Introduction: Chest radiograph is the first step in evaluation of hemoptysis, but when it is normal, some physicians choose bronchoscopy with variable results. In this study, our objective was to elucidate how we could increase diagnostic yield of bronchoscopy and bronchoalveolar lavage by looking at inflammatory cells in cytology.

Material and Methods: A retrospective study was performed on 102 patients with hemoptysis and normal chest roentgenograph. Data consisted of demographic, clinical findings such as the amount of hemoptysis and weight loss, gross findings in bronchoscopy and cytology and histopathology results. Accuracy of cytology in 2 conditions: (1) routine reports and (2) approach that used inflammatory cells in cytology for diagnosis was compared. Follow-up period was 3 months.

Results: Male to female ratio was 3/2 and average age was 43 (SD = 17) years. In bronchoscopy, gross infiltration or vegetation was seen in 14% and histopathology for malignancy was diagnostic in 4%. Thirty-seven percent of subjects showed native cells and 9% showed neutrophilia in favor of infection. Accuracy of bronchoalveolar lavage using inflammatory cells in cytology increase significantly from traditional methods (sensitivity = 89% and specificity = 93% in comparison with 40% and 83% in traditional methods).

Conclusions: Attention to cytology of bronchial washing (both malignant and inflammatory cells) increases utility of bronchoscopy in patients with hemoptysis and normal chest roentgenogram.

Key Words: hemoptysis, cytopathology, chest roentgenogram, lung cancer, interstitial lung disease, tuberculosis

(Orig Investig) J Bronchol 2007;14:95–97

Received for publication September 27, 2006; accepted February 27, 2007.

From the Departments of *Pulmonary Medicine; †General Health, Medical School of Islamic Azad University of Mashhad; and ‡Department of Pathology, Mashhad University of Medical Sciences, Mashhad, Iran.

Place of Research: Ghaem and Imam Reza Hospital, Mashhad University of Medical Sciences.

There is no conflict of interest.

Reprints: Majid Mirsadraee, MD, No. 80, 15 Kosar St, Kosar Ave, Vakilabad Blv, Mashad, Iran (e-mail: majidmirsadraee@yahoo.com, m-mirsadrae@mums.ac.ir, mirsadra@mshdiau.ac.ir).

Copyright © 2007 by Lippincott Williams & Wilkins

H emoptysis is a well-known indication for flexible bronchoscopy, especially for evaluation of malignancy, infection, and localization of bleeding.1 The role of bronchoscopy in cases where chest x-ray is normal or show only nonlocalized findings is less clear. Tak et al2 compared diagnostic yield of high-resolution computed tomography to routine bronchoscopy and they demonstrated that high-resolution computed tomography has 3 times more diagnostic yield than bronchoscopy. The purpose of bronchoscopy in such studies was the detection of incidence of malignancy, which can be as low as 0.3%.2,3 For this reason Law et al4 concluded that bronchoscopy under the circumstance has a low yield and is not cost effective. However, considering other etiologies that can lead to bleeding, such as infections and interstitial lung disease, bronchoscopy could lead to more precise diagnosis. Bronchoalveolar lavage (BAL) contain cells and mediators from lung parenchyma that can direct clinician to possible hidden cause such as malignant lesion or inflammatory process.5,6 Objective of this study was to evaluate the benefit of bronchial cell counts and differential counts besides of cytology in directing further work up and diagnosis of hemoptysis in patients with normal chest roentgenogram.

METHODS

Patients who were hospitalized for investigation and management of hemoptysis and were found to have normal chest x-ray were included into this retrospective study.

Variables such as demographic data, history of weight loss, amount of hemoptysis, results of gross findings in bronchoscopy and cytopathology were included in this study.

Bronchoscopy was performed by Olympus BF type 40 with local anesthesia and gross bronchoscopic appearance was classified as normal, superficial inflammation, exophytic lesion, ulceration, and nodularity. Bronchial washing or BAL was performed with 100 mL saline and aliquot was sent for cytology. All patients in this study underwent endobronchial or transbronchial lung biopsy. Cytology of inflammatory cells in BAL was used for diagnosing certain pathology as mentioned before.6 According to this classification, treatment with antibiotics was given if purulent sputum or neutrophils in cytology (more than 80% of inflammatory cells) was
present. In these subjects, disappearance of hemoptysis was considered to be of infection origin. When bronchoscopy was assumed unremarkable (normal), patients were followed for 3 months. If cytology report was inconclusive, a second opinion was acquired.

