Open Lung Biopsy in Patients with Acute Leukemia

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The results of open lung biopsy in 15 patients with acute leukemia, pulmonary infiltrates, neutropenia, and fever were reviewed. The patients averaged 26 hospital days of neutropenia and 20 hospital days of fever before open lung biopsy, and all patients received broad-spectrum antibacterial agents (mean 17 days) before open lung biopsy. Nine (67 percent) received amphotericin B prior to open lung biopsy (mean 22 days). Open lung biopsy yielded a specific clinically helpful diagnosis in six patients, but only two of these patients survived the hospitalization during which open lung biopsy was performed. Open lung biopsy detected fungus in four patients and leukemic infiltrates in two patients. Management was appropriately modified in these patients. In nine patients, a specific diagnosis of the pulmonary infiltrate was not obtained by open lung biopsy. Antimicrobial regimens were not changed substantially for these patients. In six patients, the results of open lung biopsy may have been misleading. Two patients had pulmonary fungal diseases at autopsy, undetected by open lung biopsy eight days and five weeks prior to death. Another patient had invasive aspergillosis and one had cytomegalovirus pneumonitis not detected by open lung biopsy. Two patients had false-positive preliminary histologic reports of pulmonary infection. On the basis of this experience, in this specific population of patients, open lung biopsy was often of little help in directing medical therapy or influencing clinical outcome.

Pneumonia is a frequent cause of morbidity and mortality in patients with acute leukemia. In one series from the Baltimore Cancer Research Center, 76 percent of patients with leukemia acquired pneumonia, and this infection proved fatal to 65 percent of them [1]. In an autopsy series reported by Chang et al [2] from the M. D. Anderson Hospital, infection alone accounted for 66 percent of the deaths in leukemic patients; 24 percent of the deaths due to infection were due to pneumonia.

The clinical situation of patients with leukemia in whom fever and diffuse pulmonary infiltrates develop greatly taxes the time, effort, and diagnostic acumen of house staff, internists, surgeons, pathologists, radiologists, and microbiologists. Frequently, these patients also present important ethical dilemmas with respect to aggressiveness of diagnostic efforts and treatment options [3]. An accurate diagnosis allows for an objective decision regarding specific therapy directed against the cause of the infiltrates, may allow elimination of unnecessary and potentially toxic antimicrobial agents from the patient's therapeutic regimen, and may facilitate a more rational approach to the management of these often fragile and critically ill patients. If

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noninvasive methods fail to provide a diagnosis, limited thoracotomy to obtain lung tissue (open lung biopsy) has been advocated due to its safe provision of the most satisfactory specimen for histopathologic examination and culture [4–11]. However, open lung biopsy is not without complications [12], and some investigators have questioned its helpfulness for management of critically ill immunosuppressed patients or for improvement in their quantity or quality of life [8,10]. The literature on the usefulness of open lung biopsy in patients with acute leukemia is difficult to evaluate, since studies have included immunosuppressed patients with a wide variety of underlying conditions and immunosuppressive drug regimens [4–12]. We therefore reviewed our experience with open lung biopsy in patients with acute leukemia—predominantly acute myelocytic leukemia—to determine the impact of this procedure on the clinical management and outcome in these patients.

PATIENTS AND METHODS

When surgical specimens are received by the pathology department at Stanford University Hospital, a surgical accession number and brief description of the specimen are recorded. These entries were reviewed for the period April 1974 through December 1982. For all entries that described specimens obtained from the thorax, file cards in the pathology department were consulted. The file cards describe the type of specimen, the procedure employed to procure it, and a brief clinical history of the patient. Patients with acute leukemia and lung biopsy by thoracotomy were identified and their hospital charts reviewed. For this review, patients were included if they had acute myelocytic leukemia, fever (temperature above 38.3°C), neutropenia (neutrophil count below 1,000/mm^3), and a new pulmonary infiltrate on chest radiography [13]. One patient with chronic myelocytic leukemia in blast crisis and one patient with hairy cell leukemia were also included.

Each complete chart for a pertinent admission was reviewed, but attention was directed particularly to the presence of antileukemic therapy, the number of days of fever and neutropenia preceding open lung biopsy, results of chest radiography, use of antimicrobial agents (number of antibiotics), days of antimicrobial therapy, type of antimicrobial therapy (antibacterial, antiprotozoan, or antifungal), detection of a specific disease process (caused by infection or by neoplasm) with use of open lung biopsy, impact of open lung biopsy on management of the patient, alternate efforts employed for diagnosis of the cause of pulmonary infiltrate, survival of the patient with respect to that hospital admission, and results obtained at autopsy.

