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CLINICAL REVIEW

FELINE VIRAL PAPILLOMATOSIS
ABCD guidelines on prevention and management

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Overview: Papillomaviruses are epitheliotropic and cause cutaneous lesions in man and several animal species, including cats.
Infection: Cats most likely become infected through lesions or abrasions of the skin. Species-specific viruses have been detected but human and bovine related sequences have also been found, suggesting cross-species transmission.
Clinical signs: In cats, papillomaviruses are associated with four different skin lesions: hyperkeratotic plaques, which can progress into Bowenoid in situ carcinomas (BISCs) and further to invasive squamous cell carcinomas (ISCCs); cutaneous fibropapillomas or feline sarcoids; and cutaneous papillomas. However, papillomaviruses have also been found in normal skin.
Diagnosis: Papillomavirus-induced skin lesions can be diagnosed by demonstration of papillomavirus antigen in biopsies of skin lesions, or detection of papillomavirus-like particles by electron microscopy and papillomavirus DNA by polymerase chain reaction (PCR).
Treatment: Spontaneous regression might be expected. In cases of ISCC, complete excision should be considered if possible.

Virus

Papillomaviruses are small viruses containing circular double-stranded DNA and belonging to the family *Papillomaviridae*, which contains 30 genera.

Epidemiology

Papillomaviruses have been detected in several animal species and in man as a cause of cutaneous lesions.[1] In each host different papillomavirus types exist, which is also true for cats.[2] The viruses tend to be species-specific, but sequences related to bovine and human papillomaviruses have been found in cats, suggesting cross-species transmission.[3,4] Papillomavirus infection has also been detected in other felids including the Florida panther subspecies of cougar (*Puma concolor coryi*), bobcat (*Lynx rufus*), Asian lion (*Panthera leo persica*), snow leopard (*Panthera uncia*) and clouded leopard (*Neofelis nebulosa*).[5]

Pathogenesis

Papillomaviruses are epitheliotropic; infections usually occur through lesions or abrasions of the skin. Initially, the basal cells of the stratum germinativum are infected, which leads to hyperplasia and delayed maturation of cells in the stratum spinosum and granulosum. In the basal cells only early gene expression occurs, whereas viral protein synthesis and virion assembly occurs in terminally differentiated

European Advisory Board on Cat Diseases
The European Advisory Board on Cat Diseases (ABCD) is a body of experts in immunology, vaccinology and clinical feline medicine that issues guidelines on prevention and management of feline infectious diseases in Europe, for the benefit of the health and welfare of cats. The guidelines are based on current scientific knowledge of the diseases and available vaccines concerned.

The latest version of the feline viral papillomatosis guidelines is available at www.abcd-vets.org

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cells of the stratum spinosum and, more specifically, the stratum granulosum. Virus is present in the differentiated keratinised cells and is shed with exfoliated cells of the stratum corneum.

Papillomaviruses are commonly found in normal skin of different animals, including the cat;[6] this makes definitive proof of a causal relationship between the presence of papillomavirus sequences and skin lesions difficult.

Clinical signs

In cats, papillomaviruses have been associated with different skin lesions.

