Comparative Medicine
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Vol 52, No 2
April 2002
Pages 152-159

Lymphosarcoma in the Laboratory Woodchuck (*Marmota monax*)

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From 1979 to 1999, 28 cases of lymphosarcoma were identified in the Cornell University woodchuck colony (prevalence rate: 152/100,000/yr). The prevalence of lymphosarcoma was similar in woodchucks not infected with the woodchuck hepatitis virus (WHV) and in chronic carriers of WHV. Males (13) and females (15) alike were affected (mean ± SD age 4.7 ± 2.92 years; range, 0.5 to 9 years). On the basis of the major organ system involved, woodchuck lymphosarcoma was classified as multicentric (12 cases, 43%), alimentary (5 cases, 18%), cranial mediastinal (5 cases, 18%), and miscellaneous (6 cases, 21%). A cutaneous form was not observed. Morphologic criteria similar to those of the Kiel classification were used for light microscopic classification. All Kiel categories—except the immunoblastic form—were found: 17 cases (61%) were centroblastic, and 6 were lymphocytic (21%). Other categories (centrocytic and plasmacytoid) were recognized less frequently. Immunophenotyping of 27 cases revealed 15 (56%) B cell ($CD3^-/CD79a^+$ or $CD3^-/BLA.36^+$), 7 (26%) T cell ($CD3^+/CD79a^-/BLA.36^-$), and 5 (18%) non-T non-B cell ($CD3^-/CD79a^-/BLA.36^-$) lymphosarcomas. Lymphosarcoma in woodchucks develops at a higher rate than that observed in humans or companion animals, and WHV infection has no effect on prevalence. The anatomic and Kiel classification used in domestic species also can be used in woodchucks. Commercially available α-CD3, α-CD79a, and α-BLA.36 antibodies were useful for immunophenotyping woodchuck lymphosarcomas.

The Eastern woodchuck (*Marmota monax*) is a valuable experimental animal model for hepatitis B virus (HBV) research including studies of pathogenesis (1) and toxicity and efficacy of antiviral drugs (2). The woodchuck hepatitis virus is a member of the hepatotropic Hepadnavirus family, for which HBV is the prototype (1). Similar to human neonatal infection with HBV, experimental infection of neonatal woodchucks with WHV results in chronic infection at a rate ≥ 60%, and the lifetime risk of developing hepatocellular carcinoma is almost 100% (1). A breeding colony of WHV-negative woodchucks was established at Cornell University in 1979, and now serves as the source of woodchucks for experimental studies.

To monitor the overall health of the colony and to be aware of possible confounding variables when analyzing experimental data, all woodchucks that die or are euthanized for medical reasons not related to the WHV-research protocols, undergo complete necropsy. Several woodchuck diseases, other than those associated with WHV infection, have been recognized and described, including glomerulonephritis (3), renal encephalopathy (4), various liver diseases (5, 6) parasitic encephalitis (7), cerebrospinal nematodiasis (8), cerebral neoplasia (9), testicular neoplasia (10), intracytoplasmic neuronal inclusions (8), congestive cardiomyopathy (11), and various skin disorders (12-14).

A review of computerized medical records of the Cornell woodchuck colony revealed a remarkable number of animals with lymphosarcoma. Woodchuck lymphosarcoma (to our knowledge) has been reported only as a case report (15) and comprehensive study of this subject has not been conducted. The purpose of the study reported here was to characterize the epidemiology, anatomic distribution, morphology, and immunophenotype of lymphosarcoma in Cornell-colony woodchucks during the first 20 years of the colony (1979-1999).

Materials and Methods[1]

Selection of cases. A computerized search of the records of the Cornell woodchuck colony from 1979 (inception of the colony) to 1999 was conducted. All cases were reviewed and, on the basis of the medical records and re-examination of the histologic material, 28 cases of lymphosarcoma were found. Histologically, a proliferative lesion was diagnosed as lymphosarcoma if it was obliterating or substantially disrupting tissue architecture without a preexisting lesion (i.e., acute or chronic inflammation) and consisted of round or oval cells with variable amount of cytoplasm and variably sized round or ovoid nucleus.

Anatomic classification. Woodchuck lymphosarcoma was classified according to the gross anatomic distribution of tumors throughout the body (anatomic pattern). Alimentary lymphosarcomas originated within the wall of the gastrointestinal tract as nodular or diffuse swellings with or without involvement of the adjacent mesenteric lymph nodes. Although tumor cells might have infiltrated other organs, the alimentary tract was the predominant organ involved. Multicentric lymphosarcoma was characterized by generalized lymphadenopathy with frequent involvement of abdominal organs. In cranial mediastinal

Received: 9/25/01. Revision requested: 11/13/01. Accepted: 2/04/02.
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[1]All research conducted on the woodchucks described in this report were approved by the Cornell University Institutional Animal Care and Use Committee.

lymphosarcoma, the largest tumor was confined to the region of the thymus or cranial mediastinal lymph nodes and was not accompanied by involvement of the peritoneal cavity or peripheral lymph nodes. The designation "thymic lymphosarcoma" for lymphosarcoma in the cranial pleural cavity was avoided, because lymphosarcomas in the cranial portion of the thorax may originate either from the thymus or from the cranial mediastinal lymph nodes. A case was classified as miscellaneous when a clear pattern of organ involvement could not be found, or a mixture of patterns was observed. This category also included solitary or regionally confined lymphosarcoma (16).

