Pulmonary granulomatous reaction: talc pneumoconiosis or chronic sarcoidosis?

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ABSTRACT A chronic pulmonary granulomatous reaction was associated with an almost identical clinical picture in two patients exposed to talc. In both patients lung biopsy showed the deposition of talc particles and a heavy granulomatous reaction. At the time of diagnosis the Kveim test result was negative in both patients, urinary calcium excretion was normal, and there were no extrapulmonary manifestations and no response to steroid treatment. These findings point against sarcoidosis. The serum angiotensin-converting enzyme level, however, was raised in both patients. It was concluded that the patient who was exposed to talc in the rubber industry had a true talc pneumoconiosis. The other patient, who was exposed to cosmetic talcum powder, suffered from chronic sarcoidosis with talc deposition in the lungs, since an enlarged axillary lymph node containing granulomatous inflammation was discovered after two years’ follow up. These cases show that it may be extremely difficult to differentiate between chronic sarcoidosis and talc pneumoconiosis even after careful clinical and histological analysis.

True talc is a hydrous magnesium silicate. Depending on where it is mined, commercially available talc also contains varying amounts of asbestos minerals which form chains or fibres and may therefore have an asbestos like effect on the lungs. Owing to the widespread industrial and private use of talc and talcum powder much interest has been directed to the biological effects of this mineral, which have been reported to cause pneumoconiosis in people employed in talc mills and talc mines, and in workers using talc in production processes—for example, in the rubber industry.1

Although widely used as a dusting powder, talc is not generally considered a health hazard when exposure is limited to cosmetic application at home. A search has found four reports of chronic granulomatous pulmonary disease referable to excessive use of cosmetic talc in adults.2–5 In all these cases the question arises whether it was a true talc pneumoconiosis or talc deposition and coincidental sarcoidosis.

We report a case of chronic pulmonary granulomatous reaction in a patient who had used cosmetic talcum powder for several years. As a comparison we describe a patient who was exposed to talc in the rubber industry and who showed a chronic granulomatous lung reaction which we believe represents true talc pneumoconiosis.

Case 1

A 58 year old woman had a history of myomectomy in 1952, cholecystectomy in 1968, and hysterectomy in 1977. She had been a smoker for 20 years. In April 1977 she was operated on because of a traumatic leg fracture. As a complication she had thrombosis in the left femoral vein and pulmonary embolism. The symptoms and signs of embolism disappeared during treatment with anticoagulants. Chest radiography was normal at that time. The patient was in good condition until summer 1980 when she began to suffer from dry cough, dyspnoea, tachycardia, and low grade fever. In November 1980 crepitant rales were heard at the bases of the lungs. Chest radiography showed fine diffuse opacities. Spirometry showed normal lung volumes. Diffusing capacity was lowered (DLCO 64% of predicted). The sedimentation rate was 38 mm/h. The following variables were within normal limits: haemoglobin, white cell count, differential and thrombocyte counts, creatinine, transaminases,
alkaline phosphatase, serum calcium, urinary calcium excretion, and urine analysis. Serum lysozyme was slightly raised (27 mg/l (normal 20 mg/l)) and serum angiotensin converting enzyme (ACE) was normal (38 U/l). Mantoux 10 TU was negative.

The concentration of serum immunoglobulins, C3 and C4, and the titres of cryoprecipitins, direct Coombs-test, Latex-fixation test, Waaler-Rose, and antinuclear antibodies were normal. The Kveim test result was negative.

Three months later, in February 1981, laboratory results were the same as before, except that the serum ACE was raised (70 U/l). For diagnostic purposes an anterolateral thoracotomy was performed. The lung showed a diffuse nodular consistency. A biopsy specimen was taken from the lingula. Cultures for tuberculosis, bacteria, and fungi were negative. Histological examination showed a heavy intra-alveolar and interstitial granulomatous inflammation (fig 1) consisting of epitheloid and giant cells forming granules, macrophages, lymphocytes, plasma cells, some eosinophils, and fibrosis. Numerous birefringent particles were discovered inside the giant cells (fig 1). For elemental electron probe microanalysis 5 μm thick tissue sections of the lung were deparaffinised in xylene, mounted on carbon coated nylon grids by conductive carbon cement, and examined by scanning electron microscopy (SEM) in a graphite holder (JEM-100 CX electron microscope fitted with a Princeton Gamma-Tech PGT System III energy dispersive x ray microanalyser). The foreign body material inside the granulomas contained magnesium and silicon in combination with chlorine, calcium, iron, and zinc (fig 2), characteristic of talc.

