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Development of multiple pigmented viral plaques and squamous cell carcinomas in a dog infected by a novel papillomavirus

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Abstract

Canine viral plaques are uncommon skin lesions that are induced by papillomaviruses (PVs). Plaques are usually of little clinical significance in dogs, although they have been reported rarely to progress to squamous cell carcinoma (SCC). Here is described a 7-year-old mixed-breed dog that developed numerous darkly pigmented plaques up to 8 cm in diameter. Multiple ulcerated nodular masses were visible within plaques on the ventrum and axilla. The dog showed no clinical evidence of immunodeficiency and appeared otherwise healthy. Over the next 2 years, five surgeries were performed to remove 23 ulcerated masses that ranged in size from 2 to 5 cm in diameter. Five masses were submitted for histology, and all were SCCs. Each was surrounded by epidermis that contained histological features consistent with those described in canine plaques. Suggestive of a PV aetiology, massive numbers of large keratohyaline granules were present throughout the thickened epidermis. Additionally, koilocytes were focally present, and one sample contained a band of keratinocytes within the superficial epidermis that contained pale cytoplasm and marginated chromatin. From two samples, DNA sequences from a previously unreported PV were amplified, and immunohistochemistry confirmed the presence of PV antigen in both. The PV DNA sequences were most similar to those of canine PVs previously associated with plaque formation. The plaques observed in this case were unusual owing to their rapid growth, large size and frequent malignant transformation. It is unknown whether this unusual behaviour was due to the specific PV detected in this case or to host factors within the dog.

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Introduction

Canine skin lesions that are caused by papillomavirus (PV) infection can be subdivided into papillomas and pigmented viral plaques.[1] Cutaneous papillomas demonstrate marked epidermal proliferation and are associated with infection by canine oral PV (COPV), *Canis familiaris* PV (CfPV)-2, CfPV-6 and CfPV-7.[1–3] Most canine papillomas resolve spontaneously, although malignant transformation has been reported in immunocompromised dogs.[4] Canine viral plaques exhibit mild orthokeratosis and are associated with CfPV-3, CfPV-4 and CfPV-5.[3,5,6] Although viral plaques do not spontaneously resolve, they typically remain small and of little clinical significance.[1] Malignant transformation of a single viral plaque has been reported in two dogs, while multiple squamous cell carcinomas (SCCs) developed from viral plaques over a 3- to 5-year period in two immunosuppressed dogs.[5,7–9] Involvement of PV was confirmed in all four dogs using immunohistochemistry; however, the causative PV was only investigated in one case and identified as CfPV-3.[5]

Described here is a dog that developed numerous large pigmented viral plaques. Many plaques transformed to SCCs over a 20-month period, necessitating multiple surgeries for neoplasm removal. This is the first report of multiple SCCs developing from viral plaques in a dog without identifiable immunosuppressive disease. In two lesions, DNA sequences from a previously unreported PV were detected.

Case report

A 7-year-old castrated male mixed-breed dog presented to a veterinary hospital in Vanuatu with numerous plaques that were widely scattered over the entire body but were most common on the ventrum and within the axilla. The majority of the plaques were mildly elevated, darkly pigmented, and 1–3 cm in diameter. However, smaller numbers of prominently raised plaques up to 8 cm in diameter were also visible. The larger plaques were confined to the ventrum and axilla and often surrounded an ulcerated nodular mass (Figures 1 and 2). Six larger ulcerated masses were surgically removed under general anaesthesia. Additionally, a single 1 cm diameter plaque was also

