Clinical, histologic, and immunohistochemical characterization of wart-like lesions on the paw pads of dogs: 24 cases (2000–2007)

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Objective—To determine clinical, histologic, and immunohistochemical findings for dogs with wart-like lesions involving the paw pads.

Design—Retrospective case series.

Animals—24 dogs (18 Greyhounds and 6 dogs of other breeds).

Procedures—Medical records were reviewed for information on signalment, physical examination findings, concurrent disease processes, location of all lesions, and, when available, results of histologic examination of biopsy specimens. Available biopsy specimens (n = 11) were submitted for immunohistochemical staining and a PCR assay to identify viral inclusion bodies.

Results—In Greyhounds, most lesions involved the pads of the third and fourth digits, had a consistent histologic appearance without evidence of inflammation, were negative for papillomavirus, and had an unsatisfactory response to treatment. In other breeds, lesions involved the pads of non–weight-bearing digits, had histologic evidence of inflammation, were positive for papillomavirus, and responded to surgical treatment.

Conclusions and Clinical Relevance—Results suggested that wart-like lesions involving the paw pads of Greyhounds were a distinct clinical entity with features resembling porokeratosis plantaris discreta in humans. In Greyhounds, these lesions were not associated with an underlying viral etiology and, therefore, should not be considered plantar warts. Alternative treatments should be investigated because current treatments were generally unsuccessful in Greyhounds. Wart-like lesions of the paw pads in other breeds were often associated with papillomavirus, and surgical excision appeared curative. (J Am Vet Med Assoc 2009;234:1555–1558)

Paw pad lesions commonly referred to as plantar warts have been discussed on the Veterinary Information Network1 and in a recent case report.2 Such lesions have been described as well-circumscribed areas of hyperkeratosis resulting in lameness of the affected limb3 and have generally been thought to be more common in Greyhounds than in dogs of other breeds.

By definition, plantar warts (verruca plantaris) are warts caused by the human papillomavirus. In people, they appear on the sole of the foot and typically resemble a cauliflower. Some may contain small black specks that bleed when the surface is shaved, and this bleeding distinguishes plantar warts from other hyperkeratotic lesions. Plantar warts may or may not be painful.4–6 Human papillomavirus is transmitted through direct skin contact and can be acquired by walking barefoot on dirty surfaces such as those encountered in public restrooms and locker rooms or by walking on littered ground. The virus thrives in warm, moist environments, making plantar warts a common occurrence in communal bathing facilities.4 Multiple treatments for plantar warts in humans have been described, including topical application of salicylic acid, 0.7% cantharidin, or 5% imiquimod; intralesional injection of bleomycin; cryotherapy; and laser therapy.5 Surgical removal by dissection, electrodessication, or curettage is recommended for refractory plantar warts.1,5

Other hyperkeratotic lesions in people that may resemble and must be distinguished from plantar warts include calluses, corns, and PPD. A callus is defined as a toughened area of skin that has become relatively thick and hard in response to repeated contact or pressure. Calluses are generally not harmful but may become infected.6,7 Corns represent specially shaped calluses that possess a central conical core of keratin. Although corns may occur on the palm and plantar skin surfaces, they more frequently occur on thin or glabrous skin surfaces such as the tops of toes or fingers. Neither calluses nor corns are consistently painful.6,7 Porokeratosis plantaris discreta is a

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dermatopathologic condition of the plantar surface of the foot. Clinically, these lesions are painful and are usually found on weight-bearing surfaces. The proposed etiology is that pressure over the orifices of eccrine sweat glands results in hypertrophy of the glands, causing pain as a result of pressure on surrounding pacinian corpuscles.12,13

Although wart-like paw pad lesions in Greyhounds have frequently been referred to as plantar warts, there is no evidence that these lesions are virally induced, and information is lacking on the underlying cause, histologic features, and natural progression of these lesions as well as on results of treatment. The purpose of the study reported here was to determine clinical, histologic, and immunohistochemical findings for dogs with wart-like lesions involving the paw pads.

Materials and Methods

Criteria for case selection—Medical records of the Tufts University Cummings School of Veterinary Medicine and the Angell Animal Medical Center were searched to identify dogs with wart-like paw pad lesions that were examined at either institution between January 2000 and October 2007.

Medical records review—Data obtained from medical records of dogs included in the study consisted of breed, sex, age, history, results of clinicopathologic testing and radiography, lesion location, treatment, outcome, and, when available, results of histologic examination of biopsy specimens. Attempts were made to contact owners of dogs included in the study to obtain follow-up information on additional treatments provided, outcome, and lesion recurrence.