- First, **cutaneous hyperkeratotic plaques** seem to be most common in older and immunosuppressed cats – eg, feline immunodeficiency virus-infected animals.[7,8] However, plaques have also been reported in cats without any recognised immunodeficiency.[9] The plaques appear as flat, slightly raised scaly and variably pigmented lesions (Figure 1).
- Second, viral plaques can progress into **Bowenoid in situ carcinomas** (BISCs), and further to **invasive squamous cell carcinomas** (ISCCs). Feline BISCs occur often in pigmented, haired skin and appear as crusting, hyperpigmented and roughly circular lesions. Sunlight plays a role in the development of ISCCs, with lesions tending to be found in sparsely haired areas such as eyelids, nose and pinnae. A clear association between papillomavirus DNA (the *Felis domesticus* papillomavirus 2 – FdPV-2) and squamous cell carcinoma has been found; it was detected in all 20 BISCs examined, and in 17/20 cases of ISCC. However, FdPV-2 DNA could also be detected in 52% of normal skin swabs.[6] In one study, 50% of the sequenced papillomavirus DNA was most closely related to human papillomavirus DNA. In a recent study, papillomavirus DNA could not be detected in any of 30 oral squamous cell carcinoma samples screened,[10] which is at variance with earlier observations.
- Third, **feline cutaneous fibropapillomas** or **feline sarcoids** may be caused by papillomavirus infection. They are rare, occurring as skin neoplasms (nodular masses) found most commonly on the head, neck, ventral abdomen and limbs (Figure 2). The finding of a papillomavirus similar to bovine papillomavirus type 1, and the higher prevalence in cats with known exposure to cattle, suggest an association with the bovine virus.[11,12] This hypothesis is in line with the known association between bovine papillomavirus and equine sarcoids.
- Fourth, papillomaviruses have been associated with **feline cutaneous papillomas**.[13]

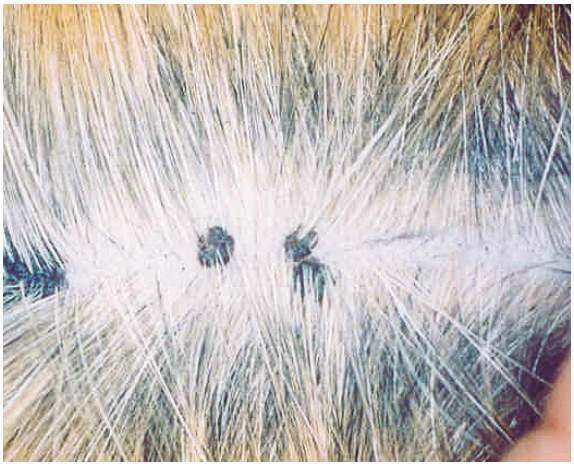

Figure 1 **Pigmented flat cutaneous papillomas.** *Courtesy of Herman Egberink, PhD thesis, Utrecht*

Figure 2 **A case of sarcoid in a patient presented at the Utrecht Companion Animal Clinic; diagnosis was verified histologically, but the viral etiology was not established.** *Courtesy of Y Schlotter, Companion Animal Clinic, Veterinary Faculty, Utrecht University*

Diagnosis

A biopsy from a skin lesion can be taken for histopathological examination and immunohistochemical staining of papillomavirus group-specific antigens. By electron microscopy, intranuclear papillomavirus-like particles might be demonstrated in keratinised cells. Also PCR can be used to demonstrate papillomavirus DNA in the lesions and for identification of the viral strain by further sequencing. However, the presence of papillomavirus DNA in normal skin of cats makes interpretation of positive PCR results of skin lesions difficult [EBM grade I].

Disease management

No specific treatment is known. In immunocompetent cats, spontaneous regression can be expected, as is also seen in dogs, but it may take a long time, up to several months

In immunocompetent cats, spontaneous regression can be expected, but it may take several months.

KEY POINTS

- Papillomavirus infections are associated with skin lesions but the virus can also be found in normal skin.
- Besides cat-specific papillomaviruses, DNA sequences most closely related to human and bovine wart viruses have been detected in skin lesions.
- The diagnosis is supported by the intralesional detection of viral antigen or DNA.
- There is no specific treatment for papillomavirus-induced skin lesions.

[EBM grade IV]. Imiquimod (Aldara), used for topical treatment of Bowen's disease in humans, has never been thoroughly evaluated in cats with this condition; a response was noted but no conclusion with respect to the efficacy of the drug in cats can be drawn [EBM grade III].[14] In this study the ISCC lesions were also papillomavirus antigen negative. Feline ISCCs tend to slowly metastasise. Therefore, if the anatomical location allows, complete excision might be curative.

There are no vaccines available for papillomatosis in cats.

EBM grades
The ranking system for grading the level of evidence of various statements within this article is described on page 533 of this Special Issue.

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Conflict of interest

The authors do not have any potential conflicts of interest to declare.

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