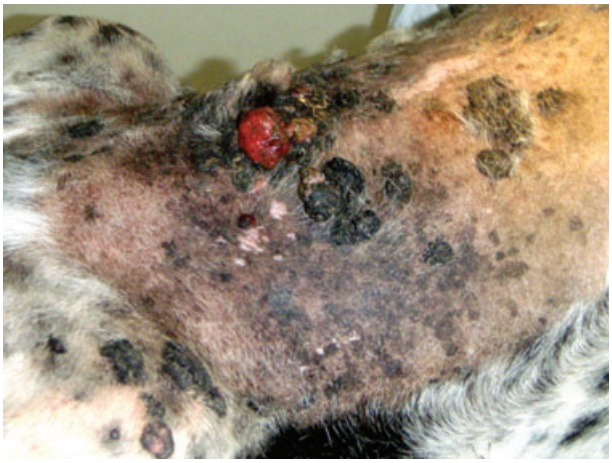

Figure 1. Multiple pigmented plaques on the ventrum of a 7-year-old mixed-breed dog. Note the presence of numerous mildly elevated plaques along with multiple large nodular ulcerated masses.

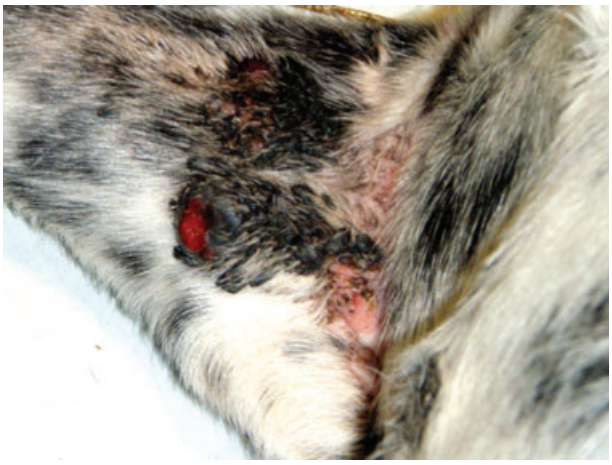

Figure 2. Two large pigmented plaques within the axilla of a 7-year-old mixed-breed dog. A nodular ulcerated mass is visible within one of the plaques.

excised. An ulcerated mass from close to the prepuce and the small plaque were fixed in formalin and submitted for histological examination. The dog was reported to be kept, along with a 3-year-old dog that had no clinical evidence of disease, outside with access to shade.

Histological examination of the large mass showed a raised papillary site of keratinocyte transformation and invasion, breaching the basement membrane and sending keratin pearls and sheets of epithelia into the dermis and outwards to form papillary processes above the epidermal contour (Figure 3). This well-differentiated SCC was associated with markedly vascular dermal sclerosis. The neoplastic cells had moderate cellular atypia and a high mitotic rate. The margins of the SCC and into the surrounding epidermis contained increased numbers of large keratohyaline granules; however, no increased granule number was present within the infiltrating epidermal cells. There was also marked hyperplasia and orthokeratosis that resulted in a scalloped appearance. Superficial layers of the epidermis contained large numbers of large keratohyaline granules, while increased melanin was visible within deeper layers of the epidermis and in melanomacrophages within the underlying dermis. Towards the periphery of the lesion, small numbers of cells with condensed nuclei surrounded by a cytoplastic clearing (koilocytes) were visible. However, koilocytosis was not a prominent feature within the surrounding plaque. The histological diagnosis was an invasive SCC developing within a viral plaque. It is unusual for cutaneous SCCs to have a nodular exophytic appearance. The nodular appearance appeared to be due to the marked fibrovascular stroma within the dermis. It is considered most likely that the increased dermal fibrous tissue was induced by the overlying hyperplastic epidermis and then infiltrated by the neoplastic cells; however, it is also possible that the fibrous tissue was directly induced by the infiltrating neoplastic cells.

