

Feline sarcoid in a 1-year-old domestic short-haired cat caused by bovine papillomavirus type 14 in Switzerland

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Summary

A 1-year-old domestic short haired cat, living on a farm in Switzerland, was presented to the veterinarian with a 5 cm in diameter mass, bulging from her left nostril. The mass was only incompletely removed because of its unfavourable location. Histologically, the lesion consisted of an infiltrative growing spindleoid proliferation in close approximation to the epidermis and was diagnosed as a feline sarcoid tumour. The presence of Bovine Papillomavirus type 14 (BPV-14) specific DNA could be identified in the tissue by using two PCR assays. The amplified sequences of 194 and 549 base pairs (bp) were 99% and 100% identical with a virus isolated after autopsy, from a cat with feline sarcoid in the USA. The cat recovered completely after an even incomplete surgical excision and no recurrence could be observed 10 months later.

Keywords: feline sarcoid, *bovine Papillomavirus type 14*, cat, spindleoid neoplasia, surgery

Felines Sarkoid bei einer 1-jährigen europäischen Hauskatze ausgelöst durch bovines Papillomavirus Typ 14 in der Schweiz

Eine einjährige Bauernhofkatze zeigte einen 5 cm grossen Knoten an der linken Nasenöffnung, der aufgrund seiner Lokalisation nur unvollständig entfernt werden konnte. Hinsichtlich der infiltrativ wachsenden, spindelförmigen Proliferation wurde histologisch ein felines Sarkoid diagnostiziert. Die aus dem Gewebe isolierte DNA konnte durch zwei PCRs als solche von bovines Papillomavirus 14 (BPV-14) identifiziert werden. Die 194 und 549 Basenpaare (bp) langen, amplifizierten Sequenzen waren 99 bzw. 100% identisch mit einer von einem in den USA isolierten Virus, welches mit felinem Sarkoid in Zusammenhang gebracht wurde. Trotz unvollständiger Exzision, ist bis 10 Monate nach der Operation kein Rezidiv aufgetreten.

Schlüsselwörter: felines Sarkoid, *bovines Papillomavirus Typ 14*, Katze, spindelzellige Neoplasie, Chirurgie

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Introduction

Feline sarcoids (synonym: feline cutaneous fibropapillomas) are rare intradermal fibroblastic proliferations of cats living in rural areas. So far, feline sarcoids were reported in North America, New Zealand, England, Sweden and Australia (Schulman et al., 2001; Munday et al., 2010). These lesions resemble those described as equine sarcoids (Gumbrell et al., 1998; Schulman et al., 2001; Gross et al., 2005). Equine sarcoids are the most common skin tumours of horses and are divided into 5 different clinical entities (Martens et al., 2000). In cats, however, these different morphologies are not described. Sarcoids are caused by small double-stranded DNA papillomaviruses (PVs), which are classified into genera

based on the coding sequences of the highly conserved major capsid protein L1. The majority of PVs only infect epithelium and are highly host specific. The bovine papillomaviruses (BVPs) of the Deltapapillomavirus genus, however, have the ability to infect both epithelial and mesenchymal cells of different species (Bernard et al., 2010; Joh et al., 2011; Munday et al., 2014). Lesions caused by PVs in domestic cats may be oral papillomas (*Felis catus* (Fca) PV-1) (Munday et al., 2015), feline cutaneous viral plaques, Bowenoid carcinomas (FcaPV-2 and FcaPV-3) (Lange et al., 2009; Munday et al., 2013) and feline sarcoids. Feline sarcoids are spindleoid sarcomas of younger cats with close connection to the epidermis, which are reported not to metastasize but often tend to develop recurrences after incomplete surgical

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excision. The entire genomic sequence of PVs involved in feline sarcoids (FeSarPV) isolated from cats was recently published and classified as a Deltapapillomavirus. However, since DNA of this virus was also amplified from samples of normal skin and fibropapillomas of cattle (Munday et al., 2010; daSilva et al., 2012), it seems likely that feline sarcoids are due to cross-species infection by BPVs (Schulman et al., 2001).