Because the examinations pointed to the possibility of talcosis a careful inquiry was undertaken into the dust exposure of the patient. She had applied non-powdering talc on her face for 20 years and after that, talcum powder two to three times a day during a 10 year period, usually in an unventilated room. The total amount of powder used was two boxes a year. In the patient’s own opinion the amount of powder used was not excessive enough to cause any disease. Elemental analysis of two different commercially available talcum powder preparations was also carried out. Electron probe microanalysis of these preparations showed magnesium, aluminium, silicon, potassium, iron, and zinc (fig 3).

In March 1981, treatment with prednisolone was started with an initial dose of 40 mg. The dose was gradually lowered to 10 mg a day over a period of four months. When the treatment was discontinued after nine months no improvement of pulmonary function or radiographs was observed. The serum angiotensin values fell to normal during the steroid treatment (26 U/l) but rose again after treatment ceased (77 U/l).

After two years’ follow up an enlarged axillary lymph node was noticed. A biopsy specimen showed granulomatous inflammation.

Case 2

A 55 year old woman had smoked 10 cigarettes a day for 30 years. From 1958 to 1968 she had packed rubber balls and was exposed to the talc used as a dusting agent to prevent adhesion of the balls. During the first five years after exposure she began to suffer insidiously from dyspnoea. In April 1973 a chest radiograph showed diffuse nodular opacities; lung auscultation was normal. All the following variables were within normal limits: sedimentation rate, haemoglobin, white cell count, differential and thrombocyte counts, creatinine, transaminases, alkaline phosphatase, serum calcium, daily urinary calcium excretion, urine analysis, titres of latex

Fig 1 Open lung biopsy specimen of case 1 showing heavy granulomatous inflammation (a) with strongly birefringent crystal inside a giant cell (b) van Gieson, × 230 (a), × 1200 (b).
fixation test, Waaler-Rose, cryoprecipitins, and antinuclear antibodies. Mantoux 10 tuberculin unit (TU) was positive. Spirometry showed normal lung volumes (FVC 107% of predicted), but diffusing capacity was lowered (DLco 60% of predicted). The Kveim test result was negative.

A lung biopsy was performed with a transthoracic TruCut needle in the right lower lobe. The biopsy specimen showed numerous small interstitial granulomas (fig 4a). Within these granulomas numerous particles were found, most of them double-refractile and resembling talc particles (fig 4b). Some ferruginous bodies were also seen. The alveolar spaces were patent.

In July 1973 treatment with prednisolone was started with an initial dose of 40 mg. The dose was gradually lowered and the treatment was terminated after two months because no objective improvement was observed in the chest radiograph or in pulmonary function.

In April 1980 spirometry showed normal lung volumes (FVC 84% of predicted) and diffusing capacity was lowered (DLco 51% of predicted). At that time serum ACE was slightly raised at 49 μmol/l (normal 40 μmol/l).

**Discussion**

Talc used in the manufacture of cosmetic talcum powder is normally of high purity. Nevertheless, x-ray diffraction analysis of 21 powders obtained through retail channels in the United States showed that few of them consisted of pure talc. Quartz, ranging from 2% to 5% was found in eight, while one sample contained 35%. Detectable amounts of fibrous tremolite and anthophyllite were reported to be present in 10, and chrysotile in two. Epidemiological studies indicate that prolonged exposure to cosmetic grade talc is not associated with the development of pneumoconiosis, though exposure to industrial grade talc may result in this condition.

Exposure to talc causes three distinct types of
et raised histological during the lung biopsy specimens was examined.

In both the cases, the granulomas showed the granulomatous reaction in the lung tissue and foreign body giant cells were found in the cytoplasm of giant cells. Except, the talc particles were not found in the lung tissue.

References

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These findings do not establish any causal relationship between the use of talc and the disease. Further studies are needed to clarify this issue.

In our patients, the lung biopsy specimens showed extracellular talc deposits. This suggests that the talc is not as harmful as previously believed. However, the exposure to dust from talc-containing products may still be a concern.

Our report shows that even after careful clinical and laboratory examinations, it may be difficult to differentiate between chronic sarcoidosis and interstitial fibrosis.