Histologic examination—Available biopsy specimens were reevaluated by a single pathologist (MB) to confirm the diagnosis, identify consistent, defining histologic characteristics, and determine a plausible etiopathogenesis. Biopsy specimens available for reevaluation had all been fixed by immersion in neutral-buffered 10% formalin, processed by use of routine methods, and embedded in paraffin. For the present study, 5-µm-thick sections were obtained and stained with H&E.

Immunohistochemical staining and PCR assay—Additional unstained sections and paraffin blocks representative of biopsy specimens available for reevaluation were sent to Michigan State University for evaluation for viral inclusion bodies by means of immunohistochemical staining and a PCR assay. Immunohistochemical staining was performed with a monoclonal antibody (SDS-disrupted bovine papillomavirus type 1 immunogen) against human papillomaviruses 1, 6, 11, 16, 18, and 31. This antibody has been reported to cross-react with a wide range of papillomaviruses in other species, including dogs.15 Immunohistochemical staining was performed with an automated staining system that incorporated a commercial detection system. Antigen retrieval was achieved by incubating slides in a high-pH antigen retrieval solution for 60 minutes. Sections were counterstained with hematoxylin.

Positive control specimens included tissues known to be infected with canine papillomavirus. For negative control specimens, the primary antibody was replaced with homologous nonimmune serum. For the PCR assay, DNA was extracted from paraffin-embedded specimens with a commercial kit and was tested with 2 PCR assays previously reported to be capable of detecting a broad range of human papillomaviruses.17 The first assay targeted a 450–base pair region of the papillomavirus L1 gene and incorporated primers MY11 (5′-CMCAGGGWCATAAYAATGG-3′) and MY09 (5′-CGTCMMARRGGAWGCTGAC-3′). The second assay targeted either an approximately 450–base pair (primers CP4 [5′-ATGGTACARTGGGCATWTGA-3′] and CP5 [5′-GAGGYTGCAACAAAMTGRCT-3′]) or approximately 320–base pair (primers PPF1 [5′-AA-CATTGTAGACATTATAACGAGC-3′] and CP5) region of the papillomavirus E1 gene.18 Assay specifications were similar to those described previously,19 with the reaction carried out in a multiplex format.

Amplification products were analyzed by means of agarose gel electrophoresis and visualized by means of UV transillumination. Amplicons were gel purified with a commercial kit and submitted to the Research Technology Support Facility of Michigan State University for automated direct sequencing.

Results

Twenty-four dogs met the criteria for inclusion in the study. There were 18 Greyhounds, 2 Labrador Retrievers, 1 Foxhound, 1 Rottweiler, 1 Golden Retriever, and 1 retriever cross. Thirteen dogs were spayed females, 10 were castrated males, and 1 was a sexually intact female. Mean age was 6.9 years (range, 1 to 15 years).

At the time of initial examination, the 18 Greyhounds had 8 wart-like lesions (Figure 1) involving the digital pads of the right forepaw (1 lesion on the second digital pad, 2 lesions on the third digital pad, and 5 lesions on the fourth digital pad), 6 lesions involving the digital pads of the left forepaw (3 lesions on the third digital pad, 2 lesions on the fourth digital pad, and 1 lesion for which location was unspecified), 1 lesion involving the fourth digital pad of the right hind paw, and 11 lesions involving the digital pads of the left hind paw (7 lesions on the third digital pad and 4 lesions on the fourth digital pad). There were 10 lesions on the second digital pad of the right hind paw. Lesion location at the time of initial examination in dogs other than Greyhounds was tested with 2 PCR assays previously reported to be capable of detecting a broad range of human papillomaviruses. The first assay targeted a 430–base pair region of the papillomavirus L1 gene and incorporated primers MY11 (5′-CMCAGGGWCATAAYAATGG-3′) and MY09 (5′-CGTCMMARRGGAWGCTGAC-3′). The second assay targeted either an approximately 450–base pair (primers CP4 [5′-ATGGTACARTGGGCATWTGA-3′] and CP5 [5′-GAGGYTGCAACAAAMTGRCT-3′]) or approximately 320–base pair (primers PPF1 [5′-AA-CATTGTAGACATTATAACGAGC-3′] and CP5) region of the papillomavirus E1 gene. Assay specifications were similar to those described previously, with the reaction carried out in a multiplex format.

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Figure 1—Photograph of the typical appearance of a wart-like lesion involving the paw pad in a dog.
Results of a serum biochemical profile (n = 5), CBC (4), and urinalysis (1) were available for only limited numbers of dogs; no consistent abnormalities were identified. Radiographs of the affected paw pads were available for 4 Greyhounds and for the retriever cross. Two Greyhounds had swelling of the soft tissues of the affected digit, and 3 Greyhounds had associated degenerative joint disease involving the metatarsophalangeal, metacarpophalangeal, or interphalangeal joint. The retriever cross had moderate to severe degenerative joint disease involving the metatarsophalangeal, third, and fifth digital pads of the left forepaw, the right metatarsal pad, and the fourth digital pad of the right hind paw.