Case history

The cat was presented to the veterinarian showing a slightly bulging mass on her left nostril measuring 1 cm in diameter. The mass was firm, alopecic and the surface slightly ulcerated (Fig. 1). A fine needle aspiration (FNA) was performed under anaesthesia with Domitor[®], (Provet AG, Lyssach, Switzerland) and Morphasol[®]-4, (Dr. E. Gräub AG, Bern, Switzerland) subcutaneously, followed by intravenous anaesthesia with Propofol[®] 2%, (Provet AG, Lyssach, Switzerland). Unfortunately, the FNA was not diagnostic. As a bacterial infection was suspected, an initial treatment with Veraflox[®], (Provet AG, Lyssach, Switzerland) 5 mg/kg b.w. (once daily) orally, was given. Six weeks later, the cat was presented again due to a massive growth of the lesion. The bulging mass on her left nostril measured now 5 cm in diameter (Fig. 2). An excision of this mass seemed inevitable.

Therapy

Under anaesthesia with the same protocol as mentioned above, the mass was surgically removed. A total excision

was not possible because of the location next to the left nostril. The wound was closed by a single button suture with Supramid[®] 3-0, (B. Braun Medical AG, Sempach, Switzerland). A small suture dehiscence occurred 10 days after surgery and was closed again with Supramid[®] (Fig. 3). Due to the incomplete excision of the mass, with “close margins”, the cat was given a Viscum Album Extract (VAE) as adjuvant treatment (injections with Iscador[®] P, Iscador AG, Arlesheim, Switzerland) followed by oral application with Viscum quercus praeparatum 3% Dilaq, (Iscador AG, Arlesheim, Switzerland).

Histology

The excised material was fixed in 4% buffered formalin for 24 h, dehydrated in a 70–95% ethanol series, followed by Xylol and paraffin embedding. Sections (2 to 3 µm) were mounted on glass slides and stained with Haematoxylin-Eosin (HE) using standard procedures. Histologically the mass consisted of spindle cells expanding the dermis and subcutis and was intimately associated with the epidermis. The neoplastic cells were oval to spindle with moderate amounts of pale basophilic cytoplasm with indistinct cell borders (Fig. 4) and round to oval nuclei showing a finely stippled chromatin pattern and only slightly visible nucleoli, moderate anisocytosis, anisocaryosis and anisonucleoliosis. The neoplastic cells were embedded in abundant extracellular matrix (mucopolysaccharides), separating the adnexa and often forming whorls around small blood vessels or hair follicles. The mitotic rate was moderate with 11 mitotic figures in 10 high power fields. Within the tumour were small areas of

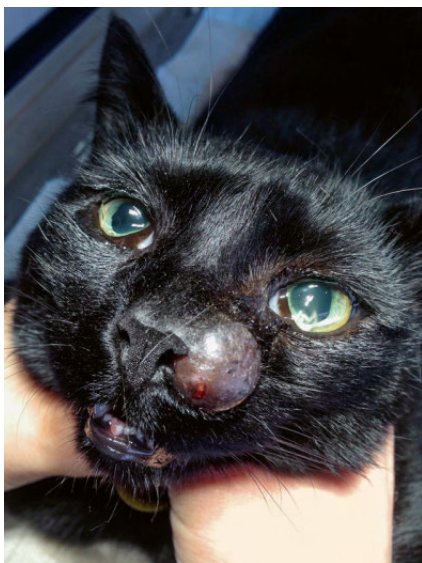


Figure 1: Cat at first presentation with a bulging mass measuring 1 cm in diameter.



Figure 2: The cat at the second presentation 2 months after the first treatment attempt. The mass grew up to 5 cm in diameter.

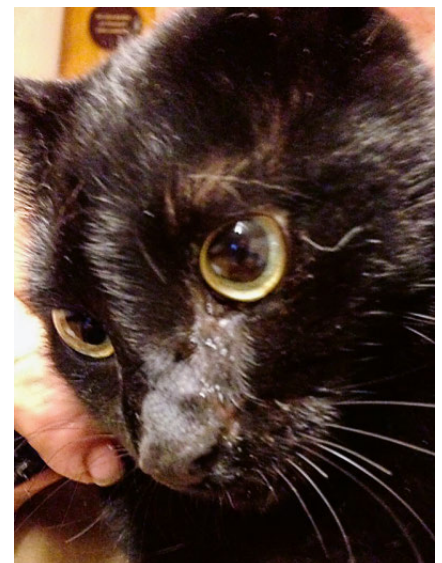


Figure 3: Complete healing of the operation field 6 months after the closure of the suture dehiscence.

coagulative necrosis randomly distributed visible. The overlying epidermis was multifocally ulcerated or if still intact, hyperplastic, forming high rete ridges and were strongly pigmented by melanin. In the stratum spinosum were deposited a moderate amount of keratohyalin granula (Fig. 5).