**Statistical Analysis**

A sample size of 100 patients with 0.05 ± risks and 90% potency was calculated. A $2 \times 2$ table was drawn for evaluating the accuracy of cytology in 2 conditions: (1) routine reports and (2) approach that used inflammatory cells in cytology for diagnosis. Then differences between the 2 groups were analyzed by $\chi^2$. Epi-info 2003 software was used for statistical analysis.

This study was approved by the university research ethics committee.

**RESULTS**

Approximately 1513 bronchoscopy files were reviewed (from year 2001 to 2004) and 113 patients with hemoptysis and normal chest roentgenogram were found. In 102 cases, a satisfactory cytology reports were available who were enrolled in this study. Men were affected more than women ($M/F = 3/2$). Average age of patients was 43 (SD = 17) years with a range of 10 to 83. Seventy-two percent of patients had previous history of lung disease such as chronic obstructive pulmonary disease or bronchiectasis, and 27% noticed significant weight loss. Ten percent of patients had streak of hemoptysis, 30% frank hemoptysis, and 60% massive hemoptysis.

Gross bronchoscopic findings in trachea and the carina are shown in Table 1 and gross bronchoscopic findings in right and left lung are shown in Table 2. In summary, gross findings suggestive of a specific diagnosis was present in 15 patients (14%). Histopathologic examination of the samples from above patients showed that 5 had neoplastic lesions (4 bronchogenic carcinoma and 1 carcinoid tumor). All of these patients were older than 45 years except 1 who was a 30-year-old woman with bronchogenic carcinoma.

Cytologic findings suggestive of malignancy were present in 4 cases and its sensitivity and specificity as sole finding was 40% and 83%, respectively (positive predicted value = 50% and negative predicted value = 76%). Other inflammatory cell in BAL that helped in establishing the diagnosis consists of neutrophils in 53%, eosinophils in 1%, and lymphocytes in 4% of patients. In 36 patients (37%), cytologic findings were mainly native lung cells such as alveolar macrophages and the follow-up revealed no organic lesions. In 9 subjects with purulent discharge or significant neutrophilia in BAL (more than 80%), follow-up showed resolution of hemoptysis with antibiotic therapy in 92%. Remainder of cases with neutrophilia in BAL consisted of bronchiolitis obliterans in 1 (1.1%) case, chronic obstructive pulmonary disease in 35 (36%), bronchiectasis in 25 (26%), idiopathic pulmonary fibrosis in 2 (2.3%), and 11 cases remained undiagnosed. Eosinophilia in BAL was due to Churg Strauss syndrome and lymphocytosis was due to sarcoidosis in 3 cases (3.2%) and hypersensitivity pneumonitis in 1 case. Using the mentioned results, interpretation of cytology using inflammatory cells had sensitivity and specificity of 89% and 93%, respectively (positive predicted value = 98% and negative predicted value = 70%) that is significantly better than former interpretation (Table 3).

**DISCUSSION**

In western countries, chronic inflammatory lung disease and bronchogenic carcinoma are the most prevalent cause of hemoptysis.7–9 The common diagnostic evaluations usually consist of a plain chest radiograph; but it fails to localize the lesion in 20% to 46% of patients with hemoptysis.10 Although there is agreement that patient with focal roentgenographic abnormalities (suggestive of malignancies) require bronchoscopic

**TABLE 1.** Frequency of Bronchoscopic Findings in Trachea and Carina of Patients With Hemoptysis and Normal Chest x-ray in 100 Subjects

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Inflammation</th>
<th>Mucosal Infiltration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trachea</td>
<td>95 (88%)</td>
<td>1 (0.9%)</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Carina</td>
<td>97 (95%)</td>
<td>1 (0.9%)</td>
<td>3 (2.7%)</td>
</tr>
</tbody>
</table>

**TABLE 2.** Frequency of Bronchoscopic Findings in Lobar and Segmental Bronchi of Patients With Hemoptysis and Normal Chest x-ray

