Pathology in Practice

History

A 3-year-old 17.2-kg (37.8-lb) neutered male Border Collie mix was evaluated because of sudden onset of glaucoma bilaterally, for which there was limited response to aggressive medical treatment. Blepharospasm and third eyelid protrusion in both eyes were first noticed 1 month earlier. Visual impairment was detected 7 days later, at which point a diagnosis of glaucoma was made and administration of medications (topical ophthalmic treatment with timolol, dorzolamide, latanaprost, and prednisolone acetate and oral treatment with methazolamide, carprofen, and amlodipine) was initiated by a local veterinarian. These treatments were ongoing at the time of this evaluation. Erythema and crusting of the skin caudal to the nasal planum developed a few days after treatments commenced. Results of a CBC and serum biochemical analysis were unremarkable, and results of an ELISA for heartworm antigen and antibodies against *Borrelia burgdorferi*, *Anaplasma phagocytophilum*, and *Ehrlichia canis* were negative.

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Clinical Findings

On physical examination, alopecia, depigmentation, and ulcerative lesions of the nasal planum, muzzle, periocular skin, and mucocutaneous lip junction were evident (Figure 1). There were also adherent crusts on the bridge of the nose and multifocal thick crusts on the lateral aspects of the thorax and cranial aspects of the stifle joints. Oral examination revealed erosions on the hard palate. Ophthalmic examination revealed bilateral panuveitis, glaucoma (intraocular pressure in each eye, 35 mm Hg; reference range, 10 to 20 mm Hg), complete serous retinal detachments, and blindness.

Prior to performing skin biopsies, affected regions of the thorax were shaved, which revealed that the thoracic lesions had an erythematous rim around the pigmented areas of the skin with multifocal, partial to complete erosions affecting only the pigmented areas (Figure 1). Eleven 8-mm-diameter punch biopsy specimens of skin from the muzzle, lip margins, and lateral aspects of the thorax were obtained, fixed in neutral-buffered 10% formalin, and submitted for histologic examination. Lesions on the hard palate were not biopsied.

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

Figure 1—Photographs of the face (A) and the partially shaved left lateral aspect of the thorax (B) of a Border Collie mix that was evaluated because of sudden-onset glaucoma and skin lesions that developed 1 to 2 weeks later. At the time these photographs were taken (approx 35 days after the onset of ocular signs), skin biopsy specimens were collected from affected sites. A—Notice the ulceration and depigmentation of the nasal planum and periocular skin and thick adherent crusts along the dorsal aspect of the muzzle. B—Partial shaving of hair on left side of the thorax revealed multifocal partial to complete erosions affecting only the pigmented areas with erythema visible at the junction of pigmented and nonpigmented skin.
Histopathologic Findings

Histologic examination of the biopsy specimens revealed granulomatous lichenoid dermatitis, with sheets of large macrophages intermingled with lower numbers of lymphocytes, neutrophils, and plasma cells forming a thick band just beneath the epidermis, occasionally blurring the dermoeipidermal junction (Figure 2). In the biopsy specimens of haired skin, these infiltrates often surrounded hair follicles and adnexal glands as well. The macrophages contained very fine, granular melanin pigment (Figure 3). The epidermis was mildly acanthotic and contained scattered necrotic cells, and there were areas of erosion with spongiosis and surface crusting.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: granulomatous lichenoid dermatitis and perifolliculitis with intrahistiocytic fine melanin granules.

Case summary: uveodermatologic syndrome in a dog.

Comments

Differential diagnoses for the depigmented and ulcerative skin lesions on the face of the dog of this report included uveodermatologic syndrome, discoid lupus erythematosus, systemic lupus erythematosus, pemphigus foliaceus, pemphigus erythematosus, and epitheliotropic lymphoma. For the lesions on the muzzle, thorax, and stifle joints, dermatophytosis and pyoderma were also considerations. On the basis of the uveitis and depigmented, ulcerative facial and mucocutaneous lesions, uveodermatologic syndrome was highly suspected. Results of histologic examination of skin biopsy specimens revealed granulomatous lichenoid dermatitis and intrahistiocytic melanin granules, which are characteristic features of uveodermatologic syndrome.1,4 In the case described in the present report, the skin lesions were unusually severe, with marked follicular involvement and involvement of the truncal skin. The lesions on the hard palate were presumed to be a part of the same disease process because similar oral lesions have been detected in other dogs with uveodermatologic syndrome.3,5,6 However, for the dog of this report, biopsy specimens of the hard palate lesions were not obtained for histologic confirmation.

In dogs, uveodermatologic syndrome is characterized by bilateral granulomatous panuveitis associated with poliosis and vitiligo.1,3,7-9 It is also referred to as Vogt-Koyanagi-Harada-like syndrome because of similarities to Vogt-Koyanagi-Harada syndrome of humans.2,10,11 Evidence indicates that the human and canine diseases both result from an autoimmune process directed against antigenic components of melanocytes, specifically tyrosinase and related proteins.12-15 In the case described in the present report, the melanocyte-specific targeting of this disease was highlighted in the affected areas of skin on the thorax, where lesions were restricted to the pigmented areas and each was clearly delineated by an erythematous rim.

