Sputum cytopathological findings in former asbestos workers

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Cigarette smoking asbestos workers constitute a high-risk group for the potential development of lung cancer. The Tyler Asbestos Workers Program was begun in July 1974 to examine 890 former asbestos workers, approximately 90% of whom are cigarette smokers. As of April 1975, 456 former workers had been studied by sputum cytopathology; 217 (48%) were found to have mild squamous epithelial atypias, 20 (4%) severe atypias, and 1 (0.3%) malignant cells of a squamous carcinoma. Sputum cytopathology has been found to be an excellent, simple, noninvasive, painless, and inexpensive means of early detection of premalignant and malignant lesions of the lungs.

One-third (33%) of these former asbestos workers had ferruginous bodies in their sputum. The ferruginous bodies were most numerous in aerosol-induced sputa specimens and could be readily identified by the routine Papanicolaou stain.

Introduction

The Tyler Asbestos Workers Program has been developed for former asbestos workers in order to provide them the most up-to-date care for the early detection and treatment of pulmonary diseases, particularly carcinoma. Approximately 90% of these men are also cigarette smokers, and this along with their previous occupational asbestos exposure renders them 90 times more likely than the general population to develop carcinoma of the lung.[1,2] The cohort for the program is composed of 890 former amosite asbestos workers, most of whom still live within a 150-mile radius of Tyler, Texas. The plant operated between 1954 and 1972. The program began in July 1974, and is ongoing. Each former worker is scheduled for a complete interview, physical examination, and laboratory diagnostic studies including complete blood count and urinalysis, roentgenogram of the chest, electrocardiogram, spirometry, and sputum cytopathology which serves as the heart of the program. Through April 1975, 1,184 sputum specimens from 456 workers had been studied and the results serve as the basis of this report.

Material and Methods

Sputum is collected by both aerosol inhalation during the initial clinic visit and early morning cough at home. All sputa are collected directly into 60% alcohol which serves as an instant fixative. Three sequential early morning home-collected sputa are mailed to the cytopathology laboratory and pooled into one. Sputum induction is carried out by transoral inhalation of a few breaths of an ultrasonic aerosol mist of 8% solution of sodium chloride in water. After inhaling as few as three to five breaths, the patient yields an adequate specimen which is collected directly into 60% alcohol in the sputum container. The sputum specimens are poured into a Petri dish and the cytotechnologist, using curettes, selects out portions of cellular aggregates, debris, and particulate matter and transfers them onto four prelabeled microscopic slides which have been coated with a thin layer of albumin. The cellular material is spread thinly and evenly over the slide by a second slide which is not albumin coated. The

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Supported in part by Contract No. 1-CN-45-66 of the National Cancer Institute, Division of Cancer Control and Rehabilitation to the Texas Chest Foundation.

slides to be stained are then placed in 95% ethyl alcohol in a Coplin jar and subsequently stained in the routine manner by the Papanicolaou technique. The remainder of the specimen is utilized for preparation of a cell block. The sediment for the cell block is placed into a tissue embedding bag, passed through the routine tissue fixatives, and embedded in paraffin. The paraffin blocks of the sediment are sectioned and stained with hematoxylin and eosin and Prussian blue for iron.

Screening of the Papanicolaou-stained sputum smears averages five to seven minutes per slide. Black ink dots are placed by atypical cells and green ink dots by ferruginous bodies. The total number of ferruginous bodies per specimen (four slides) is reported as follows: few, 1 to 14; moderate, 15 to 29; and many, more than 30. For quality control, the cytopathology slides of 10% of all negative sputa specimens are rescreened.

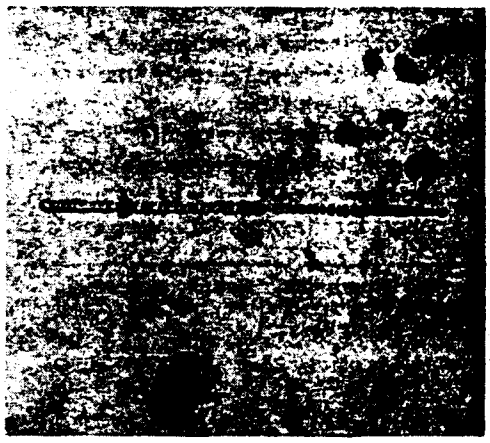
The sputa specimens are reported as unsatisfactory (saliva), no atypia, mild atypia, severe atypia, and positive for carcinoma. Free alveolar macrophages must be identified in order for the specimen to be considered adequate; otherwise it is presumed to be unsatisfactory. Mild atypias include squamous metaplasia and mild dysplasias. Severe atypias include moderate and severe dysplasias. The term "dysplasia" is used to imply dyskaryosis. The squamous metaplasia and the dysplasias are thought to be reversible atypias of the bronchial epithelium. "Positive for carcinoma" includes both carcinoma in situ and invasive carcinoma. We are applying this nomenclature of descriptive terminology to represent the progression of epithelial atypias from the mildest change of simple squamous metaplasia to the development of frank squamous carcinoma.

