

Microchip-associated fibrosarcoma in a cat

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Conflict of Interest

No conflicts of interest have been declared.

Abstract

A 9-year-old, neutered male cat was presented for a subcutaneous mass on the neck. After surgical removal of the mass, a pet identification microchip was found within the tumour. Histological examination of the mass revealed typical features of the feline postinjection sarcoma. The cat had never received injections at the tumour site; all routine vaccinations were administered in the hindlimbs. Few cases of sarcomas developing at the site of microchip application have been reported in animals, although the contributory role of vaccine administrations has not been ruled out. This is the first report of a microchip-associated fibrosarcoma in a cat. Adherence to American Association of Feline Practitioners vaccination guidelines, avoiding the interscapular area, enabled confirmation of the definitive aetiology of the neoplasia.

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In November 2009, a 9-year-old, neutered male domestic short-haired cat was examined by the referring veterinarian for a 1.5 cm × 2 cm firm subcutaneous mass at the base of the left side of the neck. According to the medical records, the cat was vaccinated for calicivirus, herpesvirus, parvovirus (FVRCP) and rabies on an annual basis and identified by a microchip. The owner reported noticing the mass 2 months prior to presentation and presented the cat for examination because of recent rapid growth.

Physical examination, thoracic radiographs, complete blood count and biochemical profile did not identify any other clinical abnormalities. The mass was excised with 2 cm surgical margins, both lateral and deep to the tumour. The tissue was fixed in 10% neutral buffered formalin for histological examination. Upon examination and trimming of the tissue, an intact animal transponder device embedded in the adipose tissue, deep to the mass, was found (Figure 1). Representative tissue specimens were routinely processed and paraffin embedded

for histopathological examination. Histologically, a poorly demarcated nodular subcutaneous mass extending into the dermis was observed. The nodule was composed of poorly differentiated spindle-shaped neoplastic cells surrounding a central area of necrosis, leading to cavitation with purulent debris (Figure 2). The spindle-shaped cells, arranged in irregular and partly interlacing bundles, showed pleomorphic elongated nuclei with prominent multiple nucleoli and abundant amphophilic cytoplasm. Mitotic rate was high (three or four per high-power field), with unusual mitotic figures (Figure 3). Numerous histiocytic cells were scattered in the mass, with the sporadic presence of multinucleated cells. Severe lymphoid infiltrate, often arranged in dense aggregates, was present at the periphery of the neoplastic growth. Neoplastic cells were not present at the surgical margins.

Immunohistochemistry was performed on 4- μ m-thick tissue sections by an automated Bond immunostainer (maXTM A; Menarini Diagnostics, Florence, Italy) using primary antibodies against vimentin intermediate filaments, S-100, smooth muscle actin, desmin and CD79 (Dako North America, Inc., Carpinteria, CA, USA); and CD18 and CD3 (Dr P. F. Moore, University of California at Davis, CA, USA). The Bond™ Polymer refine detection containing a peroxide block was used as the detection system, and 3,3-diaminobenzidine tetrahydrochloride (Leica Biosystems, Newcastle Ltd., UK) was applied as chromogen for all antibodies except for S-100, for which fast red was used. All sections were counterstained with Mayer's haematoxylin.

Neoplastic cells showed diffuse and strong expression of vimentin, and numerous peripheral bundles were also positive for smooth muscle actin (Figure 4); these find-



Figure 1. Surgically excised, formalin-fixed skin and subcutaneous mass from the cat. Cut section reveals a nodular cavity subcutaneous lesion with a microchip embedded in the adipose tissue. Scale bar represents 2.5 mm.

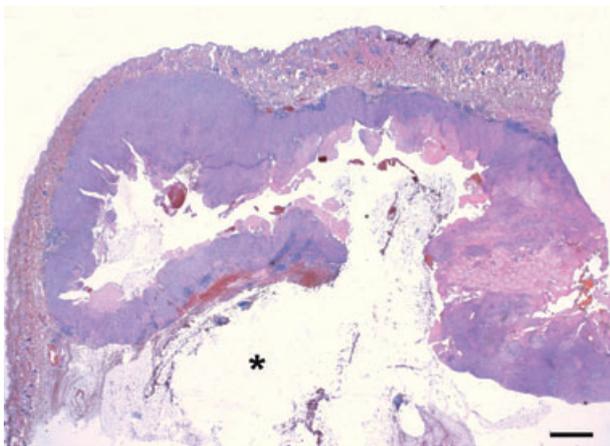


Figure 2. Excised subcutaneous mass. The tumour extends into the dermis and is composed of a dense fibroblast proliferation surrounded by lymphoid aggregates. The microchip (*) was found in the adipose tissue connected with the central cavitation of the mass. Haematoxylin and eosin. Scale bar represents 680 μm .

