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Disseminated T-cell lymphoma in a guinea pig with bilateral ocular involvement

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Abstract. A 2-year-old female shorthair guinea pig was presented to the Veterinary Medical Teaching Hospital, University of Wisconsin–Madison, for evaluation of a unilateral corneal opacity of 1 week duration. Physical examination revealed a markedly thickened right cornea and lymphadenopathy of the submandibular and prescapular lymph nodes. Cytology of a lymph node aspirate was highly suggestive of lymphoma. The animal was humanely euthanized. Postmortem examination revealed a disseminated lymphadenopathy involving the submandibular, anterior cervical, prescapular, bronchial, anterior mediastinal, and mesenteric nodes, and hepatomegaly with accentuation of lobular morphology. The right cornea was dark red, dry and dull, and diffusely thickened, and the globe was exophthalmic. Microscopically, pleomorphic neoplastic lymphoblasts were present in the lymph nodes, spleen, liver, lungs, heart, rhinarium, bone marrow, and kidneys. Bilateral infiltration of the eyes by neoplastic lymphoblasts was noted, which was more extensive on the right. The neoplastic cells stained immunohistochemically as T-lymphocytes using antibodies directed against CD3 antigen.

Spontaneous neoplasia is generally uncommon in guinea pigs, with only 319 cases from more than 42,000 animals reported up until 1976.⁸ Respiratory neoplasms are the most common tumors observed. Neoplasia rarely occurs in guinea pigs less than 3 years of age. The incidence of neoplasia varies greatly with strain. Female guinea pigs may be more likely to develop tumors. Only 22 (± 2) of the previously described tumors were leukemias or lymphomas.⁸ A further 12 cases of leukemia and lymphoma, from approximately 5,000 animals, were described in the literature in 1991.^{4,14} Rare sporadic cases have been reported since that time.³

Lymphosarcoma has been experimentally induced in guinea pigs by a number of methods. Cutaneous neoplasia has developed following chronic antigenic stimulation.¹⁵ Paren-

teral administration of chemical carcinogens has induced leukemia with pulmonary tumors.⁶ Irradiation with either X rays or gamma rays also induces the formation of disseminated lymphoma, with concurrent leukemia.¹ Additionally, a C-type retrovirus infection has been associated with lymphosarcoma and leukemia in the guinea pig^{5,10,11} and virus transmission by cell-free culture filtrate has resulted in leukemia.⁹

Lymphosarcoma is the most frequent metastatic intraocular neoplasm in dogs and cats.^{2,12} The neoplasm is usually bilateral, and the iris and ciliary body are most frequently involved. Other regions, including choroid, can be involved to a lesser extent.^{2,12} In guinea pigs, ocular involvement is rare with iris, choroid, and retina most commonly affected.^{1,7,10} Only 1 case of a primary ocular tumor, a corneal dermoid, has been described.¹³ This current report describes a spontaneous case of disseminated T-cell lymphoma with bilateral ocular involvement.

A 2-year-old pet female shorthair guinea pig was pre-

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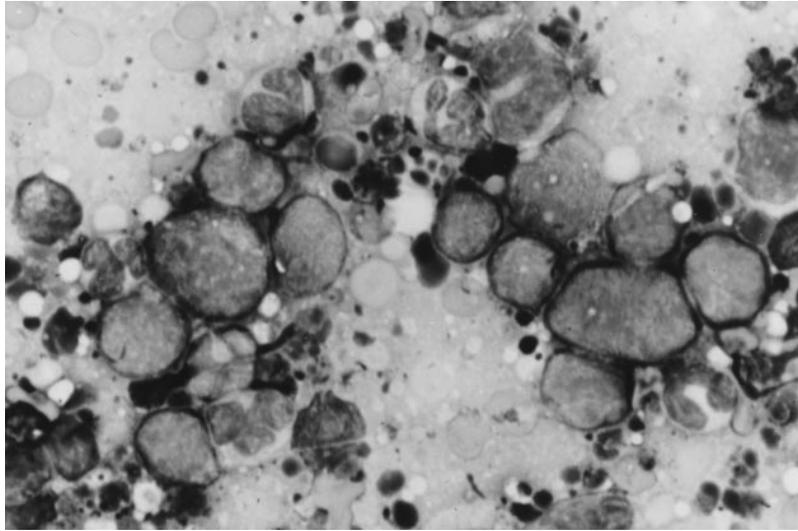


Figure 1. Cervical mass aspirate; guinea pig. Monomorphic large round cells. Wright's giemsa. 1,000X.