Results

Ferruginous bodies have been found in the sputa of approximately one-third of the former asbestos workers. Less than

1. Photomicrograph of sputum showing a dumbbell-shaped ferruginous body. Note the adjacent cluster of free alveolar macrophages. Papanicolaou stain, X 260.

2. Photomicrograph of sputum showing a lance-shaped ferruginous body. Papanicolaou stain, X 260.



1% of those tested have failed to produce satisfactory specimens. Thus far, only one former worker has been found to have cells positive for squamous carcinoma in his sputa. He was a 76-year-old Caucasian man who had worked in the asbestos plant from 1954 to 1961. He was also a chronic cigarette smoker of 180 pack years.* Initial sputum examination disclosed both ferruginous bodies (Figs 1, 2) and malignant cells of squamous carcinoma (Fig 3). A roentgenogram of the chest showed reticular infiltrates consistent with interstitial fibrosis in the lower lobes of both lungs; however, no localizing lesion was seen. Fiberoptic bronchoscopy revealed an ulcerating lesion of the bronchus intermedius which, by brushing, washing, and biopsy, was positive for squamous carcinoma (Fig 4). Mediastinoscopy and other routine laboratory studies showed no metastasis, and a right exploratory thoracotomy was performed. When visceral pleural metastases were discovered, the carcinoma was considered to be unresectable and the operation was terminated. The patient refused both radiation therapy and chemotherapy, and died of probable ventricular fibrillation six months after diagnosis. Necropsy revealed the squamous cell carcinoma of the bronchus intermedius (Fig 5) with metastases to right bronchial lymph nodes, right visceral pleura, and pericardium. Asbestosis with interstitial fibrosis was present in both lower lobes of the lungs (Figs 6, 7) and centrilobular emphysema was present in the upper lobes.

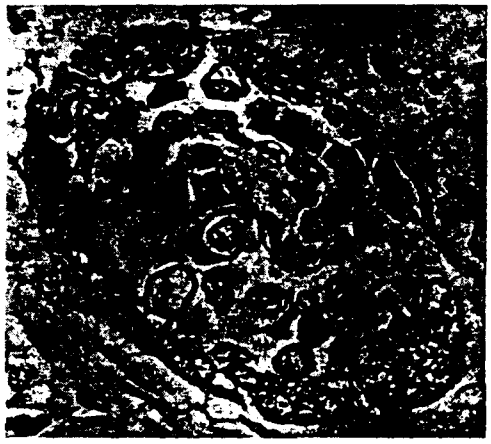
Twenty former workers (4%) have had sputa with severe epithelial atypias, and 48% have had mild atypias, the majority of which are squamous metaplasia.

In the group of former workers whose sputa has yielded ferruginous bodies, the aerosol method of sputum specimen induction has provided for more frequent recovery of the bodies than spontaneous sputa alone. Also, by our methods of quantitation, the aerosol-induced sputa specimens contain a larger number of

*Three packs of cigarettes/day/50 years.

3. Photomicrograph of sputum revealing two large malignant cells of squamous carcinoma. Papanicolaou stain, X 260.

4. Photomicrograph of the tissue preparation of the bronchial biopsy. Note nest of malignant cells of squamous carcinoma. Hematoxylin and eosin stain, X 145.



5. Gross photograph of a coronal section of the right lung. Note the irregular white squamous carcinoma (arrow) involving the bronchus intermedius.

6. Gross photograph of coronal section of right lung. There is diffuse interstitial fibrosis of the lower lobe (arrow).

ferruginous bodies. This appears to be even more significant when one considers that the aerosol-induced specimen is a single specimen, while the spontaneous specimen is a pool of three. The sputa specimens with severe epithelial atypias were equally distributed between aerosol-induced and spontaneous specimens.

Discussion

While the first cases of pulmonary fibrosis caused by asbestos inhalation were reported in 1929,[3] and the first case of lung cancer associated with asbestos in 1935,[4] it was not until 1968[2] that epidemiologic studies established the role of asbestos in the development of lung cancer in cigarette smoking asbestos workers.

The Tyler asbestos plant was in operation between 1954 and 1972, employing 890 men who processed amosite asbestos mined in South Africa.

For many years, sputum cytopathology has been known to be a useful clinical laboratory means of early detection and diagnosis of lung cancer, yielding positive results in up to 80% of cases.[5] Only recently, however, has the role of fiberoptic bronchoscopy been established in the localization of superficial endobronchial carcinomas.[6] Serial roentgenograms of the chest will not permit truly early detection of lung cancer because such a cancer must grow and double for more than five years before it becomes large enough to be seen by the radiologist.[7]

Thus far, in the Tyler Asbestos Workers Program, only one of 456 former workers has had a sputum cytopathologic diagnosis of squamous carcinoma. Although the roentgenogram of this man's chest showed no localizing lesion, the cancer found by fiberoptic bronchoscopy in the bronchus intermedius had already metastasized to the visceral pleura and was nonresectable for cure. Twenty of these 456 former workers have severe atypia of epithelial cells in their sputa. Close clinical and cytologic follow-up of these 20 patients is presently in progress. As the program continues, all 890 former workers will be examined and reexamined

routinely at six-month intervals or more often depending upon cytopathologic and clinical findings in each case.