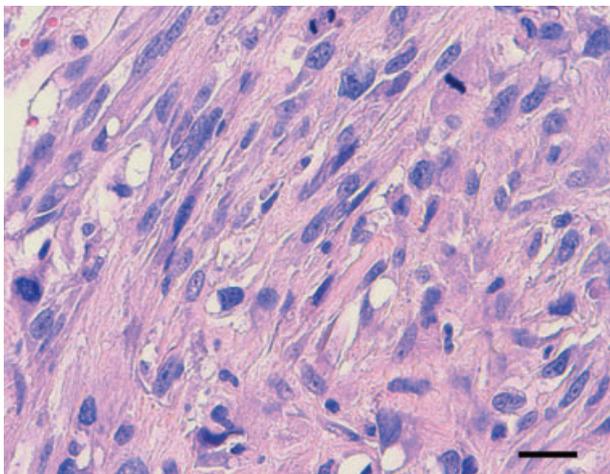


Figure 3. Photomicrograph of subcutaneous tumour. Poorly differentiated spindle cells arranged in irregular and partly interlacing bundles, showing abundant cytoplasm, pleomorphic nuclei with prominent multiple nucleoli and a high mitotic rate. Haematoxylin and eosin. Scale bar represents 25 μm .

ings were consistent with myofibroblastic differentiation. Numerous histiocytic cells were identified by CD18 immunostaining that predominantly surrounded the necrotic area. Lymphoid aggregates were primarily composed of CD3-positive lymphocytes. A diagnosis of fibrosarcoma with typical features of feline postinjection sarcoma was made. The owner declined postoperative radiation therapy, and the cat recovered from surgery without any complications. No recurrence of the tumour was seen 11 months after surgery, and the cat is still in a healthy condition at the time of writing.

The historical information, obtained from the referring veterinarian, revealed that the cat had been implanted with an Indexel (Meriel, Lyon, France) microchip in the dorsal neck area 4 years prior to the development of the neoplasia. The Indexel microchip is equipped with an antimigrational capsule, located in the anterior part of the

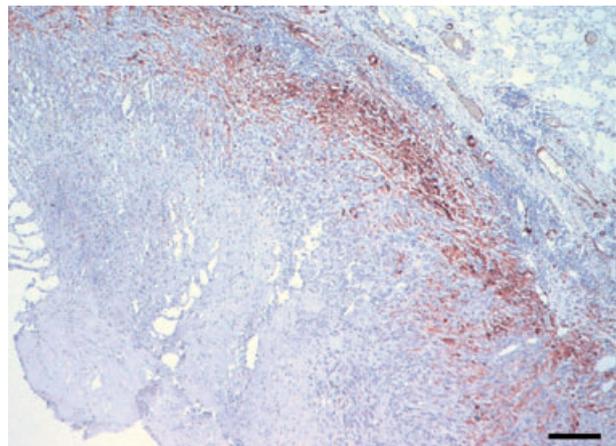


Figure 4. Photomicrograph of subcutaneous tumour. Peripheral bundles with myofibroblastic differentiation highlighted by strong immunoreactivity for smooth muscle actin antibody. Actin 1A4 immunostaining; peroxidase method with haematoxylin counterstain. Scale bar represents 100 μm .

microchip, to prevent migration after implantation. The capsule is made from bioglass, the main components of which are silicon, sodium, calcium, potassium, magnesium, iron and aluminium, and has been classified in the silicon sodium group.¹

All vaccinations had been administered in the hindlimb muscles, according to American Association of Feline Practitioners vaccination guidelines.²

Implantation of a microchip is considered a safe, relatively painless and permanent means of identification. The Indexel microchip is equipped with an antimigrational capsule, located in the anterior part of the microchip, ensuring encapsulation by fibrous tissue and preventing migration after subcutaneous implantation.^{1,3} Despite the implantation of millions of microchips,⁴ development of tumours at microchip implantation sites appears to be a rare event. One case of liposarcoma and one case of fibrosarcoma at microchip implantation sites have been reported in dogs.^{5,6} One case of fibrosarcoma adjacent to the site of microchip implantation has been recently described in a cat, although the authors could not exclude the possibility that vaccines repeatedly administered at the same site were responsible for the neoplastic growth.⁷ A leiomyosarcoma in a zoo bat,⁸ two soft tissue sarcomas in small zoo mammals⁹ and soft tissue tumours in laboratory rodents^{10,11} have been also described at the site of implanted microchips. The microchip-associated tumours so far reported were mesenchymal in origin,¹² and the mechanism of carcinogenicity is suspected to be foreign body induced.¹⁰⁻¹³ In the case reported here, the microchip was embedded in the subcutaneous adipose tissue, connected to the necrotic cavity within the tumour, and the presence of scattered macrophagic and multinucleated cells and lymphoid aggregates supported this as the aetiological hypothesis. Furthermore, on the basis of the history, the contributory role of vaccinations can be ruled out.

