

Squalene Aspiration Pneumonia : Thin-Section CT and Histopathologic Findings¹

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Purpose : The purpose of this study was to describe the thin-section computed tomography (CT) findings and histopathologic findings of squalene aspiration pneumonia.

Materials and Methods : Thin-section CT scans were obtained from nine patients with proven exogenous lipid pneumonia resulting from aspiration of squalene (derived from shark liver oil). The condition was diagnosed by biopsy (n=3), bronchoalveolar lavage (n=4), or sputum cytology and clinical history (n=2); a clinical history of squalene use was confirmed in all patients. Specimens of transbronchial lung biopsy were also reviewed and compared with thin-section CT findings.

Results : Thin-section CT findings included ground-glass attenuation (n=8), consolidations obliterating vascular marking (n=4), scattered centrilobular ground-glass attenuation (n=2), and interlobular interstitial thickening (n=6). Geographic lobular distribution with peripheral spared lobules was observed in all patients. These diseases involved multiple lobes (n=5) and abnormalities were usually located in the dependent portion of the lung. In three cases, histopathological correlation showed that ground-glass attenuation reflected intra-alveolar infiltration of lipid-laden macrophages with exudative fluid. Interlobular septal thickening represented hyperplasia of type II pneumonocytes with mild fibrosis.

Conclusion : On the basis of these results, we concluded that squalene aspiration pneumonia can be reliably diagnosed by thin-section CT findings particularly when the appropriate history is known.

Index words : Lung, aspiration
Lung, consolidation
Lung, CT
Lung, fibrosis

Exogenous lipid pneumonia is an uncommon condition resulting from the aspiration or inhalation of fat-like material. In initial reports, most patients with lipid pneumonia were either children who often had local anatomic defects such as cleft palate or debilitated

adults (1, 2). Nevertheless, several reports have indicated that the condition can also occur in healthy people (1). Exogenous lipid pneumonia now occurs less frequently than in the 1930s, but each year, one or two cases are reported in the literature (3, 4). For the following reasons, the incidence may actually be higher than reported: many clinicians are unfamiliar with this entity; patients commonly present with nonspecific clinical presentations, or no symptoms at all; and chest radiographic findings mimic other pulmonary processes.

Squalene is a lipid derived from shark liver oil, and

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in Asia, is used as a traditional folk remedy. As in most cases of mineral oil aspiration, the symptoms of squalene aspiration pneumonia are either absent or nonspecific, and chest radiographs and CT findings can simulate other diseases. Thus, squalene aspiration pneumonia is often unrecognized(5).

We therefore assessed the thin-section CT findings of squalene aspiration pneumonia and correlated them with the histopathologic findings.

Materials and Methods

We retrospectively reviewed the thin-section CT findings and medical records of nine consecutive patients (eight men and one woman; age range, 33–73 years; mean age, 59 years) with proven exogenous lipid pneumonia.

Diagnosis was based on transbronchial lung biopsy in three patients, bronchoalveolar lavage in four patients, and positive sputum examination for fat vacuole with competent radiological findings in two. In all patients, a history of taking squalene (shark liver oil) was confirmed retrospectively. The duration of taking squalene was between 1 week and 4 years.

In all patients, a CT/T 9800 scanner(GE Medical Systems, Milwaukee), was used to obtain thin-section CT scans; 1.5-mm collimation scans (140 KVp, 170 mAs, 2 or 3 seconds) were obtained, with a 15 mm scan interval. The images were reconstructed using a high-spatial-resolution algorithm, and were photographed at a window level and width appropriate for lung parenchyma(level = -750 HU; width = 1500HU). Contrast material was not administered to any patient.

The thin-section CT scans were retrospectively analysed by two chest radiologists, and final decisions were reached by consensus. The scans were assessed specifically for the pattern and distribution of pulmonary abnormalities such as ground-glass attenuation, consolidation and interstitial thickening. We also analyzed temporal changes in the CT findings.

