Polyvinyl chloride pneumoconiosis

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Arnaud, A., Pommier de Santi, P., Garbe, L., Payan, H., and Charpin, J. (1978). Thorax, 33, 19–25. Polyvinyl chloride pneumoconiosis. A 53-year-old man, who had been exposed for 23 years to polyvinyl chloride (PVC) in the bagging area of a vinyl chloride polymerisation plant, presented with a diffuse micronodular infiltrate on his chest radiograph. Light microscopy of lung obtained by drill biopsy showed a diffuse infiltration with histiocytes and multinucleated giant cells, with some collagen formation. Ultrastructural studies showed foreign particles in the macrophages, which were identical with PVC powder viewed under the electron microscope. Incubation of PVC powder with human lung macrophages in vitro showed that the macrophages engulfed the powder to give a similar ultrastructural appearance.

Pneumoconiosis due to polyvinyl chloride (PVC) was first described by Szende et al. (1970). Several epidemiological studies have since been made, which tend to demonstrate that PVC or vinyl chloride (VC) inhalation may be responsible for abnormalities of pulmonary function and chest radiograph (Lilis et al., 1975, 1976; Miller et al., 1975; Suciu et al., 1975). However, histopathological descriptions of this disease are infrequent. We describe here one such case and a study of the ultrastructure of a lung biopsy specimen.

Case report

A 53-year-old man was referred in April 1974 for investigation of diffuse micronodular chest radiographic abnormalities (Fig. 1). He gave a history of chronic productive morning cough for three years, and for three months he had noticed mild weakness and slight exertional dyspnoea. He had smoked 20 cigarettes a day since age 22.

The patient had worked from November 1945 until December 1968 in the PVC bagging area of a vinyl chloride polymerisation factory. Since 1969 he had worked as a shepherd. A chest radiograph performed in 1968 as a routine factory check-up showed the same micronodular shadows. No further investigations were done. Previous chest radiographs were said to have been normal. Physical examination was negative. A scratch tuberculin skin test was weakly positive. Sputum examination for Mycobacterium tuberculosis on three specimens was negative.

The red blood cell count was: 4.19 × 10^6/l; haemoglobin 13.2 g/dl; leucocyte count 6.6 × 10^9/l with 40% lymphocytes and 60% neutrophils; platelets 294 × 10^9/l; erythrocyte sedimentation rate 6 and 20 mm/h; cholesterol 2.11 g/l; total bilirubin 6 mg/l; serum alkaline phosphatase 53 U/l; SGOT 25 U/l; SGPT 39 U/l. Pulmonary function tests showed forced vital capacity 3.82 l (expected value 5.29 l); forced expiratory volume in 1 second 2.82 l (expected value 3.89 l). Arterial blood gases: Pao2 84 mmHg; Paco2 40 mmHg; pH 7.39. Carbon monoxide transfer factor 32.14 ml/min/mmHg (predicted value 31.75/ml/min/mmHg) (10.7 mmol/min/kPa; 10.6 mmol/min/kPa). No abnormality was seen on bronchoscopy. A lung biopsy using Steel’s pneumatic trephine was performed.

Light microscopy

The lung specimen was, for the most part, diffusely infiltrated by histiocytes, in which were seen a few alveolar ducts (Fig. 2). The cytoplasm of these histiocytes contained clear vacuoles. Giant multinucleated cells with vacuolated cytoplasm were also present (Fig. 3). PAS and alcian blue stains were negative. Polarised light revealed no intravascular birefringent particles. The cells were arranged in a collagen matrix, which was of thinly fibrillar aspect; a few smooth muscle fibres were also seen.
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**Fig. 1** Chest radiograph showing diffuse micronodular infiltrate.

**Fig. 2** Lung biopsy showing diffuse infiltration with histiocytes. (Haematoxylin and eosin ×36)
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**Electron Microscopy**

The specimen was fixed with 3.4% glutaraldehyde in a cacodylate buffer; post-fixation was with 2% osmium-tetroxide. The specimen was then dehydrated in acetone and embedded in Araldite. The sections were cut by a Reichert ultramicrotome, then stained with uranyl acetate and lead citrate. Examination and photographs were obtained by Philips EM 300 electronic microscope.

