Naltrexone for treatment of acral lick dermatitis in dogs

Stephen D. White, DVM

Summary: *Acral lick dermatitis (lick granuloma) was diagnosed in 11 dogs on the basis of history, physical examination, and histopathologic findings. A predilection for the left forelimb was noticed.*

All 11 dogs were given the narcotic antagonist naltrexone. Successful treatment (cessation of licking, reepithelialization of lesions) was seen in 7 dogs. All 7 dogs' lesions recurred when naltrexone was stopped, but reepithelialized in 5 dogs when the drug was readministered. Adverse effects (drowsiness, withdrawal from owner) were seen in 1 dog, but resolved within 48 hours of stopping the drug.

Acral lick dermatitis (lick granuloma, acral pruritic nodule) is a common self-induced dermatitis of dogs.[1-3] Lesions are usually single and are most common on the distal portion of extremities.[1-3] Although organic factors such as pyoderma, allergy, foreign body, or neoplasia are sometimes an underlying cause of acral lick dermatitis,[1-7] most reports[2, 3, 6, 8] refer to a psychogenic (learned behavior, social isolation, stress) cause. Reported treatments of acral lick dermatitis of nonorganic causation include corticosteroids (intralesional or topical),[2, 5, 8, 9] surgical excision,[4, 8] orgotein,[10] topical application of a proteolytic enzyme,[11] cobra venom,[2, 4, 8] radiation therapy,[2, 8] restrictive collars,[2, 6] acupuncture,[12] cryosurgery,[2] and topically corticoadministered steroid-flunixin meglumine-dimethylsulfoxide solution.[3] Reported success rates vary.

Self-mutilative behavior (stereotypies) has been reported in pigeons,[13] mice,[14] rats,[15] horses,[16, 17] swine,[18] and a dog.[19] Narcotic antagonists have been reported to be effective in controlling stereotypies in human beings and animals.[14-17, 20-24] The similarity of acral lick dermatitis to such stereotypies has been reported.[25, a] The exact mechanism by which narcotic antagonists suppress or control stereotypies remains unclear. Increased release of endogenous opioids such as endorphins and enkephalins have been noticed in stress-induced and self-mutilative behaviors in mice,[14] swine,[18] and human beings.[26] The dopaminergic system also has been implicated in stereotypies, and there is considerable interaction between the endogenous opioids and this system.[15] Endogenous opioids also may induce an analgesic state, decreasing pain perception, and therefore, motivation to decrease self-multilative behavior.[23] Narcotic antagonists such as naltrexone antagonize effects of endogenous opioids by binding to endogenous opioid receptors.[25] By reducing the analgesic state, the narcotic antagonists increase the perception of pain[21] and decrease the theorized endorphin-mediated reward or reinforcement of the self-injurious behavior.[27] The purpose of the study reported here was to determine the efficacy of a narcotic antagonist, naltrexone, in the treatment of acral lick dermatitis in dogs.

Materials and Methods

Dogs—Nine dogs were referred to the Foster Hospital for Small Animals, Tufts University School of Veterinary Medicine, and 2 dogs to the Colorado State University Veterinary Teaching Hospital with the presumptive diagnosis of acral lick dermatitis (Table 1). Dogs ranged in age from 1.5 to 12 years, with a median age of 5.3 years. Breeds included Doberman Pinschers (5), Golden Retrievers (3), Welsh Corgi (1) and dogs of mixed breeding (2). The latter were a Golden Retriever-type dog and a Siberian Husky X German Shepherd Dog. Seven dogs were sexually intact males and 4 were spayed females. A complete history of each dog was taken, and an attempt was made to identify any psychogenic factors affecting the dog. Duration of the

From the Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80526.

Supported by a grant from the American Academy of Veterinary Dermatology.

The author thanks Drs. Amy R. Marder, Laurie J. Stewart, David Garlick of the School of Veterinary Medicine, Tufts University, and Dr. Rod A. W. Rosychuk at the College of Veterinary Medicine and Biomedical Sciences, Colorado State University for technical assistance, and Dr. Ronald N. Ehrman for providing naltrexone.