Histologic classification and mitotic index. Hematoxylin and eosin (H&E)-stained glass slides were examined by light microscopy, and lymphosarcomas were categorized according to the Kiel classification (17). This classification was used, because we had experience using this system; it is simple to apply, and is the only classification system that can be applied without much clinical information (i.e., survival time and disease-free interval). Each case was classified independently by two pathologists (TN and SPM), and six months later, the slides were reviewed again to confirm the initial classification. The growth pattern, similar to most cases of canine lymphosarcoma (16), was principally diffuse or minimally nodular; therefore, an attempt was not made to classify the tumors into diffuse or follicular patterns. Lymphosarcomas were also classified, using an arbitrary method, which is based solely on the cumulative number of mitotic figures in 10 randomly chosen 40×-magnification fields. On the basis of total number of mitotic figures, lymphosarcomas were grouped into low (0 to 10), medium (11 to 20), or high (> 20) categories (18).

Immunophenotyping. Immunohistochemical staining was performed, using commercially available antibodies against human CD3 (rabbit polyclonal α-human CD3 antibody, DAKO, Carpinteria, Calif.), human CD79a (mouse monoclonal α-human CD79a antibody, DAKO), and human BLA.36 (mouse monoclonal α-human BLA.36 antibody, DAKO). We used these α-human antibodies, because woodchuck-specific lymphocyte markers are not commercially available and these antibodies are used successfully in rodents and in our daily diagnostic work. The streptavidin-biotin/horseradish peroxidase (HRP) method was used according to the manufacturer's instructions (Zymed Laboratories, San Francisco, Calif.). Formalin-fixed paraffin-embedded tissues were sectioned at 5-μm thickness and were mounted on Probe-On slides (Fisher Scientific, Springfield, N.J.). The following antigen-retrieval protocols were used: for α-CD3 immunostain, the mounted tissues were trypsinized at 37°C for 1 h; for α-CD79a and α-BLA.36, the mounted tissues were immersed in 0.01*M* sodium citrate (pH 6.0) and microwaved twice (10 min each) in a household microwave oven (Panasonic) at "High" setting. The chromogen was 3,3-diaminobenzidine tetrachloride (DAB; Sigma Chemical Co., St. Louis, Mo.), and all slides were counterstained lightly with Gill's hematoxylin. The specificity of CD3, CD79a, and BLA.36 for woodchuck lymphocytes was screened, using formalin-fixed paraffin-embedded 5-μm-thick sections from normal peripheral lymph nodes, thymus, and spleen. Negative controls were obtained by substituting the primary antibody either with purified normal rabbit or mouse serum (DAKO) depending on the primary antibody. For each case, usually only one tissue (most often the neoplastic mass) was evaluated. Each case was classified independently by two pathologists (TN and SPM), and six months later, the slides were reviewed again to confirm the initial classification.

Table 1. Epidemiologic analysis of woodchuck lymphosarcoma in the Cornell colony

Risk factor	No. of woodchucks		χ^2	*df*	*P*
	With lymphosarcoma	Without lymphosarcoma			
Age (yr)					
< 2	6	1,797	28.42	2	<0.001
2-6	13	3,610			
> 6[a]	9	388			
Sex					
Female	15	3,039	0.01	1	0.90
Male	13	2,756			
Source					
Colony born[b]	23	3,838	3.16	1	0.076
Wild caught	5	1,957			
WHV serostatus					
N	15	3,241	2.41	3	0.49
C	5	1,352			
R	5	552			
O	3	540			

[a]More lymphosarcoma cases were found in this age group than expected.
[b]More lymphosarcoma cases than expected were found in colony-born animals.

Statistical analysis. Associations between four risk factors (age, sex, source [colony born or wild caught[2]], and WHV serostatus) and lymphosarcoma prevalence were tested by use of χ^2-analysis. The age groupings—0 to 1 year (sub-adult), 2 to 6 years (adult) and > 6 years (elderly)—were created before testing so that the *a priori* assumptions for the χ^2 test could be met. The following categories were recognized for WHV serostatus: category "X" (serostatus unknown), woodchucks did not have serologic information available; category "N", animals did not have detected serologic markers of hepadnavirus infection (includes woodchucks exposed to hepadnaviruses that failed to develop markers); category "C" contained animals that were chronically infected with the WHV and consistently tested positive for WHV surface antigen; category "R" (resolved infection) contained animals in which serologic testing detected antibodies against the surface antigen following experimentally induced WHV infection; and category "O" (other serologic testing) contained woodchucks with antibodies to the WHV core antigen as the only marker. Animals in category "X" (unknown serologic status) were not considered in the statistical analysis, because no woodchucks with lymphosarcoma fell in this category and only 110 control woodchucks were in category "X". All statistical tests were two-tailed, with significance interpreted at $P \leq 0.05$.

Results

Epidemiology. As of May 1999, a total of 6,051 woodchucks had lived in the facility since its inception in 1979. Two-thousand twenty-two animals that died or were euthanized because of clinical signs of disease not related to the WHV-research protocols underwent complete necropsy. Twenty-eight cases of histologically confirmed woodchuck lymphosarcoma were found after reviewing the necropsy reports and re-examining the H&E-stained glass slides for these cases. The age of the affected animals ranged from 0.5 to 9 years (mean ± SD age, 4.7 ± 2.92 years). Prevalence rate of lymphosarcoma was 152/100,000/yr. Lymphosarcoma in the Cornell woodchuck colony was not related to sex or WHV serostatus ($P > 0.05$). Lymphosarcoma was significantly more prevalent in woodchucks older than 6 years.

