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Case report

TRAUMATIC BLEPHARITIS INCLUDING CUTANOUS CHANGES WITH A CLINICAL APPEARANCE OF IMMUNE-MEDIATED DISEASE

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A four-year-old intact male Labrador retriever was presented with acute onset of ulcerative lesions around both eyes, on the mucocutaneous junctions around the muzzle and nares, and on the lateral aspects of paw pads. All lesions were symmetrical and well demarcated. The rest of ocular and systemic examination was unremarkable. The onset of lesions was acute and coincided with an episode of intense hunting in switchgrass. Similar lesions were present in another dog used in the same hunting trip. The clinical presentation was suggestive of a possible immune-mediated skin disease. However, the patient responded to systemic antibiotic treatment with full recovery without recurrence upon cessation of therapy. Traumatic origin should be included into differential diagnosis of mucocutaneous ulcerative lesions presenting as a possible immune-mediated skin disease.

Key words: blepharitis, canine, mucocutaneous ulcerative lesion.

INTRODUCTION

There are many potential causes of skin erosions and ulcerations in dogs, including bacterial, yeast and parasitic infections, metabolic and neoplastic diseases, chemical sources, and immune-mediated/autoimmune diseases. Erosive lesions affecting mucocutaneous junctions, especially those involving multiple areas, are most commonly associated with immune mediated/autoimmune skin diseases, and to a lesser extent with neoplastic diseases (epitheliotropic lymphoma) or chemical causes (cutaneous adverse drug reactions). Detailed history, clinical examination, and histopathological examination of biopsy samples play a significant role in establishing the definitive diagnosis of such lesions. Treatment of immune-mediated/autoimmune skin diseases involves systemic immunosuppressive medications, which can have significant side effects [1].

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Switchgrass (*Panicum virgatum*) is a prairie perennial grass native to North America that typically grows 3–5 feet tall. It is resistant to extreme weather conditions (heat, drought, cold), and is common in the Midwestern prairie, used for pasture and hay production (when harvested before reaching maturity), as well as an ornamental grass. Other uses include erosion control and biofuel production. Switchgrass is an important source of nesting grounds and cover for birds and rabbits [2], and its seeds are a food source for many bird species (including songbirds, pheasants, quails and turkeys). Switchgrass can be toxic to horses, sheep and goats. It is palatable to cattle when young, but as it matures, switchgrass becomes hard and its nutrient content declines [3].

This article describes a case of sudden onset of multifocal mucocutaneous erosive lesions in a dog caused by exposure to switchgrass during intense hunting. Switchgrass has been implicated in gastrointestinal toxicity and liver damage with photosensitivity in horses, goats and sheep, but to the best of our knowledge, this is the first description of a case with traumatic erosive lesions on mucocutaneous junctions in a dog.

CASE REPORT

A four-year-old intact male Labrador retriever was presented for examination with a history of sudden-onset hemorrhagic and ulcerative lesions development around both eyes, immediately after an intense hunting trip in switchgrass three days earlier. According to the owner, the lesions were purely hemorrhagic at the completion of the hunting trip, and started to form crusts in the following days. The patient was otherwise systemically healthy, current on vaccinations, deworming, and heartworm prevention. Similar lesions (less extensive) were also present in another dog belonging to the same owner, and used in the same hunting episode. The second dog was not presented for the ophthalmological evaluation.

Standard hospital informed consent form was obtained for all procedures prior to initiating the clinical examination of the patient. Complete ophthalmic examination was performed with a Finoff transilluminator (Welch Allyn), slit lamp biomicroscope (Keeler PSL Classic), and indirect ophthalmoscope (Heine Omega 200). The patient had normal vision in bright and dim light conditions (positive menace response, following objects, and good visual navigational skills). Both eyes were kept comfortably open; tear production was within normal limits in both eyes (20/20 mm/min; OD/OS); and intraocular pressure was normal bilaterally (12/13mmHg; OD/OS). Erosive lesions were present on the mucocutaneous junctions of the eyelids in both eyes, and both conjunctivas were mildly hyperemic (Figure 1). Lesions were moist and non-pruritic, without easy plucking of hair in the perilesional fields.

