associated sarcomas to chemotherapy. In general, a doxorubicin-based protocol is the chemotherapy of choice for soft-tissue sarcomas. Doxorubicin is an anthracycline antitumor antibiotic isolated from *Streptomyces peucetius* var. *caesius* cultures. Its primary antineoplastic activity results from nucleotide base intercalation and interaction with topoisomerase II, thereby inhibiting nucleotide replication and formation of deoxyribonucleic acid (DNA)-cleavable complexes, respectively. Doxorubicin is often combined with cyclophosphamide, a derivative of nitrogen mustard. An alkylating agent, cyclophosphamide induces cross-linking of DNA strands as well as intrastrand breaks and linkages. The use of these two drugs together has yielded greater activity against solid tumors than either agent alone in both experimental animal models and human patients.[10,11] In addition, this combination has been used to treat solid tumors in cats with minimal toxicity.[12]

The main purpose of this study was to describe the efficacy of combining doxorubicin and cyclophosphamide in treating cats with nonresectable fibrosarcomas arising at sites associated with vaccination. The goal was to determine whether neoadjuvant chemotherapy might render nonresectable tumors amenable to surgical excision. In addition, the results from this retrospective study might serve as a basis for investigating the potential benefits of chemotherapy as an adjuvant to aggressive surgery or as part of a multimodality treatment approach to vaccine-associated sarcomas. Multimodality therapy, including chemotherapy, may be indicated for these tumors since recent studies have reported higher-than-expected rates of metastasis.[6,7] Finally, it was hoped that this study could identify prognostic factors in cats with fibrosarcomas that might influence the response to chemotherapy.

Materials and Methods

A review of the medical records of the VHUP was performed to identify cats with histopathologically confirmed fibrosarcomas treated with doxorubicin and cyclophosphamide since 1986. Further eligibility criteria included the presence of a measurable tumor at a site potentially used for vaccination (cats with tumors on the head, tail, distal extremity, or within a body cavity were excluded), treatment with two or more cycles of chemotherapy in order to fully evaluate tumor response,[a] and sufficiently detailed medical records for interpretation of treatments given and tumor response. Follow-up records regarding clinical course after the recognition of progressive disease and survival were obtained from the VHUP records or from correspondence with the referring veterinarian, owner, or both. One cat treated by one of the authors (Barber) in a private practice setting was also entered into the study.

Data collected from the records included age, sex, breed, vaccination history, tumor location, tumor size, number of tumor occurrences at that site, staging procedures performed, number of cycles of doxorubicin/cyclophosphamide chemotherapy, potential treatment-related toxicity, and other therapies employed after the development of progressive disease. Information on the date and cause of death was gathered from the medical record, when available, or through conversations with referring veterinarians or owners.

All cats received doxorubicin intravenously (IV) on day one. The initial dose administered ranged from 20 to 30 mg/m^2 of body surface area (BSA) based on the attending clinician's discretion. Cyclophosphamide was administered orally at 50 mg per cat, divided into two doses on days three and five or divided into four daily doses over days three through six. Complete blood counts (CBCs) or white blood cell counts (WBCs) with a differential were performed on the first day of each cycle and once or twice between days seven and 14. The cycle was repeated every 21 days. Adjustments in subsequent doses were made at the discretion of the attending clinician.

Responses to therapy were categorized as follows: major response (MR), defined as the resolution of all clinically detectable tumor (the choice of the term major response rather than complete remission was based on the presence of a surgical scar from prior surgery in most animals, which could not be definitely determined to be devoid of neoplastic cells on physical examination); partial response (PR), defined as 50% to 90% reduction in gross tumor burden in all sites for at least four weeks; stable disease (SD), defined as a decrease in gross tumor burden of less than 50% or an increase of less than 10% of four weeks' duration; and progressive disease (PD), defined as an increase in tumor burden greater than 10% or the development of any new tumors. Response duration was defined as the date of administration of the doxorubicin dose immediately preceding the response until the date on which tumor progression was documented or the date of surgery to remove resectable residual disease. Tumor measurements, when available, were used to determine tumor volume. When such measurements were absent from the medical record, classification of tumor response was based on the attending clinician's judgment.

Survival time was calculated as the time in days from administration of the first dose of doxorubicin until death or last communication between the owner and the authors or referring veterinarian. Differences between the curves were analyzed by applying the log-rank test. Evaluation of individual parameters for correlation with tumor response was performed by chi-square analysis. Significance was set at a p value of less than 0.05.

Results

Twelve cats were identified for inclusion in the study. Initiation of chemotherapy treatment spanned from May 1990 to November 1998. A summary of the findings for each of the cases is shown in the Table. At the time of first chemotherapy treatment, the cats ranged in age from four to 17 years, with a mean and median of 9.7 and 10.5 years, respectively. Nine (75%) of the cats were spayed females,