

## SPONTANEOUS B-CELL LYMPHOMA IN HAMSTER

LINFOMA ESPONTÂNEO DE CÉLULAS-B EM HAMSTER

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**ABSTRACT:** During anatomopathologic study, including immunohistochemistry, about chagasic pancreatitis experimentally induced in four month aged male non-isogenic hamsters, weighing  $107.8 \pm 10.9$ g, lymphoma infiltration was observed in a 15 month-aged normal control animal. The neoplasia was disclosed on the occasion of necropsy studies, 330 days after the beginning of experiment. Similar lymphoma was not found in the remainder normal controls (n=73), nor in the group of infected hamsters age and weight matched (n=94). The neoplasia histopathologic and immunohistochemical changes were consistent with non-Hodgkin diffuse large B-cell lymphoma; nevertheless, the hypothesis of eventual leukemic origin was not entirely excluded. Experimentally induced lymphomas have been related in laboratory animals; however, cases of spontaneously occurring lymphoma have been infrequently described in hamsters. In the present case, the development of the disease could have some relation with the animal aging process.

**UNITERMS:** Hamster. Spontaneous B Lymphoma. Neoplasm.

### 1. INTRODUCTION

The lymphoid segment of hematopoietic system is the most frequent site of spontaneous neoplasm development in hamsters. The frequency of lymphoid neoplasms and the occurrence of horizontally transmitted cases have strengthened the hypothesis that they have an underlying viral etiology and may appear to over a year following exposure to an infectious agent as neonates<sup>(1,2,3)</sup>.

The scanty necropsy reports of lymphoma occurring in hamsters are often cases of hematologic malignancies experimentally induced. We report a case of spontaneous diffuse large cell lymphoma of B-cell lineage detected in a normal control hamster.

### 2. MATERIALS AND METHODS

The procedures with the hamsters were in accordance to the Guide for the Care and use of Laboratory Animals from the National Institute of Health<sup>(4)</sup>, and had ethical approval in our Institution.

Four month-aged male non-isogenic hamsters (*Mesocricetus auratus*) weighing  $107.8 \pm 10.9$ g were initially infected, and reinfected each 75 days later, by peritoneal route, with 2,000 blood forms of the *Trypanosoma cruzi* Vic strain (n=94). Non-infected male hamsters, age and weight-matched, constituted the normal control group (n=73). The hamsters were housed in rigid plastic cages and fed with industrial (NUVILAB CRI®, Colombo-PR) pelleted low-fat diet

(54% carbohydrate, 23% protein and 4% fat) and tap water *ad libitum*.

Before sacrifice, each animal was submitted to light ether inhalation anesthesia<sup>(5)</sup>. The liver and spleen were weighed in a precision scale during necropsy routine. For light microscopy study, the samples were fixed in 10% neutral buffered formalin, embedded in paraffin, then cut at 5 and stained with hematoxylin-eosin (HE).

The immunohistochemical analysis to detect the antigens CD20CY (DAKO, M755), CD45RO (DAKO, M742), CD45RB (DAKO, M701), kappa (DAKO, A191) and lambda (DAKO, K614) was performed, in sections from paraffin-embedded tissue, by streptavidin-biotin-peroxidase method (LSAB plus, DAKO, K690), according to the kit instructions (DAKO, Carpinteria, USA). The primary antibodies were utilized overnight at 4°C, and in the following dilutions: CD20CY 1:500, CD45RO 1:500, CD45RB 1:800, kappa 1:40,000 and lambda 1:50. To reveal the detection system, 3-amino-9-ethyl-carbazole 0.048% (SIGMA, A5754) and hydrogen peroxide 0.0097% were used. Sections of normal human lymph node served as positive controls for the immunohistochemical study, and negative controls were sections of each sample tested without using primary antibodies.