An implant should evoke as little reaction as possible, because inflammatory cells can produce and secrete proteolytic enzymes.¹⁴ If the surface of the implanted device

causes permanent irritation following chronic inflammation, it is likely that proteolytic enzymes will be produced and released continuously, resulting in collagenolysis and/or tissue reconstruction and reduced tissue stability.

Recently, Linder *et al.*¹⁵ showed that the surface material of a microchip transponder can influence the composition of the fibrous tissue capsule and the tissue reaction *in vivo* as well as cell growth *in vitro*. The *in vivo* data were obtained from mice and the *in vitro* data using feline fibrosarcoma cell lines. *In vitro*, feline cell growth in the presence of titanium microchips was much better than in the presence of any of the other devices tested; in mice, mild to moderate granulomatous inflammation was observed around titanium particles. *In vivo*, a special polymer, parylene C (Pet-ID, UK) elicited almost no inflammatory reactions in the surrounding tissue, whereas *in vitro* only a moderate number of cells could be detected on the parylene C transponders. The results may be applicable to other species, but differences between different species and cell lines cannot be excluded. Indeed, a systematic study would add greatly to our understanding of the process of tumourigenesis as related to microchip implants. This could help demonstrate that microchip-associated tumours stem from a foreign-body reaction to the external surface of the transponder alone (i.e. glass capsule and polypropylene sheath) rather than from specific features of the device, such as its capacity as a radio-frequency transponder.

In September 1997, the British Small Animal Veterinary Association (<http://www.bsava.com/resources/microchipadvice>), in conjunction with the Federation of European Companion Animal Veterinary Associations, launched a scheme to record information on adverse reactions to microchips,^{16–18} in order to increase the knowledge of possible aetiological causes and support the standardization of materials and implanting procedures.

In general, chronic inflammation alone is not thought to be capable of inducing neoplastic transformation, and host factors are considered to be essential in the transformation of cells. In cats there is a casual relationship between chronic inflammation and development of sarcomas, as observed in postvaccinal sarcomas,^{19,20} ocular post-traumatic sarcomas²¹ and a fibrosarcoma at the site of a deep nonabsorbable suture.²² Injections of vaccines or therapeutic drugs into the subcutis can result in granulomatous nodules. Injected materials, such as adjuvants and other vaccine components, are highly antigenic and can incite a local and persistent immunological response, resulting in a palpable subcutaneous nodule.²³ Antigen load, degree of persistent inflammation and eventual fibroblastic proliferation are thought to be important factors predisposing to tumour development in cats. It is speculated that during tissue repair, fibroblasts and myofibroblasts are stimulated by the immunogenic substances in the vaccine reaction site and this, in combination with other factors, such as oncogene alterations or unidentified carcinogens, leads to malignant transformation of cells. Dubielzig *et al.*²¹ report that penetrating traumas involving the ocular globe, particularly with lenticular destruction, increase the risk of developing ocular sarcomas in cats. Lenticular capsular rupture with destruction of the lenticular substance by phagocytosis and chemical

breakdown would usually be expected to contribute to a low-grade inflammatory disease over a long period of time. Lenticular capsular rupture would also lead to the release of lenticular epithelial cells, which are known to undergo fibrous metaplasia and may contribute to proliferative ocular disease. The latency period between trauma and development of neoplasia is often several years.²¹

In the case described by Buracco *et al.*,²² an uncoated, braided, nonabsorbable material, applied 7 years before, was supposed to be responsible for a chronic granulomatous response and development of neoplasia.

Despite the huge number of microchips implanted annually in pets,⁴ the number of reported adverse reactions is limited; therefore, the use of microchips for pet identification should not be discouraged. However, veterinarians should be aware that tumours can develop at microchip sites, and owners should be educated to monitor these sites for long periods of time, in order to promote early detection as well as better definition of the incidence of tumours. Data from experimental studies showed that the length of implant exposure ranged from 6 months to 2 years in laboratory rodents.^{24,25} In the cases so far reported in dogs and cats, the length of implant exposure ranged from 7 months to 4 years. Notwithstanding, more data are necessary to better define the time of tumour development. In addition, clinicians are encouraged to follow current vaccine recommendations as described in the 2006 American Association of Feline Practitioners Feline Vaccine Advisory Panel Report.² Following Vaccine-Associated Feline Sarcoma Task Force recommendations on standardization of vaccination protocols would help veterinarians to monitor vaccine site reactions and better correlate a given vaccination and subsequent tumour development.