Specimens of transbronchial lung biopsy were fixed in 10% neutral buffered formalin, and then embedded in paraffin. Serial sections of 4um thickness were made and stained with hematoxylin-eosin and Masson-trichrome. Histopathologic findings of biopsy specimens at low magnification were reviewed and compared with thin-section CT findings.

Table 1. Findings in Nine Cases of Squalene Aspiration Pneumonia

Patient No.	Age/Sex	Duration of squalene ingestion at Time of CT	Symptoms	Location	HRCT Findings
1	73/M	4 Yr	Cough, sputum	Right medial & lateral segment, Left posterior basal segment	Patchy dense consolidation with ground-glass attenuation. interstitial thickening
2	59/M	3 Yr	cough, sputum	Right middle lobe, Left lingular division	Sharply marginated ground-glass attenuation, reticular interstitial thickening.
3	33/M	1 Mo	Cough, dyspnea	Right posterior & superior segment, Left superior segment	Patchy dense consolidation with ground-glass attenuation. Stellate centrilobular consolidation
4	55/M	2 Mo	Scanty sputum	Right posterior & superior segment	Patchy dense consolidation with ground-glass attenuation, reticular interstitial pattern. Stellate centrilobular consolidation
5	59/M	3 Yr	No Sx	Right medial segment	Reticular interstitial thickening with interlacing ground-glass attenuation.
6	68/M	16 Mo	dyspnea, scanty sputum	Right lateral segment, Left anterior basal & lateral basal segment	Sharply marginated ground-glass attenuation and dense consolidation, reticular interstitial thickening.
7	60/M	1 Mo	No Sx	Right medial basal & posterior basal segment	Patchy dense consolidation with ground-glass attenuation. interstitial thickening
8	56/M	6Mo	dyspnea, cough, sputum	Right apical segment, Left apicoposterior segment	Sharply marginated ground-glass attenuation.
9	55/M	1 Wk	No Sx	Right posterior segment	Sharply marginated ground-glass attenuation.

Results

Thin-section CT demonstrated patchy ground-glass attenuation (n=8), consolidations obliterating vascular marking (n=5), scattered centrilobular ground-glass attenuation (n=2), and interstitial thickening (n=6). Geographic lobular distribution and peripherally spared secondary pulmonary lobules were observed in all patients (Table 1). In six cases, multiple lobes were involved, and these were usually located in dependent portions of the lung. In most cases, the lower lobes were predominantly affected, although in debilitated patients in a recumbent position, the superior segment of a lower lobe or posterior segment of an upper lobe, was most likely to be involved.

In patients with a history of acute aspiration, geographic lobular distribution of ground-glass and dense consolidation obliterating vascular marking were observed on thin-section CT (Fig. 1A). Histopathologic examination showed only minimal evidence of acute inflammation; lipid-laden macrophages and exudative fluid, however, had extensively infiltrated the alveolar space. There was no evidence of interstitial fibrosis (Fig. 1B).

In patients with a two- or three-month history, ground-glass attenuation was noted in peripheral areas, and consolidation was denser than during the acute stage (Fig. 2A). Histopathologic examination demonstrated infiltration by lipid-laden macrophages

of the alveolar space. However, there were fewer such macrophages and no evidence of exudative fluid. Minimal interstitial fibrosis and hyperplasia of type II pneumocyte were present (Fig. 2B).

In patients with longer histories of repeated aspiration, thickening of interstitial septa and decreased lung volume as well as geographic patterns of distribution were found on thin-section CT. Ground-glass attenuation was observed between the thickened interstitial septa (Fig. 3A). Histopathologically, these findings represented the interstitial fibrosis and hyperplasia of type II pneumocytes. Lipid-laden macrophage was scarcely noted (Fig. 3B).

Discussion

Thin-section CT findings of squalene aspiration pneumonia observed in this study included patchy ground-glass attenuation, consolidations obliterating vascular marking, scattered centrilobular ground-glass attenuation, and interstitial thickening. In all patients, geographic lobular distribution with peripherally spared lobules was observed; these had multiple lobes and were usually located in dependent portions of the lung. During histopathological correlation, intralobular ground-glass attenuation and dense lobular consolidation reflected intra-alveolar lipid-laden macrophages with exudative fluid. The interstitial thickening represented the hyperplasia of type II pneumocytes with mild fibrosis.

