Myofibroblastic sarcoma originating at the site of rabies vaccination in a cat

Richard R. Dubielzig, Kathleen L. Hawkins, Paul E. Miller

Immunoproliferative reactions associated with subcutaneous administration of rabies vaccinations have been reported in cats. Recent reports indicate that cats are also at risk of developing sarcomas at rabies vaccination sites. Additionally, fibrosarcomas in cats have been reported as common at vaccination sites. A g-year-old spayed female Siamese cat owned by 1 of the authors (PEM) was inoculated with a deep intramuscular injection into the caudal left thigh with a commercial killed rabies vaccine. Approximately 4 months after the injection, a firm nodule was palpated at the vaccination site. The nodule grew slowly for the next 4 weeks. Upon surgical exploration 5 months postvaccination, the nodule was composed of a yellow-white firm mass, which diffusely infiltrated between and through the semimembranosus and semitendinosus muscles. The tumor was classified as a fibrosarcoma on histopathologic examination and was determined to be incompletely excised. A tumor was palpable again 12 months after vaccination, and the leg was subsequently amputated 14 months after vaccination. The cat remained free of disease until 35 months after vaccination, when the tumor recurred at the amputation stump. The cat was euthanized 50 months after vaccination. At the time of euthanasia, the cat had chronic constipation secondary to tumor infiltration into the pelvic canal. Tissues obtained from the amputation surgery were fixed in formalin and in glutaraldehyde fixatives for light and electron microscopy.

Light microscopic examination showed an invasive neoplasm composed of plump spindle cells with abundant cytoplasm and centrally positioned round nuclei with multiple nuclear folds. Mitotic figures were common. Extracellular collagen was minimal (Fig. 1). There was an intense infiltration of lymphocytes around the margins of the mass. For...
In light of recent observations on the association between spindle cell sarcomas and rabies vaccination in cats, cats may be at risk of developing malignant tumors with morphologic features of myofibroblasts at rabies vaccination sites. Spindle cell tumors expressing smooth muscle actin have also been reported to originate in the eyes of cats following severe ocular trauma.\(^{5,3,8}\) These tumors also express thick, smooth extracellular basement membrane material, and the cell of origin is speculated to be the released lens epithelial cell.\(^{1,3-8}\) Lens epithelial cells are known to express smooth muscle actin in association with proliferation and spindle cell metaplasia.\(^2\)

The phenomenon of sarcoma formation at vaccination sites deserves urgent attention. The cause-and-effect relationship between vaccination and sarcoma formation must be investigated with carefully designed prospective studies looking at the fate of cats vaccinated with different products and different techniques. The possibility that cats are at risk of cancer development associated with the proliferative phase of wound healing might be studied in vitro using tissues from wound healing.

**Acknowledgments.** We acknowledge Wendy S. Rosbury, Katherine Toy, and Thomas G. Jasper for their assistance and expertise in performing the immunohistochemistry.

---

**References**


---

**Figure 2.** Electronmicrograph of neoplastic cells from vaccination site in a cat, showing bundles of filaments adjacent and parallel to the plasma membrane. Dense areas (arrows) are seen in the filaments. The arrangement is typical of myofilaments seen in myofibroblasts. Bar = 0.4 µm.

Malin-fixed paraffin-embedded tissue was immunohistochemically stained for high- and low-molecular-weight cytokeratin, vimentin, desmin, muscle-specific actin, myoglobin, myosin, S-100 protein, glial fibrillary acid protein (GFAP), and neurofilament. Neoplastic cells stained positively for vimentin, actin, and myoglobin but were negative for all other markers, including desmin. The myosin staining was uninterpretable because of background staining.

Ultrastructurally, tumor cells had bundles of filaments with dense areas. Filaments were oriented adjacent to and parallel with the plasma membrane (Fig. 2). The pattern of filament aggregation adjacent and parallel to the plasma membrane with dense growth is typical of myofilaments seen in myofibroblasts.\(^{10}\)

Beginning approximately 6 days after inducing a surgical wound, proliferating fibroblasts are known to express smooth muscle actin.\(^1\) Under normal circumstances, the expression of smooth muscle actin in proliferating fibroblast cells continues until about 30 days postwounding and then ceases.\(^1\) Desmin and myoglobin are not expressed in proliferating fibroblasts.\(^3\) The term “myofibroblast” has been used to describe fibroblasts that proliferate in granulation tissue formation. These cells are similar to the cells found in the post-vaccinal sarcoma.

Spindle cell tumors showing myofibroblastic differentiation occur in humans. The criteria used to classify tumors as myofibroblastic are vimentin and actin expression and the finding of bundles of myofibers with electron-dense areas running parallel and adjacent to the plasma membrane.\(^{5,8}\) Desmin is occasionally expressed in myofibroblastic cells in both neoplasms and in wound healing.\(^{1,8,10}\) The cells in this case expressed vimentin and actin but not desmin. Bundles of myofibrils with electron-dense areas were also seen.