Environmental Asbestos Complicated by Lung Cancer*

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Diagnosis of asbestosis and bronchiolo-alveolar carcinoma was made in a 55-year-old Turkish woman who was a nonsmoker. She originated from and was living in an area with a high prevalence of environmental diseases attributed to tremolite asbestos. Mineralogic analysis of lung tissue revealed very high concentrations of asbestos bodies (1.64×10⁶/g of dry tissue) and tremolite fibers (173.7×10⁶ of dry tissue). This case illustrates the following points: (1) In some areas, environmental exposure can lead to cumulated fiber retention comparable to occupational exposure and thus can represent a risk for lung fibrosis (asbestosis). (2) Lung cancer as a complication of environmental asbestosis also should be considered as a potential environmental disease.

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In rural Turkey, as in other mediterranean areas (Greece, Cyprus, Corsica), the prevalence of environmental asbestos-related diseases is high. This is attributed to the presence of asbestos fibers, mainly tremolite, in the soil and to its use as a whitewash material.

Malignant mesothelioma and benign pleural lesions (plaques, thickening) are commonly reported. These diseases occur frequently in subjects with low-dose exposures, contrary to asbestosis which requires a heavy exposure to develop. We report the case of a Turkish woman who presented with asbestosis and bronchial carcinoma after only environmental exposure.

Case Report

A 55-year-old woman was evaluated for hemoptysis and left thoracic pain, at the Hacettepe Hospital, Ankara, Turkey. She had no past history of respiratory disease and was a nonsmoker. She was a housewife, originating from and living in Cezin, a village adjacent to Maden/Elazig, in the southeastern part of Turkey. She had done whitewashing, as most of the women from the rural part of Turkey.

Physical examination revealed coarse crepitations and diminished breath sounds at the left thoracic base. The standard chest x-ray film showed a large opacity in the left lower lobe with partial atelectasis of this lobe. There were also bilateral diffuse irregular opacities and diaphragmatic calcifications compatible with asbestosis and asbestos-related pleural plaques.

Fiberoptic bronchoscopy showed stenosis of the apical segment of the left lower lobe by an irregular mucosa. Biopsies were not contributive, and the patient underwent a left posterolateral thoracotomy. This procedure disclosed a 4-cm diameter mass in the left lower lobe, extending into the lingula and toward the left hilum. No radical surgery could be performed, and pulmonary biopsy specimens were taken.

Pathologic Findings

The lung tissue exhibited an interstitial and peribronchiolar fibrosis associated with an infiltration by pigmented

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Figure 1. Histologic sections showing peribronchiolar fibrosis (top, low magnification) and interstitial fibrosis with asbestos bodies (asbestosis [bottom, high magnification]. H and E. original magnifications X75 (top) and X70).

Figure 2. Histologic section showing the tumor with a typical bronchiolo-alveolar pattern. (H and E. original magnification X130).
macrophages and lymphocytes and with type 2 pneumocyte proliferation (Fig 1, top).

Asbestos bodies were numerous and closely related to these lesions (Fig 1, bottom). These changes in lung morphologic features are contiguous to a neoplastic growth of nonmucinous cells proliferating along alveolar septa, in a typical case of bronchiolo-alveolar carcinoma (Fig 2).

**MINERALOGIC STUDIES**

Mineralogic studies were performed on digested lung samples. The technique of preparation and counting has been published previously.\(^1\) The light microscopic examination count was 1.64×10⁶ asbestos bodies per gram of dry lung. The results of fiber counting and analysis by electron microscopy were as follows: 173.7×10⁶ tremolite fibers per gram of dry lung; 1.9×10⁶ anthophyllite fibers per gram of dry lung, and 25.1×10⁶ nonasbestos fibers per gram of dry lung (rutile [TiO₂] and aluminosilicates; erionite fibers were not detected).

The mean geometric length of tremolite fibers was 4.3 μ (range, 0.8 to 53 μ; median, 4 μ), the mean geometric diameter was 0.26 μ (range, 0.04 to 1.30 μ; median, 0.25 μ), with a mean geometric aspect ratio of 17 (range, 3 to 200; median, 16).

**DISCUSSION**

This observation raises two interesting issues concerning asbestos-related diseases: (1) the role of environmental exposure, and (2) the association of asbestosis with lung cancer. The diagnosis of asbestosis is undeniable: the chest x-ray film shows interstitial lung disease with pleural calcifications; peribronchiolar and interstitial fibrosis with numerous asbestos bodies is found in the lung sections.\(^2,3\)

In the diagnosis of a classic case of asbestosis, a cumulated exposure that is important enough to represent a substantial risk for fibrosis is required.\(^4\) There was obviously no occupational exposure in this case, but the village of origin is located in southeastern Turkey, in an area where the prevalence of diseases due to environmental exposure to tremolite is high.\(^5,7\) Lesions associated with tremolite exposure reported in this area are mainly pleural thickening and calcification, but radiologic signs of interstitial fibrosis have been reported to occur in about 1 percent of the population.\(^6\) An abundance of mesothelioma and bronchial carcinoma cases also are reported in this area.\(^6\) The type of exposure is similar to that in many other places in Turkey,\(^7,8\) where asbestos material is used as a whitewash product for the houses (the application of this material usually is done by women). The exposure starts at birth and can thus be considered lifelong.