[2]*Wild caught animals were born in their natural habitat, trapped as adults, and were introduced to the colony after negative serological result for the WHV.*

The data suggested that lymphosarcoma was more prevalent in colony-born animals than in wild caught animals (Table 1).

Pathologic changes. Twenty-five percent of the animals with lymphosarcoma did not have previously observed clinical signs of disease or remarkable recent medical history. In the rest, clinical signs of disease were usually non-specific: emaciation, weakness (5 animals, 18%), dyspnea (5 animals, 18%), and generalized lymphadenopathy (3 animals, 11%). These signs were observed either alone or in combination with one another in a given woodchuck. Generally, clinical signs of disease did not correlate with gross or histologic lymphosarcomatous organ involvement, with the exception of animals with generalized lymphadenopathy or dyspnea. All woodchucks with generalized lymphadenopathy had lymphosarcomatous involvement of the enlarged lymph nodes, and 60% of the animals with dyspnea had lymphosarcoma involving the lung or cranial mediastinum.

Other gross or histologic lesions encountered besides lymphosarcoma included blood vessel degeneration, intimal mineralization (7 animals, 25%), diaphragmatic hernia (4 animals, 14%), portal hepatitis, cholangitis (4 animals, 14%), pneumonia (3 animals, 11%), chronic nephritis (3 animals, 11%), hepatic lipidosis (2 animals, 7%), and myocardial degeneration (2 animals, 7%). Again, these lesions were encountered either alone or in various combinations in a given animal. Six animals were affected solely with lymphosarcoma; the most commonly involved organs were the peripheral lymph nodes, liver, spleen (4 animals, 67%), lung, kidney (3 animals, 50%), gastrointestinal tract (2 animals, 33%), and brain, heart, cranial mediastinum (1 animal, 17%). Lymphosarcoma affected these organs alone or, more commonly, in various combinations with one another in a given animal. At necropsy, all but one animal had grossly evident neoplasia. In that animal, histologic examination revealed discrete collections of abnormally large, somewhat pleomorphic lymphocytes in the Peyer's patches of the colon and within gastric and colonic lymphatic channels.

Anatomic pattern. Multicentric lymphosarcoma was found in the largest numbers in Cornell-colony woodchucks (12 cases, 43%). Sites included various peripheral lymph nodes (mandibular, retropharyngeal, superficial cervical, lumbar, popliteal, and iliac). Since all these animals had rather advanced lymphosarcoma, often the visceral organs also were involved in the neoplastic process besides the peripheral lymph nodes. The other forms were represented almost equally (Table 2).

Kiel classification. Most of the neoplastic cells in lymphocytic lymphosarcomas resembled mature lymphocytes with scant cytoplasm and small, round, heterochromatic nuclei and indistinct nucleoli (Fig. 1). Cells in centrocytic lymphosarcomas were somewhat larger, and had small to medium-sized, irregular nuclei with stippled chromatin and indistinct nucleoli (Fig. 2). Centroblastic lymphosarcomas had medium-sized to large, round to oval, single vesicular nuclei and distinct (usually multiple) nucleoli that were often located at the periphery of the nucleus. On the basis of the other neoplastic lymphoid cells that accompanied the centroblasts, three subtypes were recognized. In the centroblastic-monomorphic subtype, most neoplastic cells had centroblastic phenotype. If centrocytes accompanied the predominant centroblastic neoplastic lymphoid cells, the designation was centroblastic-centrocytic. In centroblastic-polymorphic lymphosarcomas, most of the neoplastic lymphoid cells were centroblastic, with a minor population of pleomorphic neo-

Table 2. Morphologic and immunologic classification of lymphosarcoma in woodchucks (n = 28)

Variable	Number (%)
Anatomic pattern	
Multicentric	12 (43)
Miscellaneous	6 (21)
Alimentary	5 (18)
Cranial mediastinal	5 (18)
Kiel classification	
Centroblastic	17 (61)
Lymphocytic	6 (21)
Centrocytic	2 (7)
Plasmacytoid	1 (4)
Miscellaneous	2 (7)
Immunoblastic	0 (0)
Cumulative number of mitotic figures in 10× high-power magnification fields	
High (> 20)	11 (39)
Medium (11-20)	3 (11)
Low (0-10)	14 (50)
Immunophenotype*	
B cell	15 (56)
CD79a$^+$ only	1 (4)
BLA.36$^+$ only	8 (30)
CD79a$^+$ and BLA.36$^+$	6 (22)
T cell	7 (26)
Non-T non-B cell	5 (18)

*For this variable, n = 27 woodchucks.