[a]Dodman NH, Shuster L, Court MH, et al. The antipruritic effects of narcotic antagonists in dogs (abstr), in *Proceedings*. Am Coll Vet Anesthesiol 1987, 18.

Table 1—Signalment, physical examination, and history data of 11 dogs with acral lick dermatitis treated with naltrexone

Dog No.	Age (yr)	Breed	Sex	Location of lesion(s)	Duration of lesion(s) (yr)	Possible predisposing cause
1	3	Doberman Pinscher	M	Left hock	0.25	Nervous owner
2	1.5	Doberman Pinscher	FS	Left forelimb	1	Left in cage during work day
3	6	Mixed	M	Left forelimb	2	None
4	8	Doberman Pinscher	M	Right rear foot	1	None
5	2	Golden Retriever	M	Left forelimb	0.16	None
6	2	Golden Retriever	FS	Left forelimb	1	Rock chewer
7	12	Welsh Corgi	M	Left forelimb	>3	Alone at home during work day
8	5	Mixed	M	Multiple; distal areas of all 4 limbs	3	Alone at home during work day
9	4	Doberman Pinscher	M	Left forelimb right and left thigh	2	None
10	11	Doberman Pinscher	FS	Left forelimb	0.5	None
11	4	Golden Retriever	FS	Left forelimb	3	None

M = male; F = female; FS = spayed female.

lesions lasted from 6 months to >3 years before examination. Potential psychogenic causes were identified in 5 dogs. Dogs 7 and 8 were left alone at home all day, dog 2 was frequently confined in a cage, dog 1 had a self-described nervous owner, and dog 6 was constantly being reprimanded by the owner for chewing and swallowing rocks.

Previous treatment consisted of Elizabethan collars or bandages in dogs 3, 9 and 10, topically administered corticosteroid-dimethylsulfoxide-[b] flunixin meglumine[c] solution in dogs 1 and 7, and unspecified ointments in dog 3. The Elizabethan collars and bandages improved the lesions only as long as they were kept on the dogs. Topical treatments had no effect on the lesions.

In dogs 2, 3, 5 to 7, 10, and 11, the lesions were limited to the left forelimb, over the cranial aspect of the carpal/metacarpal area. In dogs 8 and 9, both the left forelimb and other areas (similar locations on all 4 limbs [dog 8] or the right and left lateral thigh areas [dog 9]) were involved. The left hock area of dog 1 and the right rear foot of dog 4 were affected. Lesions were alopecic, ulcerated, and well demarcated. At admission to the referral institution, a CBC, serum enzyme analysis, serum uric acid concentration, and biopsy of the acral lick dermatitis for histopathologic examination and aerobic bacterial culture and susceptibility testing (the latter obtained with sterile technique), were performed. Radiographs of the underlying tissues were obtained.

If organisms were isolated in bacterial culture, an antimicrobial drug based on susceptibility results was administered to the dog for 2 weeks. If no or minimal healing of the lesion or decrease of the dog's licking was observed, or if bacteria were not isolated initially naltrexone[d] (2.2 mg/kg of body weight, q 24 h PO), was administered to the dog. If the lesion did not heal, or the dog's licking did not decrease within 10 days, treatment was increased to q 12 h. If there was still no change, treatment was considered a failure. If the lesion began to heal, and the dog's licking decreased, the dog was maintained on the effective dose for 1 month. Successful treatment was defined as cessation or substantial decrease in the amount of licking of the lesion, to the point that the acral lick dermatitis reepithelialized and healing could occur. The dog was then monitored via examinations and/or telephone calls with the owner for a minimum of 1 year to determine if relapses occurred.

[b]Synotic, Diamond Laboratories Inc, Des Moines, Iowa.
[c]Banamine, Schering Corp, Bloomfield, NJ.
[d]Trexan, du Pont Pharmaceuticals, Wilmington, Del.