Fundus examination of the right eye revealed two small focal perivascular scar lesions in the superior retina, which were presumed to be an incidental finding (likely healed inflammatory lesions). Fundus examination of the left eye was normal. The rest of the ophthalmic examination was unremarkable.

Physical examination revealed similar lesions (crusty erosions) on mucocutaneous junctions around the muzzle and nares, and on lateral aspects of the paw pads.

All observed lesions were symmetrical and well demarcated, without perilesional hyperpigmentation typical of chronic inflammation (Fig.1). The rest of the systemic examination was normal. No peripheral lymphadenopathy was noted. No lesions were noted in the oral cavity or in the anal or genital area. The owner had noted no problems/pain with defecation or urination.

Possible differential diagnoses of lesions affecting individual locations as observed in this clinical case are listed in Table 1. Due to the multifocal, symmetrical erosive lesions in mucocutaneous areas, the main differential diagnoses included the following disease groups: infectious (fungal/algae: candidiasis, protothecosis, dermatophytosis; parasitic: demodicosis; protozoal: leishmaniosis), immune-mediated (hypersensitivity: atopy/allergies, food hypersensitivity, contact hypersensitivity; auto-immune: pemphigus complex – pemphigus erythematosus, foliaceus, and vulgaris, bullous pemphigoid, lupus - discoid, and systemic, cutaneous drug reaction, uveodermatological syndrome, erythema multiforme/toxic epidermal necrolysis), metabolic/nutritional (zinc-responsive dermatosis), congenital/hereditary (canine familial dermatomyositis, juvenile cellulitis) and other (hepatocutaneous syndrome). Because of the very specific history in this particular case, traumatic origin of the lesions was also included in differential diagnoses.

Further diagnostic options were discussed with the owner and included complete cell blood count, serum chemistry panel, microbiology testing, cytology examination of impression smears and histopathology of biopsy samples from affected areas, which would provide further diagnostic differentiation and a more narrowed diagnosis (Table 2, Figure 3).

Figure 1. Patient presented with symmetrical erosive lesions around the eyes, muzzle, nares and paw pads. These lesions were first noticed by the owner 3 days prior initial examination.

Table 1. Possible differential diagnoses of lesions according to location. Bold and italic font marks lesions in all observed locations as in this patient. Numbers indicate references for specific conditions.

Etiology		Diagnosis	Periocular	Perinasal	Perioral	Feet
Infectious	Bacterial	M-C pyoderma [4, 5]	+	+	+	-
	Fungal Algae	***Candidiasis [6, 7]***	+	+	+	+
		Malassezia [6-8]	+	-	+	+
		Protothecosis [6, 7]	+	+	+	+
		Dermatophytosis [6, 7]	+	+	+	+
		Blastomycosis [6, 7]	+	+	-	+
		Cryptococcosis [6, 7]	-	+	+	+
	Parasitic	***Demodicosis [9, 10]***	+	+	+	+
	Viral	Canine Herpes Virus [11]	+	-	-	-
		Distemper [12]	+	+	-	-
	Protozoal	***Leishmaniasis [12-15]***	+	+	+	+
	Rickettsial	RMSF [12]	-	-	+	-
Immune-mediated	Hyper-sensitivity	***Allergies/Atopy [16-20]***	+	+	+	+
		Food hypersensitivity [16, 17, 20]	+	+	+	+
		Contact Hypersensitivity [16, 17, 19-21]	+	+	+	+
		Eosinophillic Granuloma [16]	-	-	+	-
		Medial Canthal Blepharitis [17, 19, 20]	+	-	-	-
	Auto-immune	***Pemphigus complex [17, 22, 23]***	+	+	+	+
		Lupus (DLE,SLE) [14, 17, 22-24]	+	+	+	+
		Cutaneous Drug Reaction [19, 22, 23, 25, 26]	+	+	+	+
		VKH [17, 18, 22, 23, 27, 28]	+	+	+	+
		Erythema Multiforme/ TEN [22, 23]	+	+	+	+
		Vasculitis [22, 23]	-	+	+	+
Metabolic/Nutritional		***Zinc-responsive dermatosis [29, 30]***	+	+	+	+
Congenital/Hereditary		***Canine Familial Dermatomyositis [31, 32]***	+	+	+	+
		Juvenile cellulitis [17, 32-36]	+	+	+	+
Other		***Hepatocutaneous sy [29, 37]***	+	+	+	+
Neoplasia		SCC [38, 39]	+	+	+	-
		Epitheliotropic lymphoma [38-41]	+	+	+	-