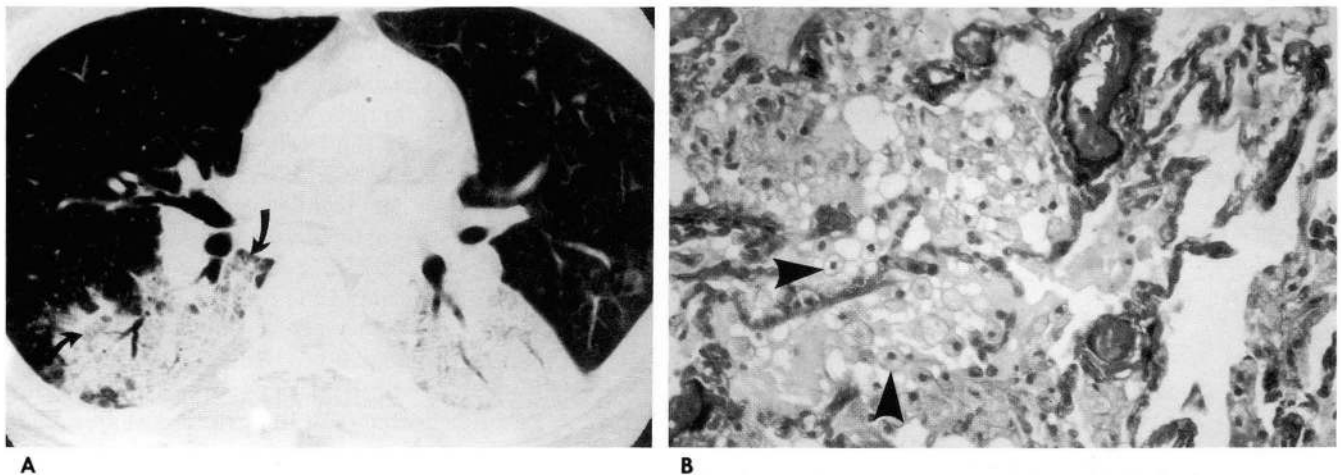


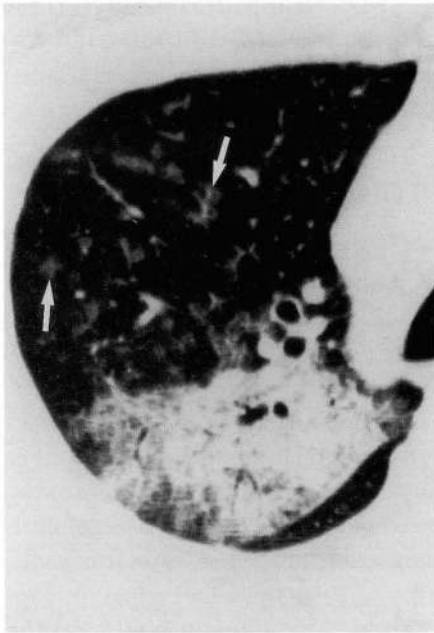
Fig. 1. Case 3. A thirty-three year-old man with a history of taking squalene for one month. During the last week, he had taken more than 10 capsules of squalene through the nose, whereupon a cough and mild dyspnea developed.

A. On thin-section CT, geographic lobular distribution of dense lobular consolidation obliterating vascular marking was observed at the superior segments of both lobes. An air-bronchogram is clearly demonstrated by the consolidation. Interposed ground-glass attenuation was peripherally located.

