Abnormal Airway Function in Individuals with the Acquired Immunodeficiency Syndrome*


Pulmonary function test results of individuals with the acquired immunodeficiency syndrome (AIDS) were analyzed to determine the prevalence of abnormally low forced expiratory flow rates and bronchial hyperreactivity. Of 99 individuals with AIDS, a total of 44 (44 percent) had either low forced expiratory flow rates or a significant response to inhaled bronchodilator. Thirty-one (31 percent) individuals exhibited significant improvement in airflow rates after bronchodilator inhalation, while 33 (33 percent) had low flow rates. Twenty (20 percent) individuals had both low flow rates and a significant response to bronchodilator. In 83 percent of symptomatic individuals treated with bronchodilators there was clinical improvement. Thus, we conclude that abnormally low forced expiratory flow rate with or without bronchial hyperreactivity is a common and treatable complication of AIDS. (Chest 1983; 84:945-48)

Individuals with the acquired immunodeficiency syndrome (AIDS) are subject to frequent and often fatal pulmonary complications. Infections due to a myriad of opportunistic and common pathogens as well as noninfectious processes such as malignancy and lymphocytic interstitial pneumonitis have been identified in this setting. In addition, anatomic obstruction of upper and central airways may occur as a result of endobronchial metastases from Kaposi's sarcoma. A bronchospastic disorder also has been described in 3 percent of 130 individuals with AIDS.

In our experience, bronchospasm occurs more frequently in AIDS than has previously been reported. Symptoms such as wheezing and chest tightness are common among those in our AIDS patient population. The recognition of an asthma-like syndrome in AIDS is particularly important since it could be confused with life-threatening disorders such as opportunistic infection and could lead to either inappropriate diagnostic evaluation or therapy. To document the prevalence of airway dysfunction in this setting, we analyzed pulmonary function test results and reviewed the medical records of individuals with AIDS who were treated at the New England Deaconess Hospital.

METHODS

Sample Selection and Testing Procedures

The New England Deaconess Hospital is a 500-bed university-affiliated hospital in Boston where approximately 25 percent of all those in Massachusetts with AIDS have received treatment since 1983. Between January 1, 1983, and July 31, 1986, 153 individuals with AIDS were treated at this institution. Of these individuals, 105 were referred to the pulmonary function laboratory. In all cases, the diagnosis of AIDS was established by the criteria outlined by the Centers for Disease Control. The records of all patients able to perform three forced expiratory maneuvers conforming to the standards established by the American Thoracic Society were evaluated. To qualify for analysis, each patient had to have an acceptable forced vital capacity as registered on a pneumotachometer-based spirometer (System 1070, Medical Graphics, St. Paul, MN). This system was tested with a calibrated rotameter and its output was determined to be linear in the normal range of human forced expiratory flows. The system was calibrated twice daily by injecting a standard volume at five different flow rates. Spirometric values were compared with the published normal values of Crapo et al.

A standard approach was employed in the assessment of forced expiratory flow rates. Flow rates were considered to be abnormally low if either the ratio of forced expiratory volume in 1 s (FEV,) to the forced vital capacity (FVC) or the mean forced expiratory flow during the middle half of the FVC (FEF 25-75%) was more than 1.65 standard deviations below the age-sex-height specific predicted value for that individual. Because individuals with abnormally low lung volumes also have low maximum expiratory flow rates, only the FEV/FVC ratio was considered in the evaluation of obstruction for individuals whose FVC was below 80 percent of predicted. Although a low FVC does not necessarily indicate restrictive impairment, we reasoned that in cases in which the FVC was reduced secondary to air trapping, as would occur with significant airflow obstruction, the FEV/FVC ratio also would be reduced. Thus, we assumed that individuals with reduced FVCs but normal FEV/FVC ratios had restrictive disease irrespective of low instantaneous maximum expiratory flows. Individuals were evaluated prior to and 15 min after two inhalations of an aerosolized albuterol solution (Proventil inhaler, Schering Corp., Kenilworth, NJ). The response to inhaled bronchodilators was considered significant if the FEV, increased by at least 12 percent, or if the FEF 25-75% increased by at least 25 percent while the vital capacity changed less than 10 percent.

