucocorticoids as monotherapy failed to control the condition in some English Springer Spaniels.[1] The treatment of cyclosporine-associated PLD consists of discontinuing or decreasing the administration of cyclosporine and, in some cases, providing additional oral or topical treatment with antimicrobial agents. The regression of skin lesions following the discontinuation of cyclosporine treatment without concurrent antimicrobial use in dogs has been reported.[3] On the other hand, institution of antimicrobial treatment without altering the cyclosporine dosage would be expected to fail to induce complete lesion resolution.

For the dog of the present report, the cyclosporine dosage was reduced to 5 mg/kg (2.2 mg/lb) orally once daily, and cephalexin[d] (25 mg/kg [11.4 mg/lb], PO, q 12 h) was administered for 14 days. During a follow-up examination 3 weeks later, the lesions of PLD had resolved completely. At the last follow-up examination 24 months after the diagnosis of PLD, these lesions had not recurred, and the VCLE was controlled with cyclosporine administration at a dosage of 5 mg/kg, orally, every other day.

a. Prednisolone, Butler Schein Animal Health, Dublin, Ohio.
b. Atopica, Novartis Animal Health, Greensboro, NC.
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d. Cephalexin, Lupin Pharmaceuticals, Baltimore, Md.

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6. Gross TL, Halliwell RE, McDougal BJ, et al. Psoriasiform lichenoid dermatitis in the Springer Spaniel. *Vet Pathol* 1986;23:76–78.
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