Table 2. List of the most frequently observed clinical symptoms and diagnostic features for diagnoses identified in Table 1 based on the anatomical localization. Numbers indicate references for specific conditions.

Etiology		Diagnosis	Typical clinical symptoms	Clinical symptoms in the patient
Infectious	Bacterial	M-C pyoderma [4, 5]	Bacteria present on cytology	Cytology not performed
	Fungal Algae	Candidiasis [6, 7]	Candida present on cytology	Cytology not performed
		Malassezia dermatitis	Malasezia present on cytology	Cytology not performed
		Protothecosis [6, 7]	Prototheca spp. present on cytology	Cytology not performed
		Dermatophytosis[6, 7]	chronic onset	Trichogram not performed
	Parasitic	Demodicosis [9, 10]	Chronic onset	Skin scraping not performed
	Protozoal	Leishmaniasis [12-15]	Macrophages with Leishmania present on cytology, Chronic onset	No history of travel
Immune-mediated	Hyper-sensitivity	Allergies/Atopy [16-20]	Pruritus	Not present
		Food hypersensitivity [16, 17, 20]	Pruritus	Not present
		Contact Hypersensitivity [16, 17, 19-21]	Pruritus	Not present
		Pemphigus complex [17, 22, 23]	Chronic onset	Acute onset
		Lupus (DLE,SLE) [14, 17, 22-24]	Chronic onset, depigmentation of the nose, loss of the normal cobblestone architecture	Acute onset, not present
		Cutaneous Drug Reaction [19, 22, 23, 25, 26]	History of drug intake	Not present
		Uveodermatological syndrome/VKH [17, 18, 22, 23, 27, 28]	depigmentation of the hair	Not present
		Erythema Multiforme/ TEN/SJS [22, 23]	Multiple clinical symptoms	Moist erosive non-pruritic lesions could be a result of the TEN
Metabolic/Nutritional		Zinc-responsive dermatosis [29, 30]	Dry lesions	Moist lesions
Congenital/Hereditary		Canine Familial Dermatomyositis [31, 32]	Dry lesions	Moist lesions
		Juvenile cellulitis [17, 32-36]	Usually affects dogs between the ages of 3 weeks and 4 months	Middle age dog (4 year)
Other		Hepatocutaneous sy [29, 37]	Usual in older dogs, Systemic signs	Middle age dog (4 year), Systemic signs not present