Results

Dog 5 had a high serum uric acid concentration of 2.03 mg/dl (normal, <2.0 mg/dl). Microscopic examination of biopsy specimens from acral lick dermatitis lesions revealed epidermal hyperplasia (acanthosis, pseudoepitheliomatous hyperplasia) in dogs 1, 3 to 5, 7 to 11, hyperkeratosis in dogs 1 to 3, 5, 6, 8 and 11, parakeratosis in dogs 1, 3, 5, and 8, and dermal fibrosis in dogs 2, 4, 8 and 11. Dermal cellular infiltrates were noticed in dogs 1, and 4 to 11. Infiltrates were characterized as mixed population (lymphocytes, neutrophils, histiocytes, plasma cells, eosinophils, mast cells) in dogs 5, 7, 8 and 10, mononuclear (lymphocytes, plasma cells, mast cells) in dogs 1, 3, and 6, and plasma cells in dogs 4 and 9. In dogs 4, 8, and 9, plasma cell infiltrate was noticed in association with apocrine sweat glands.

Bacteriologic culturing yielded no growth in dogs 6 and 9. *Staphylococcus intermedius* was isolated from dogs 1, 2, 7, 8, and 10, *Streptococcus* spp from dogs 1, 4, 8, and 10, *Escherichia coli* from dogs 3 and 4, *Pseudomonas* spp, *Proteus* spp and *Actinobacillus* spp from dog 4, *Clostridium* spp from dog 11, and *S epidermidis* from dog 5. Dog 10, with *S intermedius* and a *Streptococcus* spp isolated from biopsy specimens, had slight improvement after 2 weeks of erythromycin administration. Antimicrobial agents effected no improvement in the

lesions of the other dogs. Radiographic examination of the underlying tissues revealed soft tissue swelling in dogs 2, 3, 5, 8, 10, and 11, and periosteal reaction in dogs 3, 4, and 8.

Dogs 1 to 3 did not improve when treated with naltrexone. Dog 1 improved after being given another narcotic antagonist (nalmefene) SC. Dog 1 had a nervous owner, and after being given to a new owner, lesions resolved without treatment. Dogs 6, 7, 9, and 11 were successfully treated at 2.2 mg/kg q 24 h, and dogs 4, 5 and 10 were successfully treated at 2.2 mg/kg, q 12 h. Dog 8 had partial cessation of licking with the increased dosage regimen, but not enough to effect improvement of the lesion. Dog 6 was a rock chewer; this behavior also ceased during treatment. Adverse effects (drowsiness, withdrawal from the owner) were noticed in dog 3. These effects resolved within 48 hours of stopping the drug.

All 7 dogs that had improvement of their acral lick dermatitis relapsed after naltrexone treatment was stopped. Relapses were seen 1 week (dogs 4 and 9), 2 months (dogs 6, 10 and 11), 6 months (dog 5), or 3 years (dog 7) after stopping naltrexone treatment. Dogs 7 and 11 were euthanatized for unrelated health problems. The other 5 dogs that relapsed improved when naltrexone therapy was reinstituted. Final disposition of these 5 dogs varied. Dogs 5 and 10 were treated as needed at their original dosage (2.2 mg/kg, q 12 h) for 2 to 4 weeks at the discretion of the owners. Dog 6 has been successfully managed by giving the original daily dose (2.2 mg/kg) q 48 to 72 h. The owner of dog 9 refused to administer further treatment. Dog 4 was given the original dose (2.2 mg/kg, q 12 h) for 6 months at which time it became refractory to treatment and was euthanatized.

