Histologic Patterns of Lung Infiltration of B-Cell, T-Cell, and Hodgkin Lymphomas

Maria B.G. Costa, MD, PhD,1 Sheila A.C. Siqueira, MD,2 Paulo H.N. Saldiva, MD, PhD,2 Klaus F. Rabe, MD, PhD,3 and Thais Mauad, MD, PhD2,3

Key Words: Lung infiltration; Autopsy; Hodgkin lymphoma; B-cell lymphoma; T-cell lymphoma

DOI: 10.1309/R4BRRADYF20K49HE

A b s t r a c t

Secondary lung infiltration by lymphomas occurs frequently. To our knowledge, however, no recent studies have attempted to discriminate histologic patterns of lung infiltration in the lymphoma subtypes. We retrospectively evaluated the frequency of lung infiltration and the respective infiltration patterns by lymphomas at autopsy, during an 11-year period. Lymphomas were classified according to the 2001 World Health Organization Classification of hematologic malignancies in B-cell, T-cell, and Hodgkin lymphomas (HLs). In 21,157 autopsies, 414 reports with lymphoma diagnosis were reviewed histologically, and 85 showed lung infiltration (20.5%). We studied 14 HLs, 43 B-cell lymphomas, and 20 T-cell lymphomas. Five infiltration patterns were identified: peribronchial-perivascular, nodular, alveolar, interstitial, and pleural. Approximately half of the lymphomas had more than 1 infiltration pattern (mean, 1.7); peribronchial-perivascular and pleural were the most frequent. The frequency of nodular infiltration was larger in HL than in B-cell lymphomas. T-cell lymphomas had a larger frequency of the interstitial infiltration pattern compared with B-cell lymphomas. Recognizing the frequency and patterns of lung infiltration in the light of a more recent classification is certainly useful for physicians dealing with lymphoma diagnostic procedures, such as radiologists and pathologists.

Primary pulmonary lymphomas are very uncommon, whereas secondary infiltration of the lung by hematologic malignancies is a frequent finding. Primary pulmonary lymphomas represent 3% to 4% of the extranodal non-Hodgkin lymphomas (NHLs) and only 0.5% of all primary pulmonary malignant neoplasms.1 On the other hand, autopsy studies revealed that the lung, after the liver, is the second organ involved in the extranodal dissemination of these disease processes.2 It has been shown that parenchymal lung involvement will develop in 38% and 24% of the patients with Hodgkin lymphomas (HL) and NHL, respectively, during the disease.3

Secondary infiltration of the lungs can occur by hematogenic dissemination or by contiguous invasion from a hilar or mediastinal site of the lymphoma.1 It is believed that the intrapulmonary distribution of the lymphomas is determined by the location of the lymphoid tissue in the lung. The lymphatic drainage of the lungs occurs along peribronchial and perivascular axes, and there is organized lymphoid tissue at the bifurcation of bronchi and pulmonary vessels.4 Pleural effusions might occur by one or a combination of the following 3 mechanisms: pleural infiltration by the lymphoma, obstruction of the lymphatics draining the pleura by enlarged intramediastinal lymph nodes, and obstruction of the thoracic duct.3 Pleural effusions are considered a bad prognostic factor in NHL.3

Pulmonary patterns of lymphomatous infiltration have been characterized radiologically as bronchovascular-lymphangitic, alveolar, interstitial, and nodular.5,7 These patterns were demonstrated to have a good correlation with pathologic appearances in some studies.8 Although
pulmonary involvement in NHL frequently occurs in cases of disseminated disease, some authors believed that the anatomic pattern of lung involvement could be a biologic predictor of its behavior. For instance, demonstrated that patients with a nodular lesion have a 30% better prognosis than those with alveolar parenchymal disease. In these studies, no prognostic relation could be established with the histologic type. However, most of the studies regarding the secondary infiltration of the lungs by lymphomas date to 30 years ago. Some of these pathologic studies used now-historic lymphoma classifications such as the Rappaport classification. During the last 30 years, major progresses in the field of hematopathology occurred, culminating in the World Health Organization (WHO) Classification of hematologic malignancies in 2001. This classification has delineated well-characterized clinical-pathologic entities and grouped the lymphomas in 3 major categories (T-cell, B-cell, and HL).