Molecular analysis

DNA was extracted from the center of the formalin fixed tissue using the QIAamp DNA Mini Kit (Qiagen, Hombrechtikon, Switzerland) according to the manufacturer's instructions. For detection of viral DNA of FeS-arPV/BPV14, a previously reported primer set jmpSA-F (5'-GGAACAAACCTCACAATCAC-3') and jmpSA-R (5'-CCAGTTCTCTAATACTGAGG-3') was used (Munday et al., 2010). As these primers just amplify a short product of 194 bp, additional primers amplifying a 549 bp product in the L1 region (5771 to 6319) of the BPV14 genome BPV14for (5'-TGG TAA AGA GGT GCC CAA AG-3') and BPV14rev (5'-GCT TCC TCA GCC ATT TTG AG3-') were designed. PCR was performed with a reaction mix containing 8 µl water, 2 µl of each forward and reverse primer (10µM each), 1µl extracted DNA as template and 12µl REDTaq ReadyMIX (SIGMA-ALDRICH, Buchs, Switzerland) in a total volume of 25 µl. The cycling program for all PCR assays started with a denaturation step of 3 min at 94 °C, followed by 40 cycles of 30 sec at 94 °C, 30 sec at 55 °C and 30 sec at 72 °C. PCR products were separated by agarose electrophoresis. Both primer sets for feline sarcoid virus BPV14 amplified bands of the expected size. The PCR amplicons were excised from the agarose gel and purified using Zymoclean Gel DNA Recovery Kit (ZYMO RESEARCH, Irvine, USA) according to the manufacturer's protocol. Nucleotide sequences were determined (Microsynth, Balgach, Switzerland) and compared to the published reference sequences of BPV14 with the NCBI Basic Local Alignment Search Tool ("BLAST") (<http://www.ncbi.nlm.nih.gov/blast/Blast.cgi>) (Altschul et al., 1990). The sequencing results of the shorter and the longer amplicon showed 99% and 100% identity to the published BPV14 sequence (Genbank accession #KP276343).

Discussion

Our sequences covering 743 bp (194 bp and 549 bp) were identical to the L1 of BPV14, which was sequenced and classified from a cat in the USA (Munday et al., 2015). Similar to our case, the cat had a rapidly growing mass at the nose tip. Therapy attempts with intralesional injections of cisplatin and surgery were performed twice, but the mass regrew within only 2 months. When the

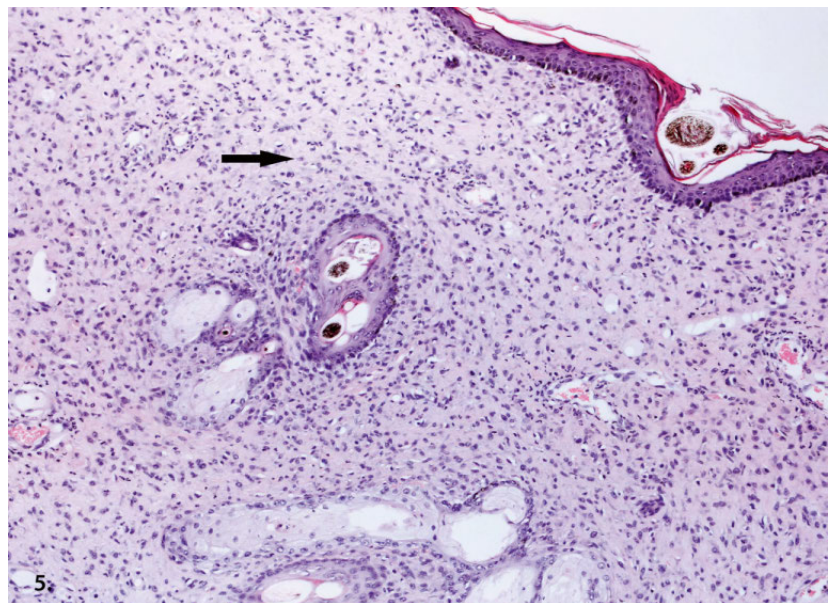


Figure 4: Mesenchymal neoplasia adjacent to the epidermis with the spindleoid to stellate cells embedded in abundant extracellular matrix (mucopolysaccharides), separating the adnexa and forming whorls around small blood vessels. HE staining, 4x magnification.