The cytoplasmic membrane of the macrophages had thin expansions; the nuclei were small, and chromatin was either irregularly disposed in clumps in the cytoplasm or placed against the nuclear membrane. The cytoplasm was, for the major part, infiltrated by a non-homogenous material surrounded by an electron dense membrane, whose outlines were irregular. This material was either granular or of a fluffy appearance; the granules were 0.3 to 0.4 microns in size (Figs 4 and 5). Between the phagosomes, thin cytoplasmic layers covered the organelles; the mitochondria were small in size and had well conserved cristi. The Golgi system was normal.

**Phagocytosis of PVC powder by alveolar macrophages**

Human alveolar macrophages were obtained by bronchial lavage. About 2 to 3\times10^6 macrophages were incubated with 0.2 ml of PVC powder for 90 minutes at 37-5°C in a mixture of 20% of compound 199 and 80% of fetal calf serum. The macrophages were then treated and examined with the electron microscope according to the method previously described. The absorption of the PVC particles in the cytoplasm of these cells was rapidly accomplished. The particles appeared in the phagosomes as either oval corpuscles or clusters which were variable in size (Figs 7 and 8). At this stage, the particles showed no evidence of degradation. Thinly granular lysosomal material was deposited against them. The cytoplasm of the macrophages contained mitochondria, bundles of microfilaments, and multiple lysosomes.

**Discussion**

In this case of discrete pulmonary fibrosis associ-
Fig. 4  Histiocyte with a small eccentric nucleus (N); the cytoplasm is mostly occupied by irregularly outlined phagosomes containing a fluffy granular substance. Collagen fibres (C). (EM ×13 900)

Fig. 5  Biopsy specimen; fluffy material with irregular outlines surrounded by a dense membrane (—). Phagosomes are confluent in places (—). (EM ×37 000)
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Fig. 6 PVC powder made of oval subunits of variable size; they are linked together by smaller particles (→). (EM ×46 000)

Fig. 7 In-vitro study of PVC particle phagocytosis by an alveolar macrophage showing oval bodies of uneven size with irregular outline, sometimes surrounded by finely granular lysosomal material (→); microfilaments (mF). (EM ×37 000)

ated with a granulomatous reaction the lesions contained particles which could not be identified by the usual stains. We suggest that this may be pneumoconiosis induced by PVC inhalation.

The chest radiographic abnormalities in our patients are the same as those described by Lilis et al. (1975); these authors showed that 48-6% of workers exposed in their work to PVC dust for at least 20 years have reticular and/or micronodular chest radiographic shadows. The histological lesions we describe are identical with those recorded by Szende et al. (1970), who reported the case of a 31-year-old man who had worked for 12 months in an environment containing high levels of PVC. This patient had severe respiratory failure. Pulmonary biopsy showed diffuse fibrosis associated with focal granulomatous lesions whose cells contained ovoid or polygonal particles. These lesions are the same as those experimentally provoked by Frongia et al. (1974), who exposed guinea-pigs and rats from two to seven months in a room where PVC powder was bagged. Examination of the guinea-pigs showed an earlier reaction at alveolar level composed of macrophages and giant multinucleated cells. These cells contained minute intracytoplasmic granules, which were not stained by the usual methods. On later examination, these lesions became focal granulo-
mas. Examination of rats showed more pronounced initial fibrotic lesions but later lesions were comparable with those observed in the guinea-pigs.

The identical morphology of the intracellular foreign particles observed in our patient, and the microscopic appearances of the PVC powder and of the inclusions in human macrophages which have engulfed PVC powder in vitro, are convincing evidence that our case can be considered to be that of PVC pneumoconiosis.

Clinically, the evolution of PVC pneumoconiosis is uncertain. Our patient had only a slight reduction in vital capacity with no reduction in gas transfer factor, suggesting that the fibrosis was not as yet of much functional significance; on the other hand, Szende and co-workers (1970) reported a case with severe respiratory impairment. Occupational exposure to PVC dust may have been different in these two cases. Our patient was exposed to PVC dust only, while Lilis et al. (1975, 1976) showed that PVC dust inhalation induced less severe respiratory function abnormalities than simultaneous inhalation of vinyl chloride monomer and PVC. This must be compared with the results described by Prodan et al. (1975), who showed that, in the guinea-pig, two hours' inhalation each day of air containing 10% vinyl chloride monomer over two weeks could produce diffuse pulmonary fibrosis. Further studies of the mechanisms of this pneumoconiosis are in progress.

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References


Fig. 8 In-vitro study of an alveolar macrophage in contact with PVC for 90 minutes. Particles of PVC are accumulated in a phagosome, which occupies almost all of the cytoplasm (>). Smaller phagosomes engulf oval corpuscles and small granules of PVC. (EM X6800)
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