### 3. PATHOLOGIC FINDINGS

In one of the normal control animals weighing 167g, ascites, lung infiltrates, discrete enlargement of the heart and right epididymis, in addition to massive enlargement of liver (19.2g; 11.5% of body weight) and spleen (2.8g; 1.6% of body weight) were observed (Figure 1). Comparatively, the mean weights of liver and spleen from other normal age-matched controls were, respectively, 5.3g (3.9% of body weight) and 0.12g (less than 0.1% of body weight). The liver and spleen showed homogeneous diffuse infiltrate of lymphoid cells containing large vesicular nuclei with one to three evident nucleoli and indistinct cytoplasm (Figure 2). Similar histopathological findings were seen in myocardium, lung, kidney, pancreas, epididymis, small and large intestine, in addition to abdominal skin and bone marrow. Another important finding was the increased number of mononuclear cells inside veins and arteries examined. No lymph node enlargement was detected, but a dermal plaque (3.0 x 1.0cm) was evident in the periumbilical area. The aspect of the organs and of the lymph nodes was normal in the re-

mainder 73 non-infected control hamsters.

The neoplastic cells were negative to T-cells (CD45RO, CD45RB), in addition to kappa and lambda markers; however, they were positive to B-cells marker CD20CY, and the diagnosis of large cell lymphoma of B-cell lineage was confirmed (Figure 3).

### 4. DISCUSSION

The authors describe a diffuse malignant non-Hodgkin B-cell lymphoma spontaneously occurring in a hamster. The disease was found in stage IV, widespread in extra nodal sites including bone marrow and blood. However, the intense mononuclear cells infiltration in bone marrow (Figure 4) and their presence in circulating blood could favor a possible leukemic origin in this lymphoproliferative process.

Hamsters are susceptible to many experimentally induced neoplasms; however, the incidence of spontaneous neoplasm in this animal is considered low under 2 years of age<sup>(6,7,8)</sup>. Lymphoreticular neoplasms are enclosed in the second group in frequency, coming after the adrenal cortex endocrine neoplasms<sup>(7)</sup>. The neoplasm's most common site is on peripheral lymph nodes. The organs more often involved are the bowel, liver, kidney and spleen, although neoplasm infiltrates and white nodular masses can be found in several other body sites. The histological appearance is variable, some showing only immature lymphocytes and others more pleomorphic cells. Large cell lymphoma is the most common cell pattern, but histiocytic or plasma cell differentiated and lymphocytic neoplasms have also been described<sup>(3,6,9)</sup>.

Spontaneously occurring lymphoma has been transplantable, both by subcutaneous and intravenous route, with metastases preferentially in lungs, liver, spleen, kidney and pancreatic lymph nodes<sup>(10)</sup>. In this case, the animal was a 15 month-aged hamster pertaining to the normal control group, and a spontaneous large cell lymphoma of B-cell lineage was characterized, in the absence of lymph node changes.

The most impressive gross finding in this case was the giant enlargement of liver and spleen especially considering that they were, respectively, 3.6 and 23 times heavier than those organs from other normal age-matched control hamsters.

As the accumulated experience in our Laboratory have demonstrated in relation to many other antibodies originally designed to human cases, those used in this study may be, as well, useful in hamsters.