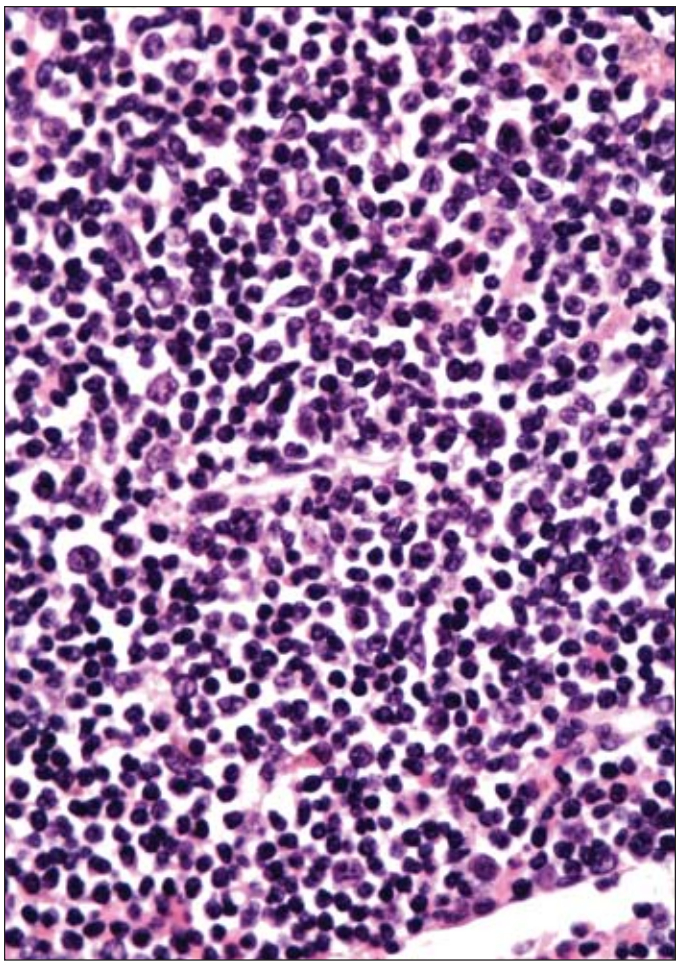

Figure 1. Photomicrograph of a section of lymphocytic lymphosarcoma from one of the woodchucks of the study. The neoplastic cells resemble small mature lymphocytes. H&E stain; magnification = 452×.

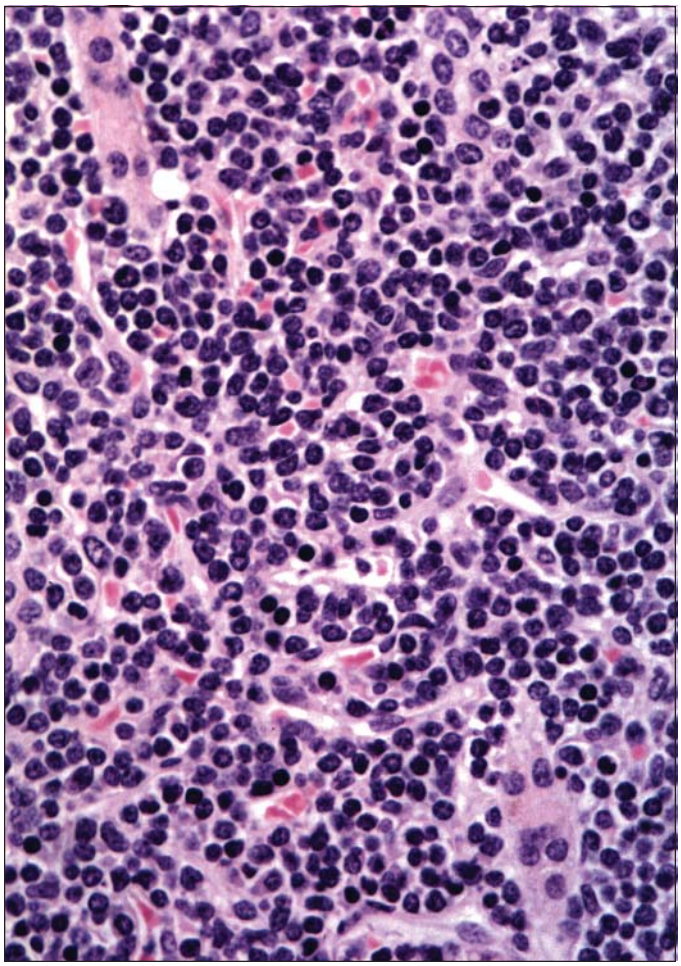

Figure 2. Photomicrograph of a section of a centrocytic lymphosarcoma. The neoplastic cells are larger than small lymphocytes and have medium-sized, irregular, single nuclei with indistinct nucleoli. H&E stain; magnification = 452×.

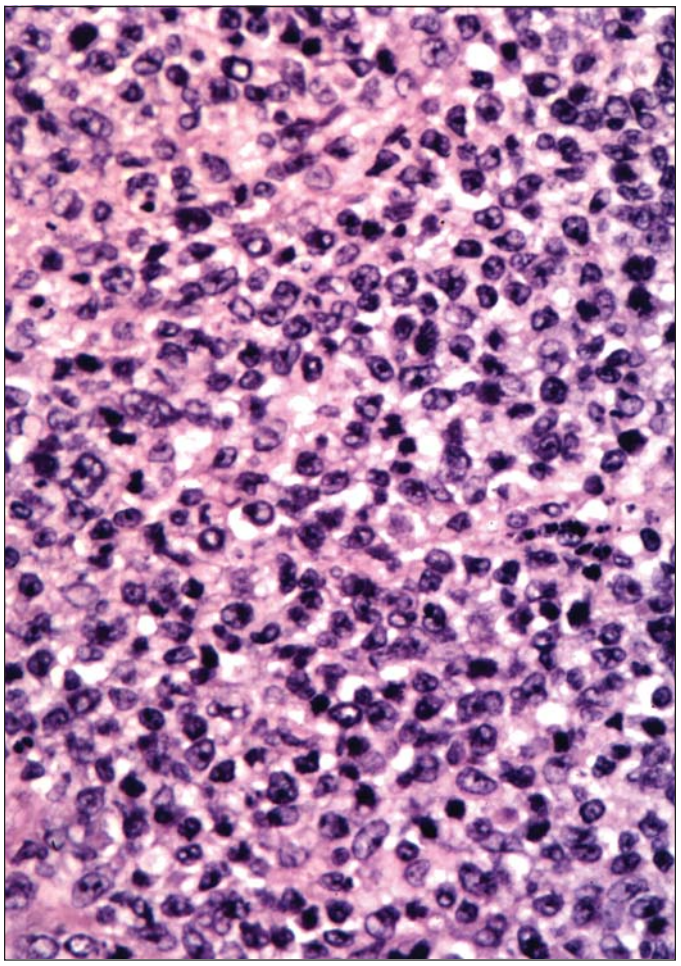

Figure 3. Photomicrograph of a section of a centroblastic polymorphic lymphosarcoma. Large cells with vesicular, single nuclei and distinct nucleoli are in the majority, and are accompanied by smaller cells with dense, small, single nuclei. H&E stain; magnification = 452×.