Mineralogic analyses not only confirmed the presence of tremolite in the lung, but also demonstrated very high concentrations of asbestos bodies and fibers in the range of those usually associated with asbestosis.\(^3,9\) In our experience of asbestos body counts, concentrations higher than 5,000/g of dry lung are exceptional in unexposed subjects and burdens of over 1 million asbestos bodies usually are associated with asbestosis.\(^1,10\) Even if absolute numbers of fibers counted by electron microscopy must be interpreted with caution, the values found in this case are very high: they are greater by about 1,000 times than the amount of tremolite usually found in a general population.\(^11\)

Moreover, the mean length and aspect ratios are high in our patient, close to dimensions of commercial amphiboles found in occupationally exposed subjects.\(^11\) Thus, this observation demonstrates that in some cases, cumulated retention of fibers resulting from environmental exposure can be comparable to what is found in patients occupationally exposed to asbestos. Lung fiber concentration can then reach levels associated with parenchymal fibrosis, and asbestos bodies can be so numerous that they readily appear in sections, allowing a histologic diagnosis of asbestosis. This confirms that environmental exposure does not necessarily mean low-dose exposure, essentially associated with pleural plaques and mesothelioma.\(^7\)

This nonsmoking woman with asbestosis also developed a bronchiolo-alveolar carcinoma. The respective roles of asbestosis and asbestos burden in the pathogenesis of cancer associated with asbestos exposure are still being debated.\(^12\) The great majority of asbestos-exposed workers with bronchial carcinoma have indeed radiologic or pathologic evidence of interstitial fibrosis.\(^13-15\) It is possible that the coexistence of asbestosis and lung cancer merely reflects the expression of two diseases with a similar dose-effect relationship. Also, it is possible that both diseases are related, the cancer being a result of long-standing parenchymal inflammation and fibrosis.

Whatever the truth, with the present state of knowledge, a carcinoma generally is ascribed to asbestos when asbestosis is present.\(^4\) All sites and all histologic types of lung cancer are reported in asbestos-exposed workers.\(^4,16\)

Bronchiolo-alveolar carcinoma, however, is a particular type of adenocarcinoma; lung cancers associated with diffuse or localized (scars) lung fibrosis mostly are adenocarcinomas.\(^18,17,20\) In lung fibrosis, type 2 pneumocyte proliferation can disclose varying degrees of atypia, with a progression between simple hyperplasia to atypical bronchiolo-alveolar cell proliferation.\(^12,17\) The latter may be considered as a premalignant lesion for bronchiolo-alveolar carcinoma.\(^21\)

Smoking does not appear to be a major factor in the development of this atypical hyperplasia, contrary to what is observed with squamous metaplasia.\(^22\) The facts that the cancer in this case was a bronchiolo-alveolar carcinoma and also that in sections, fibrosis and cancer appeared very intimately connected and intermingled, reinforce our conviction that there is a relationship between lung fibrosis (asbestosis) and cancer in this nonsmoking woman.

In conclusion, this case demonstrates that asbestosis can be associated with environmental exposure to tremolite. Bronchial carcinoma as a complication of environmental asbestosis also should be considered as a potential environmental disease.

**REFERENCES**

Acute Hypoxemic Respiratory Failure Following Intrapleural Thrombolytic Therapy for Hemothorax*

Michael D. Frye, M.D., F.C.C.P.; Mikell Jarratt, M.D.; and Steven A. Sahn, M.D., F.C.C.P.

Intrapleural instillation of thrombolytic agents has been useful in the treatment of hemothorax when thoracotomy tube drainage is unsuccessful. We present a patient who developed acute hypoxemic respiratory failure following the intrapleural instillation of both streptokinase and urokinase 24 h apart. Hypoxemia most likely resulted from a direct effect of the products of fibrinolysis on the pulmonary circulation.

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Complications of the therapeutic use of intrapleural thrombolytic agents are infrequent. Although intravascular administration has been associated with adult respiratory distress syndrome (ARDS) in two patients,1,2 intrapleural instillation has not been previously reported to lead to pulmonary complications. We recently observed a patient who developed two episodes of severe hypoxemia related to the instillation of two different thrombolytic agents.

CASE REPORT

A 58-year-old man with sick sinus syndrome developed an iatrogenic right hemothorax following placement of a permanent transvenous cardiac pacemaker. Closed thoracotomy tube drainage to suction was not sufficient in completely evacuating the hemothorax.

On the fourth day after tube placement, 250,000 U of streptokinase was instilled intrapleurally. Eight hours following instillation, the patient developed severe hypoxemia and basilar crackles. Physical examination did not suggest a cardiac cause. He remained afebrile and had no hemoptysis or arrhythmias. He had never previously received a thrombolytic agent. Baseline cardiac ejection fraction was 65 percent. The arterial blood gas (ABG) values on 100 percent oxygen were pH of 7.44, Pco2 of 31 mm Hg, and Po2 of 73 mm Hg. Prior to the instillation of streptokinase, the ABG values on 2 L/min nasal cannula O2 were pH of 7.37, Pco2 of 35 mm Hg, and Po2 of 81 mm Hg. The chest radiograph showed bilateral interstitial and alveolar infiltrates, diffuse volume loss, and the previously observed blunting of the right costophrenic angle. Pulmonary artery catheterization revealed a pulmonary artery pressure (PAP) of 24/6 mm Hg, pulmonary capillary wedge pressure (PCWP) of 5 mm Hg, and cardiac output (CO) 6.4 L/min. Fibrinogen level was 489 mg/dl (control, 175 to 400), prothrombin time was 13.3 s (control, 11.4 s), partial thromboplastin time of 22.6 s (control, 25.7 s), and platelet count of 310,000/μl.

Four hours after administration of aerosolized β-agonists,

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