The type of thoracotomy and site of biopsy were chosen by the thoracic surgery team. A single surgeon supervised thoracotomy for the majority of patients. As stated previously [14], it is vital to have an experienced team of surgeons, anesthesiologists, pathologists, and microbiologists for optimal acquisiton and processing of the biopsy specimen. Touch preparations of the biopsy specimen stained with methenamine-silver and frozen sections were routinely prepared on the day of biopsy. Results of touch preparations were available within four to six hours of the biopsy procedure. Hematoxylin and eosin histologic stains, Gram stains, and acid-fast stains for mycobacteria were routinely performed, and results were available within two days. Portions of the specimen were routinely cultured for aerobic and anaerobic bacteria, mycobacteria, fungi, and viruses. Dieterle silver stain was not performed routinely during the period covered by this review.

RESULTS

General. Open lung biopsy was performed in 15 patients. The data are summarized in **Table I.** Ages ranged from seven to 76 years, with a mean age of 49. Ten of the 15 patients (67 percent) were male. Fourteen (93 percent) were receiving cytotoxic chemotherapy to induce remission of leukemia at the time the pneumonic infiltrate was noted. The patients had a mean of 20 hospital days (range one to 120) of fever prior to open lung biopsy. The mean number of days of neutropenia prior to open lung biopsy was 26 (range one to 120). The interval between onset of pneumonia and performance of open lung biopsy ranged from approximately the day of hospitalization to 44 days. However, because the actual onset of pneumonic infiltrates was frequently difficult to define (e.g., in patients who entered the hospital with pulmonary infiltrates, in patients with chronic lung disease), this range is not completely accurate.

All patients received broad-spectrum antibacterial agents for a mean of 17 days (range three to 44) prior to open lung biopsy. Twelve (80 percent) received a combination of three antibiotics, two (13 percent) received four antibiotics, and one (7 percent) received two antibiotics. In addition, before open lung biopsy, five patients (33 percent) received either pentamidine (one patient) or trimethoprim/sulfamethoxazole (four patients) for suspected Pneumocystis carinii pneumonia. One patient (7 percent) received erythromycin for treatment of Legionella, and another received isoniazid and rifampin for possible tuberculosis before open lung biopsy. Nine of the 15 patients (67 percent) received amphotericin B for a mean of 22 days (range three to 90) prior to open lung biopsy.

Bronchoscopy and needle aspiration of the lung were each performed four times in a total of six patients. Results of these procedures failed to demonstrate a cause for any of the lung infiltrates. The only complication of the thoracotomy procedure to obtain the open lung biopsy specimen was a hematoma that developed at the site of the surgical wound and required surgical drainage (Patient 12). No other patients required reoperation, and no significant postoperative bleeding, pneumothorax, or wound infection was seen. Nine patients died during their hospitalization (median of eight days until death after open lung biopsy, range two to 35 days). Patients who died within 14 days of open lung

biopsy were critically ill prior to open lung biopsy; no death could be attributed directly to the procedure.

Results of Open Lung Biopsy. Fungus was detected histologically in biopsy specimens from four patients (27 percent; Patients 6, 10, 11, and 13). Three biopsy specimens (Patients 10, 11, and 13) showed features typical of invasive aspergillosis. The biopsy specimen from Patient 6 showed predominantly organizing alveolar pneumonitis. Hyphae atypical of Aspergillus were seen in the bronchial lumens, but invasion by fungus was not evident in the biopsy specimen. Culture of the specimen for fungus showed no growth. This patient received a total of 1.4 g of amphotericin B and was discharged 23 days after open lung biopsy.

Two biopsy specimens (13 percent; Patients 5 and 12) revealed leukemic infiltrates. Chemotherapy for leukemia was promptly started in both patients, and antimicrobial agents were stopped.

Nine biopsy specimens (60 percent) were not diagnostic for a specific disease process.

Possible Errors in Interpretation of Open Lung Biopsy Specimens. In seven different instances in six of the 15 patients (40 percent), results of open lung biopsy may have been misleading. Chest radiography in Patient 3 at the time of open lung biopsy revealed "mass-like" infiltrates in the left perihilar region, an infiltrate in the right lower lung field, and a nodular density in the right upper lung field. The biopsy specimen was obtained from a 5 cm nodular, thick density at the medial aspect of the left upper lobe. This specimen did not reveal any evidence of fungal infection. The patient died eight days after open lung biopsy. At autopsy, an extensive bilateral pneumonia due to fungi resembling Aspergillus and Candida was found. The left upper lobe contained a fungal abscess.