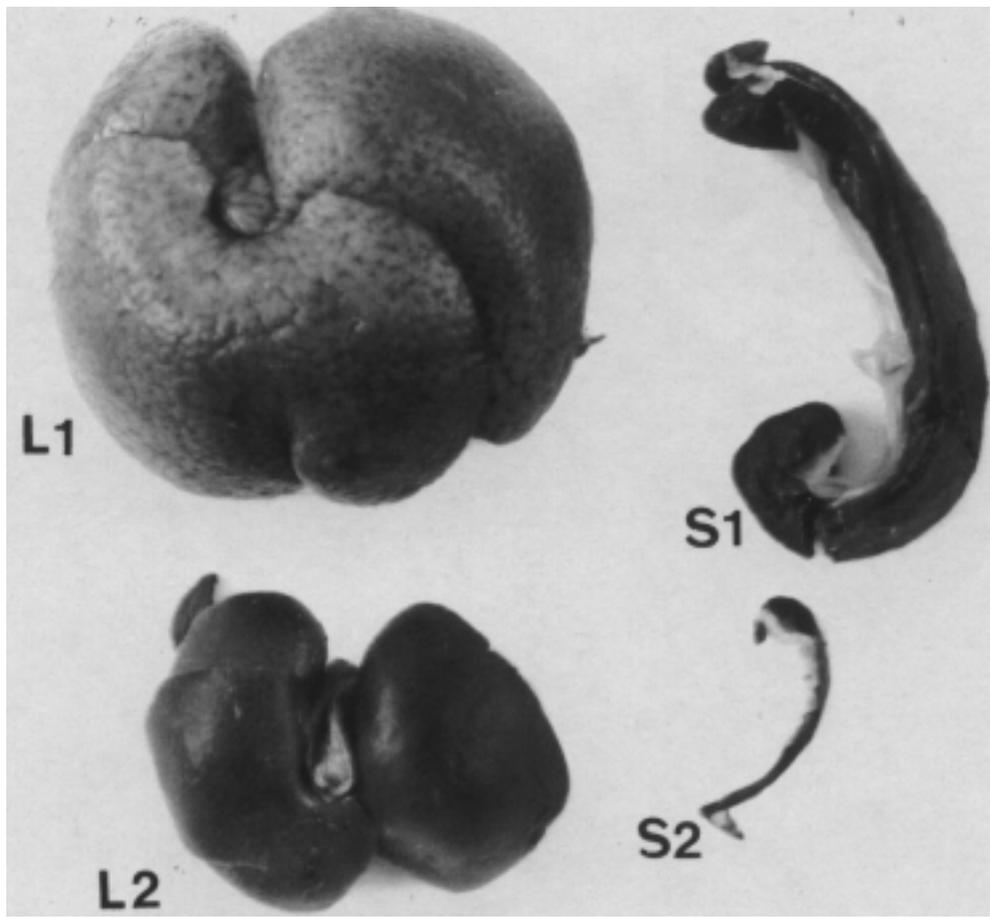


Figure 1. Comparison-between liver (L) and spleen (S) massive enlargement dueto lymphoma (L1 and S1) and the normal aspect of the organs (L2 and S2)

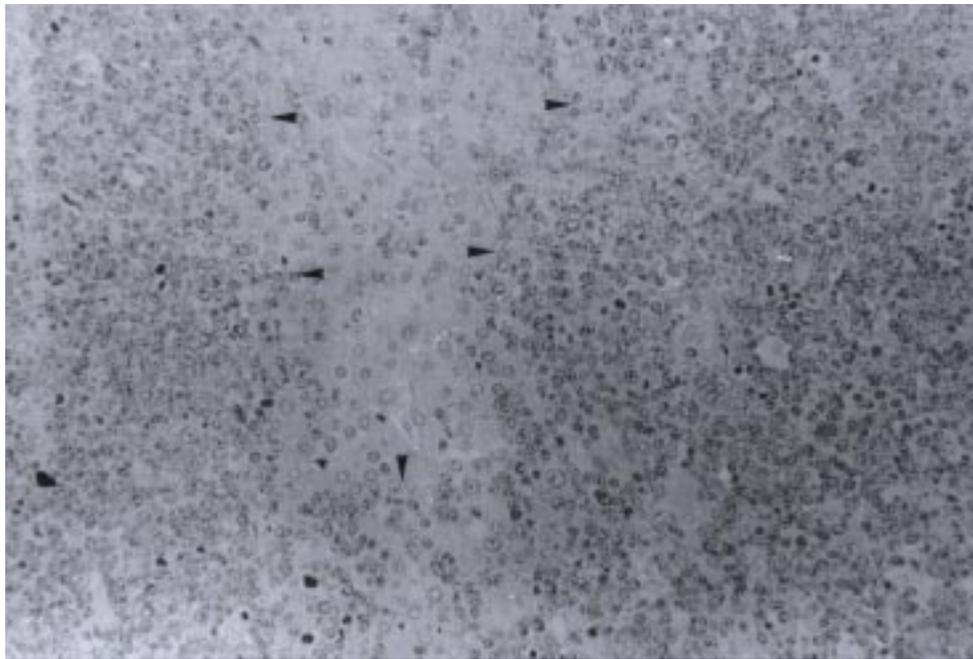


Figure 2. Liver section showing homogeneous diffuse infiltrate of lymphoid cells (arrowheads) characterizing a large cell lymphoma of B-cell lineage (HE x200).

