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ORIGINAL ARTICLE

Cytologic findings of hematologic malignancies in bronchoalveolar lavage fluid

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Introduction Bronchoalveolar lavage (BAL) is often performed in leukemia and lymphoma patients with pulmonary infiltrates, mainly to rule out infection. However, malignant hematopoietic infiltrates are uncommon and a comprehensive cytologic study has not yet been performed.

Materials and methods We retrospectively reviewed all BAL samples from our institution for the past 22 years (November 1992-October 2014).

Results There were 37 cases of hematologic malignancies identified on BAL specimens (21 female patients and 16 male patients, age 22-80 years). Eighteen patients (49%) had pneumonia-like symptoms at the time of initial diagnosis of their malignancy, including fever, dyspnea, respiratory distress/hypoxia, and cough. The biopsy-proven cases were 25 leukemia (12 acute myeloid leukemia, 6 acute promyelocytic leukemia, 2 acute monocytic leukemia, 2 acute myelomonocytic leukemia, 1 chronic myeloid leukemia in blast phase, 1 large granular leukemia, and 1 plasma cell leukemia), 11 lymphoma (8 diffuse large B-cell lymphoma, 1 mantle cell lymphoma, 1 natural killer/T-cell lymphoma, and 1 T-cell lymphoma), and 1 multiple myeloma. Chest X-ray findings included opacities, consolidation, and interstitial edema. Four patients had BAL specimens with concomitant microorganisms. Eighteen patients subsequently died (2 days to 4 years), 15 were alive (3 weeks to 8 years of follow-up), and 4 were lost to follow-up.

Conclusions BAL is especially important in distinguishing inflammatory/infectious processes from neoplastic disorders because many patients with hematologic malignancies can have pneumonia-like symptoms as part of their initial disease presentation. Causative pathogens are identified in only a minority of malignant BAL specimens from these patients. Lung involvement in patients with hematologic malignancies carries a poor prognosis.

Introduction

About 15% to 25% of neutropenic patients with hematologic malignancies develop pulmonary infiltrates.[1] Unfortunately, the presence of pulmonary infiltrates in these patients carries a nearly 50% mortality rate.[2] Though the etiology of these

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infiltrates is diverse, diagnostic delay is a significant predictor of mortality.[1] Bronchoalveolar lavage (BAL) is often performed, mainly to rule out infection. Noninfectious causes include alveolar hemorrhage, pulmonary leukostasis, and drug toxicity.[3] However, malignant hematopoietic infiltrates are an uncommon finding in BAL specimens. We present the clinical and cytologic features of 37 cases of hematologic malignancies diagnosed by bronchoalveolar lavage. To the best of our knowledge, this is the largest case series examining such an infrequent cytologic finding.

Materials and methods

We performed a retrospective database search for lymphoma, leukemia, and multiple myeloma diagnosed on BAL specimens from our institution for the past 22 years (November 1992-October 2014). We identified 37 cases accessioned between 1999 and 2014. All patients had biopsy-proven hematologic malignancies. BALs with abundant red blood cells and absent lung elements were excluded because these specimens may have had peripheral blood contamination. During this time period, 2977 total BAL specimens were accessioned and 49 specimens (1.6%) were from patients with a prior history of hematolymphoid neoplasms. Specimens were received fresh and cytospin preparations (3 cases, 8%) or CytoLyt solutions and Thin Prep smears (both Hologic Inc, Marlborough, Mass) (34 cases, 92%) were prepared and stained with Papanicolaou stain. Cell blocks were made in 11 cases and sections stained with hematoxylin and eosin. All samples were stained with periodic acid−Schiff, Gomori methenamine silver, Fite acid fast stain, and gram Brown and Brenn. In 6 cases, immunostains including CD3, CD20, and CD138, were performed. However, only 4 cases had sufficient cell block material for staining. Flow cytometry was performed in 5 cases with sufficient cells for diagnosis in 3 cases. Concurrent lung biopsy was performed in 3 cases and cytogenetic studies were performed in 1 case. To assess the sensitivity of BAL, we performed a retrospective search of surgical and autopsy specimens for malignant hematopoietic pulmonary infiltrates and then searched these cases for prior or concurrent BAL.