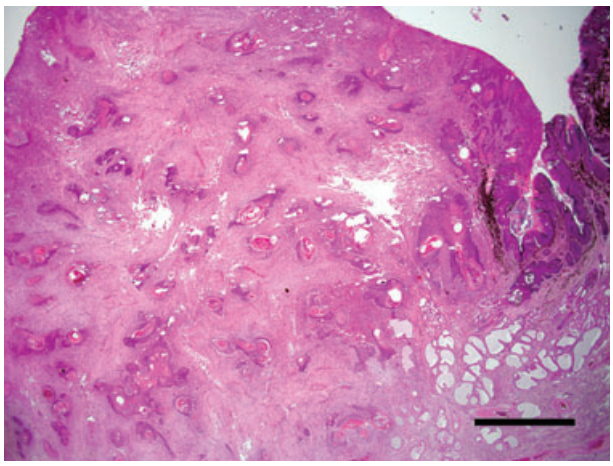

Figure 3. Photomicrograph of the large ulcerated mass close to the prepuce within Figure 1. To the left of the photomicrograph is a squamous cell carcinoma that consists of numerous nests and trabeculae of infiltrating epidermal cells supported by a marked fibrovascular stroma. The epidermis to the right is thickened, folded and hyperpigmented. The epidermal changes here are consistent with a canine pigmented viral plaque. H&E. Scale bar = 1.5 mm.

Histological examination of the small plaque revealed moderate orthokeratosis resulting in a scalloped appearance to the epidermis. Keratinocytes showed organized synchronous differentiation with no anisokaryosis. Increased numbers of large keratohyaline granules were visible within the superficial layers, with melanin granules prominent within the basal cell layer. Koilocytes were not visible within the thickened epidermis. The dermis underlying the lesion contained large numbers of heavily pigmented melanomacrophages. The histological features were consistent with previous descriptions of canine viral pigmented plaques.[1]

Additional pigmented plaques and nodular ulcerated masses developed over the next 20 months. Although small plaques developed over the entire body, ulcerated masses remained restricted to the ventrum and axilla. During this time, the dog was anaesthetized four more times to remove 14 additional 2–5 cm diameter ulcerated masses. A mass that was removed 16 months after the lesions were first observed was submitted for histology. As before, histology revealed a nodular mass consisting of neoplastic epidermal cells infiltrating a well-developed

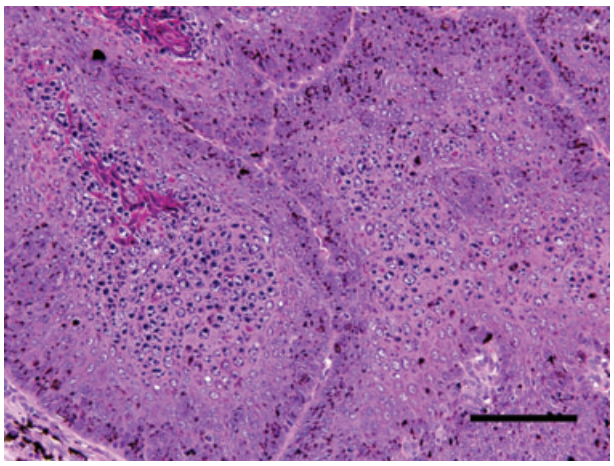

Figure 4. Photomicrograph of epidermis surrounding an *in situ* squamous cell carcinoma. Note marked thickening and folding of the epidermis. Increased melanin is visible within the deeper epidermis, while large keratohyaline granules are prominent with the superficial layers of the epidermis. The epidermis has retained an orderly maturation, and little dysplasia is visible. H&E. Scale bar = 70 μm.

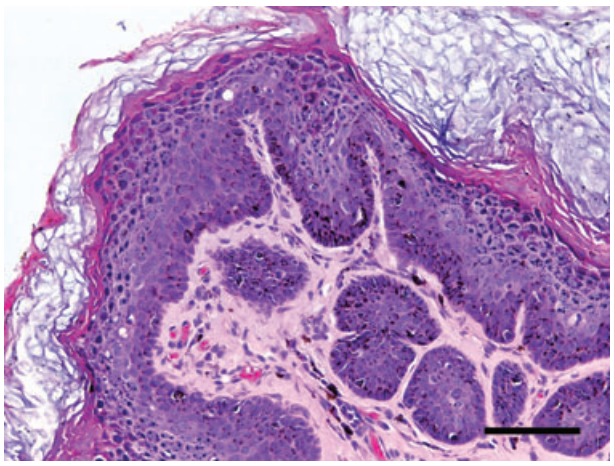

Figure 5. Photomicrograph of epidermis surrounding an *in situ* squamous cell carcinoma. Large keratinocytes with pale cytoplasm are visible within a band within the superficial layers of the epidermis. H&E. Scale bar = 70 μm.

