CHEST

Official publication of the American College of Chest Physicians

Bronchogenic Carcinoma in Patients Seropositive for Human Immunodeficiency Virus

Shawn D. Aaron, Ellen Warner and Jeffrey D. Edelson

Chest 1994;106;640-642
DOI 10.1378/chest.106.2.640

ISSN:0012-3692

washing) using partial cardiopulmonary bypass. Am Rev Respir Dis 1970; 101:877-84
2 Mazyck EM, Bonner JT, Herd HM, Symbas PN. Pulmonary lavage for childhood pulmonary alveolar proteinosis. J Pediatr 1972; 80:839-42
3 Altose MD, Hicks RE, Edwards MW. Extracorporeal membrane oxygenation during bronchopulmonary lavage. Arch Surg 1976; 111:1148-53
4 Cooper JD, Duffin J, Glynn MFX, Nelems JM, Teasdale S, Scott AA. Combination of membrane oxygenator support and pulmonary lavage for acute respiratory failure. J Thorac Cardiovasc Surg 1976; 71:304-08
5 Freedman AP, Pelias A, Johnston RF, Goel IP, Hakki HI, Oslick T, et al. Alveolar proteinosis lung lavage using partial cardiopulmonary bypass. Thorax 1981; 36:543-45
6 Hiratzka LF, Swan DM, Rose EF, Ahrens RC. Bilateral simultaneous lung lavage utilizing membrane oxygenator for pulmonary alveolar proteinosis in a 8-month-old infant. Ann Thorac Surg 1983; 35:313-17
7 Mahut B, de Blic J, Le Bourgeois M, Beringer A, Chevalier JY, Scheinmann P. Partial and massive lung lavages in an infant with severe pulmonary alveolar proteinosis. Pediatr Pulmonol 1992; 13:50-3
8 Prakash UBS, Barham SS, Carpenter HA, Dines DE, Marsh HM. Pulmonary alveolar phospholipoproteinosis: experience with 34 cases and a review. Mayo Clin Proc 1987; 62:499-518
9 Moazam F, Schmidt JH, Chesrown SE, Graves SA, Sauder RA, Drummond J. Total lung lavage for pulmonary alveolar proteinosis in an infant without the use of cardiopulmonary bypass. J Pediatr Surg 1985; 20:398-401
10 Ramirez-RJ. Alveolar proteinosis: importance of pulmonary lavage. Am Rev Respir Dis 1971; 103:666-78
11 Rogers RM, Levin DC, Gray BA, Moseley LW. Physiologic effects of bronchopulmonary lavage in alveolar proteinosis. Am Rev Respir Dis 1978; 118:255-64
12 Sunderland WA, Campbell RA, Edwards MJ. Pulmonary alveolar proteinosis and pulmonary cryptococcosis in an adolescent boy. J Pediatr 1972; 80:450-56
13 Kariman K, Kylstra JA, Spock A. Pulmonary alveolar proteinosis: prospective clinical experience in 23 patients for 15 years. Lung 1984; 162:223-31
14 Bartlett RH. Extracorporeal life support for cardiopulmonary failure. Curr Prob Surg 1990; 27:621-705
15 McKenzie B, Wood RE, Bailey A. Airway management for unilateral lung lavage in children. Anesthesiology 1989; 70:550-53
16 Spock A, Kylstra J, Lanning C, Camporesi EM. Lung lavage in two infants with alveolar proteinosis. Pediatr Res 1983; 17:390A
17 Rogers RM, Szidon JP, Shelburne J, Neigh JL, Shuman JF, Tantum KR. Hemodynamic response of the pulmonary circulation to bronchopulmonary lavage in man. N Engl J Med 1972; 286:1230-33
18 Wasserman K, Blank N, Fletcher G. Lung lavage (alveolar washing) in alveolar proteinosis. Am J Med 1968; 44:611-17
19 Smith JD, Millen JE, Safar P, Robin ED. Intrathoracic pressure, pulmonary vascular pressures and gas exchange during pulmonary lavage. Anesthesiology 1970; 33:401-05
20 Ramirez RJ. Bronchopulmonary lavage—new techniques and observations. Dis Chest 1966; 50:581-88
21 Colon AR, Lawrence RD, Mills SD, O'Connell EJ. Childhood pulmonary alveolar proteinosis (PAP): report of a case and review of the literature. AJDC 1971; 121:481-85
22 Davidson JM, Macleod WM. Pulmonary alveolar proteinosis. Br J Dis Chest 1969; 63:13-28
23 Ramirez RJ. Pulmonary alveolar proteinosis. Arch Intern Med 1967; 119:147-56
24 Paul K, Muller KM, Oppermann HC, Nutzenadel W. Pulmonary alveolar lipoproteinosis in a seven-year-old girl. Acta Paediatr Scand 1991; 80:477-81

Bronchogenic Carcinoma in Patients Seropositive for Human Immunodeficiency Virus*

Shawn D. Aaron, M.D.; Ellen Warner, M.D.; and Jeffrey D. Edelson, M.D., F.C.C.P.