sented to the University of Wisconsin–Madison Veterinary Medical Teaching Hospital for evaluation of a corneal opacity of 1-week duration. The lesion was unresponsive to topical treatment with pilocarpine, chloramphenicol, and prednisolone acetate. The owner noted rapidly enlarging ventral cervical masses. Physical examination revealed a marked chemosis of the right cornea, increased anterior chamber depth, hyphema, and scleral and conjunctival hyperemia. Enlarged retropharyngeal, submandibular, and prescapular lymph nodes were palpated. A fine-needle aspirate of a cervical mass contained high numbers of large cells with round nuclei, stippled chromatin, and a thin rim of dark cytoplasm (Fig. 1). Occasional mitotic figures were noted. The cells were admixed with heterophils and scattered macrophages with intracytoplasmic debris. A presumptive diagnosis of

lymphoma with accompanying necrosis and inflammation was made. The owner declined treatment for the guinea pig, which was humanely euthanized.

Postmortem findings included a marked diffuse lymphadenopathy; both peripheral and internal lymph nodes were asymmetrically enlarged (Fig. 2). Lymph nodes were multilobulated and bulged pale white and uniform on cut surface. The liver was enlarged and pale brown and had a prominent lobular pattern with alternating areas of light tan and white. The right eye was mildly exophthalmic, and the cornea was dry, dull, and dark red with a rough surface. After fixation in Bouin's solution, hemisection of the right eye revealed a markedly thickened (~3-mm) cornea with expansion of the adjacent sclera (Fig. 3). Tissue samples were fixed in 10% neutral buffered formalin and processed rou-



Figure 2. Mesenteric lymph nodes; guinea pig. Lymphadenomegaly with loss of distinction between cortex and medulla by uniform bulging, white, firm tissue (arrow, cut surface). Scale = 1 cm.

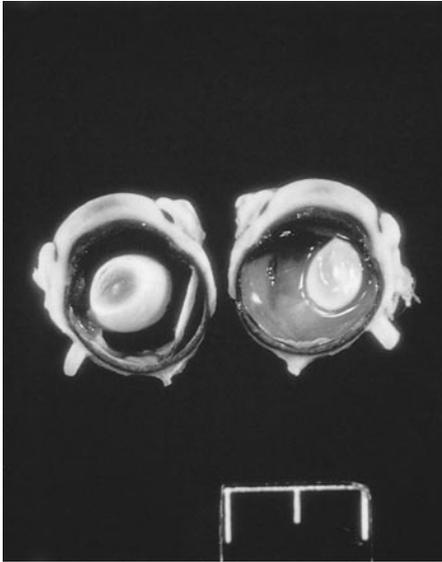


Figure 3. Right eye; guinea pig. Markedly thickened cornea with expansion of the adjacent sclera. Bouin's fixative. Scale = 1 cm.

tinely. Lymph node samples were fixed in Karnovsky's fixative and processed routinely for transmission electron microscopy.

Microscopically, all lymph nodes examined (right internal iliac, tracheobronchial, prescapular, submandibular, anterior cervical, colic, and mesenteric chain) had replacement or effacement of normal architecture by a relatively monotonous round cell population. The cells contained variable amounts of eosinophilic to amphophilic cytoplasm. Nuclei were ovoid and cleaved with finely stippled granular chromatin and up to 3 large, distinct nucleoli. Mitotic figures numbered 6–16 per high-powered field and were frequently

bizarre. Similar neoplastic cell infiltrates were present in the spleen, bone marrow, liver, lung, pericardium, and kidney.

The cornea of the right eye was edematous and expanded by diffuse infiltrates of the neoplastic cells (Fig. 4). Descemet's membrane was ruptured and the iris was adhered to the posterior cornea. Tumor cells expanded the iris and ciliary body, infiltrated the choroid, and extended into the adjoining sclera. Episcleral tissue and extraocular muscles also contained neoplastic cell infiltrates. The left eye was less severely affected. Peripheral blood was not evaluated for circulating lymphoblasts, but their presence in the bone marrow, hepatic sinusoids, spleen, and within pulmonary vasculature suggests that the guinea pig was leukemic.

Ultrastructurally, the neoplastic cells in the lymph node had a high nuclear to cytoplasmic ratio; the sparse cytoplasm contained free ribosomes, rough endoplasmic reticulum, and mitochondria. Cells had irregular, often convoluted nuclei with peripheral heterochromatin and up to 3-nucleoli (Fig. 5). No viral particles were identified.