Patient 8 had a known Aspergillus infection of his elbow in conjunction with an abnormal chest radiographic appearance. Culture of sputum specimens in the three months prior to open lung biopsy yielded Aspergillus. To determine the cause of pulmonary infiltrates that progressed despite therapy with amphotericin B, open lung biopsy was performed. The biopsy specimen was obtained from an area of the right lower lobe that was grossly abnormal by visual inspection. Culture of a sputum specimen obtained the day before open lung biopsy yielded heavy growth of Aspergillus. The open lung biopsy specimen showed organizing pneumonitis, bronchiolitis obliterans, and lipid pneumonia; culture of the biopsy specimen showed no growth. Despite continuation of amphotericin B, he died five weeks after open lung biopsy, and autopsy showed Aspergillus in all sections of lung parenchyma and fungal emboli in large and small blood vessels.

In Patient 4, bilateral pulmonary infiltrates developed during the six weeks prior to open lung biopsy. During the week before open lung biopsy, the infiltrate in the right lower lobe increased. At thoracotomy, no discrete lesions were seen in the lung, although the lung was boggy and discolored. The biopsy specimen was obtained from the area of lung considered diseased on the basis of visual inspection and radiographic findings. The open lung biopsy specimen was not diagnostic for a specific process. Cultures of specimens from the nares and a tracheal aspirate two days before and one day after open lung biopsy, respectively, yielded Aspergillus. Nine days after open lung biopsy, chest radiography showed a nodule, 4 cm in diameter, in the left upper lobe (location of the infiltrate at the time of open lung biopsy) and three complex cavitary lesions in the right lower lobe. Amphotericin B therapy was resumed, the patient's condition improved, and she was discharged.

Patient 14 had bilateral pulmonary infiltrates on chest radiography for 17 days before open lung biopsy. The open lung biopsy specimen was taken from a woody, granular area of the right lower lobe. Frozen sections suggested infiltrates due to leukemia cells or interstitial pneumonitis. Permanent sections were interpreted to show an organizing pneumonitis with focal honeycombing; a few atypical cells suggested the possibility of cytomegalovirus infection. Assays for serum antibody to cytomegalovirus performed on serum specimens obtained at approximately the time of open lung biopsy showed a significant rise in titer. Culture of the biopsy specimen yielded cytomegalovirus six weeks after the patient had died and seven weeks after the open lung biopsy.

For Patient 15, initial touch preparations of the open lung biopsy specimen were reported to show rare budding yeast. Amphotericin B therapy was started. Special stains of permanent sections did not confirm the presence of yeast, and routine histologic stains showed hemorrhagic pneumonitis. Amphotericin B treatment was continued until the patient died, nine days after open lung biopsy.

The initial pathologic report on the open lung biopsy specimen in Patient 3 indicated the presence of intranuclear inclusions in areas of fibrosing alveolitis. Use of acyclovir was initially rejected, due to the potential bone marrow toxicity of this drug. However, acyclovir therapy was started seven days after open lung biopsy and one day before the patient's death. The autopsy report did not indicate any evidence of viral pneumonitis, but rather extensive fungal invasion of the lung.

An open lung biopsy in Patient 6, hyphae consistent with Aspergillus were seen within bronchial lumens without evidence of tissue invasion, although acute alveolar injury was seen. Despite lack of demonstrable tissue invasion, this patient was treated with a course of amphotericin B and was discharged from the hospital 23 days after open lung biopsy.

TABLE I Patients with Acute Leukemia and Open Lung Biopsy for New Pulmonary Infiltrates