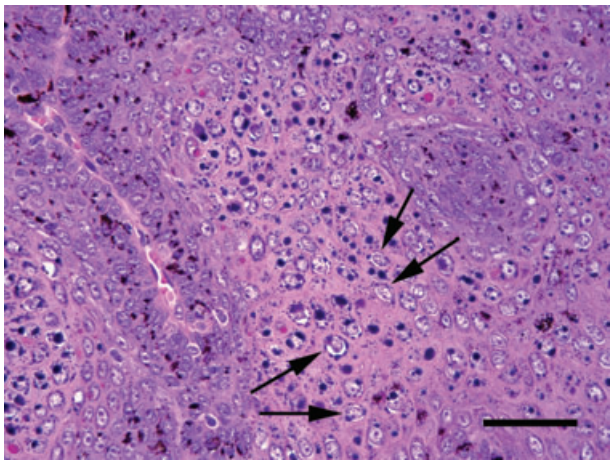

Figure 6. Photomicrograph of epidermis surrounding an *in situ* squamous cell carcinoma. Keratinocytes within the deeper epidermis show koilocytosis, with dark condensed nuclei surrounded by a clear cytoplasmic halo (arrows). H&E. Scale bar = 30 μm.

dermal fibrovascular stroma. A complete blood count and serum biochemistry panel performed at this time showed no evidence of any systemic disease, although specific testing for hypothyroidism or hyperadrenocorticism was not performed. The dog was not receiving any medication except routine heartworm prevention.

Three additional masses that were surgically removed 4 months later were examined histologically. All three contained areas of marked epidermal proliferation that contained loss of organization of keratinization and moderate to marked cellular dysplasia. The neoplastic epidermal cells remained confined by the basement membrane, and all three masses were classified as *in situ* SCCs. As before, all neoplasms were surrounded by epidermis that was markedly thickened, contained large numbers of large keratohyaline granules, and was hyperpigmented (Figure 4). Additionally, one of the *in situ* SCCs was surrounded by epidermis that contained keratinocytes with increased quantities of pale cytoplasm and vacuolated nuclei containing marginated chromatin. These cells formed a band predominantly within the granular cell layer (Figure 5). One sample contained foci of koilocytosis (Figure 6); however, koilocytes were not visible within the other two samples.

Polymerase chain reaction (PCR) was used to amplify PV DNA from the lesions. Briefly, DNA was extracted from formalin-fixed paraffin-embedded tissue as previously described.[10] Samples from which DNA was extracted included the viral plaque and SCC that were part of the initial submission and a SCC that had been submitted 16 months later. The consensus primers FAP59/64 and MY09/11 were used to amplify PV DNA.[11,12] The DNA extracted from a bovine fibropapilloma was used as a positive control, while no template DNA was added to the negative controls. The MY09/11 primers amplified PV DNA from the positive control and the viral plaque. The DNA amplified from the plaque was purified and sequenced as previously described.[10] This allowed determination of a 396 bp section of the PV *L1* gene (GenBank accession no. GU220384). Three months later, DNA was extracted from the three *in situ* SCC samples using the same methods. The MY09/11 primers amplified PV DNA from one sample. This was the *in situ* SCC sample that contained the band of keratinocytes with pale cytoplasm. The DNA sequence amplified from the *in situ* SCC sample was identical to that previously detected in the viral plaque. The amplified sequence was compared with known sequences from GenBank (see http://www.ncbi.nlm.nih.gov/genbank), using the basic local alignment search tool (http://www.ncbi.nlm.nih.gov/blast). The sequence was most similar to CfPV-5 (71%), CfPV-4 (70%) and CfPV-3 (70%), but only 60% and 59% similar to CfPV-2 and COPV, respectively. The FAP59/64 primers only amplified DNA from the positive control.