plastic lymphoid cells (Fig. 3). Plasmacytoid lymphosarcomas were composed of large neoplastic cells with abundant cytoplasm, eccentric, single, large nuclei and, sometimes, a perinuclear halo (Fig. 4). A lymphosarcoma was classified as miscellaneous if none of the previous nuclear morphologic criteria could be applied to the majority of the neoplastic cells.

Seventeen (61%) centroblastic and 6 (21%) lymphocytic lymphosarcomas were found. Other forms were encountered less frequently (Table 2). Immunoblastic lymphosarcoma was not found. We found no correlation between the Kiel classification and the immunohistochemical data, or number of mitotic figures or anatomic distribution of the neoplasm.

Number of mitotic figures. On the basis of the cumulative numbers of mitotic figures in 10 randomly chosen 40× (high power) magnification fields, 14 woodchuck lymphosarcoma cases were classified as low, 11 cases as high, and 3 cases as medium categories (Table 2).

Immunophenotyping of normal woodchuck lymphoid organs. Commercial α-CD3, α-CD79a, and α-BLA.36 antibodies were used to immunostain non-lymphosarcomatous (normal) woodchuck lymphoid organs, from animals infected (n = 1) and not infected (n = 2) with WHV. The tissue-specific immuno-staining patterns were similar in the infected and non-infected animals.

In non-neoplastic woodchuck peripheral lymph nodes of clinically normal, CD3 strongly labeled the paracortical small lymphocytes and scattered mature lymphocytes in germinal centers (Fig. 5). The CD79a antibody stained the mantle cells and the primary follicles, weakly stained the centrocytes, and did not stain the centroblasts (Fig. 6). The BLA.36 immunostain strongly labeled centroblasts in the secondary follicles, and scattered lymphocytes in the mantle zone and in the paracortex (Fig. 7).

In non-neoplastic woodchuck spleens, CD3 stained most of the mature small lymphocytes in the periarteriolar lymphoid sheaths and scattered small lymphocytes in and around the germinal centers. The lymphocytes in the splenic marginal zone stained weakly with CD79a. The BLA.36 antibody strongly labeled about 75% of the lymphocytes in the splenic germinal centers, and scattered lymphocytes in the marginal zone. Also, BLA.36 stained approximately 25% of the lymphocytes in the PALS (data not shown).

In the thymus, CD3 stained about 75% of the small lymphocytes. Cells in the thymus did not stain in response to CD79a. The BLA.36 antibody stained about 40% of the round cells in the thymic medulla and scattered (< 5%) cells in the cortex. The Hassall's corpuscules had moderate to strong staining with BLA.36 (data not shown).

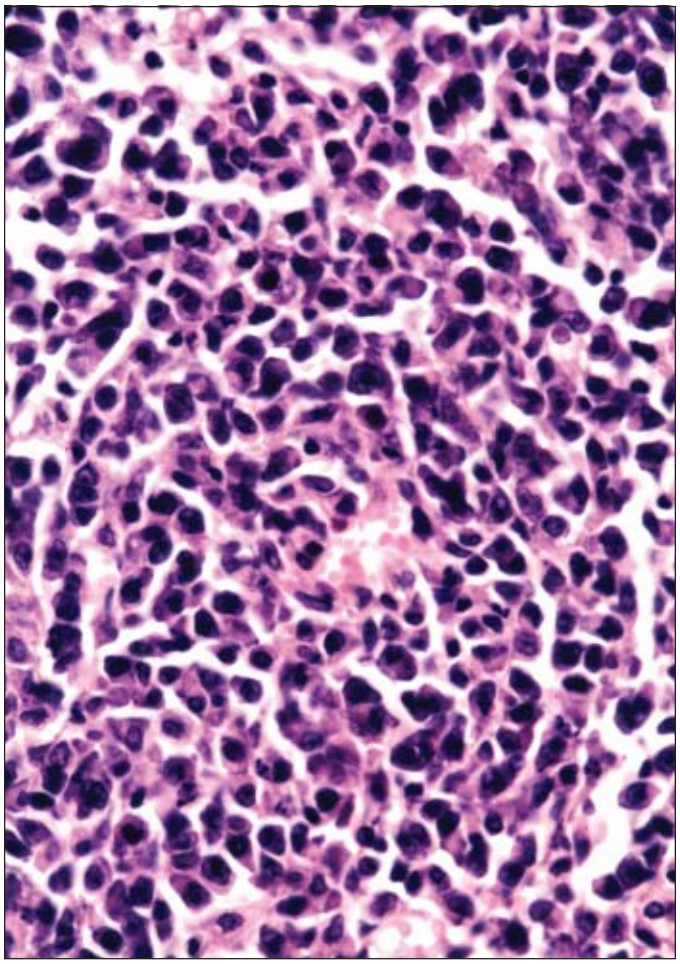

Figure 4. Photomicrograph of a section of a plasmacytoid lymphosarcoma. The neoplastic cells are large with abundant cytoplasm and single, eccentric, large nuclei. H&E stain; magnification = 452×.