Patient	Age/Sex	Year	Underlying Disease	Antileukemia Chemotherapy*	Before Open Lung Biopsy: Neutropenia (days)	Before Open Lung Biopsy: Fever (days)	Before Open Lung Biopsy: Antimicrobial Agents†	Antimicrobial Agents after Open Lung Biopsy	Open Lung Biopsy Diagnosis	Outcome	Comments
1	65/M	1979	Acute myelocytic leukemia	Yes	7	11	Three broad-spectrum antibiotics (10), amphotericin (3)	No change	Acute alveolar injury with hemorrhage	Died 10 days after open lung biopsy; no autopsy	
2	64/M	1979	Acute myelocytic leukemia	Yes	1	1	Three broad-spectrum antibiotics (1), trimethoprim/sulfamethoxazole (5)	Isoniazid and erythromycin added	Acute and organizing interstitial pneumonia	Died 14 days after open lung biopsy; no autopsy	
3	66/M	1981	Acute myelocytic leukemia	Yes	36	15	Three broad-spectrum antibiotics (31), amphotericin (21), trimethoprim/sulfamethoxazole (1)	Broad-spectrum antibiotics discontinued for five days, then resumed; amphotericin continued; acyclovir started seven days after open lung biopsy	Acute and organizing alveolar injury	Died eight days after open lung biopsy	Autopsy showed extensive Aspergillus and Candida penumonia
4	34/F	1981	Acute myelocytic leukemia	Yes	47	12	Three broad-spectrum antibiotics (44), amphotericin (19, discontinued 12 days before open lung biopsy)	Broad-spectrum antibiotics discontinued eight days after open lung biopsy; amphotericin started 11 days after open lung biopsy (see Comments).	Acute alveolar injury	Discharged 18 days after open lung biopsy	Aspergillus recovered in sputum three days after open lung biopsy, and chest radiography revealed new cavitary lesions nine days after open lung biopsy
5	76/M	1982	Acute myelocytic leukemia	No	9	9	Three broad-spectrum antibiotics (9)	Broad-spectrum antibiotics discontinued for one day	Leukemic infiltrates	Died two days after open lung biopsy; no autopsy	
6	54/M	1978	Acute myelocytic leukemia	Yes	28	24	Three broad-spectrum antibiotics (23), amphotericin (10), erythromycin (5), trimethoprim/sulfamethoxazole (7), isoniazid (6), rifampin (6)	Amphotericin and rifampin continued; other antibiotics discontinued after seven days	Organizing acute alveolar injury with dense aggregate of mycelia in bronchial lumens	Discharged 23 days after open lung biopsy	Despite lack of tissue invasion, therapy with amphotericin
7	59/M	1982	Acute myelocytic leukemia	Yes	18	17	Three broad-spectrum antibiotics (21), amphotericin (15)	All agents continued for five days until development of rash	Mild acute alveolar injury	Discharged 10 days after open lung biopsy	

8	7/M	1974	Acute myelocytic leukemia	Yes	120	120	Four broad-spectrum antibiotics (14), amphotericin (90)	No change	Diffuse interstitial pneumonitis	Died five weeks after open lung biopsy	Autopsy showed extensive Aspergillus invasion in all areas of the lung
9	27/F	1979	Acute myelocytic leukemia	Yes	23	30	Three broad-spectrum antibiotics (30), trimethoprim/sulfamethoxazole (17), amphotericin (17)	Broad-spectrum antibiotics continued for 24 days; after five days, amphotericin replaced with miconazole for an additional eight days	Alveolar injury	Discharged 21 days after open lung biopsy	
10	59/M	1981	Acute myelocytic leukemia	Yes	8	4	Three broad-spectrum antibiotics (4)	Amphotericin started; broad-spectrum antibiotics continued until death	Invasive aspergillosis	Died six days after open lung biopsy; no autopsy	
11	62/F	1977	Acute myelocytic leukemia	Yes	21	8	Three broad-spectrum antibiotics (4)	Broad-spectrum antibiotics discontinued after three days; amphotericin added	Invasive aspergillosis	Discharged 20 days after open lung biopsy	
12	30/F	1977	Acute myelocytic leukemia	Yes	8	1	Three broad-spectrum antibiotics (8)	Broad-spectrum antibiotics discontinued after three days	Leukemic infiltrates	Discharged 11 days after open lung biopsy	
13	48/F	1977	Acute myelocytic leukemia	Yes	33	24	Three broad-spectrum antibiotics (24), amphotericin (15)	Broad-spectrum antibiotics continued until death, three days after open lung biopsy	Invasive aspergillosis	Died with Pseudomonas aeruginosa septicemia three days after open lung biopsy	
14	51/M	1981	Hairy cell leukemia	Yes	27	27	Four broad-spectrum antibiotics (27), amphotericin (7)	No change	Organizing pneumonitis; few atypical cells suggestive of cytomegalovirus	Died four days after open lung biopsy	Cytomegalovirus cultured from lung biopsy specimen
15	33/M	1980	Chronic myelocytic leukemia in blast crisis	Yes	2	3	Two broad-spectrum antibiotics (3), pentamidine (1)	Amphotericin added	Hemorrhagic pneumonia	Died nine days after open lung biopsy	Initial report indicated yeast-like forms on Gomori's methenamine silver stain of touch preparation

* At time of presence of pulmonary infiltrate.
† Numbers in parentheses indicate days of drug therapy.