To our knowledge, there are no studies analyzing lung involvement by different types of lymphoma based on this recent classification. In this study, our aim was to discriminate whether WHO Classification entities also could behave differently concerning lung infiltration. Recognizing the patterns of lung infiltration of the different lymphomas in the light of the new classification might be useful for diagnostic (eg, recognition of radiologic patterns) and prognostic purposes. Therefore, we retrospectively analyzed the frequency and the histologic patterns of lung infiltration by B- and T-cell lymphomas and HL at autopsy, comprising a period of 11 years.

Materials and Methods

Autopsies

We retrieved from the files of the Department of Pathology, São Paulo University, São Paulo, Brazil, all autopsy reports with a diagnosis of HL or NHL comprising the period between January 1988 and July 1999. We further discriminated the presence of AIDS as an underlying disease and the occurrence of primary pulmonary lymphomas and lymphomatoid granulomatosis (LYG). Patients’ ages (expressed as median) and sex were obtained. For some cases, we obtained clinical data related to the presence of dyspnea, cough, and abnormal pulmonary auscultation during the last admission. The São Paulo University Medical School Institutional Ethical Committee approved the study.

Tissue Analysis

We reviewed H&E-stained slides of all hematologic autopsies and scored for the presence of lung infiltration. There were 1 to 3 slides containing lung tissue per autopsy. Exclusion criteria were associated infections. Regarding the positive cases, further subclassification according to the following histologic infiltration patterns was done: (1) nodular, unique or multiple, confluent; (2) peribronchial-perivascular, when the lymphoma cells were present along bronchial and vascular bundles; (3) alveolar, when lymphoma cells filled the alveolar spaces in a pneumonic pattern; (4) interstitial, when lymphoma cells infiltrated predominantly along the alveolar septa; and (5) pleural, when lymphoma cells were present in the pleura.
Lymphoma classification for each case was obtained from the original biopsy or excision material, by consulting the surgical pathology files of the Department of Pathology. All cases were reviewed by a hematopathologist (S.A.C.S.) who classified the archived material according to the WHO classification, using new diagnostic immunohistochemical analysis panels and histologic sections when indicated. Lymphomas were grouped as HL, B-cell, and T-cell neoplasms.

As for the immunohistochemical technique, standard procedures were used. Briefly, sections were deparaffinized, and a 0.5% peroxidase in methanol solution was applied for 10 minutes to inhibit endogenous peroxidase activity. Antibody binding was detected with a streptavidin-biotin-peroxidase immunohistochemical system (LSAB Kit, DAKO Duet System, K0675, DAKO, Carpinteria, CA) and revealed with diaminobenzidine. Positive and negative control slides were used in each staining run. Slides were counterstained with Harris hematoxylin.

We were able to retrieve the results of the oncotypic analyses of pleural effusions studied by means of cytomorphologic and cytochemical examination in 16 cases. Pleural

**Image 2**

A, Diffuse large B-cell lymphoma. Peribronchial-vascular pattern of lung infiltration. Lymphoma cells are present along the bronchovascular bundles (arrows) (H&E, ×1.6). B, Follicular B-cell lymphoma. Peribronchial pattern of lung infiltration. Lymphoma cells infiltrate all layers of the bronchiole (B) (H&E, ×100).

**Image 3**

Diffuse large B-cell lymphoma. A, Alveolar pattern of lung infiltration. Lymphoma cells fill the alveolar spaces, conferring a pneumonic aspect to the tissue (H&E, ×100). B, Detail of Image 3A. Note the large lymphocytes filling the alveolar spaces (A) (H&E, ×400). AS, Alveolar septa.
effusion results were compared with the presence or absence of pleural infiltration. We identified the interval in days between the procedure and the autopsy.