These recommendations include administering any vaccine containing rabies as distally as possible in the right hindleg, administering FeLV vaccinations as distally as possible in the left hindleg, and injecting FVRCP (with or without *Chlamydia*) vaccines in the right shoulder. This would prevent administration of vaccines at the site of microchip implantation, avoiding consequent micro-environment alterations that could increase the risk of sarcoma development and allowing researchers to determine the aetiology of tumours more easily.

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Résumé Un chat mâle castré de 9 ans est présenté pour une masse sous-cutanée sur le cou. Après exérèse chirurgicale de la masse, un transpondeur a été trouvé au sein de la tumeur. L'examen histologique de la masse a révélé des caractéristiques typiques de sarcome félin post-injectionnel. Le chat n'avait jamais reçu d'injection au site de la tumeur; tous les vaccins de routine étaient administrés dans les membres postérieurs. De rares cas de sarcome se développant au site d'injection de transpondeur ont été rapportés chez l'animal, bien que la contribution des administrations vaccinales n'ait pas été exclue. Ceci est le premier cas rapporté de fibrosarcome félin associé à un transpondeur. L'appartenance à l'AAFP (American Association of Feline Practitioners), recommandant d'éviter la vaccination dans les zones inter-scapulaires, a permis de certifier l'étiologie définitive de la tumeur.

Resumen Un gato macho castrado de nueve años se presentó debido a la presencia de una masa subcutánea en cuello. Después de la extirpación quirúrgica de la masa, se encontró un microchip de identificación dentro del tumor. El examen histológico de la masa reveló características típicas de sarcoma felino por inyección. El gato nunca había recibido inyecciones en el sitio del tumor; todas las vacunaciones rutinarias fueron administradas en los miembros posteriores. Se han reconocido pocos casos de sarcomas en el sitio de implantación del microchip en animales, aunque el papel contribuyente de administraciones vacunales no se había eliminado. Éste es el primer informe de un fibrosarcoma asociado con microchip en un gato. La adherencia a la pautas de vacunación felina de la asociación americana de veterinarios de gatos (AAFP) que evitan el área interescapular permitió confirmar la etiología definitiva de la neoplasia.

Zusammenfassung Ein neun Jahre alter kastrierter Kater wurde mit einer subkutanen Umfangsvermehrung am Nacken vorgestellt. Nachdem die Umfangsvermehrung chirurgisch entfernt worden war, wurde ein Mikrochip zur Identifizierung von Heimtieren in dem Tumor gefunden. Die histologische Untersuchung der Masse zeigte typische Merkmale des felinen Sarkoms, welches nach Injektionen auftritt. Die Katze hatte an der Stelle des Tumors nie Injektionen erhalten; alle routinemäßigen Vakzinierungen waren in den Hinterextremitäten verabreicht worden. Bei Tieren sind nur wenige Fälle von Sarkomen beschrieben, die an der Stelle der Mikrochip-Implantation entstanden waren, wobei eine beitragende Rolle der Verabreichungen von Impfungen bisher nicht ausgeschlossen wurde. Es handelt sich hierbei um den ersten Fallbericht einer Katze, die aufgrund der Mikrochip-Implantation ein Fibrosarkom entwickelte. Die Einhaltung der Richtlinien zur Vakzinierung der American Association of Feline Practitioners (AAFP), wobei die inter-scapuläre Gegend zu vermeiden ist, erlaubte die Feststellung einer eindeutigen Ätiologie dieser Neoplasie.

要約 9歳齢の去勢した雄猫が頸部の皮下腫瘍を主訴に来院した。腫瘍の外科的切除のあと、腫瘍内にペット認識用マイクロチップが発見された。腫瘍の組織学的な検査は猫の注射後肉腫の典型的な特徴を示した。その猫は腫瘍部位に一度も注射されたことがなかった；すべての定期的なワクチン接種は後肢に接種されていた。ワクチン接種が原因となった要因は除外されていないが、動物において、肉腫がマイクロチップ投与の部位に発生した報告はほとんどない。これは猫のマイクロチップ関連性線維肉腫の初めての報告である。米国ネコ科開業医協会(AAFP)のワクチンガイドラインを厳守するのであれば、腫瘍の明らかな原因と主張されている肩甲間へのワクチン接種は避けるべきである。