Effect of Open Lung Biopsy on Patient Management. Nondiagnostic open lung biopsy often did not materially affect management of patients with respect to use of antimicrobial agents. Of the nine patients who had nondiagnostic open lung biopsy, eight (89 percent) continued to receive broad-spectrum antibiotics. Six of seven patients (86 percent) continued to receive amphotericin B. In Patient 4, in whom amphotericin B was discontinued, administration of this drug was resumed 11 days after open lung biopsy, because of the appearance of new cavitary pulmonary lesions and recovery of Aspergillus from culture of sputum samples. Four of four patients (100 percent) continued to receive either trimethoprim/sulfamethoxazole or pentamidine for suspected infections with P. carinii. In addition, isoniazid and erythromycin in Patient 2 and acyclovir in Patient 3 were added to the antimicrobial regimens after open lung biopsy.

Prior to open lung biopsy, the nine patients in whom open lung biopsy was nondiagnostic received an average of 4.3 antimicrobial agents per patient; after official interpretations of histologic slides from the open lung biopsy specimen became available, they received an average of 3.9 agents.

In six patients (40 percent), an etiologic agent was identified on open lung biopsy, and clinical management was modified accordingly. For the four patients in whom fungus was detected on open lung biopsy (Patients 6, 10, 11, and 13), amphotericin B was added to the regimens of two patients and continued in the other two patients. Broad-spectrum antibiotics were discontinued in three of these patients. One (Patient 13) had concurrent Pseudomonas septicemia for which broad-spectrum antibiotics were continued.

Two patients (Patients 5 and 12) had leukemic infiltrates detected on open lung biopsy, and antimicrobial agents were discontinued.

Patient Survival after Open Lung Biopsy. Six of 15 patients (40 percent) who underwent open lung biopsy survived hospitalization. Two of four patients (50 percent) in whom fungus was detected on open lung biopsy lived to be discharged from the hospital; two patients died on Days 3 and 6 following open lung biopsy. One of two patients (50 percent) in whom leukemic infiltrates were detected on open lung biopsy was discharged from the hospital; the other patient died two days after open lung biopsy. Three of nine patients (33 percent) with nondiagnostic open lung biopsy survived hospitalization; six patients died at a median of nine and a half days after open lung biopsy.

COMMENTS

In recent reports of series of open lung biopsy in immunocompromised patients, open lung biopsy by limited thoracotomy was considered a safe procedure that provided the most satisfactory tissue samples for pathologic and microbiologic studies [4–12]. Because needle aspiration, needle biopsy, and transbronchial biopsy of the lung provide little control for the person performing the procedure in the event of an untoward complication, they are infrequently employed at our institution in patients with severe neutropenia and thrombocytopenia. Despite the safety record of open lung biopsy, neither the quantity nor the quality of life has been shown to be increased by use of this procedure in patients with acute leukemia [10]. Most reviews of open lung biopsy in immunocompromised patients have lumped together all immunocompromised patients, usually without clear delineation of the data for particular subsets of patients such as those with acute leukemia [6,8–12]. For this reason, we reviewed retrospectively the results of open lung biopsy in patients with acute leukemia (predominantly acute myelocytic leukemia) who presented with neutropenia, fever, and acute pulmonary infiltrates of unknown cause. Open lung biopsy aided establishment of the cause of pulmonary infiltrates in six of the 15 patients (40 percent): fungal infection in four patients and leukemic infiltrates in two patients. These diagnoses resulted in appropriate modification of the treatment regimens in these patients. Such modifications of drug regimens did not occur in the nine patients in whom open lung biopsy did not provide a definitive diagnosis. Thus, the attending physicians appeared to place little reliance on open lung biopsy findings that did not reveal a specific disease process.

