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Lipoid Pneumonia: A Review

Hanaa Banjar, MD, FRCPC*

Exogenous lipoid pneumonia is an uncommon condition resulting from aspiration or inhalation of fat-like material, such as mineral oil found in laxatives and various aerosolized industrial materials. A historical review of the literature, which includes: sources of lipoid pneumonia, patho-physiology, clinical features, diagnosis, complications and treatment are presented.

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Exogenous lipoid pneumonia is an uncommon condition resulting from aspiration or inhalation of fat-like material, such as mineral oil found in laxatives and various aerosolized industrial materials. These substances elicit a foreign body reaction and proliferative fibrosis in the lung. Because symptoms are absent or nonspecific and the roentrogeno- graphic findings simulate other disease, exogenous lipoid pneumonia is often unrecognized. Yet appropriate historical inquiries and simple laboratory tests can lead to the correct diagnosis. Removal of the offending agent, may lead to improvement in lung function before serious complications develop[1].

In 1925 Laughlen[1] first described what is now called *exogenous lipoid pneumonia* when he reported oil droplets in the lung during the autopsies of three children and one adult who had received mineral oil nose drops or oral laxatives during life. In 1929, Quinn and Meyer [2] illustrated how aspiration of the oil apparently failed to provoke two important protective responses of the airway, glottic closure and coughing, and by-passed mucociliary transport mechanism.

Initially, most patients with lipoid pneumonia were children – often with local anatomic defects such as cleft palate – or debilitated adults, but several reports indicated that it could occur in healthy people as well[3]. By 1941 more than 400 cases, many were fatal, had been reported[4] and the hazards of mineral oil became appreciated. In 1942 the Council of Pharmacy and Chemistry removed nasal inhalant preparations containing petroleum from the medications included in its list of New and Nonofficial Remedies[5], and manufacturers of nose drops and sprays began to use saline instead as the vehicle for their products.

* Consultant Paediatric Pulmonologist
Department of Pediatrics
King Faisal Specialist Hospital and Research Center (KFSH&RC)
Riyadh
Saudi Arabia

Endogenous Vs Exogenous Lipoid Pneumonia

Lipids, fat-like compounds of mineral, animal, or vegetable origin contain long –chain fatty acids with alcohol; they are called oils when liquid at room temperature. Lipoid, often used as a synonym for lipid. Lipid pneumonia can have either an external or an internal source. Exogenous lipoid pneumonia, also called "cholesterol" or "golden" pneumonia, usually develops when lipids that normally reside in the lung tissue – most commonly cholesterol and its esters – escape from destroyed alveolar cell walls distal to an obstructing, usually malignant, airway lesion or from lung tissue damage by a suppurative process[6]. Less commonly, endogenous lipids appear in the lung with fat emboli, pulmonary alveolar proteinosis, and lipid storage disorders[7]. Microscopic findings and fat stains can distinguish endogenous from exogenous lipoid pneumonia.

Source of Exogenous Lipids

Most cases of lipoid pneumonia occur from aspirating or inhaling mineral oil[8]. Oil-based laxatives[9,10]. Excessive use of lip balm (Chap Stick)[11] and of flavored lip gloss (Kissing Potion)[12] led to lipoid pneumonia in both. Inhalation of oils may also cause lipoid pneumonia[13].

Several reports of lipoid pneumonia, especially in infants and small children, have originated from traditional folk remedies. In Saudi Arabia oily nose drops are still used, and animal fats, such as ghee (clarified butter made from goats' milk), are often fed forcibly to establish regular bowel habits or administered in tranasally to treat coughs and colds[14,15]. In India (sesame seed) was used to flush the secretions out through the nose[16]. In Brazil mineral oil used to relieve partial small-bowel obstruction due to *Ascaris lumbricoides*[17]. An Oriental practice is to instill medicated oil into the nose and then sniff it[18].

Although rare, lipoid pneumonia has occurred following bronchography, which employs iodized peanut, sesame seed, or olive oils[19]. Gastro esophageal reflux with aspiration causes lipoid pneumonia when medium-chain triglyceride oil given as a nutritional supplement via a nasogastric tube[20].