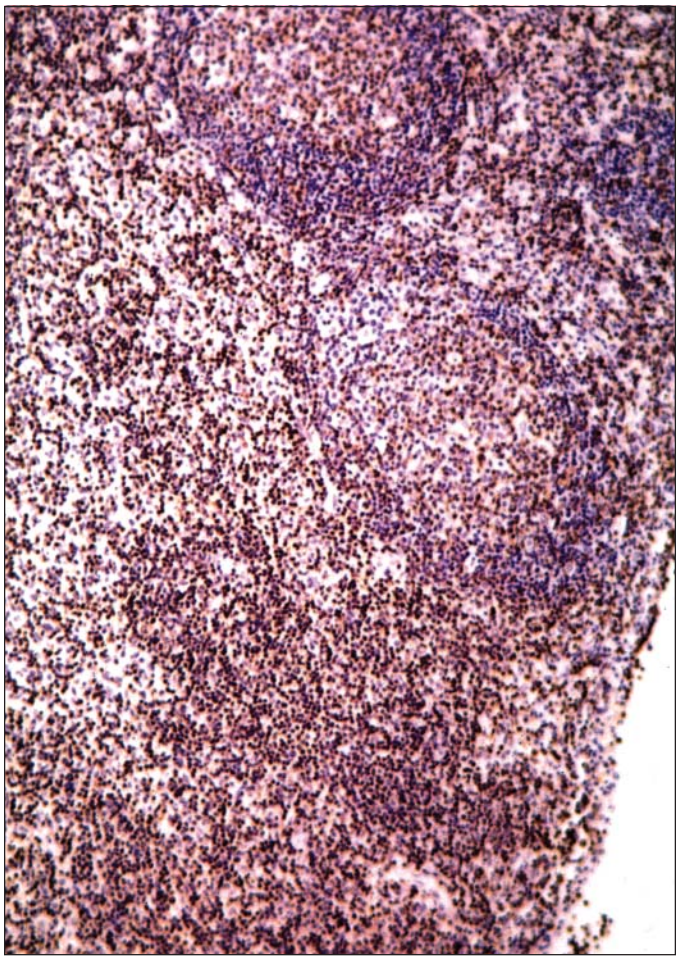

Figure 5. Photomicrograph of a section of normal woodchuck lymph node cortex after CD3 immunostaining. Most of the lymphocytes in the paracortex are staining, as well as are lesser numbers in the germinal centers. Streptavidin-HRP method, DAB chromogen, Gill's hematoxylin counterstain; magnification = 113×.

Immunophenotyping of woodchuck lymphosarcomas. Immunophenotyping was performed for 27 of the 28 cases. The T-cell lymphosarcomas were positive only with CD3 and did not stain with either CD79a or BLA.36. The B-cell lymphosarcomas were CD3 negative and positive with CD79a or BLA.36, or both. Lymphosarcomas that did not stain with any antibody were designated as non-T non-B cell lymphosarcomas. Most commonly, woodchuck lymphosarcomas were B cell in origin (n = 15, 56%, Fig. 8). The T-cell immunophenotype was found in seven cases (26%, data not shown). Tissues from five cases did not stain with any of the antibodies used (non-T non-B lymphosarcomas, 18%; Table 2). The immunostaining was consistent in our cases: no lymphosarcoma co-expressed CD3 with either CD79a or BLA.36 and, among those cases where more than one organ was immunostained, there was no case in which there was a change of the immunostaining pattern within the same animal. Correlation was not found between the Kiel categories and the immunophenotypic data.

Discussion

Epidemiology. The prevalence rate of woodchuck lymphosarcoma (152/100,000/yr) is higher than that of human non-Hodgkin's lymphoma (15.5/100,000/yr for both sexes in all races) (19), canine lymphosarcoma (24.0/100,000/yr) or feline lymphosarcoma (41.6/100,000/yr) (20). The prevalence of lymphosarcoma was not related to WHV serostatus. With the exception of the WHV-induced hepatocellular carcinoma, other neoplasms in the Cornell woodchuck colony develop at low prevalence. The exact reason for the high prevalence rate of lymphosarcoma in the Cornell-colony woodchucks is not known. The Cornell woodchuck colony has been a closed population for over 10 years, but it is not considered specific pathogen free. Serologic screening of the colony animals is only aimed to determine the serostatus for WHV; serologic data are not available for other viruses. However, there have been no gross, histologic, or electron microscopic lesions in the necropsy material that would suggest that these colony woodchucks harbor any other virus that could cause lymphosarcoma. Moreover, reports are not available in the scientific literature about any specific woodchuck virus (including a retrovirus) that could cause lymphosarcoma. Similar to canine lymphosarcoma, lymphosarcoma in colony woodchucks was not related to sex (21). In contrast, feline (18) and human (19) lymphosarcoma more commonly affects males.