The presence of PV antigen was investigated using immunohistochemistry (Immunogen sodium dodecyl sulphate-disrupted bovine PV type1; Chemicon International Inc., Temecula, CA, USA) within both samples that contained amplifiable PV DNA. Immunoreactivity

against PV antigen was visible within the superficial epidermis overlying both lesions.

Additional large ulcerated masses have continued to develop within the ventrum and axilla during the 2 years since the plaques were first observed. During this time, the dog has not shown evidence of systemic or metastatic disease.

Discussion

Pigmented viral plaques are a well-recognized clinical entity of dogs. While pug and miniature schnauzer dogs are predisposed, plaques have also been reported in other breeds, often in association with immunosuppression.[5,9] Viral plaques typically develop on the ventrum or medial surfaces of the legs, reaching a maximal size of 1 cm in diameter before stabilizing.[1] While the plaques in the presently described dog had the same distribution as that previously described, the plaques did not stabilize at a small size, and multiple plaques 5–8 cm in diameter were observed. Histologically, viral plaques have been reported to contain mild to moderate epidermal hyperplasia and orthokeratosis.[1,9,13] In contrast, the epidermis in the presently described plaques was often markedly thickened with prominent folds. While large keratohyaline granules have been previously described in viral plaques,[1,13] the number and size of the granules in the present case was greater than in previous descriptions.

Malignant transformation of a viral plaque has been previously reported in four dogs. Single plaques were reported to progress to *in situ* SCC in a Rhodesian ridgeback[5] dog and in a miniature schnauzer dog.[9] Eight viral plaques on a fox terrier dog receiving immunosuppressive therapy progressed to *in situ* SCC during a 3-year period,[8] while four transformed to SCCs over a 5-year period in a hypothyroid Pomeranian dog.[7] The present dog was anaesthetized five times to remove 23 large ulcerated masses during a 20-month period. Although only five were confirmed histologically to be SCCs, all the masses had a similar gross appearance, suggesting that all were likely to be neoplastic. Therefore, the viral plaques in the presently reported dog underwent malignant transformation more rapidly and more frequently than in previous reports. Additionally, this is the first report of malignant transformation of multiple viral plaques in a dog without detectable immunodeficiency. Since there are few reports describing the malignant transformation of canine viral plaques, prediction of which plaques will become neoplastic is difficult. However, results from the present case suggest that larger viral plaques that contain greater histological changes may be predisposed to malignant transformation.

The role of PVs in inducing canine plaques is well established.[6] However, it is less certain whether or not malignant transformation of a viral plaque is also influenced by PVs. In humans, PVs cause neoplasia by disrupting normal cell regulation.[14] In the present case, the large size of the plaques and advanced histological lesions suggested that significant disruption of cell regulation had occurred, possibly causing neoplasm development. However, malignant transformation was limited to the sparsely haired skin of the ventrum and axilla, suggesting that exposure to sunlight was important in SCC development. In humans, some evidence suggests that cutaneous PV infection promotes skin cancer by preventing apoptosis, and stimulating proliferation, of epidermal cells containing DNA that has been damaged by sun exposure.[14] It is possible that PV infection and sun exposure also act as cofactors to promote the malignant transformation of canine viral plaques.

