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 often 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)

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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.\textsuperscript{6,13} Although wart-like 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)\textsuperscript{9} 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.\textsuperscript{16} Immunohistochemical staining was performed with an automated staining system\textsuperscript{2} that incorporated a commercial detection system.\textsuperscript{7} Antigen retrieval was achieved by incubating slides in a high-pH antigen retrieval solution\textsuperscript{8} 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\textsuperscript{22} and was tested with 2 PCR assays previously reported to be capable of detecting a broad range of human papillomaviruses.\textsuperscript{23} The first assay targeted a 450–base pair region of the papillomavirus L1 gene and incorporated primers MY11 (5’-CMCAGGGWCATAAYAATGG-3’) and MY09 (5’-CGTCCMARRGGAWACTGATC-3’). The second assay targeted either an approximately 450–base pair (primers CP4 [5’-ATGGTACARTGGGATWGA-3′] and CP5 [5’-GAGGYYTGCAAAAAATGRC-3′]) or approximately 320–base pair (primers PPF1 [5’-AA-CAATGTGTAGACATTATAACGAGC-3′] and CP5) region of the papillomavirus E1 gene.\textsuperscript{16} Assay specifications were similar to those described previously,\textsuperscript{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). Additionally, the medical record for 1 Greyhound indicated that multiple early plantar warts were present, and the medical record for another Greyhound indicated that warts were present on the second and third digits of all 4 feet. Lesion location at the time of initial examination in dogs other than Greyhounds...
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 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 euthanized 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 dog’s 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-

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Figure 2—Photomicrograph of a section of a wart-like paw pad lesion from a Greyhound. Notice the local, extensive thickening of the stratum corneum and severe compact hyperkeratosis (CH). This results in a cylindrical or conical mound of keratin raised above the surrounding skin surface. The underlying epithelium is moderately hyperplastic with epidermal acanthosis (EA) and accentuation of epidermal rete pegs (RP). H&E stain; bar = 2 mm.
ond, third, or fourth digital pads, with most located on the weight-bearing third and fourth digital pads. By contrast, 4 of the 6 lesions identified in dogs other than Greyhounds were located on the fifth digital pad, which is not weight-bearing, or on the metacarpophalangeal or metatarsophalangeal pad. Treatment of paw pad lesions in Greyhounds was generally unsatisfactory, whereas excision was curative in other breeds, and lesions commonly recurred in Greyhounds but not in dogs of other breeds.

In the present study, histologic examination of 6 lesions from Greyhounds revealed a consistent microscopic appearance characterized by locally extensive thickening and marked compact hyperkeratosis of the stratum corneum that projected above the skin surface. The epithelium was often moderately hyperplastic with acanthosis and accentuation of the epidermal rete pegs, and there was no evidence of a surrounding inflammatory response typical of trauma or an underlying foreign body. Viral inclusion bodies were not detected, and results of immunohistochemical staining and a PCR assay for papillomavirus were negative. Thus, our findings suggested that these wart-like paw pad lesions in Greyhounds were not virally induced. In addition, lesions did not resemble corns or calluses, as described in humans, and findings were more consistent with PPD. However, although PPD is believed to be associated with occlusion of the eccrine sweat glands in humans, there was no histologic evidence of eccrine sweat gland orifice occlusion, ductular dilation, or glandular hypertrophy in any of the biopsy specimens examined in the present study. In humans, these histologic characteristics may be absent if biopsy specimens of adequate depth are not obtained, and it is possible that specimens examined in the present study were of inadequate depth. Regardless, because papillomavirus was not identified in any of the paw pad lesions from Greyhounds in the study, use of the term plantar warts to describe these lesions should probably be avoided.

In contrast with findings for Greyhounds in the present study, 3 of the 5 lesions from dogs of other breeds were positive for papillomavirus, and 2 of these 3 lesions had histologic evidence of viral inclusions. The remaining 2 lesions had histologic evidence of perilesional inflammation. Thus, we suggest that wart-like paw pad lesions in dogs other than Greyhounds may be associated with papillomavirus infection or inflammation associated with a foreign body or other inflammatory cause. In the present study, treatment of paw pad lesions in Greyhounds was typically unsuccessful, although follow-up was generally inadequate to assess the effectiveness of surgery. After surgical removal or cryotherapy of lesions in humans with PPD, patients are counseled to wear soft, padded shoes. Similarly, we currently recommend that Greyhounds with paw pad lesions avoid firm surfaces if possible and that owners consider using soft, protective booties. Five of the Greyhound owners in the present study who were available for follow-up mentioned that the only thing that appeared to alleviate signs of pain in their dogs was use of some form of padded footwear, although several owners mentioned that their dogs did not tolerate such footwear very well. Regardless of treatment, owners should be advised that lesions may recur or persist or that new lesions may develop. Prospective studies evaluating effectiveness 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