**Statistical Analysis**

Patterns of lung infiltration were expressed as percentages. The $\chi^2$ or the Fisher exact test was used to compare the frequency of histologic type and patterns of lung infiltration. $P$ values smaller than .05 were considered significant. SPSS, version 11.0 (SPSS, Chicago, IL) was used for statistical analysis.

**Results**

We analyzed the reports of 21,157 autopsies performed between January 1988 and July 1999, and 414 cases (1.957%) in which the diagnosis of primary disease was NHL or HL: 82 autopsies had HL and 332 had NHL as the diagnosis. Of the 414 cases, 85 (20.5%) of them showed lung infiltration. The frequency of infiltration was 17% (14/82) for HL cases and 21.4% (71/332) for the NHL cases. We were not able to study 8 of 71 NHLs, mostly because the original biopsy specimens were not available in

---

**Image 4** Peripheral T-cell lymphoma. A, Interstitial pattern of lung infiltration. Lymphoma cells infiltrate along the alveolar septa that become thickened (H&E, ×100). B, Detail of Image 4A. The alveolar septa (AS) become thickened owing to the infiltration of lymphoma cells (H&E, ×200). A, alveolar space.

**Image 5** Diffuse large B-cell lymphoma. A, Pleural infiltration pattern. Lymphoma cells are present in the pleural compartment (P), which is visibly thickened (H&E, ×50). B, Detail of Image 5A. Large lymphoid cells are infiltrating the pleura (H&E, ×400).
the Department of Pathology or material was not appropriate for adequate diagnosis. Therefore, among the NHLs, there were 43 B-cell and 20 T-cell lymphomas. In 2 HLs, the primary diagnosis was made at the autopsy.

Table 2 shows patient age and sex and the infiltration patterns of all B- and T-cell lymphomas and HLs. Of the lymphomas, 38 (49%) of 77 showed 2 or more infiltration patterns; the average number of infiltrations per case was 1.7. Peribronchial-vascular involvement was the most frequent and alveolar the least frequent infiltration pattern (Table 2). HLs had a higher frequency of nodular involvement than did B- and T-cell lymphomas. The \( \chi^2 \) test revealed a trend of .07 for the nodular pattern when all 3 subtypes were compared and statistical significance when HL was compared with B- and T-cell lymphoma combined (\( P = .023, \chi^2; P = .033, \text{Fisher exact test} \)). There was a larger frequency of the nodular infiltration pattern in the HLs than in the B-cell lymphomas (\( P = .036, \chi^2; P = .059, \text{Fisher exact test} \)) and a similar trend between HL and T-cell lymphomas (\( P = .048, \chi^2; P = .08, \text{Fisher exact test} \)). There was a larger frequency of interstitial infiltration in the T-cell lymphomas than in the B-cell lymphomas (\( P = .056, \chi^2; P = .085, \text{Fisher exact test} \)). The pleural infiltration pattern was common in the 3 groups, and pleural infiltration alone was present in 5 (7%) of 75 cases.

Table 3 shows the patient age and sex and infiltration patterns for the B-cell subtypes. Diffuse large B-cell lymphoma (DLBCL) was the most prevalent type, followed by small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL) and Burkitt lymphoma (4 patients). SLL/CLL had a lower frequency of nodular involvement than the other types, except follicular lymphoma. There was statistical significance when nodular involvement was compared in the 2 major subgroups SLL/CLL and DLBCL (\( P = .003, \chi^2; P = .04, \text{Fisher exact test} \)). There was no pleural infiltration in any of the 4 Burkitt lymphoma cases in this series. There was a lower frequency of the pleural infiltration pattern in the Burkitt lymphomas compared with DLBCL and SLL/CLL cases (\( P = .001 \) and \( P = .011 \), respectively, \( \chi^2; P = .002 \) and \( P = .023 \), respectively, Fisher exact test).

