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Case Report

Liquid Paraffin Pneumonia – With Chemical Analysis and Electronmicroscopy

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Summary. Liquid paraffin pneumonia was diagnosed after open lung biopsy in a woman age 73 with a hiatus hernia and rheumatoid arthritis who had been taking liquid paraffin nightly for fifty two years. Histological examination showed a lipid type pneumonia with involvement of alveoli, interstitial tissues and brochioles.

Chemical analysis of the lung showed total lipids of 17.7% (w/w), 86% was liquid paraffin which was positively identified by infrared spectroscopy. Transmission electronmicroscopy showed macrophages in the alveoli filled by phagosomes. The alveoli were mainly lined by alveolar type II cells. Scanning electronmicroscopy showed alveoli filled by a mass of vacuoled material.

Key words: Lung biopsy – Pneumonia – Liquid paraffin – Infra-red spectroscopy – Electronmicroscopy.

Introduction

Liquid paraffin has been a well recognised cause of localised and diffuse lesions in the lung (Laughlen, 1925; Ikeda, 1937; Volk et al., 1951; Wagner et al., 1955) but in recent years it has become a rarity so that the diagnosis may easily be missed, as occured in this case.

There have been few reports of chemical analysis in these cases and most of these have not proved entirely satisfactory (Wagner et al., 1955); however Elston (1966) unequivocally identified liquid paraffin by infra-red spectroscopy which was also used in the present case. Electronmicroscopic findings in liquid paraffin pneumonia have not previously been reported.

Case Report

A 76-year-old woman who lived and worked on a farm was admitted to hospital in October 1975 for investigation of recurrent iron deficiency anaemia. Two years previously she had been

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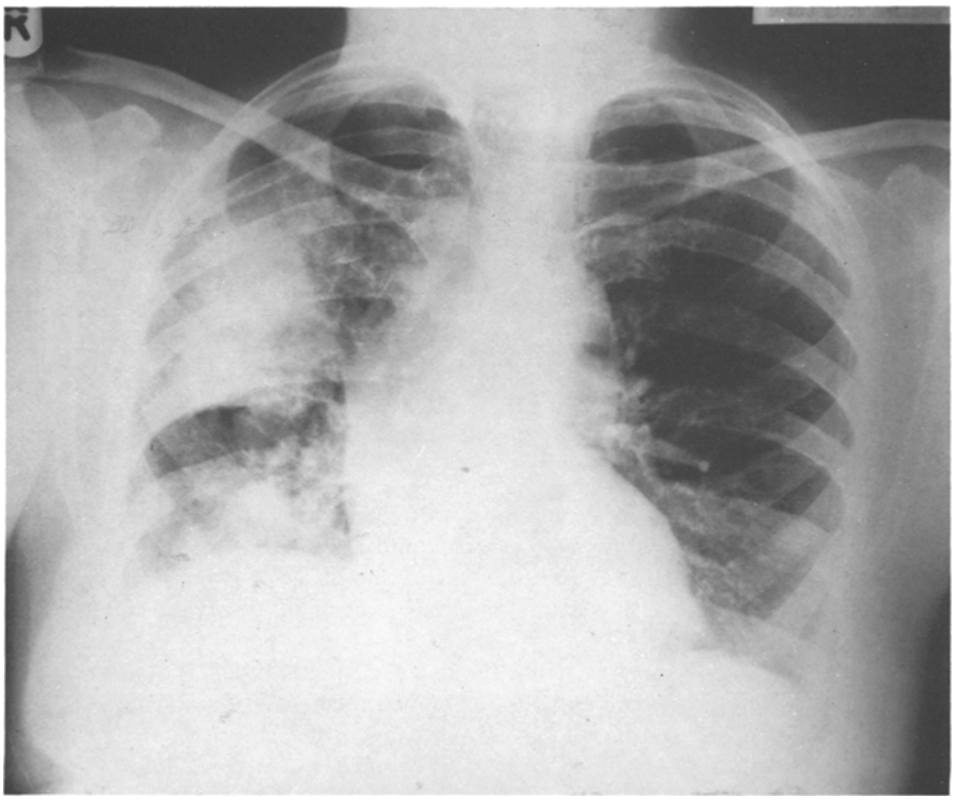