Pathophysiology and Predisposing Factors

Mineral oil, being bland and nonirritating, can enter the tracheobronchial tree without stimulating glottic closure or the cough reflex, and, once there, is expelled with difficulty because it impairs the mucociliary transport system. Reported cases of lipoid pneumonia have been most frequent in debilitated infants and adults older than 50 years, many with neurological or gastrointestinal disorders affecting swallowing, palatal or cough mechanisms and thus predisposing to aspiration of oropharyngeal or gastric contents[1,21,22].

Figure 1A. Lipid laden macrophage on hematoxylin and eosin stain

Figure 1B. Red dots in pil red O stain

Pathologic Findings

Pinkerton's showed that simple vegetable oils – sesame seed, poppy seed, and olive oil – provoke little reaction and are apparently removed from the lung largely by expectoration. Animal oils - such as milk fat, rabbit fats, and cod-liver oil, caused mononuclear and giant cell inflammation, connective tissue proliferation. Mineral oils, which are relatively inert, are emulsified (finely subdivided) and then ingested by macrophages (lipid laden macrophage on hematoxylin and eosin stain (Fig1A) and as red dots in oil red O stain (Fig 1B) After several months, giant cells and fibrosis forms around large masses of oil, which apparently develop from a coalescence of droplets liberated from the phagocytic cells. On electron-microscopic examination these macrophages lack lysosomes, an absence that may partly explain the tendency for increased infections in these patients[24]. The alveolar septa may be edematous, and the oil may elicit a foreign body reaction in the alveoli consisting of lymphocytes, plasma cells, and giant cells. Dense pleural adhesions may be present[25]. The process can involve several lobes in each patient with an overall predilection for the right lung[26]. Elastic tissue degeneration of the walls of the bronchi and bronchioles can lead to bronchiectasis[27].

Although most of the oil remains within the alveoli, some droplets and lipophages escape into the interlobular septa and travel via the lymphatics to regional lymph nodes, leaving a trail of chronic inflammation, including lymphoid follicles, and fibrosis along the interstitium[27].

Clinical Features

About half of the patients have no symptoms, their disease being evident only because of an abnormal chest roentgenogram. Occasionally, patients have the abrupt onset of fever and cough, mimicking an acute bacterial pneumonia[29]. More frequently, those with symptoms complain of chronic cough, sometimes productive, and dyspnea. Less common problems include chest pain, hemoptysis, weight loss, and intermittent fevers, perhaps due to the inflammatory reaction to oil or to secondary infection related to bronchiectasis or pneumonia[30]. Physical examination of the chest may be normal or may disclose dullness on percussion, crackles, wheezes, or rhonchi. Routine laboratory test results are usually normal, but leukocytosis and an increased erythrocyte sedimentation rate may occur, especially when the lipoid pneumonia or a complicating infection causes fever [29]. Patients may be hypoxemic[22,30]. Pulmonary function test results, infrequently reported, are sometimes normal[30], but most have shown a restrictive pattern[9,10,31].

Roentgenographic Findings

Although plain chest roentgenograms may be unremarkable in patient with lipoid pneumonia[26], most show abnormalities. In early disease, a homogenous dense consolidation, often with air bronchograms and sometimes a fine, "spun-glass" appearance[32]. The involvement may be diffuse or focal, unilateral or bilateral. Cavitation is occasional[7]. A pattern of reticular markings may develop as the emulsified oil leaves the alveoli and enters the interstitium and lymphatic, creating edema, inflammation, and fibrosis in those sites. Fibrosis and coalescence of the oil may result in nodules or masses, sometimes with well-defined borders, but often with irregular margins and radiating specules that resemble lung cancer[32,33]. Atelectasis occasionally develops from bronchial occlusion by granulation tissue or oil[34], Concomitant pleural effusions sometimes occur[7,30,35].