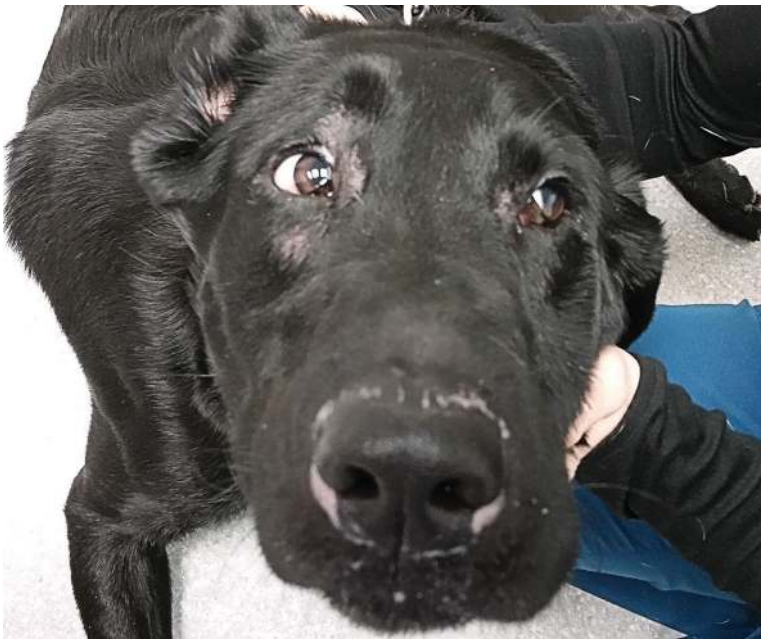

Figure 2. Same patient 2 weeks after initial presentation. All lesions are completely healed and no recurrences were noted since.

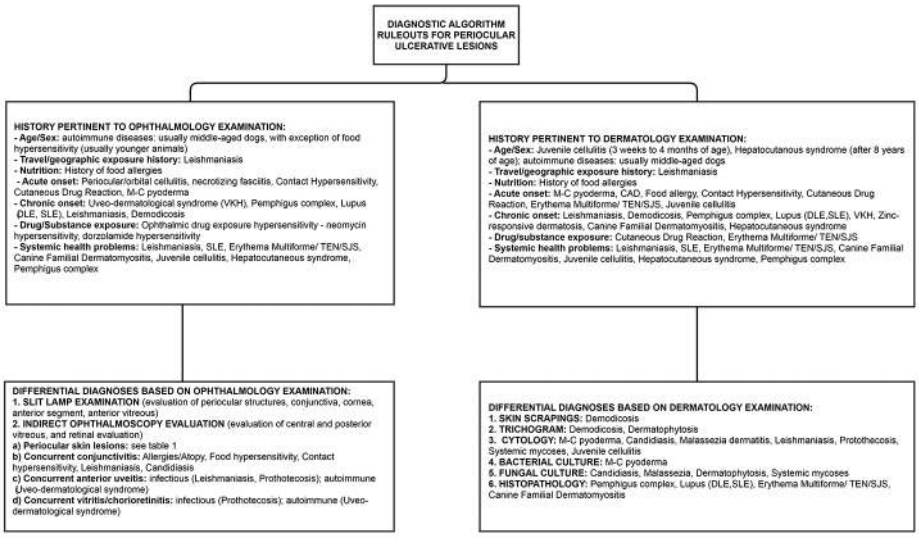

Figure 3. Diagnostic flow chart for the common ophthalmology and dermatology process in the clinical case with erosive periocular lesions.

Due to the extremely precise history of lesion onset immediately after hunting in switchgrass, as well as the occurrence of similar lesions in another dog on the same trip

(a non-related older Labrador Retriever), the decision was made to pursue preventative treatment with systemic antibiotics to avoid secondary infections of traumatic lesions initially. The owner agreed to pursue further diagnostic steps should the observed lesions persist or fail to improve with systemic antibiotics. The patient was treated with Amoxicillin/Clavulonic Acid (20mg/kg BID PO) for 14 days. Due to the rapid improvement in the clinical condition of the patient, and spontaneous resolution of lesions in the other dog without any medical therapy, the owner elected not to pursue any additional diagnostics (laboratory evaluation, biopsy, cytology evaluation, microbiology). At the 2-week recheck, all ulcerative lesions were completely healed with no new flare-ups (Fig. 2). The patient was discharged without further treatment, and has experienced no recurrence since then.