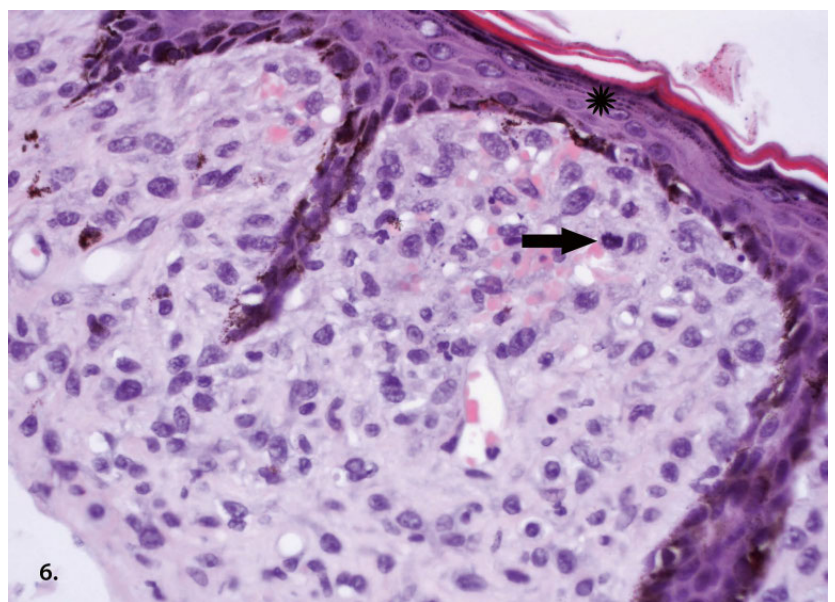


Figure 5: Round to oval nuclei with moderate anisocaryosis. A mitotic figure (arrow) is visible just underneath the epidermis. In the stratum spinosum a moderate amount of keratohyalin granula (star) were deposited. HE staining, 40x magnification.

tumour interfered with eating the cat was euthanized (Munday et al., 2015). Veterinarians tend to classify mesenchymal tumours of the skin and subcutis into soft tissue sarcomas and apply then a grading system. Such grading systems are applied for canine and human tumours (Coindre et al., 2006; Dennis et al., 2011) but not for those from cats. Adaption and implementation of these grading systems would classify the herein described tumour as soft tissue sarcoma grade II according

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to the morphology of the neoplastic cells, the mitotic rate and necrotic area within the tumour. Higher mitotic rate is often prognostic for reduced survival time in many tumours (Coindre et al., 2006; Esplin et al., 2008; Dennis et al., 2011; Thompson et al., 2011). and such grading would imply a short disease free period with a risk of metastasis that might have led to euthanasia of the cat. Although the tumour resembles closely equine sarcoids, it could readily have been misdiagnosed as fibrosarcoma, which is another kind of mesenchymal neoplasia with some risk to metastasize (Morrison and Starr, 2011). Our case taught us the importance to differentiate and to recognize these lesions as feline sarcoids since, feline sarcoids are not reported to metastasize. The accurate diagnosis of the origin of cells and aetiology is particularly more important than the classification with a grading system, which could lead to wrong prognostic outcome. If the neoplasia cannot be excised completely, radiation therapy is recommended to prevent recurrence (Gross and Affolter, 1998). The

owner of the cat reported herein disapproved the radiation because it is extensive, costly and the cat has to deal with frequent anaesthesia and possible side effects. If the VAE treatment had any immune-modulating effect as reported in the literature, remains unanswered in our case (Bussing, 2006).

In summary, if a radiation therapy is not an option, we suggest it is still worth to attempt surgery even when it is difficult to excise the mass completely. The cat has now been free of disease for 10 months. Although we cannot assure its cancer free state, the measures have prolonged its life and may even lead to complete recovery.

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