The purpose of this report is to describe an association between bronchogenic carcinoma and HIV. Three HIV-seropositive patients are described who developed bronchogenic cancer (two large cell, one adenocarcinoma) before developing an AIDS-defining illness. A critical review of the literature revealed 22 other patients in which the association of HIV infection and lung cancer is reported. These patients are characterized by a relatively young age at diagnosis (median, 43 years) and prevalence of the adenocarcinoma subtype (13 of 25 patients). Twenty of 21 patients had a history of smoking. Among 21 patients for whom data were available, 6 patients (28 percent) had AIDS at time of diagnosis of lung cancer while 11 patients (55 percent) did not have AIDS or AIDS-related complex at diagnosis.

(Chest 1994; 106:640-42)

AZT=zidovudine

Patients infected with HIV frequently develop pulmonary complications.[1,2] Although lung abnormalities in AIDS usually result from pulmonary infection, malignancies such as Kaposi's sarcoma and non-Hodgkin's lymphoma occur with markedly increased frequency in AIDS patients.[3,4] Lung cancer, however, has not classically been associated with HIV infection. This report details three cases of HIV-infected patients who developed bronchogenic carcinoma. Other published reports are reviewed, suggesting a causal association between HIV infection and lung cancer.

Case Reports

Case 1

A 50-year-old HIV-positive, bisexual man presented in November 1991 with a 3-month history of an intermittent right-sided chest and shoulder pain. He had a 30-pack-year smoking history and had been taking zidovudine (AZT) for 4 years. He had a CD4 count of 240 in October 1991. There was no history of lymphadenopathy or AIDS-defining illness. The patient reported a 4.5-kg weight loss over the previous 8 months but had no fever, cough, dyspnea, or hemoptysis. Physical examination revealed

*From the Department of Medicine, St. Michael's Hospital, University of Toronto, Ontario, Canada.
Reprint requests: Dr. Edelson, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario, Canada M5B 1W8

marked finger clubbing and tachypnea. There were several 0.5-cm mobile lymph nodes in the posterior triangle of the right side of the neck and bilateral distention of the external jugular, arm, and chest veins. A chest radiograph revealed a 4×5×5-cm soft-tissue mass in the right hilum. A computed tomographic (CT) scan of the thorax revealed a 5×7-cm right hilar mass causing near total compression of the superior vena cava along with a 1.5-cm right upper lobe nodule and another 1-cm nodule in the lingula. A percutaneous needle biopsy specimen from the right hilar mass revealed a large-cell anaplastic carcinoma. A bone scan and abdominal scan did not reveal extrapulmonary metastases. The patient was treated with radiotherapy, receiving 2,000 cGy in five fractions in December 1991. He developed a recurrence of right-sided chest pain and hemoptysis in March 1992 and received a second course of palliative radiotherapy. In October 1992, the patient developed symptoms of urinary incontinence without evidence of spinal cord compression. He was admitted to hospital for palliative care and died in December 1992.

Case 2

A 51-year-old bisexual man presented in January 1992 with a 3-month history of cough and hemoptysis. The patient had a 24-pack-year smoking history and had stopped smoking 6 years prior to presentation. In 1988, he developed generalized lymphadenopathy, was found to HIV-positive, and began therapy with AZT. In September 1991, the patient's CD4 count was 170. He then developed hemoptysis in October 1991. A chest radiograph showed a right lower lobe interstitial infiltrate for which he was treated empirically with trimethoprim-sulfamethoxazole. In January 1992, his chest radiograph demonstrated increasing infiltrative changes in the right lung and right perihilar region as well as atelectasis of the right base. An endobronchial biopsy specimen of tumor seen in the right lower lobe bronchus demonstrated large-cell anaplastic cancer. Metastatic workup disclosed no abnormalities. In February 1992, a new right pleural effusion developed. Cytologic examination of pleural fluid was consistent with adenocarcinoma. Pleurodesis of the right pleural cavity was performed; however, the patient had progressive parenchymal lung infiltration with tumor and recurrence of bilateral malignant pleural effusions. He died in hospital in March 1992.