DISCUSSION

Eyelid inflammation can be a result from either unilateral or bilateral local disease, or may be associated with generalized skin condition or systemic disease as summarized in Table 1, frequently dictating a close collaboration of an ophthalmologist and dermatologist. The primary cause of blepharitis is not always immediately apparent, as it is often masked by secondary infections resulting from opportunistic pathogens. However, the primary cause can be often suspected based on the distribution of the lesions (one or multiple eyelids, other areas of the skin), appearance of the lesions, presence of pruritus, or other systemic symptoms. Pruritus can be primary (caused by the disease process itself), or secondary (the result of secondary skin infection, most commonly due to automutilation). Other factors, such as age or breed of the animal, can help in differential diagnosis [4,5]. Possible causes of blepharitis include bacterial, protozoal (leishmaniosis), mycotic and parasitic infections, immune-mediated or autoimmune diseases, and allergic reactions or adverse drug reactions. Parasitic infections (such as demodicosis) and certain bacterial infections (such as juvenile cellulitis) are typically present in very young dogs, immune-mediated diseases in middle-age dogs (3-8 years), and neoplastic diseases in older dogs (over 8 years; [6,7]), with one case described in an 8-month-old dog [8].

Certain inflammatory diseases in older dogs can mimic juvenile cellulitis, such as in the case described by Neuber et al. of dermatitis and lymphadenitis in a four-year-old dog [9]. Some breeds (including Labrador retriever) can have a predisposition to certain diseases (including immune-mediated diseases [6]). Clinical symptoms of leishmaniosis usually include systemic signs (malaise, weight loss, diarrhea, renal and/or liver failure, anemia, lameness, dermatitis or epistaxis), but occasionally, ocular disease may be a presenting complaint. In this case the patient was born and raised in Iowa and did not leave Iowa for any Leishmania endemic areas (southern part of the USA). The most common ocular signs of leishmaniosis include blepharitis, keratoconjunctivitis and uveitis. Less commonly, chorioretinitis, retinal detachment, glaucoma, orbital cellulitis or cataracts can be seen [10].

In general, multifocal mucocutaneous erosions [5] are a typical presentation of immune-mediated or autoimmune diseases, such as mucocutaneous lupus erythematosus [11], mucocutaneous pyoderma[12], mucous membrane pemphigoid, or erythema multiforme. Less common causes include adverse drug/chemical reactions (including photosensitivity), contact dermatitis [13], neoplastic diseases (epitheliotropic lymphoma [14,15]) or local bacterial, protozoal or parasitic infections [6]. Mucocutaneous lupus erythematosus (MCLE) is typically diagnosed in middle-aged dogs (4-8 years). Most patients develop lesions, which are typically multifocal and symmetrical, in the perianal and/or genital area. MCLE lesions can sometimes be clinically distinguished from other forms of autoimmune or infectious diseases by the presence of hyperpigmentation around mucocutaneous ulcers [11].

Mucocutaneous pyoderma (MCP) is clinically characterized by lesions around mucocutaneous junctions, which typically respond well to a combination of topical and systemic antibiotics. However, prolonged treatment (4 weeks, followed by several months of pulsed antibiotic therapy) is often necessary and relapses are common [12,16]. MCP is typically less erosive than MCLE, and more commonly affects the perinasal and perioral areas [11], including lips, nose, nares, perioral skin, and less commonly, eyelids, vulva, prepuce and anus. Lesions include erythema, swelling, crusting, erosions, ulcerations, and focal depigmentation [12]. Patients with mucocutaneous pyoderma often suffer from allergies and repeated bacterial skin or ear infections [12,17]. In addition to mucocutaneous lesions, some patients will also develop cutaneous lesions in the inguinal area or axilla [12].

Mucous membrane pemphigoid (MMP) is autoimmune disease with circulating antibodies against skin collagen. Lesions typically cross onto mucosa and are generally present in the oral cavity. Predominant lesions include erosions and ulcerations, but vesicles, crusts and scars often occur [11, 18]. Erythema multiforme (EM) is a cutaneous pattern of variable etiology, which is thought to be caused by T-cell mediated hypersensitivity reaction associated with keratinocytes. Mucocutaneous erosions are typically accompanied by extensive macules, papules and plaques with central clearing [11,19]. Despite subtle distinctions in clinical appearance, the only definitive way to distinguish between MCLE, MMP, EM and MCP is histopathological evaluation of multiple biopsy samples [11].