A review of several series[32,34,36] suggests that about half of the cases have unilateral pneumonic consolidations, with a predilection for the lower lobes and the right middle lobe. The location of the abnormalities may partly depend on the patient's position when asleep. Between one third and one half have nodules or masses, usually single; diffuse, bilateral infiltrates are uncommon.

Computed tomographic scan and magnetic resonance imaging can detect fat within pulmonary tissues. Bottled mineral oil has a computed tomographic attenuation value of – 132 Hounsfield units (HU)[37]. Magnetic resonance imaging shows a high-intensity signal on T_1-weighted images, which a slow decreased of signal on T_2-weighted images, findings characteristic of blood or fat[38,39].

Diagnosis

The diagnosis of lipoid pneumonia depends on detecting fat-laden macrophages in the specimen. Microscopic identification of cytoplasmic vacuolization without fat-staining, found in many disorders, is nonspecific[40]. The type of oil present in tissue is discernible by various stains, which must be performed on frozen sections because routine preparation for paraffin embedded samples removes the oil. Chromatography (thin-layer or gas) and infrared spectroscopy, which compare the oil present with several pharmaceutical preparations or reference aliquots of liquid paraffin [22,41,42].

While demonstrating lipid-laden macrophages in the alveoli, or interstitium of lung tissue is definitive evidence of lipoid pneumonia the reliability of examining expectorated sputum is unsettle. Bronchoalveolar lavage may reveal turbid or whitish fluid with oil droplets visible on its surface. Fine-needle aspiration may be diagnostic but false-negative results occur[43]. Lung biopsy specimens – or even surgical resection – may be necessary, particularly in some patients with an equivocal history and solitary masses or nodules of unknown duration[43].

Natural History and Complications

The disease is usually indolent although some cases can be acute and fatal. Concurrent debilitating illness and continued oil use are associated with a more progressive disease[32,26]. These patients may have recurrent bacterial pneumonias. In addition, nontuberculous mycobacteria including *Mycobacterium chelonei*[44], *Mycobacterium fortuitum*[45,46,] and an unidentified rapid growth have caused super infection, possibly related to the fact that lipids enhance the growth of these organisms and impede their phagocytosis by the host's macrophages. With tissue specimens, contact smears of the lung may demonstrate the mycobacteria than routine processed sections because not only oil but organisms as well are lost during the dehydration and staining[46]. Colonization with the fungus *Cryptococcus neoformans* has also occurred[30].

With protracted exposure to the lipoid material, respiratory insufficiency may develop, occasionally leading to corpulmonale[47,48]. More commonly, symptoms improved, but roentgenographic findings persist or worsen[22,30]. One unusual complication of the granulomatous response is hypercalcemia, probably from inflammatory cells producing calcitriol, a phenomenon observed in other granulomatous disease such as sarcoidosis, tuberculosis, and systemic fungal disease[48,49]. In one case resection of a paraffinoma[48], in the other, oral corticosteroids[49] corrected the hypocalcaemia.

Lung cancer, most commonly the bronchoalveolar type, has developed in areas of preexisting exogenous lipoid pneumonia. While mineral oil could be carcinogenic, the fibrous tissue itself may predispose to cancer, as in diffuse interstitial fibrosis[50]. The association with lipoid pneumonia is, however, rare; only 21 cases have been reported[51,33,27,52,53]. Furthermore, in 100 patients with lipoid pneumonia followed for up to 20 years revealed no lung cancer [54].

Treatment

The treatment of lipoid pneumonia comprises discontinuing exposure to the offending agent, treating any complicating infection, and providing supportive care. Some have striking improvement after corticosteroid therapy[31,55] but others have experienced little effect. Resection of nodules and masses may be curative[25], but because lipoid pneumonia is typically indolent and sometimes regresses, surgical removal is usually unwarranted unless a high suspicion of cancer exists.

CONCLUSION

Lipoid pneumonia is an uncommon disease encountered in all age groups. Physician should enquire about oil intake in all patients with persistent cough and chest symptoms. Treatment involves removal of the offending agent and steroid.

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