Fig. 1. Chest radiograph showing opacities in the right upper and lower lobes

investigated at another hospital where she was found to have a hiatus hernia and deformity of the duodenal bulb, rheumatoid arthritis and a chest x-ray that showed "patchy consolidation in the right mid and lower zones". She was treated with blood transfusions and injections of iron and the anaemia improved. On this admission the haemoglobin was 10 g/dl, she had a persistent raised temperature in the mornings 38–38.4° C which dropped to 36.5° C in the evenings. She lived mainly on milk and since 1923 had been taking at least one large tablespoonful of liquid paraffin before going to bed. In the mornings she often found "fatty" droplets on her pillow. Chest x-ray (Fig. 1) showed opacification in the anterior segment of the right upper and lower zones which persisted unchanged over a period of four weeks. An oesophagoscopy showed a hiatus hernia with three shallow healing ulcers at the lower end of the oesophagus. There was occult blood in the stools and the appropriate investigations for brucellosis, tuberculosis and systemic lupus erythematosus were negative. Tests for rheumatoid factor were strongly positive. A bronchial biopsy showed no significant abnormality. In view of the persistence of the lung changes and no clinical diagnosis being made, an open lung biopsy was performed by a short right anterior thoracotomy incision through the third intercostal space. There was nodularity in the upper lobe of the right lung particularly laterally. A wedge of lung $3 \times 2.5 \times 1.5$ cm was removed, and showed a diffuse nodular infiltrate by whitish grey tissue.–The patient made a rapid recovery from the operation, her temperature subsided and the chest x-ray improved without any treatment. The patient was advised to stop taking liquid paraffin

One small piece was removed immediately and placed in Karnovsky fixative for transmission (TEM) and scanning (SEM) electronmicroscopy. For TEM the tissue was fixed for four hours at 4° C, washed overnight in cacodylate-sucrose buffer at 4° C, and then post fixed in 1% aqueous

osmium tetroxide for 1 h at 4° C. After rinsing in distilled water it was dehydrated to absolute ethanol, then placed in epoxypropane and fresh warm "araldite"; and was finally embedded in fresh "araldite". For SEM the specimen was dehydrated to pure acetone which was replaced by liquid carbon dioxide and then critically point dried. The specimen was sputter coated with gold. Another piece was kept frozen and subsequently used for chemical analysis. Specimens were cultured for bacteria, fungi and viruses and nothing was grown. The remainder of the specimen was fixed in 4% neutral formaldehyde.

Histological Findings

The changes are those of liquid paraffin pneumonia. There are large amounts of foamy, vacuolated material free and within macrophages in the alveoli, interstitial tissues and bronchioles (Fig. 2). With frozen sections only of fresh and fixed unprocessed tissue the foamy material stains a light orange with Sudan IV and light blue with Sudan black. There is no reaction with periodic acid Schiff(PAS), phosphorine 3R or nile blue sulphate and the material is not birefringent. There is plasma cell, lymphocyte and histiocyte infiltration of interstitial tissues and the subpleural region, and large collections of lymphoid tissue with germinal centres mainly associated with bronchioles (Fig. 2). In places the alveoli are lined by cuboidal cells and there is some increase in reticulin fibres in the alveolar walls and slight fibrosis. There is a fibrinous exudate on the pleural surface. The blood vessels are normal.