To correlate abnormal function with clinical events, the medical records of all individuals were reviewed with the aid of a specially prepared questionnaire. The presence or absence of lower respiratory tract infection was substantiated in each case by results of diagnostic fiberoptic bronchoscopy, chest x-ray film, and a compati-

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able clinical illness. Respiratory tract involvement with Kaposis sarcoma was documented by: (a) a characteristic radiologic pattern including the presence of diffuse parenchymal nodules, or pleural disease and/or interstitial infiltrates associated with hilar or mediastinal adenopathy in the absence of microbial pathogens in respiratory secretions; and (b) direct visualization of characteristic violaceous endobronchial masses during bronchoscopy.

Chi-square tests were used to assess the strength of observed associations; results were considered significant at the 0.05 probability level.

RESULTS

Prevalence of Abnormal Airway Function in AIDS

From January 1983 to July 1986, 105 AIDS patients were referred for pulmonary physiologic assessment. Ninety-nine (94.3 percent) of these individuals were able to perform three FVC maneuvers acceptable for analysis. The 105 patients referred to the PFT lab represent 68.6 percent of those with AIDS who were treated as either inpatients or outpatients at the New England Deaconess Hospital. The mean age of this group was 34.6 (± 8.2 SD) years. Seventy-two percent of these individuals were tested on an outpatient basis. Ninety-six percent were male and 92 percent were homosexual.

In this sample, decreased airflow rate was observed in 33 (33 percent) cases, while a significant response to bronchodilators was detected in 31 (31 percent) cases. The distribution of pulmonary function test results is shown in Figure 1. Overall, among those with AIDS, 44 (42 percent) individuals had abnormal airway function. Eleven individuals had a significant bronchodilator response in the presence of normal baseline flow rates. In six instances, obstruction was present in association with an FVC of less than 80 percent of predicted. Twenty-five individuals had an abnormally low FEV₁/FVC ratio, while an additional eight subjects had low FEF 25-75% values with a normal 1 s ratio. Among those with a significant bronchodilator response, 16 had improvement in the FEV₁, and an additional 11 had improved FEF 25-75% values alone.

Comparison of individuals with and without abnormal test results revealed no differences with respect to mean age or duration of AIDS. Cigarette smoking, defined as a minimum of five pack-years total exposure, was not more common among individuals with airflow obstruction. Fourteen of 35 smokers (40 percent), as compared with 30 or 64 nonsmokers (47 percent), had abnormal airway function. Of six individuals with a history of asthma, four had a significant response to bronchodilator.

Relation of Abnormal Airways Function to Clinical Events

We examined the temporal relationship of PFT results to episodes of Pneumocystis carinii pneumonia (PCP) and the presence of systemic Kaposis sarcoma (KS) for possible clues to the pathogenesis of airway dysfunction. Among the 99 AIDS patients reported here, 54 percent had developed PCP while 29 percent had developed systemic KS within three months prior to testing.

Eight of 18 (44 percent) cases with KS alone and nine of 42 (21 percent) cases with PCP alone had evidence of airway dysfunction. Among individuals with coexistent PCP and KS, abnormal airway function was present in seven of 11 (63.6 percent) cases. Fifteen of 29 (52 percent) individuals who had KS with or without PCP and 16 of 53 (30 percent) individuals who had PCP with or without KS had airway dysfunction. Twenty of 28 (71 percent) individuals with AIDS had abnormal tests of airway function that were not associated with PCP or KS. Of the 29 individuals with systemic KS analyzed in this study, only four had endobronchial KS visualized at bronchoscopy, while one additional patient had chest x-ray findings suggestive of pulmonary involvement with KS. There was a significant association between the presence of symp-
toms such as cough, wheeze, and chest tightness, and the occurrence of abnormal tests of airway function (Table 1). Twenty-two of 32 (68.8 percent) symptomatic individuals had abnormal function as compared with 18 of 67 (26.9 percent) AIDS patients who did not have such symptoms. Bronchodilator therapy was instituted in 24 of the symptomatic individuals, with clinical improvement in 20 cases.

