Primary Pulmonary AIDS-Related Lymphoma*

Radiographic and CT Findings

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Study objectives: To describe the radiographic and CT findings of primary AIDS-related lymphoma (ARL) of the lung (ARLL), and to evaluate percutaneous transthoracic needle biopsy (PTNB) in the diagnosis of primary ARLL.

Materials and methods: Seven chest radiographs and seven CT scans of HIV-infected patients with histologically proved primary pulmonary non-Hodgkin’s lymphoma (PPL) were reviewed at our institution. All of the patients had fibroscopy with BAL. The diagnosis of PPL was established histologically by means of PTNB (n = 4), open-lung biopsy (n = 2), or autopsy (n = 1).

Results: All but one patient had multiple peripheral well-defined nodules of various sizes on the chest X-ray film and CT scan. One patient had a subpleural parenchymal infiltrate and another had a main peripheral mass with spontaneous cavitation. Hilar/mediastinal adenopathies and pericardial/pleural effusion were never associated with the parenchymal abnormalities. Fibroscopy with BAL was always negative. PTNB, done in six cases, was diagnostic in four cases and suggested primary ARLL in two cases. No complications occurred during these procedures.

Conclusion: After excluding infectious causes, multiple peripheral nodules and/or masses without hilar or mediastinal adenopathies and without pleural effusion are suggestive of primary pulmonary ARL. A specific diagnosis can be obtained by means of PTNB.

Patients with AIDS have a higher risk of neoplastic disease. Lymphoma occurs in 3 to 10% of patients with AIDS and is the second most common malignancy in this group (the first is Kaposi’s sarcoma [KS]). AIDS-related lymphoma (ARL) is almost exclusively non-Hodgkin’s lymphoma (NHL), usually of the high-grade B-cell type. In immunocompromised patients without AIDS, the most common is primarily extranodal. The most frequent disorders are identified histologically in the CNS, GI system, liver, spleen, and bone marrow. Thoracic disorder occurs in < 10% of the cases. Various aspects of ARL in the chest have been described, including pleural effusion, interstitial and alveolar lung disease, nodules, and occasionally, hilar and mediastinal adenopathies. One major limitation in previous reports is that they did not distinguish primary from disseminated ARL of the chest. Primary pulmonary ARL is defined by exclusive lymphomatous parenchymal involvement with no other sites of involvement at diagnosis or within 3 months following diagnosis. The aims of this study were to review radiographic and CT findings in seven consecutive AIDS patients with primary pulmonary lymphoma and to evaluate percutaneous transthoracic needle biopsy (PTNB) in this setting.

Materials and Methods

Study Design

From December 1985 to December 1996, 536 CT scans were performed for 536 episodes of pulmonary manifestations in 424 HIV-infected patients. The frequency of primary ARL in this series of CT scans was 1.3%. This is not the real prevalence of the disease in HIV-infected patients, however, because not all

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Key words: AIDS; CT; lung biopsy; lymphoma

Abbreviations: ARL = AIDS-related lymphoma; ARLL = ARL of the lung; KS = Kaposi’s sarcoma; NHL = non-Hodgkin’s lymphoma; OLB = open-lung biopsy; PCCP = Pneumocystis carinii pneumonia; PTNB = percutaneous transthoracic needle biopsy

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Pulmonary manifestations were explored by means of CT. We reviewed the medical charts, chest radiographs, and chest CT scans of seven patients with AIDS and primary pulmonary lymphoma (five patients were seen in the last 5 years). The diagnosis of primary ARL was proved by means of PTNB (n = 4), open-lung biopsy (OLB; n = 2), or autopsy (n = 1). All but one of the lymphomas were high grade, the last being intermediate grade. These lymphomas were either of the B-cell type (n = 6) or indeterminate (n = 1). Extrapulmonary involvement was ruled out by normal findings on the abdominal ultrasound and/or CT scan, CNS CT scan or MRI, and bone marrow biopsy.

Patients

All of the patients were men. Six were homosexual, one was an IV drug user, and one was infected by blood transfusion. Their mean age was 37 years old (range, 31 to 52 years old). All had already had AIDS-related infections and their CD4+ cell counts were < 50 cells/μL. None had cutaneous KS. All presented with weight loss and fever between 38.5°C and 40°C; no opportunistic infections were found, except for a case of Pneumocystis carinii pneumonia (PCP). The correct diagnosis was delayed by erroneous diagnoses in five of the seven patients (four infections and one suspected thromboembolism). Fiberoptic bronchoscopy and BAL were performed in every case and did not reveal macroscopic lesions. BAL was negative in all seven cases for the diagnosis of primary pulmonary NHL. The case of PCP was diagnosed by BAL. The mean survival rate was 6.4 months (range, 1 to 17 months).