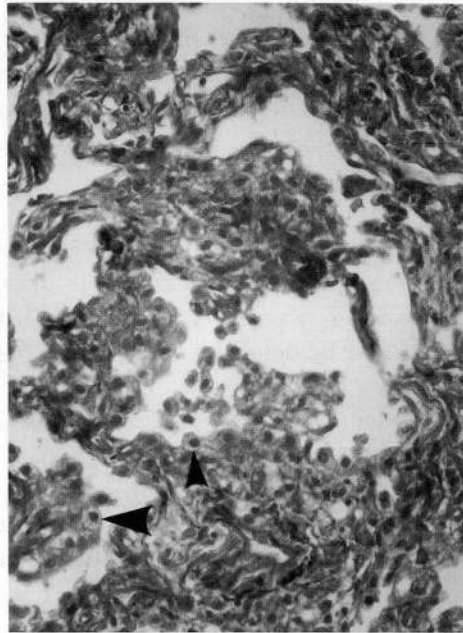
B. A photomicrograph (Masson-trichrome stain; original magnification, $\times 200$) of a transbronchial lung biopsy specimen obtained two days after the CT scan shows lipid-laden macrophages (arrowheads) and exudative fluid in the alveolar space. There is no demonstrable infiltration of inflammatory cells or interstitial fibrosis.

In 1925, Laughlen (2) first described exogenous lipoid pneumonia. He reported that during the autopsies of three children and one adult who had received mineral oil nosedrops or oral laxatives, oil droplets were discovered in the lungs. He delineated the pathogenesis of this disorder by showing that mineral oil instilled into the trachea or pharynx of rabbits subsequently appeared in their lungs and elicited a histologic

response identical to that seen in human cases. Squalene capsules are readily available in Asian health food stores, and squalene is also widely used in cosmetics. An oriental practice is to instill medicated oil into the nose and then sniff it(5—7), and Asnis (5) and Lee (8) reported cases with histories of squalene ingestion. Several reports of lipoid pneumonia have originated from traditional folk remedies, though squalene aspir-



A



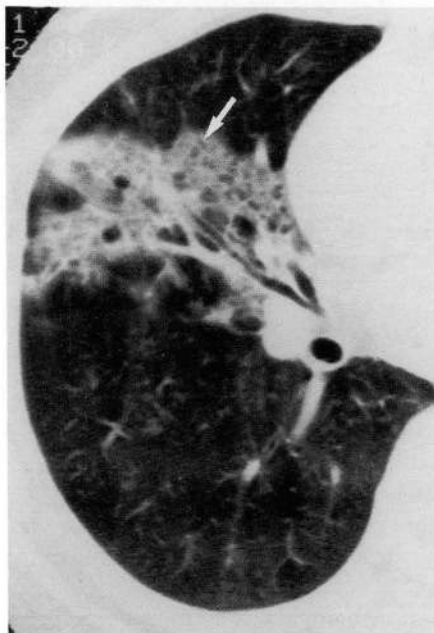
B

Fig. 2. Case 4. A fifty-five year-old male with a history of taking squalene for two months.

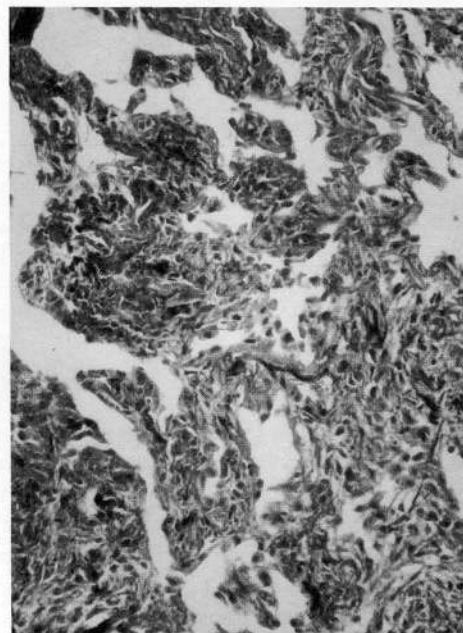
A. Thin-section CT scans of the right lung obtained at the level of the carina. Dense consolidation obliterating bronchovascular marking is located at the posterior segment of the right upper lobe. An air-bronchogram is visualized by the surrounding air space consolidation. Scattered centrilobular ground-glass attenuation (arrows) is also noted in the anterior segment of the right upper lobe. This may have been caused by scattered droplets of squalene. Interstitial thickening is not definite.

