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Reaction of human lungs to aspirated animal fat (ghee): a clinicopathological study

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Abstract We report the clinical findings and pathological lung changes in four children following a cultural practice of forced feeding with animal fat (ghee) during infancy. The clinical presentation was of acute or chronic chest infection which failed to respond to antimicrobial therapy. The radiographic features ranged from extensive bronchopneumonia to collapse/consolidation and bronchiectasis. The light microscopy findings included diffuse mononuclear interstitial pneumonia, intraalveolar desquamation of pneumocytes, lipid granuloma formation, lung atelectasis and bronchiectasis. In the two children with longstanding reactions, the striking feature was the minimal lipid engulfment by the macrophages, the continuation of the mononuclear interstitial pneumonia, bronchiectasis and minimal lung fibrosis. In these two older children, the lung lymphatics were probably the main channels for drainage of the aspirated ghee.

Key words Lipoid pneumonia · Ghee · Pathological changes · Saudi Arabia

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Introduction

The first clinicopathological description of lipoid pneumonia due to aspiration of mineral oils was made by Laughlen in 1925 [11]. It was subsequently observed that mineral oil is a pure hydrocarbon incapable of undergoing hydrolysis but apparently sufficiently irritating to evoke a tremendous cellular reaction causing damage to the lung. Simple vegetable oils, in contrast, were relatively less harmful because they are practically free from fatty acids [13, 14]. Numerous cases of lipoid pneumonia have since been reported mainly due to mineral oil [4, 6, 8, 18, 19], milk [12] and cod liver oil [10]. In lipoid pneumonia due to animal fat, the quantity, the amount of free fatty acids it contains and the presence or absence of bacterial infection have influenced the severity of the tissue reaction [17]. With the decline in the usage of mineral and cod liver oils, there has been a corresponding decrease in the incidence of lipoid pneumonia. Unfortunately, lipoid pneumonia is still encountered in some parts of the world where traditional or cultural practices involve the use of oil based substances, with its inherent risk of aspiration [2]. Forced feeding or nasal administration of rendered animal fat, "ghee", to infants and children is a tradition in South-West Saudi Arabia. It is often practised by elderly relatives, and believed to add to the well being of the newborn. This practice is the commonest cause of lipoid pneumonia in our population [1, 7, 15]. This paper is based on the clinico-pathological study of acute and chronic changes of ghee induced lipoid pneumonia in four Saudi children.

Materials and methods

Three lobectomies and one open lung biopsy specimen from children with lipoid pneumoniae were collected. Up to date clinical records, follow up data and paraffin blocks from the surgical specimens were available in the four patients.

Two of the lobectomy specimens and the open lung biopsy were received in 10% buffered formalin. Sections 4.5 μm thick were cut from paraffin embedded tissue blocks and were stained

with haematoxylin and eosin for light microscopy. The third lobectomy specimen was received fresh ("unfixed") and frozen sections were stained with oil red O for lipid identification. The remaining tissue was fixed in 10% buffered formalin and routine haematoxylin and eosin stained sections were produced.

Results

Clinical Data

The age and sex of the four children, the nature and duration of their symptoms, the radiological features and follow up data are listed in Table 1. All four children failed to respond to medical treatment and were subjected to surgery.

Gross and light microscopy examinations

In case 1 the specimen consisted of a pale tan portion or lung tissue (from right upper lobe) measuring 0.5×0.5×0.2 cm. Light microscopy showed that the parenchymal architecture was obliterated by multiple scattered ganulomata showing occasional central microabscess formation and some granulomas with entrapped lipid vacuoles (lipogranuloma; Fig. 1). In between the granulomatous reaction there was dense, interstitial, non-specific mononuclear inflammation with occasional acute microabsess formation. Silver and Ziehl Neelsen stains were negative for microorganisms.