CT and PTNB

The CT scans were obtained at 10-mm intervals throughout the chest with 1- to 2-mm collimation (n = 4) or 10-mm collimation (n = 3). The 1- to 2-mm collimation scans were reconstructed with a high-spatial-frequency algorithm. CT was performed with IV-administered contrast material in all but one patient. Images were viewed at the lung and mediastinal window settings. CT scans were assessed for the presence and anatomic location of parenchymal disease, pleural effusion, and mediastinal adenopathies. Nodules were defined as focal opacities of various sizes (< 30 mm in diameter), and could be well defined or ill-defined. Tumor masses (> 30 mm in diameter) were defined with or without air bronchograms. Mediastinal lymphadenopathy was considered to be present when the short-axis diameter of the nodes was ≥ 10 mm.

All but one patient underwent PTNB evaluation for the diagnosis of ARL. The patient without PTNB was first suspected of having a pulmonary embolism and was the first patient in this series. CT guidance was used for PTNB, which was done using a coaxial technique in every case. An 18-gauge outer needle served as a conduit for an inner 20-gauge needle. A cytopathologist, who was present during all of the procedures, performed fast staining of aspirated specimens followed by immediate microscopic examination.

All tissue samples were reviewed by the same pathologist. Primary pulmonary NHL was classified according to the updated Kiel classification and equivalents in the National Cancer Institute Working Formulation on the basis of sections routinely stained with hematoxylin-eosin and Giemsa. Histologic assessment was completed with immunohistochemical analysis of paraffin sections using the streptavidin biotin peroxidase method. The following T-cell, B-cell, and epithelial cell markers were studied: anti-CD20, CD3, CD45, and CD30 (DAKO; Trappes, France) antibodies, anti-KL1 (Immunotech; Marseille, France), and anti-EMA antibodies (DAKO, Trappes, France), respectively. In some cases, additional immunohistochemical studies were done on frozen sections by using anti-CD19, CD2, CD4, CD5, CD7, and CD8 antibodies (DAKO). Genotypic evaluation based on Ig or T-cell receptor gene rearrangement analysis was not performed because of the retrospective nature of the study.

Results

The chest radiographs in the seven patients showed isolated or multiple peripheral nodules in the lung bases, which were homogeneous in all but one case (Fig 1). We noted an isolated peripheral mass located in the middle lobe of one patient and bullous lesions associated with parenchymal subpleural infiltrates in the right upper lung in another patient. Neither definite hilar or mediastinal adenopathy nor pleural effusion was noted in any of the patients.

The CT findings confirmed the predominantly parenchymal disease, represented by well-defined nodules of various sizes and/or masses (Table 1). These nodules were peripheral and were predominantly present in the lower lung zones (Fig 2). They were bilateral in three of the seven patients and multiple in six. An air bronchogram was seen in the nodules and/or masses of four patients (Fig 3). One mass spontaneously cavitated. Enlarged hilar and/or mediastinal nodes were never observed. The only case of pleural effusion was unilateral and was observed postoperatively after lung biopsy. Pericardial effusion was never observed.

Thin-section CT was performed in four of the seven patients. A halo of ground-glass attenuation

Figure 1. A chest radiograph shows a huge isolated mass with spontaneous cavitation near the right hilum.
around the different nodules was never observed. One patient had diffuse areas of ground-glass attenuation related to PCP associated with nodules in relation to ARL (Fig 4). The ground-glass aspect disappeared on follow-up CT during specific treatment of PCP.

The relative diagnostic value of bronchofibroscopy, biopsy, BAL, PTNB, and OLB or autopsy is shown in Table 2. PTNBs of the pulmonary masses were performed in six patients. Histologic analysis led to the diagnosis of NHL in four cases. In the other two cases, the diagnosis of NHL was finally obtained by OLB or at autopsy. A malignancy was suggested by PTNB in these two cases, but the precise nature of the tumor, ie, epithelial or lymphoid, could not be ascertained even after immunohistochemical analysis.

**DISCUSSION**

In the general population, Hodgkin’s lymphoma is the most frequent lymphoma encountered in young adults. ARL is almost exclusively of the non-Hodgkin type (generally, high-grade B-cell type). The Epstein-Barr virus, which can induce lymphoma in AIDS patients, was present in all seven patients in our study.8 The most common sites of involvement are the CNS, bone marrow, bowel, and mucocutaneous tissue. Intrathoracic involvement in ARL occurs in < 10% of cases.9,10 Previous reports on CT findings in ARL are available,2–4 but none distinguish disseminated ARL from primary pulmonary ARL.