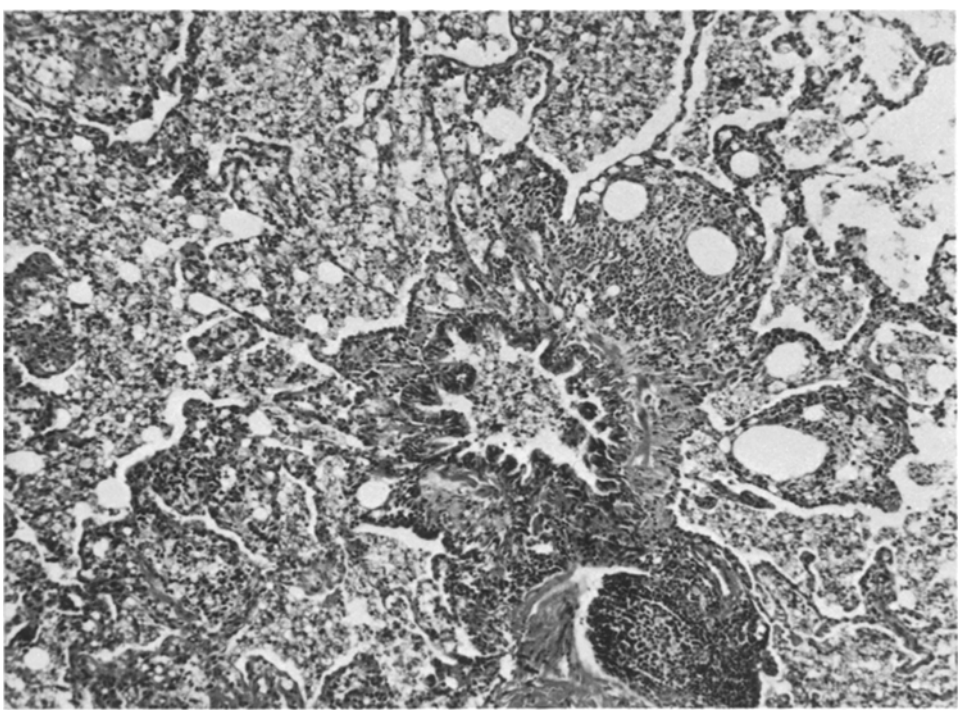

Fig. 2. Foamy material in alveoli, interstitital tissue and bronchiole with peribronchial lymphoid tissue. H. and E × 60

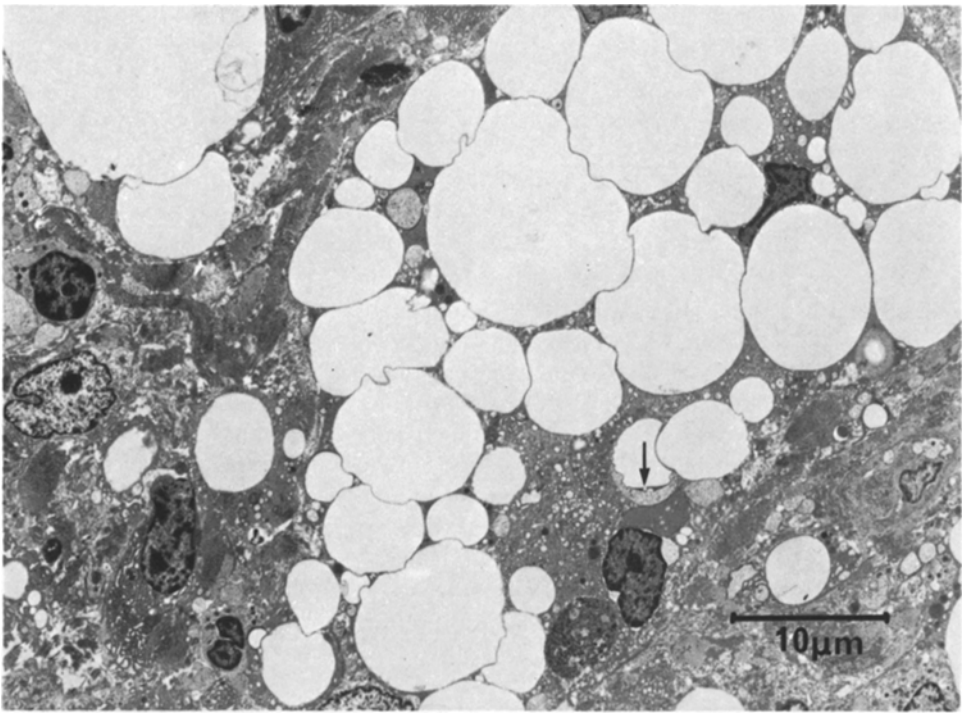

Fig. 3. Macrophages with membrane bound clear vesicles and electron dense material (*arrow*) in interstitial tissue. TEM × 3,300

Electron-Microscopic Findings

T.E.M. show many clear vacuoles varying in size from 0.5 µm to 6 µm free and within macrophages in the alveoli, and the interstitial tissue (Fig. 3). The vacuoles within the macrophages appeared to be within phagosomes which are bound in places by a single membrane (Fig. 3) but in other areas no membrane is seen. In some vacuoles there is a thin rim of smooth endoplasmic reticulum which is attached to the single membrane giving the appearance of a double membrane. There are occasional crescents of electron dense material presumably undissolved liquid paraffin in some of the vacuoles (Fig. 3). The macrophages show only occasional mitochondria and no lysosomes are seen. Plasma cells, lymphocytes and mast cells within interstitial tissue appear normal. The alveoli are mainly lined by type II cells and there is only small amounts of collagen within the alveolar wall. In places the alveolar capillary wall is normal. SEM show that the alveolar spaces are filled by sheets of foamy material, which are attached to the alveolar walls (Fig. 4).