Immunohistochemical staining by indirect streptavidin–biotin complex techniques using commercial kits^a was performed on samples from spleen, right internal ileac and mesenteric lymph nodes, and liver along with positive control tissues. Commercially produced antibodies to B-cells (CD20cy), T-cells (CD45RO and CD3), leukocyte common antigen (LCA), and guinea pig immunoglobulin were used.^a The neoplastic cells stained positively for the T-cell marker CD3 but not for the marker for mature activated T-cells, CD45RO. Neoplastic cells did not stain for the B-cell marker (CD20cy), guinea pig immunoglobulin, or with antibodies against LCA. Positive guinea pig control tissues stained appropriately for CD20cy, CD45RO, CD3, and guinea pig immunoglobulin. Anti-LCA antibody failed to stain the control guinea pig spleen. Based on the cytologic, histologic, and ultrastructural features, location and distribution of the neoplastic cells, and immunohistochemical staining results, a di-

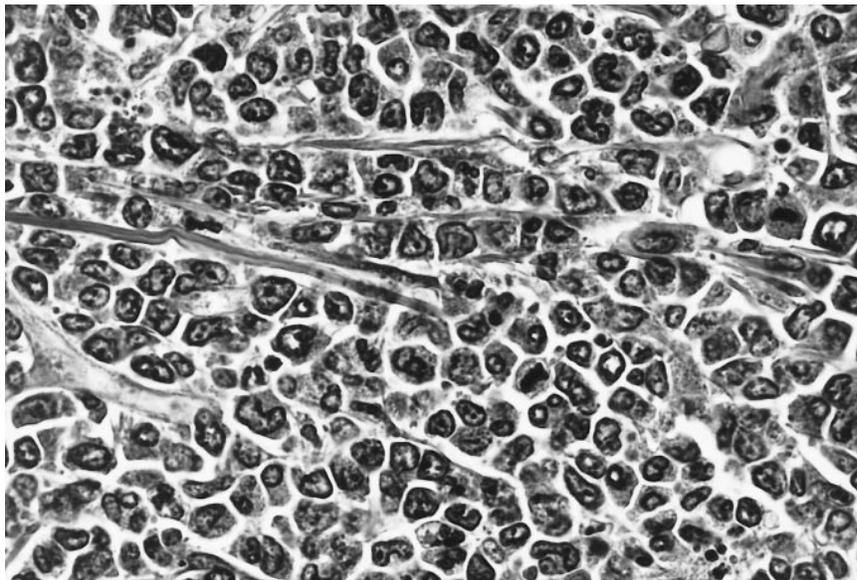


Figure 4. Cornea, right eye; guinea pig. Markedly pleomorphic neoplastic lymphocytes. HE. 400 \times .

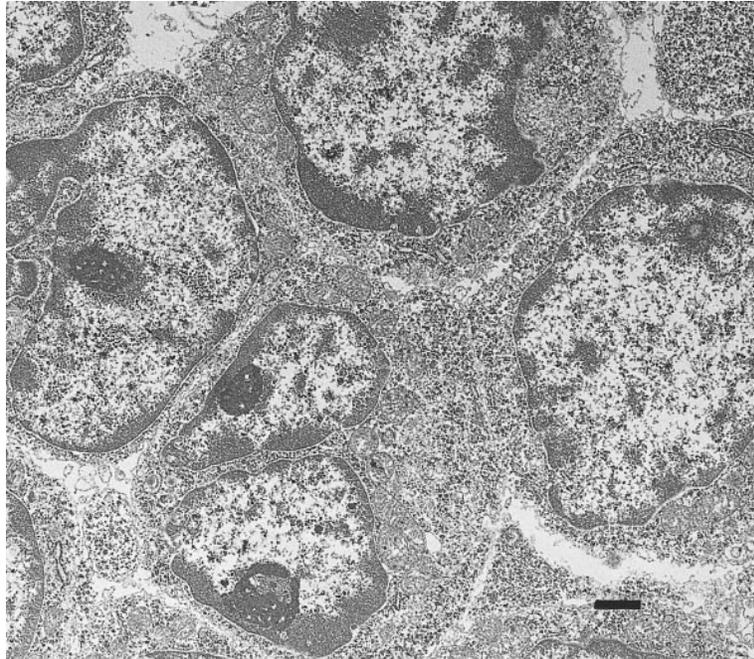


Figure 5. Electron micrograph. Mesenteric lymph node; guinea pig. Neoplastic lymphocytes. Bar = 3 μ m.

agnosis of malignant T-cell lymphoblastic lymphoma was made.

The macroscopic and microscopic features are consistent with lymphosarcoma as described in the guinea pig.^{8,11} Factors associated with the development of lymphoma in the guinea pig were not seen in this animal and consequently the tumor is thought to have developed spontaneously.^{1,5,6,11,15} The clinical presentation in this case is unusual because it centers on ophthalmic disease. Ocular involvement with lymphosarcoma after experimental irradiation¹ with viral infection¹⁰ has been seen. The current case represents a T-cell lymphoblastic lymphoma with probable leukemia.

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Sources and manufacturer

- a. DAKO Corporation, Carpinteria, CA.

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