As yet, no statistical correlations can be made between the association of ferruginous bodies (Fig 8) and atypical epithelial cells in the sputa, but in the future, as more data are gained, this will be of great interest. Even now, one can state that the finding of ferruginous bodies in such numbers indicates significant asbestos exposure, because from 1972 to 1975, not one such body had been found in similar cytopathologic examinations of 12,000 sputa specimens from the general public in the Cytopathology Laboratory of the Harris County Hospital District, Houston, Texas.

Conclusion

Sputum cytopathology is an excellent, simple, noninvasive, painless, and inexpensive means for early detection of malignant and premalignant lesions of the lung, and no special techniques are necessary for the identification of ferruginous bodies.

7. Photomicrograph of tissue preparation from right lower lobe of lung showing a deeply stained ferruginous body with associated free alveolar macrophages and fibroblasts. Prussian blue stain, X 170.

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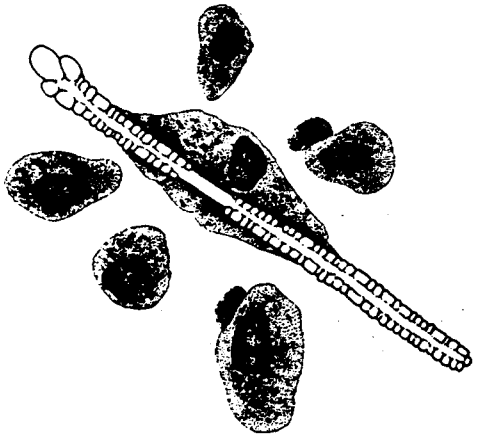
8. Artist's sketch of a club-shaped ferruginous body with associated free alveolar macrophages.



Lead health hazards from smelter emissions

The El Paso City County Health Department began an investigation of a large custom smelter in its city in December 1971 in preparation for a court case filed by the city for violations of Texas rules and regulations governing air pollution. The smelter has been in operation since 1887, producing lead, copper, and zinc from over 800,000 metric tons of ore concentrates shipped to this central location. During the investigation, it was determined that the smelter had emitted 1,012 metric tons of lead, as well as 508 metric tons of zinc, 11 metric tons of cadmium, and 1 metric ton of arsenic from its stacks into the surrounding atmosphere from 1969 through 1971.[1-2]

The emission of particulate lead into atmosphere has been of concern not only in El Paso but throughout the United States, where it is estimated that 166,000 metric tons of particulate lead alone is emitted into the atmosphere each year.[3] The principal source of this emission is from the automobile, and this has led to a growing realization that this source may be a widespread and potentially important source of lead absorption among children.[4,5,28,29,31] Chronic ingestion and inhalation of particulate lead from contaminated dust, soil, and air may account in part for the higher mean blood lead levels of urban as compared to rural children,[4] and may account for the increased lead levels seen in children living near busy roadways.[6]

While automobiles may be the major source of lead-bearing particulate matter, stationary sources such as smelters can create environmental concentrations of lead which should be closely watched and monitored. High levels of lead concentrations in the vicinity of stationary sources[7-10] are particularly possible where climatic conditions such as aridity, low wind velocity, and frequent thermal inversions minimize opportunities for pollutant dispersion. Studies of human lead absorption in such areas as described might illustrate further the potential health hazard posed by particulate lead and its role and route of absorption from the environment.

In our studies, first we determined lead concentrations in particulate matter collected with high-volume samplers throughout El Paso from 1969 through 1971. After consulting with appropriate authorities concerning the measured lead levels in the ambient air, we then proceeded to determine blood lead levels in a sample of persons living throughout El Paso. Results of this initial study caused us concern and thus began an extensive study of exposure of these people to lead in dust, soil, paint, food, water, and pottery. Our purpose was to ascertain the prevalence and severity of lead absorption in this locale, and to evaluate the role of particulate lead in lead uptake (Fig 1).

Background

El Paso is located in the extreme western part of Texas alongside the Rio Grande River adjoining Ciudad Juarez,Chihuahua, Mexico. According to the 1970 United States census, it has a population of 322,261.

The topography of the area is mountainous with the City of El Paso separated by the Franklin Mountains and the Juarez Mountains to the south in Mexico. The area is semidesert and arid to the extent that rainfall supports only limited vegetation (10 to 25 cm of rainfall per year).[11] Winds are moderate (annual average 13.5 km per hour)[12] but a fine, gritty dust be-