Vaccine-Associated Feline Sarcoma Symposium

Introduction

On July 25, 1998, a symposium on vaccination site sarcomas in cats was held during the 135th Annual Meeting of the AVMA in Baltimore, Md. The symposium was cosponsored by the Vaccine-Associated Feline Sarcoma Task Force and the Arm & Hammer Division of Church & Dwight Co. Inc. Dr. William Inskeep, a member of the AVMA Council on Research, presided over the symposium, during which up-to-the-minute information on these tumors was presented. Topics included historical review, risk factors, pathogenesis, etiology, and treatment of the disease; formation of the task force and its funding of studies; and education of and communication between the public and veterinarians regarding the disease. This was the first such symposium to be convened devoted to the subject.

Historical review and current knowledge of risk factors involved in feline vaccine-associated sarcomas

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In the late 1980s, an increase in some rather stereotypical inflammatory injection site reactions was recognized in canine and feline biopsy specimens sent to the University of Pennsylvania surgical pathology service. Questionnaires sent to veterinarians confirmed that these reactions were in sites of rabies vaccine administration. Pennsylvania had recently mandated rabies vaccination in cats. Shortly thereafter, sarcomas were observed at these vaccination sites in cats. These sarcomas had histologic features similar to those of injection site inflammatory reactions; association with the panniculus muscle, peripheral lymphoid aggregates, and macrophages containing gray-brown globular material. With help from collaborators, this material was documented to be aluminum, a common vaccine adjuvant. The association between injection site reaction and sarcoma development was circumstantial, but compelling. It was so compelling that the author wrote a letter to the editor of the Journal of the AVMA warning veterinarians of the possible link between vaccination and sarcoma formation in cats. Shortly thereafter, Kass et al., at the University of California, using sophisticated statistical analyses in a retrospective study of 345 cats in California and Hawaii, confirmed causal and temporal relations between FeLV and rabies vaccinations, and sarcoma development. Moreover, they reported that reaction to the vaccines was additive (i.e., the likelihood of sarcoma development increased with the number of vaccines given simultaneously at the vaccine site).

At about the same time, the author, in conjunction with Tufts University School of Veterinary Medicine, was conducting a retrospective study (n = 239 cats) comparing fibrosarcomas arising at vaccination sites and at nonvaccination sites. Results indicated that vaccine-associated sarcomas were larger and more aggressive, had a higher recurrence rate than did fibrosarcomas in other sites, and that they developed in younger cats. In neither retrospective study was there evidence of sex or breed predilection, or any obvious association with FeLV or FIV infection. In a later study by Ellis, neither FeLV glycoprotein 70 nor the FeLV long terminal repeat region was detected in 130 feline vaccine-associated sarcomas. Specific vaccines were not incriminated in either study, and adjuvanted and nonadjuvanted vaccines were found to be associated with sarcoma development.

One thing that results of either retrospective study could not define was the true incidence or prevalence of vaccine-associated sarcomas. By polling 29 regional...
hospitals that used the local biopsy service as to the number of vaccinations they gave, Kass et al. came up with a crude estimate of 1 to 2 tumors/10,000 vaccinated cats. In a study published in 1997, Coyne et al. evaluated the responses of 235 members of the American Academy of Feline Practice regarding number of cats seen at their practices, number of vaccines given, and number of sarcomas developing at vaccine sites during 1992. They estimated prevalence of 3.6 tumors/10,000 vaccinated cats. In an ongoing prospective study begun in 1992 and conducted at a local feline practice, the author has followed approximately 2,000 cats with known vaccination history. Each vaccine was given singly in a predesignated site. Five sarcomas have developed, each at the site of rabies vaccination. The average interval between tumor development and last rabies vaccine given was 26 months, and 1 vaccine was the sole rabies vaccine used. On the basis of all the information garnered by these various studies, it was recommended that veterinarians keep complete records of vaccine administration and that they vaccinate at separate sites.

As this story began to unfold and various reports appeared in veterinary and human medical journals, the response from the profession and the public was mixed. Many were skeptical; some were outraged and made proclamations that were inflammatory. Articles began to appear in lay publications across the country. Concerned owners developed web pages devoted to vaccine-associated sarcoma. There were rumors of lawsuits. In response to these events, the California Veterinary Medical Association in August 1996 brought together experts from around the country to discuss the issue and make recommendations. In November of that same year, the AVMA and the American Animal Hospital Association jointly sponsored a meeting of many of the same people and the Vaccine-Associated Feline Sarcoma Task Force (VAFSTF) was formed. Using the recommendations of the California task force as a guide, the VAFSTF came up with its own recommendations regarding vaccination protocols, future research goals, and education of veterinarians and the public.

In searching for the etiopathogenesis of vaccine-associated sarcomas, many theories are based on evidence that is anecdotal at best. Claims have been made regarding the importance of variables, such as needle gauge, syringe reuse, temperature of the vaccine when injected, and whether the syringe is shaken or the vaccinated area massaged. It has been speculated that orange tabby cats are more commonly affected. All of these variables have existed since cats were first vaccinated and it is unlikely that they have a major role in the pathogenesis of vaccine-associated sarcoma development. More likely, there is interaction between an individual cat's genetically programmed wound healing responses and some component in the killed organism vaccines that were developed in the mid- to late-1980s, an interaction that goes awry and leads to neoplasia. A favored hypothesis, on the basis of histologic and immunohistochemical findings, is that vaccine-associated sarcomas arise from inappropriate or overzealous inflammatory or immunologic reactions, or both, associated with the presence of vaccine components in vaccination sites, which then leads to uncontrolled proliferation of fibroblasts and myofibroblasts. Studies at our laboratory and others have focused on the interplay of growth factors and oncogenes with local inflammatory cells and proliferating fibroblasts at the vaccine site. However, detailed epidemiologic studies may help identify the specific vaccines or vaccination protocols that must be used to allow this interaction to occur. The VAFSTF has funded a multicenter epidemiologic study, headed by Dr. Philip Kass. According to Dr. Kass, this study will be more “powerful” than his previous study and will address the following questions: is the risk of nonadjuvanted vaccines equal to that of adjuvanted vaccines; is the risk of attenuated organism vaccines equal to that of inactivated organism vaccines; is there homogeneity of risk within antigen classes; and do protocols (same location throughout lifetime, reuse of syringes, mixing of vaccines in 1 syringe) affect the incidence of sarcomas? It is hoped that studies such as these will lead to an understanding of the pathogenesis of vaccine-associated sarcomas and resultant improvements in prevention and treatment.

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References

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