In case 2 the left lower lobe weighed 54.4 g and measured 6.5×6.4×4 cm. Serial sections revealed consolidated, airless dark brown parenchyma with multiple irregular greyish-white firm areas. The light microscopy features of this case were of patchy acute suppurative bronchopneumonia. Most of the smaller bronchi and bronchioles were filled with neutrophils infiltrating into the surrounding lung parenchyma with patchy signs of early organization. The lung parenchyma away from the bronchopneumonic areas was densely infiltrated by an interstitial mononuclear inflammatory reaction, leaving behind alveoli as duct-like spaces lined by plump cuboidal epithelial cells. Some of the latter cells had large hyperchromatic irregular nuclei with intranuclear eosinophilic, inclusion-like structures. There was intraalveolar desquamation of pneumocytes.

In case 3 the right middle lobe weighed 24.4 g and measured 5.5×5×2.5 cm. Serial sections of the lung parenchyma showed multiple dilated bronchial spaces some of which contained semi-solid yellowish pus-like material in the lumen. The rest of the lung parenchyma was fleshy, airless and dark brown. The histological picture was dominated by a massive diffuse peribronchiolar and interstitial mononuclear inflammatory cell infiltrate. In many areas, the intense non-specific chronic inflammation replaced the normal lung parenchyma and entrapped residual, small, rounded alveoli lined by short cuboidal epithelium. Bronchiectasis was also evident with plugging of the dilated bronchi by amorphous inspissated pinked material containing scattered inflamma-

Table 1 Clinical data and follow up of four cases of ghee induced lipoid pneumonia (*RUL* right upper lobe, *RML* right middle lobe, *LLL* left lower lobe)

Case number	Age	Sex	Age at initial ghee administration	Age at onset of symptoms	Age at diagnosis	Presenting complaint	Radiological features	Course
1	6 months	Male	Birth	2 months	6 months	Fever, cough and failure to thrive for 4 months	Extensive bilateral confluent consolidation of entire RUL and posterior aspects of both lower lobes	Alive and well
2	2.5 months	Female	Birth	1 months	2.5 months	Cough, fever and difficulty in breathing for 1 month	Bilateral consolidations involving anterior segment of RUL, RML, lingula and left lower lobe sparing lateral basal segment	Died on the 11th post--operative day
3	5 years	Female	Infancy	Infancy	5 years	Recurrent cough since infancy, worse 6 months prior to admission productive of sputum	Bilateral perihilar lung infiltration, RML and LLL collapse/consolidation	Clinical and radiological improvement but died 2 years after lobectomy from severe chest infection
4	6 years	Male	Birth	Infancy	6 years	Recurrent cough since infancy, worse 2 years prior to adminission productive of sputum	Collapse/consolidation of LLL with bronchiectatic changes	Alive and well