Among the T-cell neoplasms, the most common type infiltrating the lungs was peripheral T-cell lymphoma, not otherwise specified, followed by adult T-cell lymphoma/leukemia and anaplastic cell lymphoma. Table 4 shows patient age and sex and infiltration patterns in the lung

<table>
<thead>
<tr>
<th>Table 11</th>
<th>Antibodies Used in the Study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antigen</strong></td>
<td><strong>Source</strong></td>
</tr>
<tr>
<td>CD3</td>
<td>DAKO A/S, Glostrup, Denmark</td>
</tr>
<tr>
<td>CD5</td>
<td>Novocastra, Newcastle upon Tyne, England</td>
</tr>
<tr>
<td>CD10</td>
<td>Novocastra</td>
</tr>
<tr>
<td>CD15</td>
<td>DAKO A/S</td>
</tr>
<tr>
<td>CD20</td>
<td>DAKO, Carpinteria, CA</td>
</tr>
<tr>
<td>CD30</td>
<td>DAKO A/S</td>
</tr>
<tr>
<td>CD43</td>
<td>Novocastra</td>
</tr>
<tr>
<td>CD45RO</td>
<td>DAKO A/S</td>
</tr>
<tr>
<td>bcl-2</td>
<td>DAKO A/S</td>
</tr>
<tr>
<td>Ki-67</td>
<td>DAKO A/S</td>
</tr>
<tr>
<td>Epithelial membrane antigen</td>
<td>DAKO A/S</td>
</tr>
<tr>
<td>Leukocyte common antigen</td>
<td>DAKO</td>
</tr>
<tr>
<td>AE1/AE3</td>
<td>DAKO</td>
</tr>
<tr>
<td>Anaplastic lymphoma kinase-1</td>
<td>DAKO A/S</td>
</tr>
<tr>
<td>Cyclin D1</td>
<td>DAKO A/S</td>
</tr>
</tbody>
</table>

Table 2

Number of B-Cell, T-Cell, and Hodgkin Lymphomas That Showed Lung Infiltration at Autopsy (\( N = 77 \))

<table>
<thead>
<tr>
<th>Infiltration Pattern</th>
<th><strong>Histologic Lymphoma Type</strong></th>
<th><strong>No. (%) of Cases</strong></th>
<th><strong>Median Age (y)</strong></th>
<th><strong>Sex Ratio (M/F)</strong></th>
<th><strong>Peribronchial-Vascular</strong></th>
<th><strong>Nodular</strong></th>
<th><strong>Alveolar</strong></th>
<th><strong>Interstitial</strong></th>
<th><strong>Pleural</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>B-cell</td>
<td>43 (66)</td>
<td>57</td>
<td>33:10</td>
<td>30 (70)</td>
<td>14 (32)</td>
<td>6 (14)</td>
<td>11 (25)</td>
<td>31 (76)†</td>
<td></td>
</tr>
<tr>
<td>T-cell</td>
<td>20 (26)</td>
<td>38</td>
<td>12:8</td>
<td>15 (75)</td>
<td>6 (30)</td>
<td>6 (30)</td>
<td>10 (50)</td>
<td>11 (55)</td>
<td></td>
</tr>
<tr>
<td>Hodgkin</td>
<td>14 (18)</td>
<td>27</td>
<td>11:3</td>
<td>11 (79)</td>
<td>9 (64)</td>
<td>4 (29)</td>
<td>5 (36)</td>
<td>9 (64)</td>
<td></td>
</tr>
</tbody>
</table>

† Data are given as number (percentage) unless otherwise indicated.

‡ Pleural tissue was not represented in tissue sections of 2 B-cell lymphomas, so the percentage is based on 41 cases.
for the T-cell lymphoma subtypes. The adult T-cell lymphoma group had a higher frequency of interstitial involvement than the other types. However, the Fisher exact test performed among the 3 major T-cell lymphoma groups yielded no significant differences, probably because of the small sample.