Epidermodysplasia verruciformis (EV) is caused by an inability to mount an immune response against cutaneous PV infection.[15] Although EV was first described in people with inherited defects in the *EVER*1 and *EVER*2 genes, histological lesions consistent with EV can also occur due to immunosuppression.[15,16] Humans with inherited EV develop multiple cutaneous plaques during infancy or childhood that often progress to SCC in sun-exposed skin before 40 years of age.[15] Although canine viral plaques have been proposed as analogous to EV,[9] canine viral plaques typically progress to SCC less frequently than human EV lesions.[1] Furthermore, in contrast to previously reported canine plaques,[1] histology of human EV reveals marked epidermal hyperplasia, with koilocytosis and the presence of nests or bands of large cells with pale cytoplasm and vacuolated nuclei with marginated chromatin within the superficial layers of the epidermis.[15,16] In the presently reported dog, viral plaques frequently and rapidly progressed to SCCs within sun-exposed skin. Additionally, although histology revealed only rare foci of koilocytosis, epidermal hyperplasia was prominent, and one section contained bands of keratinocytes with increased quantities of pale cytoplasm. Therefore, the viral plaques on the presently described dog demonstrated greater behavioural and histological similarity to human EV than those previously reported. Since the plaques did not develop until the dog was 7 years of age, an inherited immunodeficiency appears unlikely. However, if these lesions were due to an acquired inability to prevent cutaneous PV infection, the cause of this immunosuppression could not be identified. To the authors' knowledge, there has not been any investigation to determine whether *EVER* genes are present in dogs and have a comparable function to those in humans.

The PV DNA sequence amplified from both samples has not been previously reported. Papilloma viruses are classified according to their *L1* genes and, since only a portion of the *L1* gene was amplified, definitive classification is not possible.[17] However, as the sequence was only 71% similar to previously reported PV sequences, the detected PV may represent a new species.[17] The amplified sequence was most similar to the sequences of CPV-3, -4 and -5.[17] These PVs are all closely related and all cause canine viral plaques.[3] Supporting a causal association between the new PV and the viral plaques is the histological and immunohistochemical evidence of viral infection within the plaques and the failure to detect any other PVs. The consensus primers used in this study have previously been used to amplify COPV, CfPV-2 and CfPV-4 DNA[10,18] and are expected to amplify all seven previously reported canine PVs.[3]

In the present case, a novel PV DNA sequence was detected within viral plaques that had an atypical behaviour and histological appearance. It is possible

that these plaques were atypical because they were caused by a new species of PV. However, host factors more frequently determine the clinical effects of PV infection in humans.[15] Therefore, it is possible that the unusual features of the plaques in the present case were due to host factors within the dog rather than a function of the specific PV. Of the four dogs that have been previously reported to develop SCCs from viral plaques, PCR was used to identify the causative PV in only one.[5] This revealed the lesions to be associated with CfPV-3.[5] Since a different PV was detected in the present case, this suggests that multiple PVs can cause canine viral plaques that are predisposed to malignant transformation. This supports the hypothesis that host factors, rather than the specific PV type, may determine lesion behaviour.

The presence of increased numbers of large keratohyaline granules within the epidermis is considered evidence of PV infection.[1,16] Since such granules were present in all samples, it was surprising that PV DNA was amplified from only two of six samples. Possible explanations include the PV infection being only transient within the lesions and a low sensitivity of the primers for the PV DNA. In humans, infection of epithelium by PVs decreases as dysplasia within the epithelium increases.[19] If dysplasia similarly reduces PV infection in canine skin lesions, it is possible that PV DNA was not present in samples that contained more advanced lesions. The two samples that contained amplifiable PV DNA were a small pigmented plaque and a sample of *in situ* SCC, both of which may contain less dysplasia than a sample of invasive SCC. Alternatively, the detection limits of the primers for the PV amplified in this case are unknown. Papilloma virus DNA was detected in the *in situ* SCC sample that contained greater histological evidence of viral infection. If this sample contained a higher concentration of PV DNA, this could have allowed amplification. Other samples may have contained insufficient viral DNA to allow amplification by primers with low sensitivity. A low sensitivity of the consensus primers for the new PV may explain why this virus has not been detected in previous investigations of PVs within canine skin.[11,20]

In conclusion, the presently described case was unusual owing to the extensive development and frequent malignant transformation of the viral plaques. To the authors' knowledge, this is the first time that multiple viral plaques have undergone malignant transformation in an immunocompetent dog. The disease in this dog showed clinical and histological similarities to human EV; however, the old age of the dog at presentation suggests that an inherited defect is unlikely to be the cause of the disease. The use of PCR revealed DNA sequences from a previously unreported PV. Whether the atypical clinical and histological appearance of the plaques was due to infection by this specific PV or due to an unidentified underlying host factor remains uncertain.