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Clot</th>
<th>Inflammation</th>
<th>Mucosal Infiltration</th>
</tr>
</thead>
<tbody>
<tr>
<td>RUL</td>
<td>86 (85%)</td>
<td>10 (10%)</td>
<td>3 (3%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>RML</td>
<td>92 (90%)</td>
<td>8 (7%)</td>
<td>3 (2.5%)</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>RLL</td>
<td>96 (93%)</td>
<td>4 (3%)</td>
<td>2 (1.5%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>LUL</td>
<td>90 (88%)</td>
<td>6 (5%)</td>
<td>5 (4%)</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>LLL</td>
<td>93 (91%)</td>
<td>6 (5%)</td>
<td>4 (3%)</td>
<td>2 (1.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Inflammation</th>
<th>Mucosal Infiltration</th>
</tr>
</thead>
<tbody>
<tr>
<td>RUL</td>
<td>86 (85%)</td>
<td>10 (10%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>RML</td>
<td>92 (90%)</td>
<td>8 (7%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>RLL</td>
<td>96 (93%)</td>
<td>4 (3%)</td>
<td>2 (1.5%)</td>
</tr>
<tr>
<td>LUL</td>
<td>90 (88%)</td>
<td>6 (5%)</td>
<td>5 (4%)</td>
</tr>
<tr>
<td>LLL</td>
<td>93 (91%)</td>
<td>6 (5%)</td>
<td>4 (3%)</td>
</tr>
</tbody>
</table>

**P**

<table>
<thead>
<tr>
<th></th>
<th>True positive</th>
<th>True negative</th>
<th>False positive</th>
<th>False negative</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
<th>$\chi^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine Cytology</td>
<td>2</td>
<td>10</td>
<td>2</td>
<td>3</td>
<td>40%</td>
<td>83%</td>
<td>76%</td>
<td>50%</td>
<td>21.13</td>
<td>0.00001</td>
</tr>
<tr>
<td>Cytology Considering Inflammatory Cells</td>
<td>50</td>
<td>14</td>
<td>1</td>
<td>6</td>
<td>89%</td>
<td>93%</td>
<td>70%</td>
<td>98%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NPV indicates negative predicted value; PPV, positive predicted value.
evaluation, the indication for patients with normal or nonlocalizing roentgenographic abnormalities remains controversial. Previous studies have been at odds regarding the risk of bronchogenic carcinoma in this group of patients. Kallenbach et al.\textsuperscript{11} and Zavala\textsuperscript{12} identified bronchogenic carcinoma in 16\% and 22\%, respectively. These authors recommend early bronchoscopy in all patients with unexplained hemoptysis. Others have reached a different conclusion. Ackert et al.\textsuperscript{3} reported 1 neoplasm in 331 patients with hemoptysis and normal chest roentgenogram. Heimer et al.\textsuperscript{13} found cancer in none of their 45 patients. These authors suggested that routine bronchoscopy was not always indicated. Weaver et al.\textsuperscript{14} further suggested the following as criteria to determine the need for bronchoscopy: presence of an abnormal chest roentgenogram, age more than 40 years or hemoptysis last more than 1 week. Poe et al.\textsuperscript{15} identified bronchogenic carcinoma in 6\% of 196 bronchoscopies performed for hemoptysis in patients with nonlocalizing chest roentgenogram. Age more than 50 years, male sex and more than 40 pack-year smoking history was the significant risk factors in this study. These authors found that limiting bronchoscopy to patients with 2 or more risk factors would have identified 100\% of the carcinoma and reduce the number of procedure by 28\%,\textsuperscript{14,15}

In our population, bronchogenic carcinoma was an uncommon finding, presented in only 4\% (4/113). This rate was similar to 2.5\% by Heimer et al.\textsuperscript{13} and 3\% by Jackson et al.\textsuperscript{16}

Some authors carried out a thorough investigation to find other causes of hemoptysis such as infection. McGuinness et al.\textsuperscript{17} found bronchiectasis in 25 of 57 of patients as the most common cause of hemoptysis. Knott-Craig et al.\textsuperscript{18} reported tuberculosis in 73\% of the patients as the most prevalent cause. Haro et al.\textsuperscript{9} found bronchiectasis in 20\%, chronic obstructive lung disease in 14\%, and pneumonia in 8\%. These etiologies need special attention according to its treatable nature and good prognosis. Neutrophile in BAL may act as a clue for diagnosing infectious diseases, although some interstitial lung disease and bronchiolitis obliterans can increase neutrophils in BAL, but its incidence in hemoptysis patients is not as high as infectious process.\textsuperscript{10}

In this study, we tried to increase utility of bronchoscopy by 2 apparent parameters that were ignored in routine approach of hemoptysis: (1) diagnosing no pathologic lesion in subjects with native lung cells in cytology and considering follow up and (2) diagnosing infection in subjects with more than 80\% neutrophile in cytology and considering antibiotic therapy. By this method accuracy of bronchoscopy was increased (Table 3), although it is not ideal.

ACKNOWLEDGMENT

The authors thank staff of bronchoscopy ward of Imam Reza and Ghaem Hospital in Mashhad city.

REFERENCES