**DISCUSSION**

This study demonstrates the frequent occurrence of abnormal airway function among individuals with AIDS. In this sample, we found that 44 percent of subjects had either abnormally low forced expiratory flow rates or a significant response to inhaled bronchodilator. Abnormal function was more prevalent among individuals with systemic KS than it was among those with the diagnosis of PCE, but was most common among those with neither PCE nor KS.

Although a prevalence rate for bronchospastic disorder in AIDS has been reported in an earlier study, the prevalence cited in that report (3 percent) was considerably lower than that found here, and, in fact, was close to the rate of airway hyperreactivity found in the general population. This discrepancy is not attributable to physiologic criteria used to assess airway dysfunction, since we employed similar criteria derived from closely related normal population studies. In the previous study only 27 of 130 patients (21 percent) underwent pulmonary function testing, and selection criteria for testing were not adequately described. Therefore, the discrepancy in reported prevalence of airway dysfunction between that study and the current one may be related to differences in patient selection.

We also considered whether the high prevalence of abnormal airway function we observed could have resulted from selection bias. For example, could it be that from among all those with AIDS who were treated at this hospital only those with suspected airway dysfunction were referred for testing? This possible bias in the selection of subjects can be addressed in the following manner. During the study period a total of 153 AIDS patients were treated at the New England Deaconess Hospital (NEDH). For the sake of argument, it could be assumed that all 48 patients not referred to the pulmonary laboratory had normal function. This is equivalent to using the total of 153 AIDS patients followed at the NEDH as the denominator for calculating prevalence. In this scenario, we still find that 29 percent of all those with AIDS who were treated as either inpatients or outpatients have airway dysfunction. Since this figure is several times greater than the prevalence of airway dysfunction among the general population, we believe that our results do not merely reflect a bias in sample selection. Furthermore, even if we employ only the FEV₁ as a reliable indication of airflow obstruction and bronchial reactivity, we still find that 30 of the total 153 (20 percent) AIDS patients treated at this institution had abnormal airway function.

Recognition of abnormal airway function had clinical importance in our patients. The symptoms of cough and wheeze led to diagnostic bronchoscopy in three cases where no other cause was found. Moreover, abnormal airway function was significantly associated with clinical signs and symptoms (Table 1). Recognition of an asthma-like syndrome led to bronchodilator therapy in 24 individuals. No unusual complications of treatment were observed, and in 20 cases, there was clinical improvement. Thus, airway dysfunction was a frequent, and highly treatable complication of AIDS.

The pathophysiology of abnormal airway function could not be ascertained in this retrospective analysis, although infection of the upper and lower respiratory tract is common in AIDS. Post-infectious asthma is a well recognized complication of respiratory infections, particularly those caused by viral pathogens, but is not generally thought to be an important complication of opportunistic infection in the immunosuppressed host. Furthermore, antecedent infection could not be implicated in the 71 percent of our patients with abnormal airway function who had neither evidence of active or recent pulmonary infection. Therefore, the role of infection in the pathogenesis of airway dysfunction is uncertain.

In summary, airway dysfunction is more common in the setting of AIDS than previously believed. Recognition of this phenomenon may lead to specific therapy with bronchodilators, and on occasion may obviate the need for diagnostic procedures such as bronchoscopy. Future prospective evaluation of this population may provide greater insight into the pathogenic mechanisms underlying the development of airway dysfunction.

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