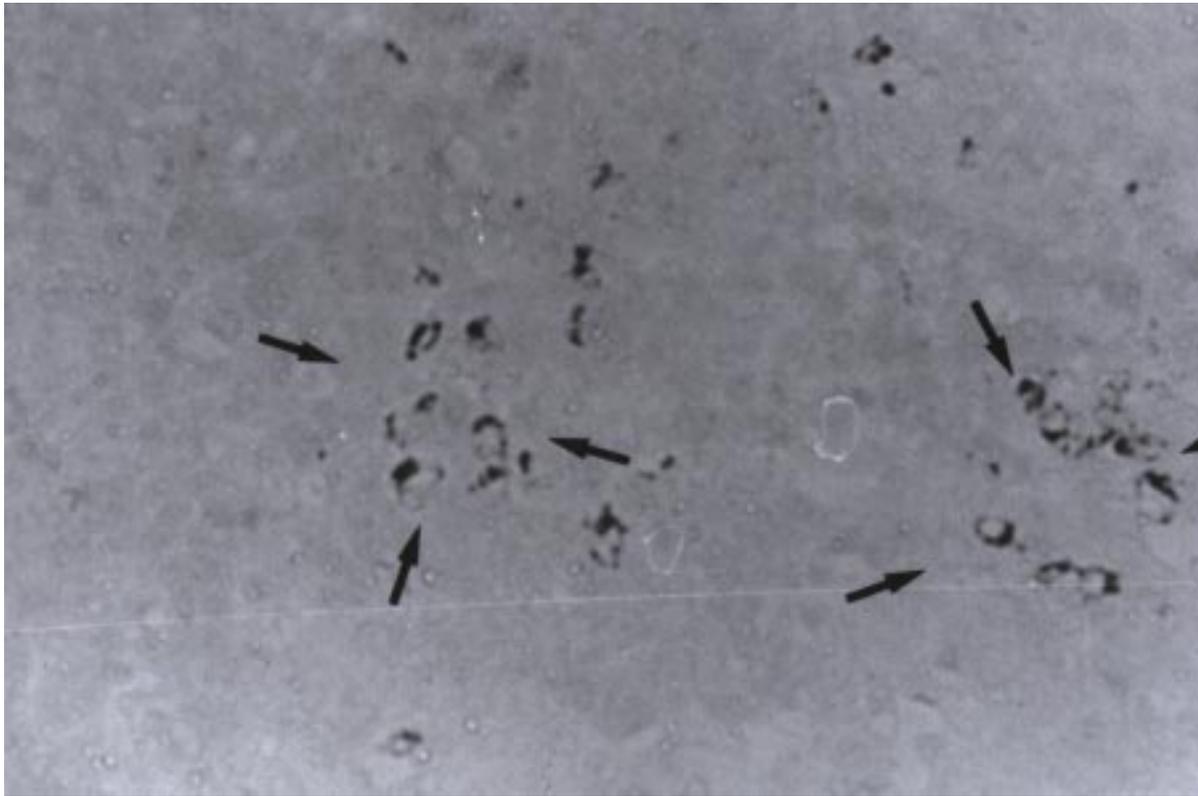


Figure 3. On immunohistochemistry of liver section, the lymphoma cells permeate the normal hepatic parenchyma, and are positive (arrows) to B-cells marker CD20CY (x400).

