LUNG FIBROSIS ASSOCIATED WITH RARE EARTH EXPOSURE

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Diffuse interstitial lung fibrosis (DILF) with the most prominent clinical sign of progressive restriction of respiratory function may have a variety of causes. The spectrum of disorders in this category is very large and still growing.[1] Besides cases with known etiology — viral, bacterial, environmental etc. — the group of so called cryptogenic or idiopathic interstitial pulmonary fibrosis deserves special attention. Among these primarily obscure cases those originating from unrecognized inhalation of organic or inorganic particles may be hidden. In recent years the application of sophisticated methods for the search of inorganic noxious particles often has been most successful in finding the true cause of pulmonary fibrosis, for instance in workers exposed to hard metals[2] or in asbestosis mimicking interstitial pulmonary fibrosis induced by mica.[3]

Presently we wish to concentrate on diffuse interstitial lung fibrosis (DILF) observed in reprophotographers. Until 1960 in Switzerland in large printing laboratories carbon arc lamps have been used as powerful light sources for reproducing photographs. The carbon rods contain coal and a wick of rare earth metal compounds such as Lanthanum, Cerium, Praseodymium, Neodymium and also Thorium. The reprophotographers have been exposed to fumes occurring during burning of the carbon rods.

After years of exposure the workers developed a slowly progressive dyspnoea. Radiographs showed a diffuse interstitial pulmonary fibrosis. From the 9 patients reported only three were diagnosed during life by lung biopsy as suffering from rare earth exposure. The majority of the cases were diagnosed as "idiopathic" interstitial pulmonary fibrosis, since etiology and relation to occupational fume exposure were not recognized during life.

The average exposure time was about 31 years, the latency period (interval between onset of exposure to time of analysis) was on the average 43 years. Data on the concentration of fume and dust at the workplace are not available. The first cases were traced and shown to be related to reprophotographer occupation more than ten years after cessation of the use of carbon rod lamps. We analyzed our first case in 1972, the last of our series in 1987 (Table I). Because of that, for the recognition of the lung disorder as due to occupational injury the histopathological and mineralogical examination of the diseased lung tissue with a variety of modern methods and a careful occupational history is crucial.

The techniques applied were: histology, transmission elektronmicroscopy, energy dispersive X-ray analysis (EDXA), selected area electron diffraction (SAED), and X-ray spectroscopy.[4,5,6]

PATHOLOGY

Gross pathology in all autopsied cases of interstitial pulmonary fibrosis was similar and sometimes difficult to assess. Extensive severe bilateral involvement occurred in only one case. Focal irregular scarring resembling honeycombing was also observed. Emphysematous areas were seen in all cases.

Microscopically the prominent features were marked interstitial fibrosis with mild interstitial infiltration. Lobular and interlobular septa were fibrosed and occasionally showed proliferation of smooth muscle cells. Interstitial infiltrates of macrophages containing small non birefringent particles less than 10 micrometer were present and there was perivascular accumulation of small deposits of dust particles. Granulomas were absent. Some alveolar spaces contained groups of macrophages with dust inclusions. The type II pneumocytes were proliferating in some areas. There was focal honeycombing with septal retraction. The pulmonary vessels showed mild hypertensive changes with muscularization of arterioles.

ELECTRON MICROSCOPY

In alveolar macrophages as well as in extracellular interstitial spaces electron dense irregular deposits ranging from 0.1 to 10 micrometer were seen. They consisted of densely packed rodlike mineral particles 0.01 micrometers in diameter and 0.1 micrometer in length.

Energy dispersive X-ray analysis (EDXA) revealed elements of the lanthanides series. Lanthanum, Cerium were regularly found, less often Praseodymium and Neodymium were noted. Selected area electron diffraction (SAED) of the aggregates resulted in diffraction patterns characteristic of brockite and rhabdophane respectively according to the ASTM Standards. Brockite and rhabdophane are carbonates and phosphates of the lanthanides.[7]

X-ray spectroscopy (Debye-Scherrer) revealed Samarium, Holmium and Thorium in one case and Ytrium in another. The results are summarized in Table II.

DISCUSSION

Although Lanthanides are widely used in industry, (nowadays also in superconductivity material Bednorz & Müller Nobelprize 1987) little is known about their effects on human health. The first radiological report on the lung disease of

workers exposed to rare earth was published in 1955 by Scheppers.[8] As in our material most of the diseased persons were engaged in reprophotographic work, and worked for years with carbon arc lamps producing fumes containing Lanthanides and root.[9] Unfortunately no data are available concerning concentration and particle size of the original fumes. Retrospectively the patients or their relatives described the working place as dusty and covered with a fine white powder.

Clinical symptoms occurred in most cases many years after cessation of exposure. At the time of the clinical diagnosis of a restrictive lung disorder with the radiologic feature of pulmonary fibrosis neither the patients nor the physicians were aware of a rare earth exposure.

The slowly progressive restrictive lung disease and its unknown origin led to the diagnosis of "idiopathic" pulmonary fibrosis.

Pathological findings were not specific. The search for exogenous particles proved to be successful and diclosed fume particles consisting of rare earth compounds. Microscopically it was difficult to visualize them. Electron microscopy, however, led to the discovery of particles of ultramicroscopic size in places where their presence was unsuspected. The size of the particles ranged from 0.1 to 10 micrometer. They were aggregates of crystals measuring approximately 0.01 micrometer in diameter and 0.1 micrometer in length.

Pathogenetically rare earth pneumoconiosis resembles the pulmonary fibrosis of hard metal workers which is similarly caused by very small dust particles. Rare earth interstitial lung fibrosis is another example of a lung disorder formerly called cryptogenic and ultimately elucidated by mineralogic analysis of the diseased lung tissue. The correlation with a careful occupational history is also a prerequisite for precise diagnosis.

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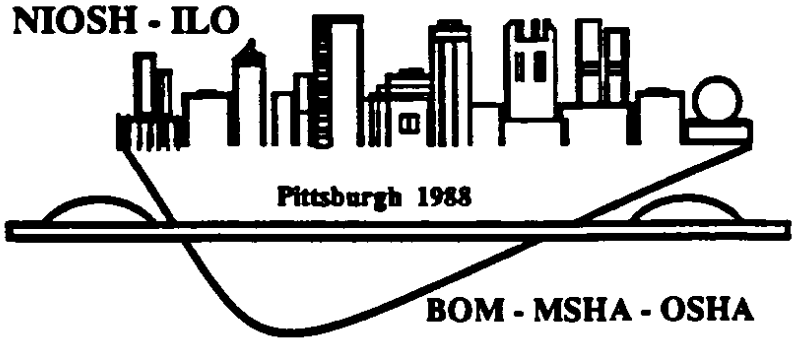
II



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