Of particular interest is the discovery that open lung biopsy may have been misleading in as many as six of the patients (40 percent). In four of them, we consider open lung biopsy to have given false-negative results. In one case each, initial pathologic reports indicated viral and fungal pneumonitis; these diagnoses were not substantiated in the final pathologic reports. Rossiter et al [8] noted two cases in which pulmonary infections due to Nocardia or Aspergillus were missed by open lung biopsy, but details of these cases were not provided. Hiatt et al [10], in a review of open lung biopsy in 68 immunosuppressed patients, were able to compare autopsy data with open lung biopsy data in 28 patients. Ten significant diagnostic errors were apparent when results from open lung biopsy were compared with the autopsy results. Four patients had invasive aspergillosis not detected by culture and microscopic examination of the biopsy specimen. Two patients each had Hodgkin's lymphoma of the lung, bacterial pneumonia, and cytomegalovirus pneumonia that were missed by open lung biopsy. These authors concluded that open lung biopsy had a diagnostic accuracy of 64 percent in their cases. However, they did not state the length of time between open lung biopsy and death, whether or not disease present at autopsy was either in the same location as the radiographic infiltrate or in

the tissue sampling site at the time of open lung biopsy, and whether or not clinical evidence of new pulmonary disease appeared between the time of open lung biopsy and autopsy. As was true for our study, Hiatt et al did not (probably could not) rule out the possibility that infection had become established between the time of open lung biopsy and death.

Diffuse pulmonary infiltrates in patients with acute leukemia are perhaps due most often to noninfectious or non-neoplastic causes, and thus a nonspecific diagnosis from the open lung biopsy specimen is not surprising. Tenholder and Hooper [15] reported their experience with 38 patients with acute leukemia (acute myelogenous leukemia, acute myelomonocytic leukemia, and the blastic phase of chronic myelocytic leukemia) and 40 episodes of diffuse pulmonary infiltrates. Twenty-six of the 40 episodes (65 percent) were attributed to noninfectious causes such as hemorrhage (28 percent), congestive heart failure (18 percent), and leukemia (20 percent). The remainder were caused by infectious agents, 13 (93 percent) of which were opportunistic pathogens (Aspergillus in three, Candida in seven, Pneumocystis in two, and cytomegalovirus in one). All diagnoses were established by histologic criteria, including autopsy data in 90 percent of the 40 cases. Open lung biopsy was infrequently employed in these patients, and these authors did not comment whether or not antemortem histologic diagnoses correlated with autopsy data. In our series, 53 percent of the infiltrates could be explained by infection with opportunistic pathogens; in 33 percent no infectious agents were detected; and in 13 percent, infiltrates were caused by leukemic infiltrates. Tenholder and Hooper point out that, for patients with acute leukemia, pulmonary infiltrates that appear in the period before treatment or within 72 hours of initiation of cytotoxic therapy were not caused by opportunistic pathogens [15]. In our series, there were three such patients (Patients 2, 5, and 12): two with leukemic infiltrates and the other with a nonspecific histologic diagnosis from open lung biopsy.

The reliability of a nonspecific diagnosis obtained from open lung biopsy is uncertain. Our results indicate that a nondiagnostic open lung biopsy does not reliably exclude infection, but noninfectious processes cause a large proportion of the pulmonary infiltrates in patients with acute leukemia [15]. As expected, results of open lung biopsy that indicated the presence of infection or leukemia correlated well with clinical response and outcome. However, Patient 14 illustrates that multiple concurrent infections occur in these patients; she died with Aspergillus pneumonia and Pseudomonas septicemia three days after open lung biopsy. It cannot be assumed that an organism detected on open lung biopsy is the sole infecting organism in a patient.

Our results, as just described, reveal that a definitive diagnosis of pulmonary infiltrates established by open lung biopsy in the specific category of febrile neutropenic patients with acute myelocytic leukemia allowed for initiation of specific therapy directed against the cause of the infiltrate. Diagnosis permitted elimination of unnecessary therapeutic agents from a patient's regimen and a more rational approach to management. Unfortunately, although open lung biopsy yielded a specific, clinically helpful diagnosis in six of our 15 patients, only two of the six survived hospitalization. On the basis of our data, open lung biopsy that does not identify a specific cause for a pulmonary infiltrate does not eliminate the need for antimicrobial therapy (particularly antifungal therapy) or further efforts to identify a specific disease process. Information other than that from open lung biopsy (such as culture of sputum specimens, evolution of radiographic abnormalities) must be considered in management of a patient's antimicrobial regimen.

In view of our experience, it is uncertain whether open lung biopsy improves the quality or quantity of life for this specific population of critically ill, severely immunocompromised patients. Future studies of the value of open lung biopsy or other diagnostic procedures in immunocompromised patients should carefully define the groups of patients included in order to determine those patients most likely to benefit from an aggressive diagnostic approach.

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