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Résumé Les plaques virales canines sont des lésions cutanées rares induites par des papillomavirus (PVs). Les plaques sont en général de faible importance clinique chez les chiens, bien que de rares évolutions en carcinome épidermoïde (SCC) aient été rapportées. Nous décrivons ici le cas d'un chien croise de 7 ans qui a développé de multiples plaques pigmentées mesurant jusqu'à 8 cm de diamètre. De multiples masses nodulaires ulcérées étaient visibles avec les plaques sur l'abdomen et les plis axillaires. L'animal ne montrait aucun signe clinique d'immunodéficience et semblait par ailleurs, en bon état général. Au cours des deux années suivantes, cinq chirurgies ont été réalisées pour retirer 23 masses ulcérées qui variaient de 2 à 5 cm de diamètre. Cinq masses ont été soumises à l'histopathologie et étaient toutes des SCC. Chacune était entourée par un épiderme présentant les caractéristiques histologiques compatibles avec celles décrites dans les plaques canines. Suggérant une étiologie virale, un grand nombre de granules de kératohyaline étaient présents dans tout l'épiderme épaissi. De plus, des koïlocytes étaient présents focalement et un prélèvement contenant une bande de kératinocytes au niveau de l'épiderme superficiel contenant un cytoplasme pâle et une chromatine marginée. Les séquences d'ADN provenant d'un précédant PV non rapporté, ont été amplifiées à partir de deux échantillons et l'immunohistochimie a confirmé la présence d'antigène de PV. Les séquences d'ADN de PV étaient semblables à celles des PV canins précédemment associés avec la formation de plaques. Les plaques observées dans ce cas étaient inhabituelles compte tenu de leur rapidité de croissance, leur large taille et leur transformation maligne fréquente. On ne sait pas si ce comportement inhabituel est lié au PV spécifique détecté dans ce cas ou à des facteurs d'hôte de l'animal.

Resumen Las placas víricas caninas son lesiones poco comunes de la piel inducidas por papilomavirus (PVs). Las placas tienen generalmente poca significación clínica en perros, aunque en raras ocasiones se ha indicado la progresión a carcinoma de células escamosas (SCC). Aquí describimos el caso de un perro mestizo de siete años de edad que desarrolló numerosas placas pigmentadas de hasta 8 cm en diámetro. Múltiples masas nodulares ulceradas eran visibles en las placas en el vientre y axila. El perro no mostraba evidencia clínica de inmunodeficiencia y aparecía sano en otros aspectos. A lo largo de los dos años siguientes se realizaron cinco cirugías para remover 23 masas ulceradas que variaban en tamaño de dos a cinco cm de diámetro. Cinco de las masas se remitieron para estudio histopatológico y todas se diagnosticaron como SCC. Cada una estaba rodeada por epidermis que contenía características histológicas consistentes con las descritas en las placas caninas. Gran numero de gránulos de queratohialina estaban presentes en la epidermis engrosada, sugestivo de etiología vírica por PV. Además, se observaron focos de coilocitosis y una muestra contenía una banda de queratinocitos en la epidermis superficial con cromatina pálida y marginada. Se amplificaron secuencias de DNA de un PV no reportado previamente en dos muestras, y la inmunohistoquímica confirmó la presencia de antígeno de PV en ambos. Las secuencias de DNA de PV fueron similares a aquellas de PVs previamente asociados con la formación de placas. Las placas observadas en este caso eran poco usuales debido a su crecimiento rápido, gran tamaño, y transformación maligna frecuente. Se desconoce si este comportamiento poco habitual fue debido al PV específico detectado en este caso o debido a factores del hospedador canino.