Results

Of 2977 BAL specimens accessioned, 37 (1%) were positive for a hematologic malignancy. Patient characteristics and BAL findings are summarized in Tables 1 and 2. The cases included 16 male and 21 female patients with a mean age of 55 years. There were 25 leukemia cases, 11 lymphoma cases, and 1 multiple myeloma case. The leukemia cases included 12 acute myeloid leukemia, 6 acute promyelocytic leukemia, 2 acute monocytic/monoblastic leukemia, 2 acute myelomonocytic leukemia, 1 chronic myeloid leukemia in blast crisis, 1 T-cell large granular lymphocyte leukemia, and 1 secondary plasma cell leukemia (PCL). Twelve of the leukemia cases were previously published at our institution.[4] Of the 23 acute leukemia cases, 15 patients (65%) had pneumonia-like symptoms as part of their initial disease manifestation. The lymphoma cases included 8 diffuse large B-cell lymphomas (DLBCL), 1 mantle cell lymphoma, 1 natural killer/T-cell lymphoma, and 1 peripheral T-cell lymphoma. All lymphoma cases except 1 pulmonary DLBCL were secondary. Of all 37 cases, 18 (49%) had pneumonia-like symptoms as their initial disease manifestation. The 19 patients with a prior hematologic history had previously undergone chemotherapy (12 patients), radiation (1 patient), or both (4 patients). Two had prior stem cell or bone marrow transplants. Remarkably, 2 patients (11%) were in bone marrow remission at the time of presentation with malignant pulmonary infiltrates. Thirteen patients (68%) had bone marrow involvement at the time of presentation, and 4 patients had lymphomatous lung infiltrates with no current or prior bone marrow involvement.

Time between diagnosis of hematologic malignancy and BAL was on average 120 days (range 5 to 2920 days). Patient symptoms were nonspecific and included fever (20 patients), dyspnea (13), cough (13, including 2 with hemoptysis), respiratory distress or hypoxia (11), and chest pain (4).

Chest X-ray findings included opacities, consolidation, and interstitial edema (Fig. 1). Most patients (24 of 37, 65%) had bilateral involvement whereas the remaining 13 patients had single lung involvement.

Twenty-two specimens (17 leukemia, 5 lymphoma, and 1 multiple myeloma) were submitted for fluid cell counts with differential. Average white blood cell count was 665/UL (range 55-5398/UL). Atypical cells were reported in 18 cases (15 leukemia and 3 lymphoma cases). Large cells with cytoplasmic vacuoles or granules were reported in 13 cases, blasts were reported in 4 cases, and large cell lymphoma was reported in 1 case. The patient with chronic myeloid leukemia in blast crisis had atypical monocytes reported in addition to blasts.

The thin layer preparations showed readily identifiable individual malignant cells. In contrast, cytospin preparations from older cases showed clumped cells and distinguishing malignant cells from alveolar macrophages and benign inflammatory cells was more difficult. Nuclear borders were somewhat more distinct on thin layer preparations. However, cytoplasmic features such as vacuoles and granules were better appreciated on cytospin preparations. Both preparations showed sufficient nuclear features for identifying tumor cells, such as chromatin patterns, nuclear membrane irregularity, and prominent nucleoli.

The acute myeloid leukemia patients had similar BAL findings, including sheets of myeloblasts with open chromatin and scant cytoplasm admixed with alveolar macrophages and bronchial epithelial cells (Fig. 2a). The acute myeloid leukemia inv16 cases also showed scattered eosinophils. The blasts in the acute myelomonocytic leukemia cases had indented kidney-bean-shaped nuclei. In 1