Case 3

In October 1990, an asymptomatic 60-year-old homosexual man was found to be HIV-positive with a CD4 count of 180. Therapy with AZT was begun. The patient had a 30-pack-year history of smoking but had quit 3 years earlier. Following the diagnosis of HIV infection, the patient had a routine chest radiograph that disclosed the presence of a right upper lobe mass and right hilar adenopathy. A CT scan of the thorax showed an irregular 2-cm mass in the anterior segment of the right upper lobe and right-sided mediastinal adenopathy. A fine-needle aspirate of the right upper lung lesion was done in March 1991, demonstrating adenocarcinoma. Metastatic workup disclosed no abnormalities. In April 1991, he had a mediastinoscopy that revealed adenocarcinoma in the right paratracheal nodes. The patient underwent radiation therapy in July 1991 to his primary lung tumor. He remained well until June 1992 when he noted cough and weight loss. Chest radiograph showed partial collapse of the right upper lobe with a right pleural effusion as well as multiple soft-tissue nodules that had developed in both lung fields. When last assessed in July 1992, he was still alive but his condition was clinically deteriorating from progressive cancer.

Discussion

This report identifies three patients infected with HIV who subsequently developed bronchogenic carcinoma. Two of these tumors were of the large-cell anaplastic histologic subtype and one was an adenocarcinoma. All three patients had significant smoking histories, although two had quit smoking several years prior to diagnosis of lung cancer. None of the patients had a diagnosis of AIDS established prior to the recognition of lung cancer, although patient 2 had AIDS-related complex. CD4 counts at the time of lung cancer diagnosis, however, were depressed (240, 170, and 180, respectively). None of the patients were IV drug abusers and all identified homosexual contact as their risk factor for HIV infection. All three patients presented with locally advanced (stage III)[5] lung cancer without evidence of metastatic disease. Patient 2 died within 6 weeks of diagnosis without receiving specific therapy. The other two patients received radiotherapy to the primary tumor site. Patient 1 died 13 months after diagnosis and patient 3 is alive with active disease 22 months after presentation. For both patients local-regional tumor progression was the cause of their clinical deterioration.

An association between AIDS and bronchogenic lung cancer has not been well documented. Including the three patients described in the present report, 25 such individuals have been identified to date.[6-14] Of tumors described in these 25 patients, 13 (52 percent) were adenocarcinomas, 6 (24 percent) were small-cell carcinoma, 3 (12 percent) were squamous cell carcinoma, 2 (8 percent) were large-cell carcinoma, and 1 (4 percent) was an adeno/squamous carcinoma. This differs from the usual distribution of tumor types in most lung cancer series, wherein squamous cell, adenocarcinoma, and small-cell cancer each account for approximately one third of cases.[15] The median age of 17 patients in whom specific age was published was 43 years. In a subgroup of seven other patients,[13] individual ages were not cited but the median age of this subgroup was 34 years. Of the 25 HIV-infected patients with lung cancer reported in the literature, 23 were male. Among the 21 patients for whom data were available, 6 patients (28 percent) satisfied the CDC criteria for AIDS at the time of diagnosis of lung cancer, and 11 patients (55 percent) were HIV-positive but were asymptomatic and did not have AIDS at the time of diagnosis of lung cancer. One patient had generalized adenopathy and three patients had AIDS-related complex at time of diagnosis. Known risk factors for HIV infection were identified in 24 of 25 patients. Fourteen of 25 (56 percent) were IV drug abusers, 9 (36 percent) were homosexual, and 1 (4 percent) had received multiple blood transfusions. Twenty of the 21 cases in which smoking history was documented were current or previous smokers. Thus, it appears that lung cancer in HIV is characterized by a distinct distribution of histologic subtypes, younger age, and an aggressive clinical course of disease.

In addition to the well-recognized predisposition of HIV-infected individuals to develop Kaposi's sarcoma and lymphoma, several studies have reported an apparent association of nonpulmonary epithelial tumors in such patients. One report cited an increased prevalence of squamous cell carcinomas of the oral and anal regions in patients with AIDS.[16] Cervical dysplasia and cancer are emerging as major challenges in the growing number of HIV-infected women.[17] Other studies have documented

series of patients with HIV-associated epithelial malignancies of the cervix,[12] colon,[18] conjunctiva,[19,20] skin,[21] and genitourinary tract.[22]

This report confirms the previously noted association between HIV infection and lung cancer and raises the possibility that the two conditions may be related. Although base population data are not available for previously published studies, the development of record linkage systems between HIV infection registries and cancer registries is now occurring in some areas and may be able to better characterize the statistical magnitude of the apparent link between HIV infection and the development of lung cancer.