Discussion

Acral lick dermatitis is a common and frustrating dermatologic disease in dogs. Predisposition of age or sex was not noticed in this study. All but dog 7 were large breeds or large mixed breeds, which agrees with previous reports.[2, 3, 5, 9, 28] However, because data are not available on breed distribution in the general hospital population at one of the referral institutions, it was difficult to draw definitive conclusions. Gross features and distribution of acral lick dermatitis in this study are similar to previous reports.[1-5, 8] A predisposition for the left forelimb has been reported.[28]

Etiologically and therapeutically, acral lick dermatitis must be differentiated from organic causes of similar lesions. Histopathologic examination, bacterial culture, and radiographic examination of underlying tissues are important to rule out differential diagnoses such as bacterial infection, fungal infection, or neoplasia of skin or underlying bone. The results of these tests on the dogs in this study were similar to those of other authors,[2, 3] although the number of dogs with plasma cell infiltrate of the aprocrine sweat gland[3, 29] and with periosteal reaction of underlying bone was less than previously reported.[3] The slight improvement in dog 10 when treated with erythromycin was not indicative of a concurrent pyoderma, because erythromycin has anti-inflammatory properties as well.[30]

Acral lick dermatitis has been attributed to psychogenic causes, including boredom, learned behavior (initial organic cause stimulates licking that continues after the organic disease is resolved), and introduction of new animals or people into a household.[1-3, 6] Such an underlying cause is not always identifiable,[3, 4] as was the case in dogs 3-5 and 9-11.

Of the 11 dogs, 7 (63%) had healing of their lesion and a decrease or cessation of their licking behavior when naltrexone was administered. Dog 8 had partial decrease in licking behavior but without healing of the acral lick dermatitis, and dogs 1 to 3 (27%) had no improvement. Although our dosage protocol was empirical, it was similar to effective doses previously used in persons treated with naltrexone,[23, e] and in a dog treated with the closely related narcotic antagonist, naloxone.[19] Dog 1 did not respond to naltrexone but improved after being given another narcotic antagonist, nalmefene, SC.[31] These results may indicate individual variation in sensitivity to different narcotic antagonists, and/or routes of administration. Failure of the other dogs to respond to naltrexone may indicate that acral lick dermatitis has causes other than stereotypies, such as dysfunction in sensory nerves.[28]

Naltrexone has a role in the treatment of acral lick dermatitis in the dog. Although the drug is expensive (approximately $2.25 for a 50-mg tablet), decreased frequency of administration was effective in dog 6, which may ameliorate financial considerations.

[e]Herman BH, Hammock MK, Feinstein C, et al. Naltrexone induces dose-dependent decreases in self-injurious behavior (abstr). *Soc Neuroscience* 1985;11:468.

References

1. Veith L. Acral lick dermatitis in the dog. *Canine Pract* 1986;13(4):15–22.
2. Muller GH, Kirk RW, Scott DW. *Small animal dermatology*. 4th ed. Philadelphia: WB Saunders Co, 1989:750–757.
3. Scott DW, Walton DK. Clinical evaluation of a topical treatment for canine acral lick dermatitis. *J Am Anim Hosp Assoc* 1984;20:565–570.
4. Doering GG. Acral lick dermatitis: medical management. *Canine Pract* 1974;(5):21–25.
5. Bagnall BG. Lick granuloma: a self-inflected skin problem. *Pedigree Dig* 1977;4(2):4–5.
6. Young MS, Manning TO. Psychogenic dermatoses. *Dermatol Rep* 1984;3(2):1–8.
7. Thomsen MK, Kristensen F. Contact dermatitis in the dog. *Nord Vet Med* 1986;38:129–147.
8. Reid JS. Acropruritic granuloma. In: Kirk RW, ed. *Current veterinary therapy V*. Philadelphia: WB Saunders Co, 1974:441–443.
9. Panel Report: lick granuloma. *Mod Vet Pract* 1974; 55:139–145.

10. Neibert HC. Orgotein treatment of canine lick granuloma. *Mod Vet Pract* 1975;56:529.

11. Holobek J. Clinical experience with a proteolytic enzyme. *VM SAC* 1973;68:148–150.

12. Bullock JE. Acupuncture treatment of canine lick granuloma. *Calif Vet* 1978;32(4):14–15.

13. Goodman I, Zacny J, Osman A, et al. Dopaminergic nature of feeding-induced behavioral stereotypies in stressed pigeons. *Pharmacol Biochem Behav* 1983;18:153–158.