Of 82 HLs, 14 showed lung infiltration. The most common subtype infiltrating the lungs was the mixed cellularity subtype, followed by the lymphocyte depletion subtype. Table 3 shows patient age and sex and infiltration patterns for the classic HL subtypes. The distribution of the infiltration patterns was similar between the 2 principal subtypes.

We identified 1 case of primary pulmonary lymphoma in this series, a mature peripheral T-cell lymphoma, from the subtype adult T-cell lymphoma/leukemia, human T-lymphotropic virus (HTLV)-1+. Three patients had AIDS-associated lymphoma, 2 with the DLBCL subtype and 1 with Burkitt lymphoma, with plasmacytoid differentiation. All patients with AIDS had disseminated lymphoma at autopsy. We identified 4 patients with clinically diagnosed LYG of different primary locations: skin, lungs, brains, and nose. At autopsy, 3 had infectious or congestive abnormalities of the

Table 3
Histologic Subtypes of B-Cell Lymphomas That Showed Lung Infiltration at Autopsy (n = 43)*

<table>
<thead>
<tr>
<th>Histologic Subtype</th>
<th>Infiltration Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%) of Cases</td>
</tr>
<tr>
<td>DLBCL†</td>
<td>18 (42)</td>
</tr>
<tr>
<td>SLL/CLL</td>
<td>15 (35)</td>
</tr>
<tr>
<td>Burkitt lymphoma/leukemia§</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Follicular lymphoma</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Mantle cell lymphoma</td>
<td>3 (7)</td>
</tr>
</tbody>
</table>

DLBCL, diffuse large B-cell lymphoma; SLL/CLL, small lymphocytic lymphoma/chronic lymphocytic leukemia.

* Data are given as number (percentage) unless otherwise indicated.
† Two patients had AIDS.
§ One patient had AIDS, with the plasmacytoid variant.

Table 4
Histologic Subtypes of T-Cell Lymphomas That Showed Lung Infiltration at Autopsy (n = 20)†

<table>
<thead>
<tr>
<th>Histologic Subtype</th>
<th>Infiltration Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%) of Cases</td>
</tr>
<tr>
<td>Peripheral T-cell lymphoma, NOS</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Anaplastic lymphoma, T-cell/null type</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Adult T-cell lymphoma/leukemia (HTLV-1+)†</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Angioimmunoblastic lymphoma</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Precursor T lymphoblastic lymphoma</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Enteropathy type T-cell lymphoma</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Mycosis fungoides/Sézary syndrome</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>

HTLV, human T-lymphotropic virus; NOS, not otherwise specified.
† Data are given as number (percentage) unless otherwise indicated.
‡ Includes 1 case of primary pulmonary lymphoma.
lungs. One patient had extensive angiocentric necrotic lesions of the lungs with secondary bacterial infection, but no remnants of an atypical lymphoid infiltrate were observed.

In 49 cases, we were able to obtain clinical data related to pulmonary abnormalities during the last admission: 28 (57%) had dyspnea, 18 (37%) had a cough, and 35 (71%) had altered pulmonary auscultation findings. There was no significant association of lymphoma subtypes and patterns of lung infiltration with these clinical parameters.

In 5 of 16 cases in which cytologic examination of pleural effusions was done, there was concordance between pleural effusion and pleural findings (31%). In 2 cases, oncocytic analysis was positive, but no pleural infiltration could be detected at autopsy. Nine patients had pleural infiltration at autopsy but negative pleural fluids. The median number of days between the procedure and death was not different among positive (8 days) and negative (8 days) pleural effusions ($P = .280$, $\chi^2$; $P = .528$, Fisher exact test).

## Discussion

In this large, 11-year, retrospective autopsy study, we found that the lung was infiltrated in 20.5% of patients with a previous diagnosis of HL and NHL. To our knowledge, we are the first to attempt to verify the pattern of lung infiltration in different histologic types according to the recent WHO Classification. Our results show that, at autopsy, lung infiltration is predominantly peribronchial-perivascular and pleural in all 3 subtypes examined. Our results confirm previous radiologic studies showing that frequently more than 1 infiltration pattern is present in the lungs infiltrated by lymphomas. We further observed that, in comparison with B-cell lymphomas, HLs have a large frequency of the nodular infiltration pattern. T-cell lymphomas, in turn, have a larger frequency of the interstitial pattern than do the B-cell lymphomas.