Chemical Analysis

The tissue was extracted twice by shaking with diethyl ether (10 ml) for 15 min. The extracts were combined, filtered and washed once with distilled water.

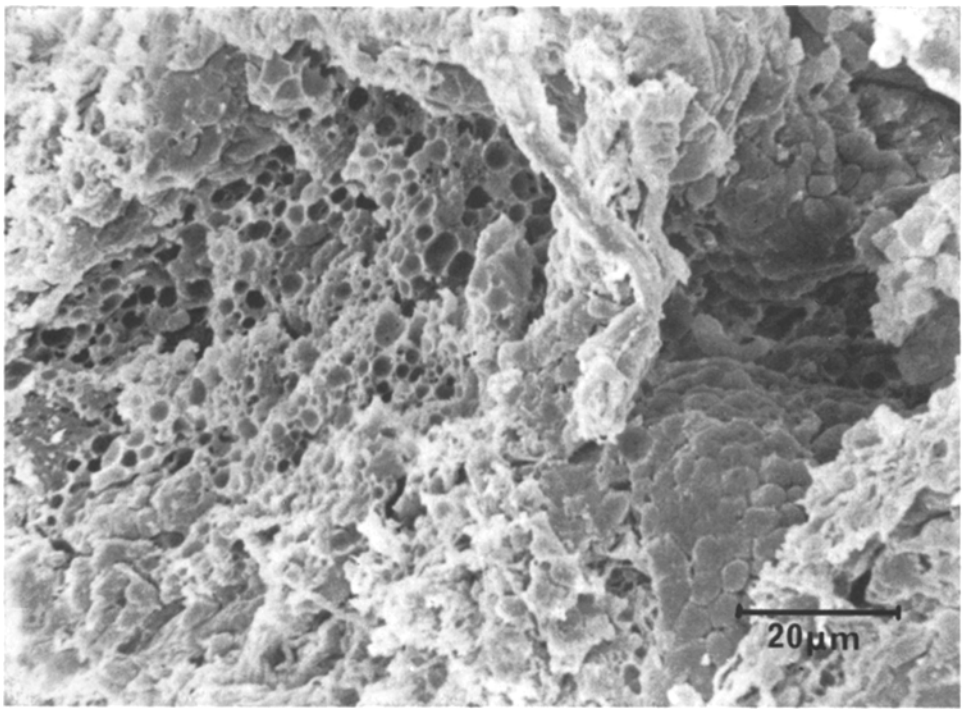

Fig. 4. Foamy material in alveoli on left; alveolar duct on right. SEM × 1,250

Table 1. A comparison of the infra-red spectra of an ethereal extract of lung tissue and liquid paraffin

Extract		Liquid paraffin	
Peak λ	Relative peak height (a)	Peak λ	Relative peak height (a)
6.88	1.8	6.84	1.7
7.28	1.0	7.27	1.0
3.415	1.6	3.415	1.3
3.505	1.0	3.505	1.0

For the first two peaks, the values are relative to the height of 7.28 µ peak, and for the second two peaks relative to the 3.505 µ peak

The ethereal extract was evaporated to dryness using a filtered stream of nitrogen, then dissolved and dried in ethanol and finally dried in vacuo over phosphorus pentoxide. Initially the extract was a viscous yellow brown liquid which hardened on standing into a grease. The iodine test for liquid paraffin was negative on the grease. Liquid paraffin usually extracts iodine from an aqueous solution to produce a violet colour in the paraffin phase.

Infra-red spectroscopy showed that the bulk of the material present in the grease must be paraffin-like hydrocarbons as the only significant peaks in the spectrum were those which arise from a hydrocarbon chain. Furthermore the

relative heights of the peaks at 6.88 and 7.28 (Table 1) suggest that the chain length of the hydrocarbon in the lung extract is of the same order as in liquid paraffin. As there was a possibility that the patient was also inhaling milk, the specimen was examined by Dr. G.C. Cheeseman, National Institute for Research in Dairying, University of Reading. The wet weight of tissue was 0.4074 g. which was emulsified into 5 ml of 0.88% potassium chloride 0.5 ml was used for immunochemistry, the rest for lipid analysis. The immunochemistry showed no reaction against the major proteins of milk. The sample of lung was extracted by the Folch procedure and lipids examined by thin layer chromatography. The total lipids were equivalent to 17.7% (w/w) and was composed of triglycerides 5%, phospholipid 5.7%, cholesterol 0.8%, cholesterol esters 0.3%, free fatty acids 2% paraffin 86.2%. The low triglyceride content and the negative immunochemical reactions suggested that the lung did not contain bovine milk.