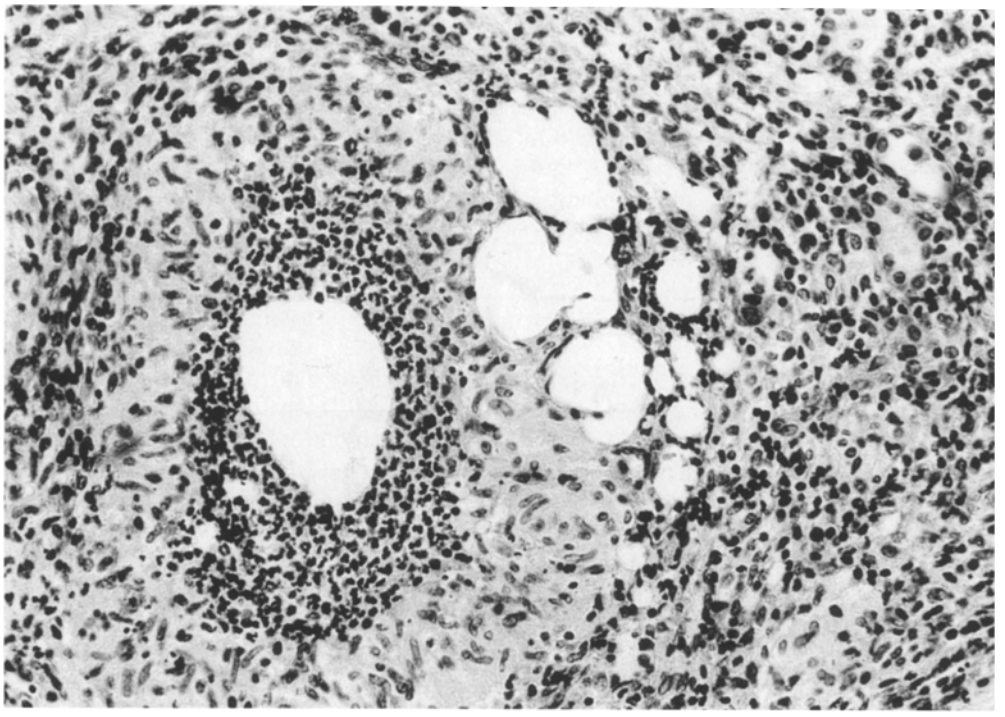

Fig. 1 Lipogranuloma with central acute microabscess formation and surrounded by intense interstitial lymphoplasmacytic inflammatory reaction. (Haematoxylin and eosin, ×230)

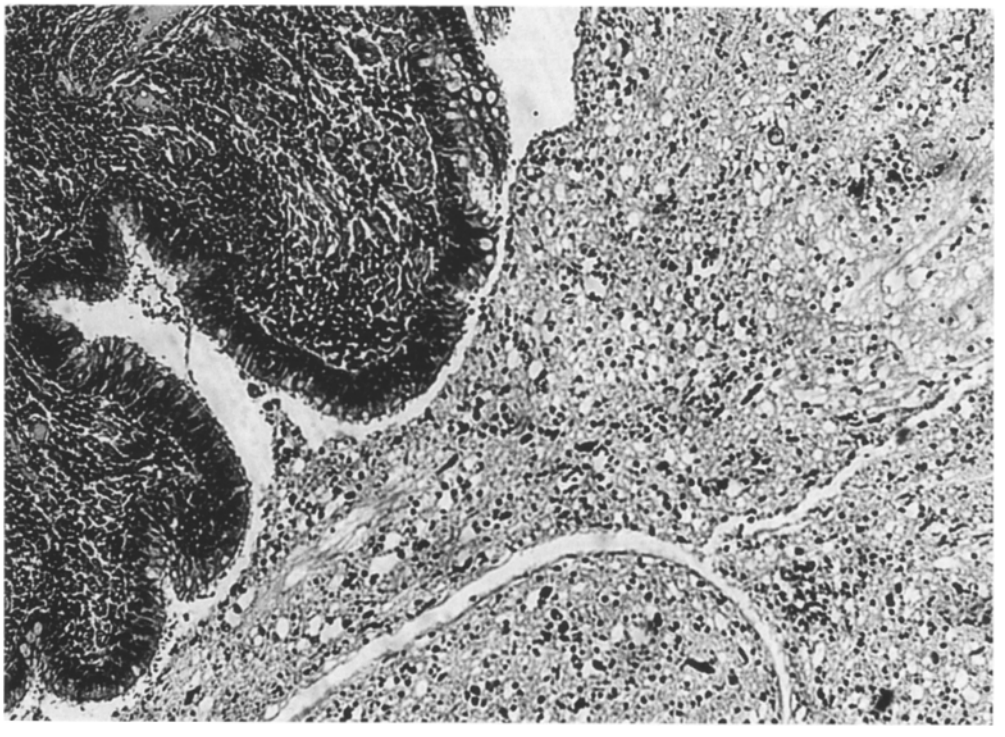

Fig. 2 Dilated bronchus "filled" with amorphous material containing lipid droplets (clear vacuoles). (Haematoxylin and eosin, ×230)

tory cells and empty smalll globules (Fig. 2). The latter was most probably lipid. However, no fresh tissue was available to do the oil red O stain. A bronchial secretion smear shows multiple lipid droplets, on staining with oil red O.

In case 4 a fresh left lower lobe weighing 50 g and measuring 6×4×3 cm was received for histopathology. The outer surface was markedly congested and serial sectioning showed fleshy, airless dark brown parenchyma with scattered dilated bronchial spaces. Some of the bronchial spaces were occluded by sticky, mucoid greyish material. The light microscopy picture in this case is similar to that of patient 3. Bronchiectasis predominated with intrabronchial accumulation of inspissated secre-

tions, chronic bronchiolitis, mononuclear interstitial pneumonia, peripheral lung collapse (atelectasis) and prominent intraalveolar haemorrhage. Only very small microscopic foci near the terminal bronchioles showed organizing and desquamative pneumonia. Oil red O stain for fat in frozen section of fresh lung tissue showed large globules of lipid mainly in lymphatic channels around medium sized bronchi and blood vessels.