Similar studies date back to the 1970s and 1980s. Most of them analyzed patterns of lung infiltration through radiologic methods and used histologic examination to confirm the lymphoma diagnosis. Furthermore, most of these studies used historic nomenclatures such as the Rappaport classification, making comparisons with present data difficult. Mentzer et al reviewed the medical records of 651 patients with lymphoma and identified lung involvement in 8.4% of the surgical specimens. The lung was involved secondarily in 61% of the cases, and diffuse NHL was the predominant lymphoma type. These authors verified that the histologic diagnosis did not predict the gross anatomic pattern of lung involvement, analyzed by means of radiologic techniques. In our study, we detected similar percentages of lung involvement by NHL and HL (21.4% [71/332] and 17% [14/82], respectively). Although some authors assert that parenchymal lung involvement is more common in HL than in NHL, our study and other autopsy studies have shown similar frequencies of infiltration.

The majority of the studies dealing specifically with lung infiltration by different B- and T-cell lymphomas are case reports. In our series, we were able to analyze 43 B-cell and 19 T-cell lymphomas that had lung infiltration at autopsy. DLBCLs and SLL/CLLs accounted for the majority of the B-cell lymphomas in our series. When comparing SLL/CLL with DLBCL (Table 3), a distinguishing pattern was the low frequency of the nodular infiltration pattern in SLL/CLL. None of the 4 Burkitt lymphomas studied in this series showed pleural infiltration. Nzeh stated that pleural involvement also was uncommon in Nigerian children with Burkitt lymphoma, while it seems to be more frequent in white patients. In Brazil, Burkitt lymphoma manifests with characteristics intermediate between the epidemic and sporadic types of this lymphoma.

Peripheral T-cell lymphomas seem to involve the lung frequently, 20% at diagnosis and a further 20% during the course of the disease. In our study, T-cell lymphomas represented 26% of the lymphomas that had lung infiltration (20/77). This percentage might reflect an increased incidence of T-cell lymphomas in Brazil, although no official data are available. In fact, a single-center study published in a Brazilian journal, in which 145 NHLs were classified into subtypes, revealed that 22.7% of the cases were T-cell lymphomas, contrasting with 12% worldwide. HTLV-1 infection is endemic in some regions of Brazil, and this fact could partially explain the high incidence of T-cell disorders in our country.
T-cell lymphomas represent several entities that have clinicoradiologic features different from those of lymphomas with the B-cell phenotype. A distinguishing feature of the T-cell lymphomas in this study was an increased frequency of the interstitial pattern compared with the B-cell lymphomas. Interestingly, there were 4 cases of anaplastic T-cell lymphoma infiltrating the lungs. In a large series of 146 patients with anaplastic large cell lymphoma, lung infiltration without mediastinopathy was one of the peculiarities of this type of neoplasia compared with other cases of nonanaplastic large B-cell lymphoma.22 All the adult T-cell lymphomas/leukemias had an interstitial pattern of involvement, which was more frequent in the leukemic lung infiltrates.23

HL frequently infiltrates the lungs, in up to 20% at diagnosis and to 40% during the clinical course of the disease, and several radiologic studies have examined the patterns of intrathoracic infiltration in this lymphoma.7 In an autopsy study, Colby et al24 demonstrated that 39% of patients with HL had lung involvement. Diederich et al7 demonstrated that radiologically, the most common infiltration pattern was nodules (88% of the computed tomography scans). In the present series, the lungs were infiltrated in 17% of the patients with HL (14/82), a percentage considerably less than in the study by Colby et al24 but similar to that found by Mentzer et al6 (20%). We confirmed that the nodular pattern is a characteristic of lung infiltration in HL, but no differences could be detected in the subtypes. HL infiltrates commonly are associated with a fibrohistiocytic reaction, a fact that possibly can explain the frequent nodular infiltration pattern observed in the present study.