14. Cabib S, Puglisi-Allegra S, Oliverio A. Chronic stress enhances apomorphine-induced stereotypic behavior in mice: involvement of endogenous opioids. *Brain Res* 1984;298:138–140.

15. Moon BH, Feigenbaum JJ, Carson PE, et al. The role of dopaminergic mechanisms in naloxone-induced inhibition of apomorphine-induced stereotypic behavior. *Eur J Pharmacol* 1980;61:71–78.

16. Dodman NH, Shuster L, Court MH, et al. Investigation in the use of narcotic antagonists in the treatment of a stereotypic behavior pattern (crib-biting) in the horse. *Am J Vet Res* 1987;48:311–319.

17. Dodman NH, Shuster L, Court MH, et al. Use of a narcotic antagonist (nalmefene) to suppress self-mutilative behavior in a stallion. *J Am Vet Med Assoc* 1988;192:1585–1586.

18. Cronin GM, Wiepkema PR, van Ree JM. Endorphins implicated in stereotypies of tethered sows. *Experientia* 1986; 42:198–199.

19. Brown SA, Crowell-Davis S, Malcolm T, et al. Naloxone-responsive compulsive tail chasing in a dog. *J Am Vet Med Assoc* 1987;190:884–886.

20. Richardson JS, Zaleski WA. Naloxone and self-mutilation. *Biol Psychiatry* 1983;18:99–101.

21. Sandman CA, Datta PC, Baron J, et al. Naloxone attenuates self-abusive behavior in developmentally disabled clients. *App Res Ment Retard* 1983;4:5–11.

22. Gilman MA, Sandy KR. Opiatergic and dopaminergic function and the Lesch-Nyhan syndrome (letter). *Am J Psychiatry* 1985;142:1226.

23. Herman BH, Hammock MK, Arthur-Smith A, et al. Naltrexone decreases self-injurious behavior. *Ann Neurol* 1987; 22:550–552.

24. Broderick PA, Blaha CD, Lane RF. *In vivo* electrochemical evidence for an enkephalinergic modulation underlying stereotyped behavior: reversibility by naloxone. *Brain Res* 1983;269:378–381.

25. Dodman NH, Shuster L, Court MH, et al. Behavioral effects of narcotic antagonists. *J Assoc Vet Anesthetists* 1988; 15:56–64.

26. Coid J, Allolio B, Rees LH. Raised plasma metenkephalin in patients who habitually mutilate themselves. *Lancet* 1983;2:545–546.

27. Kelsey JE, Belluzzi JD, Stein L. Does naloxone suppress self-stimulation by decreasing reward or by increasing aversion? *Brain Res* 1984;307:55–59.

28. van Nes JJ. Electrophysiological evidence of sensory nerve dysfunction in 10 dogs with acral lick dermatitis. *J Am Anim Hosp Assoc* 1986;22:157–160.

29. Gradzki Z, Winiarczyk S. Acral lick dermatitis in a dog. *Med Wet* 1984;40:736–737.

30. Scott DW, Buerger RG. Nonsteroidal anti-inflammatory agents in the management of canine pruritus. *J Am Anim Hosp Assoc* 1988;24:425–428.

31. Dodman NH, Shuster L, White SD, et al. The use of narcotic antagonists as therapeutic agents to modify stereotypic scratching and licking behavior in dogs. *J Am Vet Med Assoc* 1988;193:815–819.

Correction: Comparison of the complement fixation and agar gel immunodiffusion tests for diagnosis of subclinical bovine paratuberculosis

In the abstract, "Comparison of the complement fixation and agar gel immunodiffusion tests for diagnosis of subclinical bovine paratuberculosis" (*JAVMA,* February 15, 1990, p 604), the second sentence of the last paragraph should read, "However, specificities of the CF test and, particularly, the AGID test appear to be high enough that any positive test result should be regarded as a presumptive diagnosis of *M paratuberculosis* infection, and confirmatory fecal culture testing of each animal and of the herd of origin is warranted." The *JAVMA* regrets the error.