Similar presentation of mucocutaneous erosions on eyelids, lips and nose (and sometimes paw pads) can be seen in dogs with uveodermatological syndrome (VKH-like syndrome). Uveodermatological syndrome is an autoimmune disease, involving T-cell (ocular lesions) and B-cell (skin lesions)-driven autoimmunity against melanocyte cells. Skin (vitiligo) and hair (poliosis) depigmentation around the eyes, lips and muzzle is a common presenting sign. Apart from mucocutaneous and skin changes, VKH also commonly affects the anterior and posterior uvea. Characteristic findings in VKH include anterior and posterior uveitis, which can progress to secondary glaucoma, retinal detachment and blindness. These lesions are typically bilateral and may or may not be

symmetrical [20-22]. As with other immune-mediated skin disease, final diagnosis of VKH is confirmed on histopathological examination of biopsy specimens.

Cutaneous drug adverse reactions have been described in association with the use of various drugs, including meloxicam [23], imepitoin [24] and phenobarbital. Similar changes to drug adverse reactions can be also seen in chemical (photosensitivity) or contact dermatitis.

In the present case, diagnosis was established on the basis of history (acute onset of lesions after exposure to switch grass, occurrence in two different dogs who were exposed to the same conditions), fast and complete recovery with supportive antibiotic treatment, and absence of recurrence after therapy was discontinued. To the best of our knowledge, similar clinical appearance of blepharitis mimicking immune-mediated disease has not been previously described, and potential traumatic etiology should be included in differential diagnosis in similar cases.

Authors' contributions

SG and HK performed clinical examination of the patient. HK, TL, and NM prepared manuscript and tables, including differential diagnoses for different dermatology and ophthalmology categories. SG prepared the final form of manuscript. All authors read and approved the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Statement of Informed Consent

Standard hospital informed consent form was obtained for all procedures prior to initiating the clinical examination of the patient.

REFERENCES

1. Lebwohl MG, Heyman WR, Berth-Jones J, Coulson I: *Treatment of skin disease. Comprehensive therapeutic strategies.* 4th ed. 2014: Sounders Elsevier.
2. USDA. *https://plants.usda.gov/factsheet/pdf/fs_pavi2.pdf.* 2001.
3. *Oklahoma State University; http://switchgrass.okstate.edu/*. 2008.
4. Stades FC, van der Woerdt A: *Diseases ans surgery of the canine eyelid.* , in *Veterinary Ophthalmology, 5th ed.*, K.N. Gelatt, Gilger, B.C., Kern, T.J., Editor. 2013, Wiley-Blackwell. p. 877-880.
5. Hnilica KA, Petterson AP: *Differential diagnoses*, in *Small Animal Dermatology: A Color Atlas and Therapeutic Guide, 4th ed.* 2017, Elsevier. p. 1-29.
6. Miller WHJ, Griffin CE, Campbell KL: *Diagnostic methods*, in *Muller&Kirk's Small animal Dermatology, 7th ed.* 2013, Elsevier Mosby. p. 57-108.