Some studies have reported predominance of the nodular sclerosis HL subtype infiltrating the lungs,7,24 while our study indicated predominance of the mixed cellularity subtype. Such a difference might be explained by the distribution of the different HL subtypes in Brazil, ie, a predominance of the mixed cellularity subtype rather than a special predilection of this subtype to infiltrate the lungs.25

Primary pulmonary lymphomas are uncommon. They are low-grade B-cell lymphomas in 80% of the cases, especially the bronchus-associated lymphoid tissue–associated lymphomas, and have a low mortality rate.26 We were able to identify 1 case of primary pulmonary lymphoma in this series, confirming its rarity and low mortality rates, and it was a T-cell lymphoma, HTLV-1+, infiltrating primarily the lungs, an entity that has been described rarely.27

In our series, the lymphomas infiltrating the lungs in AIDS were, as expected, high-grade B-cell lymphomas, including 1 case of the new WHO subtype Burkitt lymphoma with plasmacytoid differentiation. Lung infiltration occurred as a result of extensive disease dissemination in all patients. The introduction of highly active antiretroviral therapy in AIDS seems to be related to an increase in pulmonary involvement by lymphomas,28 and pathologists and radiologists should be prepared to recognize these entities.

LYG was described classically as an angiocentric and angiodestructive lymphoreticular proliferation frequently involving the lungs.29 It is now accepted that, in most cases, LYG is an Epstein-Barr virus–related B-cell lymphoma with a prominent T-cell response. In the WHO classification, LYG is considered a variant of DLBCL.11 although T-cell LYG also has been described.30 In our study, 1 patient with LYG had extensive necrotic lesions of the lung. Although we could not identify remnants of the atypical infiltrate at autopsy, the histologic pattern of angiocentric necrotic lesions is characteristic of this entity.

The presence of a pleural effusion in a patient with lymphoma is associated with a poor overall prognosis.3 There is some controversy in the literature whether pleural effusion in lymphomas is caused by direct tumor invasion of the pleura or by lymphatic obstruction.31,32 In our series, the pleural infiltration pattern was a common finding in all B- and T-cell lymphomas and HLs (31/41 [76%], 11/20 [55%], and 9/14 [64%], respectively; Table 2) and was accompanied by pulmonary parenchymal involvement in the large majority of cases.

One autopsy study showed that 50% of patients with HL and 72% of patients with NHL with pleural effusion had malignant pleural infiltration.33 Obviously, these populations most likely reflect cases of extreme disease dissemination and cannot be compared with cases of limited disease. The results suggest, however, that pleural effusion could be the result of tumor invasion in the majority of the cases. The fact that pleural involvement alone without parenchymal involvement occurred in a few cases (5/75 [7%]) confirms the fact that pleural involvement alone is an unusual finding in lymphomas.31 In our series, there was concordance between positive pleural effusions and pleural infiltration at autopsy in 5 (31%) of 16 cases. The analysis of lymphomatous pleural effusions might pose diagnostic difficulties with reactive conditions, and some studies have shown that the use of ancillary techniques such as immunohistochemical analysis and flow cytometry increase the sensitivity of this procedure.34

Indeed, 2 cases had positive results in oncocytochemical analyses, but no lymphoma infiltration was detected at autopsy.

A limitation of this study lies in the fact that it reflects cases of extreme disease dissemination, and some of the results have to be interpreted in this context, such as the multiple patterns of lung infiltration in approximately half of the cases. Also, detailed knowledge about clinical and radiologic data would have enriched our data. Our findings might be used as a basis for prospective radiologic studies.

In this autopsy study, we determined the frequency of lung infiltration and described the histologic infiltration patterns of lymphomas, classified according to the WHO Classification.
Increasing this kind of knowledge clearly seems desirable for the physicians dealing with the diagnosis of pulmonary infiltration in lymphomas, such as radiologists and pathologists.

References