Immunophenotyping of normal woodchuck lymphoid organs. The commercial α-CD3, α-CD79a, and α-BLA.36 antibodies had staining patterns in the woodchuck that were simi-

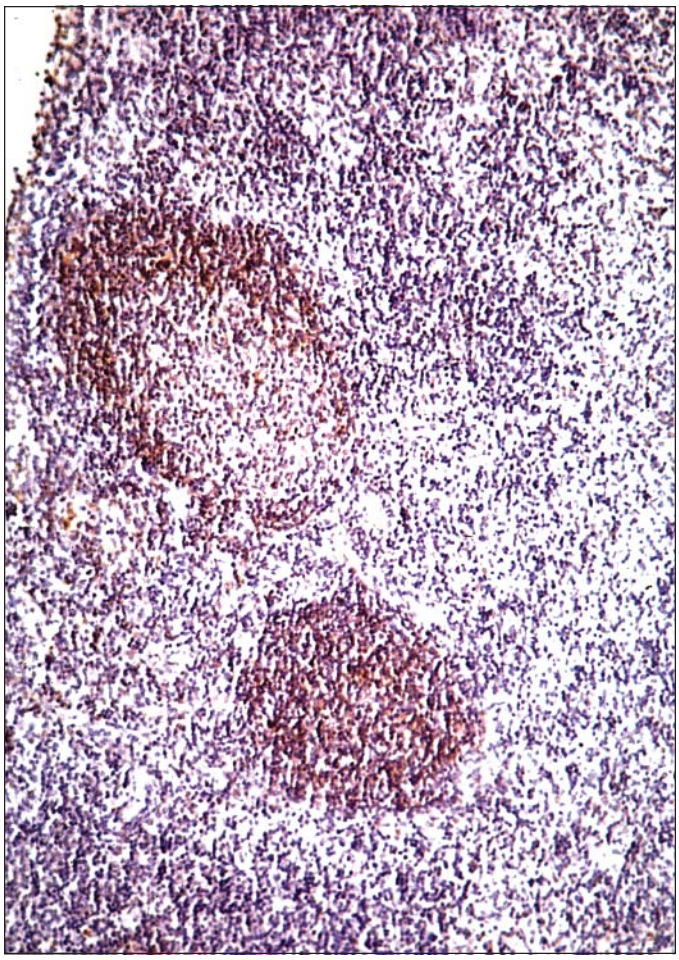

Figure 6. Photomicrograph of a section of normal woodchuck lymph node cortex after CD79a immunostaining. The positively staining lymphocytes are mostly within the lymphoid follicles. Streptavidin-HRP method, DAB chromogen, Gill's hematoxylin counterstain; magnification = 113×.

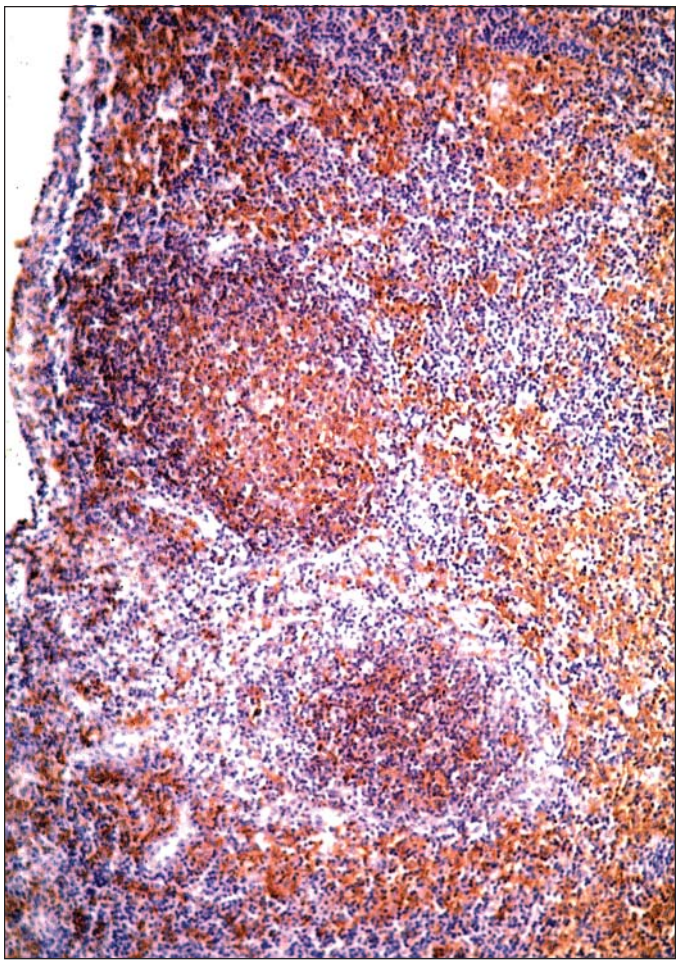

Figure 7. Photomicrograph of a section of normal woodchuck lymph node cortex after BLA.36 immunostaining. Notice the intense staining in the lymphoid follicles and the scattered positive-reacting cells in the paracortex. Streptavidin-HRP method, DAB chromogen, Gill's hematoxylin counterstain; magnification = 113×.

lar to those in the lymphoid organs of other animals (22, 23). Their staining pattern was similar in WHV-infected and non-infected woodchucks and in woodchucks with or without lymphosarcoma, establishing the specificity of these antibodies, their usefulness in woodchucks, and that infection with WHV does not influence the staining pattern.

The pattern of staining observed was similar to that of lymphosarcoma in other animals, including humans, but with a few interesting points. In the woodchuck spleen, CD79a strongly labeled the lymphocytes in the marginal zone and weakly labeled the lymphocytes in the secondary follicles. In contrast, BLA.36 labeling was stronger in the germinal centers and weaker in the marginal zone than was CD79a staining. The possible explanation for this observation is that BLA.36 and CD79a label different subsets of B lymphocytes in the woodchuck spleen. Normally, the thymus contains B lymphocytes in small numbers (24); however, only BLA.36, and not CD79a, labeled substantial numbers of small mature lymphocytes (presumably B cells) in this organ. Additionally, BLA.36 labeled the Hassall's corpuscules in the woodchuck thymus. On the basis of reports involving other species, however, BLA.36-labeling of Hassall's corpuscules is still debated (23, 25).