Discussion

The diagnosis of liquid paraffin pneumonia was made only after open lung biopsy. In retrospect the diagnosis seems straight forward; however clinical awareness of this condition is not high and the history of ingestion of liquid paraffin and the fact of changes in the chest x-ray two years previously were only obtained after the lung biopsy. The clinical diagnosis of liquid paraffin pneumonia or granulomata has always been difficult even when these conditions were more common (Wagner et al., 1955). Most cases have been diagnosed at necropsy (Buechner and Strug, 1956), following operations for suspected bronchial carcinoma (Wagner et al., 1955 Siddons, 1958) or after lung biopsy (Ayvazian et al., 1967; Burhenne et al., 1974). However Volk et al. (1951) in chronically ill patients suspected of having liquid paraffin pneumonia made the diagnosis by examination for oil in the sputum and in the lung after aspiration biopsy.

Aspiration of liquid paraffin is the cause of the pneumonia and although it is most frequently seen in debilitated infants and the elderly (Ikeda, 1937; Volk et al., 1951) aspiration in this case was almost certainly due to the hiatus hernia (Graef, 1935, Belcher, 1949). The more common lesion in adults is a foreign body granuloma with fibrosis (Ikeda, 1937) and Wagner et al. (1955) thought there was a progression from pneumonia to a foreign body granuloma with fibrosis. However it is apparent that other factors may be involved because in the present case the lung lesions had been present for at least two years and there were no granulomata and only minimal fibrosis.

Histologically liquid paraffin pneumonia has to be differentiated from endogenous lipid pneumonia seen with obstructive lesions of bronchi, particularly carcinoma (De Navasquez and Haslewood, 1954) bronchiectasis and bronchiolitis obliterans (Gosink et al., 1973). The inertness of liquid paraffin in histochemical reactions is in sharp contrast to the reactions found in endogenous lipid pneumonia. With liquid paraffin the only positive reaction is a salmon pink colour with Sudan IV and in this case a light blue colour with Sudan black whereas in obstructive pneumonia cholesterol is present, which is birefringent,

and gives a positive PAS reaction, and lipids which stain deep red with Sudan IV and black with Sudan black. The lymphoid collections around bronchioles were almost certainly related to rheumatoid arthritis and were not a reaction to liquid paraffin. This is only the second occasion in which liquid paraffin in the lung has been unequivocally identified. Prior to Elston (1966) most cases were diagnosed on histological grounds and only occasionally was chemical extraction attempted. Wagner et al., (1955) tried chemical identification but found the techniques difficult and the results uncertain. The use of chromatography and infra-red spectroscopy is a way of positively identifying liquid paraffin. The iodine test is usually a good spot test for liquid paraffin, but the negative result in this case was possibly due to small amounts of other lipid materials which altered the physico-chemical nature of the extract (Reaveley and Vaughan, 1976). There have been no previous reports of electronmicroscopic findings in liquid paraffin pneumonia. The liquid paraffin is nearly completely extracted during processing so one mainly sees large vacuoles most of which are single membrane bound phagosomes. The absence of lysosomes in these macrophages is probably because the material is indigestible, but it is possible that liquid paraffin may also inactivate lysosomal enzymes. The lack of lysosomes may be associated with decrease in microbicidal activity (Golde et al., 1976) which would be the explanation for opportunistic infections described in liquid paraffin and other forms of lipid pneumonia (Gibson, 1953; Cotton and Lloyd, 1960). The alveolar lining cells have frequently been described as cuboidal in type (Graef, 1935; Wagner et al., 1955) and TEM shows them to be type II alveolar cells, the cell which regenerate after alveolar wall damage (Brooks et al., 1978). This case illustrates the difficulties encountered in making the diagnosis of liquid paraffin pneumonia, at one time a fairly common condition but now a rarity. The electronmicroscopic findings suggest an explanation for the opportunistic infections which occasionally occur in this condition.

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