Bleomycin chemotherapy for metastatic squamous cell carcinoma in a ferret

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A 5-year-old 0.9-kg castrated male ferret (*Mustela putorius furo*) was referred for evaluation of a recurrent mass on the right lower lip. A mass at the same site had been excised 2 weeks earlier. The histologic diagnosis was squamous cell carcinoma.

Physical examination revealed a 1.8 cm × 1.0 cm × 0.6-cm mass that was firm, pink, and ulcerated (Fig. 1). The mass was freely movable. The right submandibular lymph node was firm and larger than normal. The owner reported that the ferret's behavior was normal.

Results of a CBC and thoracic radiography were normal. A biopsy specimen from the recurrent lip mass confirmed the previous diagnosis of squamous cell carcinoma. Cytologic examination of a needle aspirate specimen from the submandibular lymph node revealed clusters of epithelial cells with pale cytoplasm, large nuclei, and marked chromatin clumping suggestive of metastasis. Clinical staging according to World Health Organization criteria was T3 N1b M0 with T representing the lip mass, N representing the involved lymph node, and M representing no distant metastasis.[1]

Surgical resection of the tumor and regional lymph node was advised, but the owner rejected this recommendation. As an alternative, treatment with bleomycin[a] was recommended. The toxicity of bleomycin in ferrets was not known; however, its use in treatment of squamous cell carcinoma in dogs and cats has been associated with minimal risk of acute toxicosis.[2-4] Bleomycin can be given subcutaneously, thereby avoiding more difficult routes of administration. Bleomycin treatment was initiated at a dosage of 10 U/m^2, SC once a week.[3]

Three weeks after initiation of treatment, the tumor had increased in size to 2.4 cm × 1.1 cm × 0.9 cm. The dosage of bleomycin was increased to 20 U/m^2, SC once a week.

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[a]Blenoxane, Mead Johnson Oncology Products, Evansville, Ind.

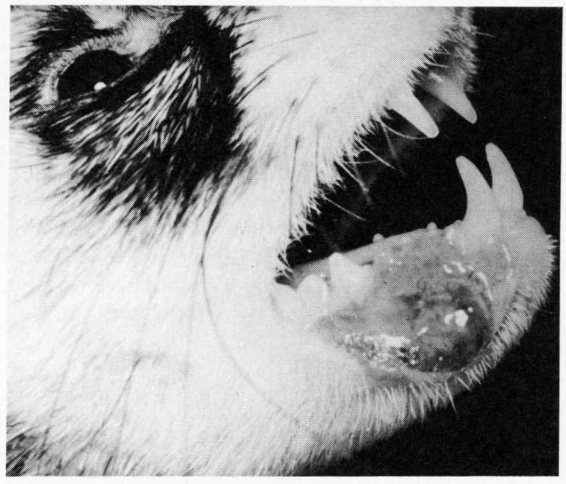

Figure 1—Gross appearance of squamous cell carcinoma in a ferret.

The size of the tumor decreased to 2.0 cm × 0.7 cm × 0.5 cm during the ensuing 3 weeks. Treatment with bleomycin was continued at 20 U/m^2, SC, once a week. Sixty-four days after initiation of treatment, the ferret was examined by the referring veterinarian because of a substantial increase in tumor size from the point of maximal regression. The owner requested euthanasia. Permission for a necropsy was denied.

Squamous cell carcinomas in ferrets are not rare.[5-9] Surgical resection is reported to be curative.[5,7,8] Successful chemotherapy for squamous cell carcinoma of ferrets has not, to our knowledge, been reported. One ferret with a nonresectable squamous cell carcinoma was treated with melphalan, but died of hemorrhagic diarrhea within 10 days of initiation of treatment.[9]

Bleomycin is a water-soluble antitumor antibiotic that is isolated from *Streptomyces verticillus*.[3,4] After administration of bleomycin in normal and tumor-bearing mice, the concentration of the drug was highest in skin, lungs, kidneys, and neoplastic tissue.[4] Bleomycin has activity against many experimentally induced tumors in mice and rats, as well as lymphoma, squamous cell carcinoma, and malignant testicular tumors in human beings.[3,4] In one study, tumors in 3 of 4 cats and

2 of 6 dogs decreased in size when bleomycin was used alone.[3]

We chose to use bleomycin because of its ease of administration, low acute toxicity, and documented activity against squamous cell carcinoma in dogs and cats.[2-4] Bleomycin is one of the few cytotoxic drugs that is not associated with bone marrow suppression.[2-4] It has been reported to cause pulmonary fibrosis in dogs after cumulative dosage exceeds 200 U/m^2.[2-4]

The initial dosage was determined on the basis of the recommended dosage in dogs.[3] Body surface area was calculated by using the formula $m^2 = K \cdot W^{2/3}/10^4$. The K factor is a constant for each species and W is weight in grams.[3] Because the K factor has not been calculated for ferrets, the K factor for cats was substituted.[3] Failure of bleomycin at the initial dosage may have been attributable to use of an inappropriate K factor. When the dose was doubled, the size of the tumor decreased.

Regression of the tumor in this ferret was not complete. There was, however, a 70% decrease (1.24 cm^3 to 0.37 cm^3) in tumor size during the 3-week period after the dosage of bleomycin was doubled. This ferret received a cumulative dosage of 150 U/m^2, less than that associated with pulmonary fibrosis in dogs. Although necropsy was not permitted, the ferret did not have clinical signs indicative of pulmonary lesions at the time of death.

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New Veterinary Biological Product

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