Zusammenfassung Virale Plaques beim Hund sind seltene Hautveränderungen, die durch Papillomavirus (PVs) verursacht werden. Plaques haben normalerweise bei Hunden eine geringe klinische Signifikanz, obwohl beschrieben wurde, dass sie sich in seltenen Fällen zu einem Plattenepithelkarzinom (SCC) entwickeln können. Hier wird ein sieben Jahre alter Mischlingshund beschrieben, bei dem sich zahlreiche, im Durchmesser bis zu 8cm große dunkel pigmentierte Plaques entwickelten. Multiple ulzerierte knotige Umfangsvermehrungen waren innerhalb der Plaques am Bauch und in den Achseln sichtbar. Der Hund zeigte keine klinischen Anzeichen einer Immundefizienz und erschien ansonsten gesund. Im Verlauf der nächsten zwei Jahre wurden fünf chirurgische Eingriffe durchgeführt, um 23 ulzerierte Massen, die im Durchmesser von zwei bis fünf cm variierten, zu entfernen. Fünf dieser Umfangsvermehrungen wurden zur histologischen Untersuchung eingeschickt und alle wurden als SCC diagnostiziert. Jede war von Epidermis umgeben, die histologische Merkmale aufwies, die mit caninen Plaques vergleichbar waren. In der gesamten verdickten Epidermis kam eine große Anzahl an keratohyalinen Granula vor, was auf eine PV Ätiologie hinwies. Zusätzlich kamen stellenweise Koilozyten vor und eine Probe enthielt innerhalb der oberflächlichen Epidermis ein Band aus Keratinozyten, die ein blasses Zytoplasma und umrandetes Chromatin aufwiesen. Die DNA Sequenzen von einem früheren, noch nicht beschriebenen PV wurden aus zwei Proben amplifiziert und mittels Immunhistochemie wurde das Auftreten eines PV Antigens in beiden Proben bestätigt. Die PV DNA Sequenzen waren jenen caninen PVs äußerst ähnlich, die zu einem früheren Zeitpunkt mit der Bildung von Plaques in Verbindung gebracht worden waren. Die Plaques, die in diesem Fall beobachtet wurden, waren aufgrund ihres raschen Wachstums, ihrer Größe und der häufigen malignen Transformation untypisch. Es ist nicht bekannt, ob dieses untypische Verhalten auf das spezifische PV, welches in diesem Fall gefunden wurde, oder auf die Wirtsfaktoren innerhalb dieses Hunden zurückzuführen ist.

要約　犬のウイルス性局面はパピローマウイルス（PV）が誘発する一般的ではない皮膚病変である。局面はめったに扁平上皮癌（SCC）に進行しないため、犬では通常臨床的に重要ではない。7 歳の雑種の犬でみられた複数の最大直径 8 cm になる暗色の色素沈着した局面 について述べる。複数の潰瘍化した結節状の腫瘤が、腹部と腋窩の局面に認められた。犬には臨床的に免疫不全の兆候は認められず健康であった。2 年の間に、直径 2 cm から 5 cm の、潰瘍化した腫瘤 23 個を取り除くために 5 回の手術を行った。5 つの腫瘤について組織学的検査を行い、全てが SCC であった。SCC の組織のそれぞれは、犬のウイルス性局面の病理組織学的所見と一致する特徴を示す表皮に囲まれていた。肥厚した表皮全体に PV の病因を示唆する、多数の大型のケラトヒアリン顆粒が存在した。さらに空胞細胞が巣状に存在し、1 つの検体では表層表皮に染色性の低い細胞質と境界明瞭なクロマチンを含む帯状のケラチノサイトが見られた。DNA シークエンスで、今までに報告されていない PV が 2 つの検体から増幅され、免疫組織化学染色により両方の検体で PV 抗原を確認した。PV の DNA 配列は局面形成と関連した従来の犬の PV にもっとも類似したものであった。この症例で観察された局面は急速に増殖すること、大型であること、悪性への形質転換が頻繁であるという点で他と異なっていた。この一般的でない性質が、この症例で検出された特定の PV に起因するものか、犬の宿主要因であるかは不明である。