Seven dogs, all Greyhounds, were examined on multiple occasions because of paw pad lesions, with 3 dogs examined twice, 3 dogs examined 3 times, and 1 dog examined 4 times. During follow-up examinations in these dogs, 7 lesions were identified on the right forepaw (2 involving the second digital pad, 1 involving the third digital pad, and 4 involving the fourth digital pad), 3 lesions were identified on the left forepaw (1 involving the second digital pad, 1 involving the third digital pad, and 1 for which location was unspecified), 2 lesions were identified on the right hind paw (both involving the fourth digital pad), and 3 lesions were identified on the left hind paw (all involving the third digital pad). In addition, 1 dog was reported to have wart-like lesions involving all 4 paws, and 1 dog was reported to have multiple wart-like lesions involving the right forepaw. Six of the 7 Greyhounds that were examined more than once had lesions involving the same foot as initially, and 5 of the 7 had lesions involving the same digit as initially.

Biopsy specimens from 11 lesions were available for reevaluation, including 6 lesions from Greyhounds and 5 lesions from dogs of other breeds. All 6 lesions from the Greyhounds had a consistent histologic appearance characterized by local, extensive thickening of the stratum corneum and severe compact hyperkeratosis often resulting in a cylindrical or conical mound of keratin raised above the surrounding skin surface. Morphology of the thickened stratum corneum was similar to the morphology of the adjacent paw pad keratin. The underlying epithelium was often moderately hyperplastic with acanthosis and accentuation of epidermal rete pegs (Figure 2). There was no evidence of hypergranulosis or viral cytopathic effects, and the underlying dermis lacked evidence of inflammation, although mild dermal atrophy associated with loss of dermal collagen, edema, and mild neovascularization were sometimes seen.

Histologic findings for dogs other than Greyhounds were similar with a few notable differences. This includes lesions in 3 dogs with immunohistochemical evidence of papillomavirus infection and a lesion in 1 dog that reportedly was a callus that had developed secondary to an infected barbed wire laceration. In 1 dog, the lesion had been removed surgically by the owner’s primary veterinarian, and the dog had healed without complications; however, a biopsy specimen had not been submitted for examination. In the remaining dog, the lesion had been treated by means of amputation of the affected digit. The histologic diagnosis was focally extensive, neutrophilic and lymphoplasmacytic dermatitis with chronic hemorrhage likely secondary to blunt trauma.

For all 6 lesions from Greyhounds, results of immunohistochemical staining for papillomavirus were negative, whereas results of immunohistochemical staining for papillomavirus were positive for 3 of the 5 lesions from dogs other than Greyhounds, including 2 lesions with histologic evidence of viral inclusion bodies. For these 3 lesions, results of the PCR assay were suggestive of a previously unrecognized strain of papillomavirus.

Owners of 17 of the 24 dogs, including 11 of the 18 Greyhounds, could be contacted by telephone to obtain follow-up information. One Greyhound was euthanatized for unrelated reasons 6 months after surgical removal of a paw pad lesion, and the owner reported that the lesion had not recurred by the time of euthanasia. Owners of the remaining 10 Greyhounds reported that results of treatment of the paw pad lesions were unsatisfactory. All 10 had had a recurrence of the original lesions or developed new lesions, either on the same digit or on a different digit or paw, and owners of all 10 reported some degree of distress related to the dogs’ level of discomfort. Two owners had considered euthanasia because they were concerned about the dogs’ well-being. Treatments that had been attempted in these dogs included excision or debridement of the lesions, topical application of tea tree oil or other ointments, application of duct tape, and use of padded boots. All 6 dogs other than Greyhounds for which follow-up information was available reportedly had a single lesion, and in all 6, surgical removal was reportedly curative.

**Discussion**

Results of the present study suggested that wart-like lesions involving the paw pads of Greyhounds may be a distinct clinical entity different from similar-appearing lesions involving the paw pads in other breeds. For Greyhounds in the present study, all lesions involved the sec-
Small Animals

of treatments for wart-like paw pad lesions in dogs are warranted.

Important limitations of the present study included its retrospective nature, small sample size, and lack of objective follow-up data. Because published reports documenting an effective treatment for similar paw pad lesions in dogs are lacking, treatments were variable, making it impossible to draw conclusions about the effectiveness of any particular treatment. However, we currently do not uniformly recommend surgical removal of these lesions in Greyhounds.

References