As in the report by Carignan et al,4 nodules of various size or mass were the most common finding in our series. These nodules were multiple in 85.7% of the cases and were exclusively located in the subpleural areas of the lung bases. In three patients, an air bronchogram was present, and one patient had a mass with cavitation before treatment. A diffuse ground-glass pattern was present once and was attributed to PCP. A halo sign has

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<th>Table 1—CT Findings*</th>
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<td><strong>Patients</strong></td>
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<td>Nodule</td>
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<tr>
<td>Consolidation</td>
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<tr>
<td>Pleural effusion</td>
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<td>Enlarged nodes</td>
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<td>Percardial effusion</td>
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<td>Alveolar or interstitial</td>
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<td>Reticulonodular</td>
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<td>Cavitation</td>
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*A = Absent; P = present.
been described in ARL.\textsuperscript{4} In this latter paper it corresponded to a nodule with a halo of ground-glass attenuation, this aspect being very different from the diffuse ground-glass pattern observed in our series.

Right-sided pleural effusion was observed once, but only after OLB. This postoperative effusion was not related to lymphoma because an autopsy, done 1 month after the OLB, confirmed the exclusive involvement of the lung. The absence of pleural effusion and/or a pleural mass is a major difference with other reports of lymphoma of the chest. In the report of Sider et al.\textsuperscript{3} pleural effusion was the most common finding, occurring in 72.7\% of the cases; in 62.5\% of these cases, the diagnosis of ARL was based on cytologic study of fluid obtained at thoracentesis or histologic study of pleural biopsy material.

Lymphadenopathy can occur in ARL, but by definition, was absent in our cases. The presence of adenopathies may point to disseminated disease. Indeed, two of nine patients had mediastinal adenopathies in the report of Carignan et al\textsuperscript{4}; one had lymphomatous heart invasion and the second had pleural effusion. The latter authors considered that mediastinal adenopathies were present when the long-axis diameter (and not the short-axis diameter as in our study) was > 10 mm.

In our patients with primary ARL of the lung (ARLL), multiple nodules and/or masses were the most frequent finding. However, these features are nonspecific, and the fever, which is always present, at least in our series, can be misleading. Differential diagnoses include tumoral lesions (eg, KS, lung cancer, and metastasis) and infections (mycobacteriosis, cryptococcosis, cytomegalovirus pneumonia, nocardiosis, and others). In four patients, nonspecific antibiotic therapy was begun because the parenchymal abnormalities were initially attributed to various potential infections. All our patients previously underwent bronchofibroscopy with BAL, which, except for one case in which PCP was associated with ARLL, was always negative for ARLL but ruled out infectious diseases and Kaposi's lesions.

All but one of our patients had PTNB, which had a high diagnostic yield (two suggestive diagnoses and four definitive diagnoses). The high diagnostic yield of PTNB for lymphomatous disease seems to be related to the high malignant grade of the tumoral process. This indicates that small specimens are sufficient for diagnosis. Our data do not agree with those of Scott and Kuhlman,\textsuperscript{11} who suspected that the success rate of PTNB in lymphoma would be lower than it is in other malignancies because of the larger specimen size required for diagnosis. Indeed, in four of six patients, a specific diagnosis of lymphoma was obtained by means of PTNB. In one patient, the biopsy showed a tumoral process suggestive of a sarcoma. The final diagnosis obtained by OLB was that of a non-B, non-T lymphoma with a pseudosarcomatous aspect. In another patient, the biopsy showed lymphomatous infiltration, and the final autopsy diagnosis disclosed a B-cell lymphoma. No PTNB-related complications were observed in our series. The absence of complications (especially pneumothorax) may be attributed to the peripheral topography of the parenchymal lesions (ie, their location near the chest wall).

In conclusion, after excluding infectious diseases, multiple peripheral nodules and/or masses without associated hilar or mediastinal adenopathies and without pleural effusion are suggestive of primary pulmonary ARLL. Like Gruden et al,\textsuperscript{12} we think that PTNB is a safe and effective diagnostic procedure for focal thoracic disease, particularly, suspected primary ARLL.

Table 2—Relative Diagnostic Value of Bronchofibroscopy, Biopsy, BAL, PTNB, OLB, and Autopsy\textsuperscript{*}.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Fibroscopy</th>
<th>BAL</th>
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\textsuperscript{*} = negative; + = positive; +/- = suggestive; ND = not done.

\textbf{REFERENCES}