ACKNOWLEDGMENT: The authors wish to thank Ms. Shirley Chan for expert secretarial assistance.

REFERENCES

1 Edelson JD, Hyland RH. AIDS and the lung. Curr Pulmonol 1990; 11:273-311
2 White DA, Matthay RA. State of the art: noninfectious pulmonary complications of infection with the human immunodeficiency virus. Am Rev Respir Dis 1989; 140:1763-87
3 Polish LB, Cohn DL, Ryder JW, Myers AM, O'Brien RF. Pulmonary non-Hodgkin's lymphoma in AIDS. Chest 1989; 96:1321-26
4 Ziegler JL, Beckstead JA, Volberding PA, Abrams DJ, Levine AM, Lukes RJ. Non-Hodgkin's lymphoma in 90 homosexual men: relation to generalized lymphadenopathy and the acquired immunodeficiency syndrome. N Engl J Med 1984; 311:565-70
5 Moutin CF. A new international staging system for lung cancer. Chest 1986; 89:225-33
6 Irwin LE, Begandy MK, Moore TM. Adenosquamous carcinoma of the lung and the acquired immunodeficiency syndrome [letter]. Ann Intern Med 1984; 100:158
7 Moser RJ, Tneholder MF, Ridenour R. Oat cell carcinoma in transfusion-associated acquired immunodeficiency syndrome [letter]. Ann Intern Med 1985; 103:478
8 Nusbaum NJ. Metastatic small cell carcinoma of the lung in a patient with AIDS [letter]. N Engl J Med 1985; 312:1706
9 Lake-Lewin D, Arkel YS. Spectrum of malignancies in HIV positive individuals [abstract]. Proc Am Soc Clin Oncol 1988; 7:20
10 Fineberg SA, Schinella R. Human immunodeficiency virus infection in women; report of 102 cases. Mod Pathol 1990; 3:575-80
11 Monfardini S, Vaccher E, Pizzocaro G, Stellini R, Sinicoo A, Sabbatani S. Unusual malignant tumors in 49 patients with HIV infection. AIDS 1989; 3:449-52
12 Braun MA, Killam DA, Remick SC, Ruckdeschel JC. Lung cancer in patients seropositive for human immunodeficiency virus. Radiology 1990; 175:341-43
13 Nguyen VQ, Ossorio MA, Roy TM. Bronchogenic carcinoma and the acquired immunodeficiency syndrome. Ky Med Assoc J 1991; 89:322-24
14 Fraire AE, Awe RJ. Lung cancer in association with human immunodeficiency virus infection. Cancer 1992; 70:432-36
15 Fraire AE, Cooper S, Buffler P, Greenberg SD. Carcinoma of lung: changing histopathologic cell types. In: Fenoglio-Praisser CM, Wolff M, Rilke F, eds. Progress in surgical pathology (vol 12). Blue Bell, Pa: Field and Wood Medical Periodicals, 1992; 129-49
16 Safai B, Lynfield R, Lowenthal DA, Koziner B. Cancers associated with HIV infection. Anticancer Res 1987; 7:1055-68
17 Maiman M, Fruchter RG, Serur E, Remy JC, Feuer G, Boyce J. Human immunodeficiency virus infection and cervical neoplasia. Gynecol Oncol 1990; 38:377-82
18 Cappell MJ, Yao F, Cho KC. Colonic adenocarcinoma associated with the acquired immunodeficiency syndrome. Cancer 1988; 62:616-19
19 Kestelyn P, Stevens AM, Ndayambaje A, Hanssens M, Van de Perre P. HIV and conjunctival malignancies. Lancet 1990; 336:51-2
20 Wynward KE, Cortin VT. Conjunctival squamous carcinoma in a patient with human immunodeficiency virus infection. Am J Ophthalmol 1989; 107:554-55
21 Sitz KV, Keppen M, Johnson DF. Metastatic basal cell carcinoma in acquired immunodeficiency syndrome-related complex. JAMA 1987; 257:340-43
22 Adjiman S, Zerbib M, Flam T, Brochard M, Desligneras S, Boissonas A. Genitourinary tumors and HIV-1 infection. Eur Urol 1990; 18:61-3