

compensate for less radical surgery. The owners of the two other cats (case nos. 5 and 7) that responded to chemotherapy declined further surgery. The relatively rapid onset of PD in these two cases (41 and 153 days, respectively) also indicates that responses to chemotherapy are unlikely to be durable. Two more cats had regression of the primary tumor but were not candidates for surgery due to the presence of pulmonary metastatic disease.

The finding of prolonged survival times for cats that responded to chemotherapy is rewarding but may not reflect a true advantage of the treatment. The number of cats in this study is small, and two cats among the nonresponders were lost to follow-up relatively early. The small sample size was also thought to hamper efforts to identify any prognostic factors that might influence or predict response to treatment, such as drug dose, tumor site, number of tumor occurrences, age, or recent debulking surgery. This is disappointing, because response to treatment is a more important measure of efficacy; overall survival time may be influenced by the owner's perseverance in continuing treatment or the willingness to consider euthanasia.

Nevertheless, the chemotherapy treatments were generally well tolerated, with toxicity being mostly mild to moderate and self-limiting. The most common complaints were anorexia and lethargy. It was impossible to accurately quantify toxicities from the medical records, as owners often were not asked to specifically record the number and severity of clinical signs. In addition, a few of the cats had histories of mild, chronic, intermittent gastrointestinal disturbances, which were difficult to distinguish from treatment-related toxicity. It is also difficult to determine the interaction between treatment and disease progression in the two cats that developed clinically significant toxicity at the time of tumor progression. Although nephrotoxicity has been reported as a chronic toxicity of doxorubicin in cats, azotemia unrelated to pyelonephritis was detected in only one cat. This may reflect a lack of vigilant monitoring for this toxicity (particularly after chemotherapy treatments were discontinued), the relatively short survival time of many of the cats, or an insufficient dose. In contrast to a previous study,<sup>12</sup> no cats in this report developed clinically significant anemia during treatment.

Reports of chemotherapy for feline fibrosarcoma are few. A study of feline soft-tissue sarcomas included two animals with tumors located over the pelvis that were treated weekly with low doses of vincristine, methotrexate, and cyclophosphamide in conjunction with surgery and mixed-bacterial vaccine. The cats survived 15 weeks and greater than 36 weeks, respectively.<sup>13</sup> A toxicity and efficacy study of mitoxantrone reported that one of nine cats with a fibrosarcoma in an unspecified location underwent a complete response of 90 days' duration.<sup>14</sup> It is difficult to compare and draw conclusions from such small numbers.

The overall response rate of 50% is similar to that reported for combination doxorubicin and cyclophosphamide

chemotherapy in other solid tumors in cats. A 48% response rate was observed among 23 cats with malignant tumors treated with these chemotherapy agents.<sup>12</sup> Three cats with oral fibrosarcomas were included in the Mauldin *et al.* study,<sup>12</sup> with one partial and one complete response. In another study, a 50% response rate was observed among cats with nonresectable mammary tumors treated with doxorubicin and cyclophosphamide.<sup>15</sup> The dose intensity in these two studies was similar to that reported here.

In dogs, doxorubicin-based chemotherapy protocols have demonstrated efficacy in the postoperative management of high-grade soft-tissue sarcomas (e.g., hemangiosarcoma, which can arise in the SC tissues).<sup>16</sup> The efficacy in other sarcomas arising in the skin and subcutis has not been reported, largely because these tumors are considered low grade and chemotherapy is not indicated in their treatment.

Preoperative or neoadjuvant chemotherapy with protocols containing doxorubicin has been evaluated to be of questionable benefit in human patients with soft-tissue sarcomas. Of 29 patients with large, high-grade, nonmetastatic soft-tissue sarcoma enrolled in a prospective trial, only one tumor met the criteria for partial response.<sup>17</sup> Nevertheless, similar to the authors' experience with cats, the patients in another study that responded to preoperative chemotherapy had superior survival times to nonresponders.<sup>18</sup>

When doxorubicin was evaluated as a single agent in postoperative management of human patients with soft-tissue sarcomas in several small studies, no significant difference in disease-free or overall survival times was detected.<sup>19,20</sup> A criticism raised about the results of these studies has been the inclusion of patients with low- to moderate-grade tumors, which are known to be less sensitive to chemotherapy.

Ideally, when employing combination therapy, each agent should have demonstrated activity individually against the specific tumor type treated. This has not been evaluated in feline fibrosarcomas. It is generally accepted that doxorubicin is likely to be the more effective agent in this combination, so it would be helpful if the response to doxorubicin alone could be compared to its combination with cyclophosphamide in feline fibrosarcomas.

The biological behavior of vaccine-associated sarcomas has been the source of debate in veterinary medicine, with some proposing that vaccine-associated sarcomas are truly high-grade neoplasms. This is supported in some studies by the finding of distant metastasis among cats with these tumors in excess of 20%.<sup>6,7</sup> In addition, these tumors are reported to be larger at the time of first recognition compared to sarcomas present in nonvaccine-associated sites,<sup>4</sup> suggesting that the vaccine-associated tumors have a higher growth rate consistent with a high-grade malignancy. Nevertheless, this may simply reflect pet owners' inability to recognize and seek early veterinary care for a mass on the trunk or caudal thigh as compared to the head or distal extremity. The 50% response rate of cats reported here is