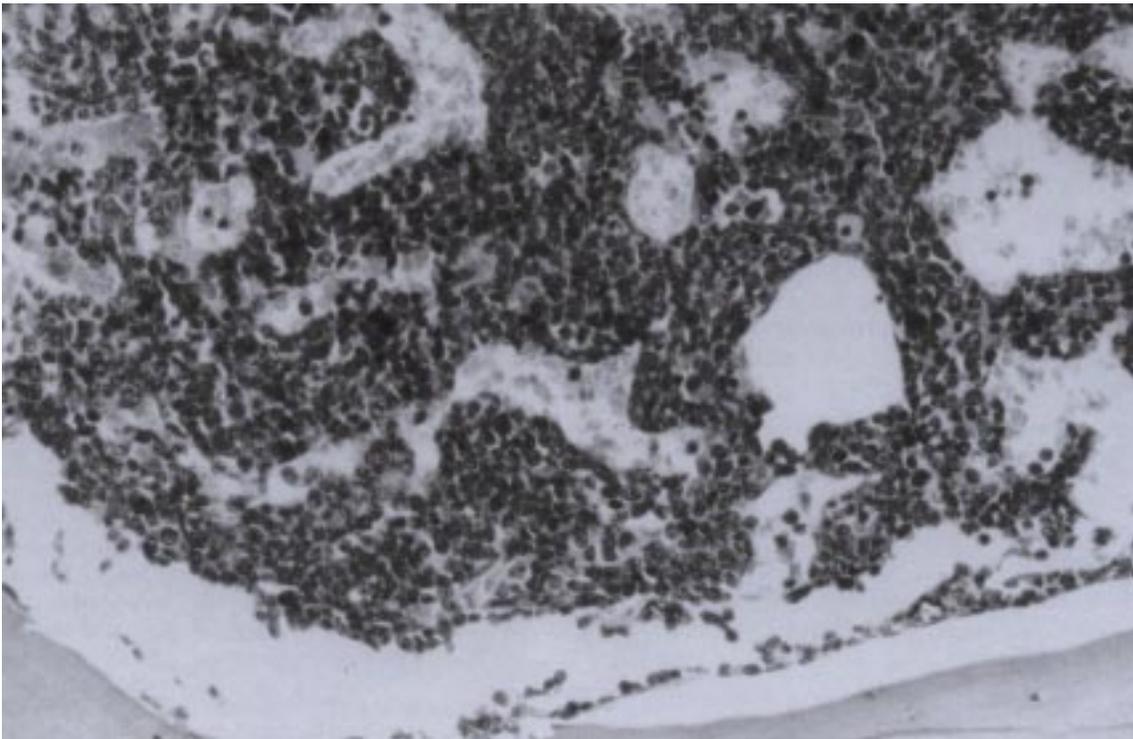


Figure 4. Bone marrow section showing diffuse and massive mononuclear cells infiltration (HE x200).

Considering the fact that lymphoma may appear over a year after neonate hamster exposure to viral infections<sup>(3,11)</sup>, it could be an eventual possibility in the present case. Nevertheless, as this animal had already surpassed 60% of the hamster's 2 years mean lifespan other likely explanation would be the lymphoma development naturally associated to the animal aging, as have been postulated in some cases<sup>(7,8,11)</sup>.

Another concern in this case is about the distinction between lymphoma and lymphocytic leuke-

mia. Moreover, the lymphoma involvement of bone marrow plus increased number of mononuclear cells in blood may indicate an evolution to leukemia.

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SANTOS VM; LIMA MA; MARQUEZ DS; CABRINE-SANTOS M; LAGES-SILVA E; MATHEUS JM; OLIVEIRA JUNIOR JV & RAMIREZ LE. Linfoma espontâneo de células-B em hamster. **Medicina, Ribeirão Preto**, 35: 179-183, abr./jun. 2002.

**RESUMO:** Durante estudo anatomopatológico, incluindo imunoistoquímica, sobre pancreatite chagásica, experimentalmente induzida em hamsters machos, não-isogênicos, com quatro meses de idade, pesando  $107,8 \pm 10,9$ g, infiltração por linfoma foi observada em um animal-controle normal, com 15 meses de idade. A neoplasia foi notada na ocasião da necropsia, 330 dias após o início do experimento. Linfoma similar não foi achado nos demais controles normais (n=73), nem nos hamsters do grupo infectado, pareados para peso e idade (n=94). As alterações histopatológicas e imunoistoquímicas foram consistentes com linfoma difuso, não-Hodgkin, de grandes células-B; porém, a hipótese de eventual origem leucêmica não foi inteiramente excluída. Linfomas experimentalmente induzidos têm sido relatados em animais de laboratório; entretanto, relatos de caso de linfoma, ocorrendo espontaneamente em hamsters, não têm sido frequentes. No presente caso, o desenvolvimento da doença poderia ter alguma relação com o processo de envelhecimento.

**UNITERMOS:** Hamster. Linfoma B Espontâneo. Neoplasia.

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