7. Whitley RD: Canine and feline primary ocular bacterial infections. Vet Clin North Am Small Anim Pract 2000, 30(5):1151-1167.
8. Basset RJ, Burton GG, Robson DC: Juvenile Cellulitis in an 8-month-old Dog. Austr Vet J 2005, 83:280-282.
9. Neuber AE, van den Broek AH, Brownstein D, Thoday KL, Hill PB: Dermatitis and lymphadenitis resembling juvenile cellulitis in a four-year-old dog. J Small Anim Pract 2004, 45(5):254-258.
10. Peña MT, Roura X, Davidson MG: Ocular and periocular manifestations of leishmaniasis in dogs: 105 cases (1993-1998). Vet Ophthalmol 2000, 3(1):35-41.
11. Olivry T, Rossi MA, Banovic F, Linder KE: Mucocutaneous Lupus Erythematosus in Dogs (21 cases). Vet Dermatol 2015, 26: 256–e55.
12. Basset R, Burton G, Robson D: Antibiotic responsive ulcerative dermatoses in German Shepherd dogs with mucocutaneous pyoderma. Austral Vet J 2004, 82:485-489.
13. Ho KK, Campbell KL, Lavergne SN: Contact dermatitis: a comparative and translational review of the literature. Vet Dermatol 2015, 26:314-e67.
14. Fontaine J, Bovens C, Bettenay S, Mueller RS: Canine cutaneous epitheliotropic T-cell lymphoma: a review. Vet Comp Oncol 2009, 7(1):1-14.
15. Donaldson D, Day MJ: Epitheliotropic lymphoma (mycosis fungoides) presenting as blepharoconjunctivitis in an Irish setter. J Small Anim Pract 2000, 41(7):317-320.
16. Gross TL, Ihrke PJ, Walder EJ, Affolter VK: *Lichenoid diseases of the dermis*, in *Skin diseases of the dog and cat, Clinical and histopathologic diagnosis, 2nd ed.* 2005, Blackwell. p. 261-263.
17. Wiemelt SP, Goldschmidt MH, Greek JS, Jeffers JG, Wiemelt AP, Mauldin EA: A retrospective study comparing the histopathological features and response to treatment in two canine nasal dermatoses, DLE and MCP. Vet Dermatol 2004, 15:341-348.
18. Gross TL, Ihrke PJ, Walder EJ, Affolter VK: *Bullous and acantholytic diseases of the epidermis and the dermal-epidermal junction*, in *Skin diseases of the dog and cat, Clinical and histopathologic diagnosis, 2nd ed.* 2005, Blackwell. p. 30-32.
19. Gross TL, Ihrke PJ, Walder EJ, Affolter VK: *Interface diseases of the dermal-epidermal junction*, in *Skin diseases of the dog and cat, Clinical and histopathologic diagnosis, 2nd ed.* 2005, Blackwell. p. 65-68.
20. Hendrix DVH, *Diseases and surgery of the canine anterior uvea.* , in *Veterinary Ophthalmology, 5th ed.*, K.N. Gelatt, Gilger, B.C., Kern, T.J., Editor. 2013, Wiley-Blackwell. p. 1165-1166.
21. Bistner S: Allergic- and immunologic-mediated diseases of the eye and adnexae. Vet Clin North Am Small Anim Pract 1994, 24(4):711-734.
22. Vercelli A, Taraglio S: Canine Vogt-Koyanagi-Harada-Like Syndrome in two siberian husky dogs. Vet Dermatol 1990, 1:151-158.
23. Niza MM, Félix N, Vilela CL, Peleteiro MC, Ferreira AJ: Cutaneous and ocular adverse reactions in a dog following meloxicam administration. Vet Dermatol 2007, 18(1):45-49.
24. Royaux E, Bhatti S, De Cock H, Van Ham L, Kitshoff A, Vandenabeele S: Cutaneous adverse drug reaction in a dog associated with imepitoin. Vet Dermatol 2016, 27(2):118-21e32.

TRAUMATSKI BLEFARITIS SA KLINIČKOM SLIKOM IMUNSKI USLOVLJENE BOLESTI

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Četiri godine star mužjak rase labrador retriver je prezentovan sa istorijom akutnog razvoja mukokutanih ulcerativnih lezija u periokularnoj i perioralnoj regiji, i na lateralnom aspektu jastučića šapa. Sve lezije su bile simetrične i sa jasnom demarkacijom. Tokom opšteg kliničkog i oftalmološkog pregleda nisu detektovane druge patološke promene. Razvoj lezija je usledio posle intenzivne fizičke aktivnosti tokom lova u polju obraslom vrlo oštrom travom (*Panicum virgatum* - switchgrass). Slične lezije su se pojavile i kod drugog psa koji je takodje bio u lovu. Klinčki, lezije na koži su ukazivale na imunski posredovano oboljenje, ali je tretman sistemskim antibioticima doveo do potpunog povlačenja svih klinickih simptoma. Traumatske promene na koži treba da budu uključene u listu diferencijalnih dijagnoza kod pasa sa mukokutanim ulcerativnim lezijama, koje kliničkom slikom odgovaraju imunološki posredovanom obolenju.