Results of a recent study14 have suggested that, in dogs with uveodermatologic syndrome, skin lesions are mediated by T cells and macrophages (T-helper cell 1–related immunity), whereas B cells and macrophages (T-helper cell 2–related immunity) are responsible for ocular le-
sions. The disease is thought to be hereditary and most commonly affects the Akita, Samoyed, Siberian Husky, and Alaskan Malamute breeds, although affected dogs of many other breeds have been described.\(^{1,3,7,8,14,16,17}\) No sex predilection has been reported.

Ophthalmic signs usually precede dermatologic signs and include uveitis (anterior or panuveitis), with secondary changes such as glaucoma, cataracts, bullous retinal detachment, and blindness.\(^{5,8,14-17}\) Skin lesions predominantly affect the face (dorsal aspect of the muzzle, periorbital regions, nasal planum, and lips) and may include poliosis and vitiligo with erythema, ulceration, and crusting of variable severity.\(^{1,3,8}\) Lesions can also develop on the scrotum or vulva, footpads, or pinnae and within the oral cavity but rarely become generalized.\(^{3,5,6}\) Unlike Vogt-Koyanagi-Harada syndrome in humans,\(^{2,10,11}\) CNS signs are extremely rare in dogs,\(^{16}\) and there have been no reports of dogs with uveodermatologic syndrome—associated auditory signs, to our knowledge.

Diagnosis of uveodermatologic syndrome is mainly based on signalment and characteristic clinical signs. Histologic examination of skin lesion samples can aid in diagnosis. Histopathologic features of uveodermatologic syndrome include lichenoid dermatosis of predominantly histiocytic macrophages containing finely granular melanin pigment.\(^{3,5,8,14}\) Occasionally, similar inflammation can involve the adnexa,\(^{14}\) as in the dog of the present report. In dogs with chronic inflammation, dermal inflammation may be minimal, with epidermal melanin present in low amounts or absent.\(^{1}\) The mainstay of treatment is oral administration of immunosuppressive doses of corticosteroids, which is often combined with azathioprine.\(^{1-3,5,7,8}\) In 1 report, a dog with uveodermatologic syndrome that did not tolerate azathioprine was administered cyclosporine, with successful treatment of the skin disease. In addition, topical ophthalmic application of corticosteroids, NSAIDs, and atropine are used to control the uveitis; if secondary glaucoma is present, ocular hypotensive treatments (eg, topically and orally administered carbonic anhydrase inhibitors and topically administered \(\beta\)-adrenergic receptor antagonists) are essential.\(^{1,2,5}\) In general, the prognosis for dogs with uveodermatologic syndrome is good with regard to the skin disease but the long-term prognosis is poor with regard to vision.\(^{1,3,5,8}\)

After the skin biopsy specimens were obtained, the dog of this report was administered prednisone (1.7 mg/kg [0.77 mg/lb], PO, q 24 h for 2 weeks). The dosage of prednisone was subsequently decreased (1.2 mg/kg [0.55 mg/lb], PO, q 24 h) to minimize adverse effects, and azathioprine (2.2 mg/kg [1 mg/lb], PO, q 24 h for 2 weeks, then 2.2 mg/kg, PO, q 48 h) was initiated. Other medications prescribed for the ocular disease were methazolamide (+.3 mg/kg [1.95 mg/lb], PO, q 8 h), timolol (0.5%) solution (in both eyes, q 8 h), dorzolamide (2%) solution (in both eyes, q 6 h), flurbiprofen (0.03%) solution (in both eyes, q 6 h), and prednisolone acetate (1%) suspension (in both eyes, q 6 h). Administration of amlodipine (0.14 mg/kg [0.064 mg/lb], PO, q 24 h) was continued because of its protective effects on the optic nerve head through improvement in blood flow and reduction in vascular resistance in the ophthalmic artery.\(^{18}\) At a 2-week recheck examination after initiation of oral administration of prednisone, anterior uveitis was in remission, secondary glaucoma was well controlled (right eye, 10 mm Hg; left eye, 13 mm Hg), retinas had completely reattached, vision had returned, and the skin lesions were markedly improved with partial hair regrowth and repigmentation. By the time of the 5-week recheck examination, skin lesions had completely resolved. Despite the initial positive response, however, ocular disease continued to progress. At the 10-week recheck examination, bilateral optic nerve atrophy was noted and it was apparent that secondary glaucoma had become refractory to the aggressive medical treatment. Skin disease remained in remission at that time.

a. SNAP 4DX Test, IDEXX Laboratories Inc, Wesbrook, Me.

References