Immunophenotyping of woodchuck lymphosarcomas. The B-cell lymphosarcomas were the most frequently encountered, similar to human, canine, and feline lymphosarcoma (26-29). The non-T non-B cell lymphosarcoma represented a higher proportion (18%) than that in other species, in which non-T non-B lymphosarcomas usually are found in < 5% of the cases (26). The lack of immunostaining with the antibodies used could be the result of the neoplastic cells being natural killer cells (truly not expressing any of the examined antigens), or undifferentiated lymphocytes that have lost these marker antigens. Additionally, various post mortem artifacts (inadequate fixation, overfixation, and autolysis) could have accounted for lack of immunostaining.

Cranial mediastinal lymphosarcomas were either B or T cell in origin. The B-cell lymphosarcomas in this region may arise either from the B lymphocytes in the mediastinal lymph node or from the BLA.36^{+} cells within the thymus. A recent report by Suster (24) underscores the importance of recognition of a native B-lymphocyte population in the thymus, which can give rise to B-cell lymphosarcoma; therefore, immunophenotypically B-cell lymphosarcomas in the cranial mediastinal region could be true extranodal primary B-cell neoplasms. The T-cell lymphosa-

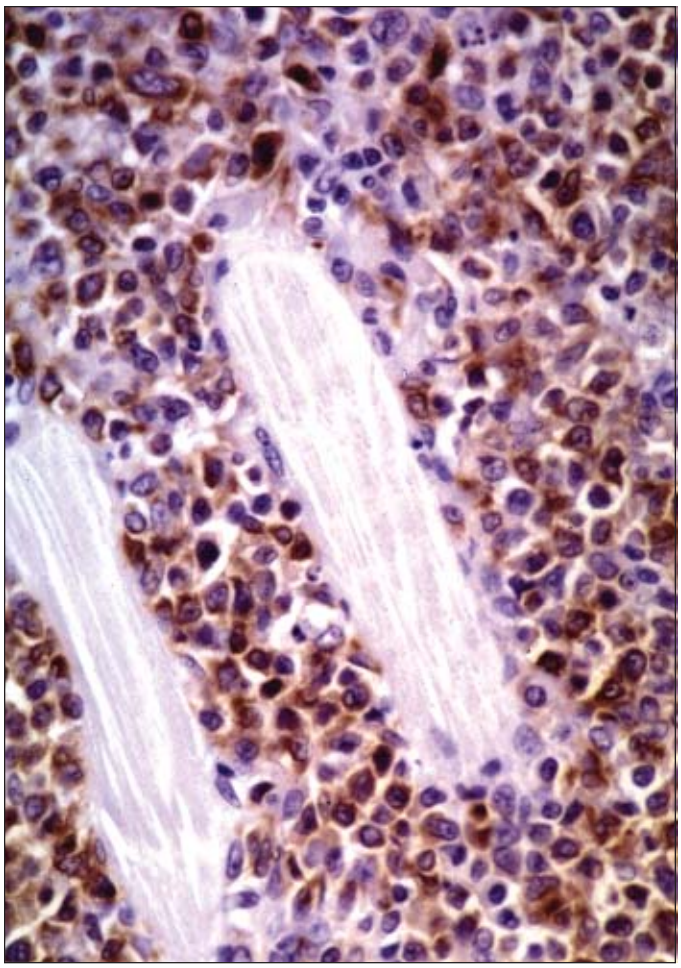

Figure 8. Photomicrograph of a section of a B-cell lymphosarcoma of the diaphragm. Intensely staining neoplastic cells obliterate the normal tissue architecture; two myofibers remain intact (center and lower left hand corner). α-CD79a immunostain, streptavidin-HRP method, DAB chromogen, Gill's hematoxylin counterstain; magnification = 452×.

rcomas in the cranial mediastinal region could arise from the thymic T cells or from T cells in the cranial mediastinal lymph nodes. This possibility stresses the importance of nomenclature of lymphosarcomas arising in the thymic region.

On the basis of our observations, the woodchuck might be an alternative (non-mouse) animal model for human non-Hodgkin's lymphoma. The advantages to use of this colony are: presence of a well established, well researched, immunocompetent, outbred woodchuck colony at Cornell University, and use as a model for a human neoplastic condition and in pharmacologic research. Lymphosarcoma is a spontaneous disease in members of this colony, and has an unusually high prevalence. We have described the first (to our knowledge) comprehensive study of woodchuck lymphosarcoma. Anatomically, microscopically, and immunophenotypically, woodchuck lymphosarcoma was similar to human and canine lymphosarcomas. However, the prevalence rate of lymphosarcoma was remarkably higher than that in other domestic animals or humans. The disadvantage would be that colony woodchucks develop lymphosarcoma usually later in life (at 3 to 4 years of age).

Acknowledgments

This work was supported by contracts NO1-AI-35164 and NO1-AI-05399 to the College of Veterinary Medicine, Cornell University with the National Institute of Allergy and Infectious Diseases. We thank the staff of the Histology Laboratory of the Department of Biomedical Sciences at the College of Veterinary Medicine, Cornell University for tissue processing and glass slide preparations. We are also grateful to the necropsy staff, residents, and pathologists whose cases were used in this study.

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