Non-neoplastic asbestos-related respiratory diseases: what relationship with other lung diseases?

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Abstract

Non-neoplastic asbestos-related respiratory diseases in practice are represented by asbestosis and pleural plaques. Clinical features and architectural tissue abnormalities of asbestosis do not differ from those of other causes of interstitial fibrosis which allows a confident diagnosis without a history of significant exposure to asbestos. But the relationship between non-neoplastic asbestos-related diseases and other lung diseases is not only represented by the need for differential diagnosis. Developing lung diseases not classified as Asbestos-Related Diseases.

The article reviews the existing relationship between non-neoplastic asbestos-related respiratory diseases and interstitial lung diseases, lung function and risk of pleuropulmonary neoplastic diseases.

Background

The epidemic of Asbestos-Related Diseases (ARDs) is spread all over the world. If in USA illnesses due to occupational asbestos exposure are decreasing, in other Countries, such as Italy and Japan they are still increasing. In Italy, asbestos production reached a peak in the period between 1976-1980, but remained steady over 100,000 tons/year until 1987. These temporal patterns delayed the peak in asbestos consumption in Italy compared to other European countries and in the United States [1]. Moreover, the use of asbestos continues to increase in Asia. Most ARDs are pleuropulmonary. In practice, non-neoplastic ARDs are represented by asbestosis and Pleural Plaques (PPs). Clinical features and architectural tissue abnormalities of asbestosis do not differ from those of other causes of interstitial fibrosis which does not allow a confident diagnosis without a history of significant exposure to asbestos [2,3]. Epidemiologic data on occupational interstitial lung diseases in general is limited by non-standardized diagnostic criteria, varied physician awareness and training, limitations inherent to the various data sources and the long latency period [4]. This leads to underreport occupational lung diseases. But the relationship between non-neoplastic ARDs and other lung diseases is not only represented by the need for differential diagnosis. A diagnosis of non-malignant ARDs does imply a lifelong elevated risk to asbestos-related cancer, while asbestos exposure itself could increase the risk of developing lung diseases not classified as ARDs [5].

This article reviews the existing relationship between non-neoplastic ARDs and interstitial lung diseases, lung function and risk of pleuropulmonary neoplastic diseases.

Asbestosis and other interstitial lung diseases

Asbestosis is an interstitial lung fibrosis caused by the inhalation of all types of asbestos fibers. A histological diagnosis of asbestosis requires the identification of diffuse interstitial fibrosis plus the presence of either 2 or more asbestos bodies in tissue with a section area of 1 cm\textsuperscript{2} or a count of uncoated asbestos fibres that falls in the range recorded for asbestosis by the same laboratory [3]. Being the fibrosis dose-dependent, asbestosis can be induced by cumulative asbestos exposure amounting to an estimated 25 fibres/ml-yrs lower levels can also cause disease in some workers [4,6]. It is well known that the presence of asbestosis increases the risk of lung cancer. In contrast to the asbestosis seen in the past, today most cases of asbestosis are asymptomatic disease identified on radiologic investigation or by histologic assessment of lung parenchyma remote from a resected lung cancer [7]. Usually the diagnosis of asbestosis is based on clinical findings and radiology in the absence of histology. The main differential diagnosis is with idiopathic lung fibrosis, in particular Usual Interstitial Pneumonia (UIP). Pathologically asbestosis is characterized by the fibrosis of alveolar walls adjacent to the respiratory bronchioles, which extend to involve the surrounding lung in the centrifugal direction. In contrast UIP begins at the periphery of the secondary pulmonary lobule and progresses in the centripetal direction. These anatomical differences of lung fibrosis could be appreciated by High-Resolution Computed Tomography (HRCT) images to some extent, not without difficulty [8]. HRCT features include increased intralobular septal markings, subpleural curvilinear lines, parenchymal bands and small cysts [7,9]. The clinic can help since progression of asbestosis, as in other pneumoconiosis, is slower compared to idiopathic interstitial fibrosis. To complicate matters it is suspected that asbestos influences the risk of developing UIP, but the findings are inconclusive [4]. A significant linear relationship was demonstrated in the UK between mortality due to interstitial lung fibrosis and historic asbestos imports.

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The decrease of lung function should be influenced by the progression of ARDs even after the cessation of exposure. Actually, both radiographic and functional pulmonary deterioration may occur long after asbestos exposure [3]. The changes in pulmonary function tests (FEV₁, FVC, total lung capacity TLC, DLCO) and CT imaging of the thorax over a 15-year period after cessation of exposure to asbestos were described in a cohort of Israeli power plant workers [18]. Comparison of the initial and follow-up examination findings revealed a significant increase in calcification of the PPs and a deterioration in pulmonary function tests results. This progression of ARDs in workers formerly exposed to asbestos who had not been exposed to it for over a decade recommends the continued monitoring of individuals exposed to asbestos after the cessation of exposure.