Discussion

The reaction of lung tissue to aspirated lipids depends largely on the nature of the flat [13, 14]. Vegetable oils generally produce little or no pulmonary reaction. Mineral oils are free from fatty acids but hydrocarbon is more irritant to lung tissue [13]; this reaction produces diffuse pulmonary parenchymal reaction [8, 14, 16] or may produce localized masses known as "paraffinomas" [3, 8]. Most paraffinomas are the result of the prolonged presence of mineral oil (in the form of liquid paraffin) in the lung parenchyma of patients using nasal drops or laxatives. Animal fats are most irritant to lung tissue, producing tissue necrosis and severe inflammatory reaction, because they are rapidly hydrolyzed to give free fatty acids [13]. The aspirated lipid, ghee in our 4 cases, is a product of goats milk with highly concentrated milk fat. Ghee induced lipoid pneumonia has now become a recognised complication related to the local custom of forced feeding ghee to infants and children in Saudi Arabia [1, 9, 15].

Inhalation of animal fats by infants is known to produce diffuse rather than localized lung injury with variable pulmonary lesions varying from mild acute bronchitis to diffuse interstitial mononuclear pneumonitis [5]. Our histological observations in the two infants (patients 1 and 2) were similar to previously described features of the acute stage of milk inhalation lipoid pneumonia [6, 12]. These features include proliferative interstitial mononuclear inflammation, intraalveolar desquamation of pneumocytes, lipid granuloma formation and confluent bronchopneumonia with microabscess formation due to superadded infection. Previous studies have reported that the most striking histological feature in acute lipoid pneumonia is the presence of numerous macrophages in the alveolar spaces and alveolar walls laden with fat droplets [5]. The macrophages were few in our histological sections and in the bronchial washings. Rather, most of the fat globules in our cases were not intracellular but were free within lipid granulomata, in bronchial lumina, in bronchial smears and in lymphatic channels. The explanation of these findings is not clear but we speculate that the lung macrophages were overwhelmed by the very high concentration of animal fat present in ghee. This led to the suppression of the process of phagocytosis leaving pulmonary lymphatics as the main pathway to drain and get rid of the inhaled fat. Previous reports have described prominent pleural lymphatics associated with lipoid pneumonia that could be mistaken for lymphatic carcinomatosis [19].

Bronchiectasis is a common finding in chronic stage of lipoid pneumonia [5] and was seen in the two older patients although the hallmark of chronicity, namely lung fibrosis, was minimal. Earlier reports have described two forms of lung fibrosis in the chronic stage of lipoid pneumonia. One form was localized with central accumulation of lipid laden macrophages surrounded by dense fibrous tissue [5] and the other was diffuse thickening of the alveolar wall by fibrous tissue entrapping lipid laden macrophages morphologically similar to mural fibrosing alveolitis [20]. Minimal pulmonary fibrosis was seen in our two older children where ghee had been in the lung tissue for 4–5 years. Here, there was minimal engulfment of the lipid (ghee) by the macrophages and pulmonary fibrosis was minimal. The proliferative mononuclear interstitial pneumonitis continued to be seen 4–5 years after the ghee lipid inhalation. The longstanding history and the presence of bronchiectasis suggested that aspiration of ghee occurred during the early months of their lives.

Sante showed in 1948 [17] that mineral oils were effectively removed undigested by macrophages leading to a localised inflammatory reaction and fibrosis (paraffinoma) at the lung hila where most of the oil-laden macrophages accumulate. In milk aspiration pneumonia, fibrosis occurs predominantly within the alveolar wall where lipid laden macrophages accumulate. Therefore we speculate that activation of macrophages during lipid phagocytosis might be important in inducing lung fibrosis in chronic stages of lipoid pneumonia. This hypothesis might explain the minimal lung fibrosis in our two older patients where lipid phagocytosis by lung macrophages was minimal.

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