**Plural plaques, lung function and risk of malignant asbestos-related diseases**

Several studies investigated the possible relationship between PPs and lung function, but the results are inconclusive. In various articles in literature an association between PPs and a slight degree of lung function impairment without clinical relevance was observed. However, most studies have demonstrated no significant association between PPs and abnormal pulmonary function tests [19]. Spanish guidelines for the diagnosis and management of asbestos-related plural and interstitial fibrosis that was judged to be most consistent with smoking-associated pulmonary fibrosis. They conclude that the clinical diagnosis of mild asbestosis cannot be reliably distinguished from interstitial fibrosis in heavy smokers. Asbestos bodies and fibres in bronchoalveolar lavage fluid and in lung specimens are of great assistance in the differential diagnosis [6,14].

**Asbestos, non-neoplastic asbestos-related respiratory diseases and lung function**

The possibility that asbestos exposure, in the absence of clinically diagnosed ARDs, may be associated with lung function impairment is discussed. A systematic review and meta-analysis demonstrated a statistically significant reduction in Vital Capacity (VC), Forced Expiratory Volume in 1 s (FEV₁) and FEV₁/VC, even in those workers without radiological changes. Even in the absence of radiological evidence of parenchymal or pleural diseases there was a trend for functional impairment. Authors concluded that asbestos exposure is related to restrictive and obstructive lung function impairment [15]. Another study described lung function profiles among patients with ARDs [16]. Significant differences in lung function in individuals with asbestos-related diseases compared to currently healthy individuals with a history of previous exposure to asbestos were found. Since occupational exposure to asbestos is strongly related to an increased decline in lung function, regular monitoring of lung function among asbestos-exposed populations represents a simple tool to facilitate earlier interventions. Wang et al. studied the adverse effects of exposure to asbestos and smoking on pulmonary function analysis on 468 asbestos-exposed workers and 282 controls [17]. Multivariate regression showed that exposure to asbestos was more strongly associated with decreased Forced Vital Capacity (FVC) and CO Diffusing Capacity (DLCO), and asbestosis more strongly associated with decreased FVC, while smoking was a major contributing factor to reduced FEV₁/FVC. This analysis suggested that asbestos and smoking might play independent roles, in which asbestos caused mainly a restrictive impairment, and smoking was a major causal factor for airway obstruction in the workers who were intensively exposed to asbestos.

Asbestos exposure may be associated with fibrosis of the walls of the respiratory bronchioles and alveolar ducts [7]. These lesions do not represent asbestosis. The asbestos Committee of the College of American Pathologists and Pulmonary Pathology Society proposed the term *asbestos airways disease* for bronchiolar wall fibrosis associated with asbestos bodies [7]. This respiratory bronchiolitis is similar to those observed from exposure to cigarette smoke and mineral dust. At the initial stage, it may be very difficult to diagnose asbestosis in cigarette smokers. Bledsoe et al. evaluate the correlation of radiographically detected pulmonary fibrosis with fibrosis established histopathologically as attributable to asbestos, in a cohort referred for diagnosis of an asbestos-related malignancy [13]. Criteria used for the diagnosis of smoking-associated interstitial fibrosis was a history of heavy smoking (>20 pack-years), interstitial fibrosis of the pattern seen in smoking-associated fibrosis and presence of emphysema or respiratory bronchiolitis. Of 24 cases judged to have asbestosis radiographically 6 showed asbestosis histopathologically. The remaining 18 cases (mean smoking history of 53 packs-years) showed interstitial fibrosis that was judged to be most consistent with smoking-associated pulmonary fibrosis. They conclude that the clinical diagnosis of mild asbestosis cannot be reliably distinguished from interstitial fibrosis in heavy smokers. Asbestos bodies and fibres in bronchoalveolar lavage fluid and in lung specimens are of great assistance in the differential diagnosis [6,14].

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pulmonary disease consider that PPs in general do not cause a decrease in occupational exposure to asbestos. On the other hand, a number of studies demonstrated no significant association between PPs and lung function impairment, although there is still debate on this issue [19].

Data in the literature very often are conflicting and to date there are few certainties in the specific field. The results of health surveillance on the exposed workers populations probably will help to better understand the problem.

References


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