B. A photomicrograph (Masson-trichrome stain; original magnification, $\times 200$) of a transbronchial lung biopsy specimen obtained 14 days after the CT scan of a. Lipid-laden macroph-

phages (arrowheads) is still observed, but exudate is not. Only a small amount of interstitial fibrosis and hyperplasia of type II pneumonocytes is noted.



A



B

Fig. 3. Case 2. A fifty-nine year-old man with a history of taking squalene for three years.

A. Thin-section CT scans of the right lung were obtained at the level of the right middle lobar bronchus. There is geographically distributed interstitial thickening (arrow) at the lateral segment of the right middle lobe. Involved area is sharply margined from uninvolved normal parenchyma which is located at the peripheral portions of the lung. Interposing ground-glass attenuation is also noted.

B. Photomicrograph (Masson-trichrome stain; original magnification, $\times 200$) of a transbronchial lung biopsy specimen obtained nine days after the CT scan of a. shows hyperplasia of type II pneumonocytes and interstitial fibrosis. Lipid-laden macrophages are scarcely observed.

ation pneumonia has rarely been reported.

In previous reports(9, 10-12), the diagnosis of lipoid pneumonia was established on CT by detecting areas of fat attenuation in a lung lesion. Hounsfield unit numbers, however, are average values from both lipids within the alveoli and surrounding inflammatory exudate, so CT attenuation values are not always characteristic of fat. Thus, fatty attenuation (-35 HU to -75 HU) in lung lesions was not always specific for a diagnosis of lipoid pneumonia. For evaluating squalene aspiration pneumonia, the distribution patterns of ground-glass attenuation and lobular consolidation were more diagnostic than the CT attenuation values of lung lesions. When squalene is aspirated, droplets can be scattered in adjacent pulmonary lobules, and this may cause scattered centrilobular ground-glass opacity. Irregular mass-like lesions were reported by Lee et al(8), but were not found in our nine cases.

Thin-section CT of pulmonary alveolar proteinosis, bronchioloalveolar carcinoma or lymphoma can show a geographic distribution of consolidation or ground-glass opacity and smooth thickening of the interlobular septa. These findings are almost the same as those of squalene aspiration pneumonia(13-15). Distribution at dependent locations and a history of taking squalene are, however, differentiating factors.

The degree and quality of tissue reaction to aspirated oil are quite variable, being related to the quantity and frequency of aspiration, the chemical characteristics of the oil itself, and the complicating effects of other substances which may be aspirated at the same time. The reaction to many animal oils and some vegetable oils is an acute bronchopneumonia characterized by edema, intra-alveolar hemorrhage, and a mixed polymorphonuclear and mononuclear infiltrate(16). In contrast, aspirated mineral oil is sometimes associated with a minimal acute inflammatory reaction. An intra-alveolar infiltrate of macrophages is, however, present and this rapidly phagocytoses the oil(17). With time, these macrophages become predominantly interstitial in location and decrease in number(19). Because the oil is carried from the alveoli into the interstitial space by macrophages, a predominantly interstitial pattern can develop during the chronic stages(19).

Although squalene is extracted from shark liver, it is an intermediate form of the biosynthesis of cholesterol and different from the usual animal fat hydrolyzed into fatty acid by lipase(9, 17). Thus, at the acute stage, aspirated squalene elicits only infiltration of lipid-laden macrophages in the alveolar space, with a minimal

inflammatory lung tissue reaction. It is similar to the reaction caused by mineral oil rather than animal fat.

We conclude from the results of this study that squalene aspiration pneumonia can be reliably diagnosed by thin-section CT findings and appropriate historical inquiries, and that these findings reflect the histopathologic changes involved.

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Squalene에 의한 흡인성 폐렴 : 고해상 CT 소견과 조직병리학적 소견¹

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목적 : Squalene에 의한 흡인성 폐렴의 고해상 전산화단층촬영(computed tomography, CT) 소견과 조직병리학적 소견을 알아보려고 하였다.

대상 및 방법 : Squalene의 흡입에 의하여 발생한 외인성 지방 폐렴으로 진단된 9명의 환자에서 고해상 CT 소견을 분석하였고, 경기관지 폐조직 생검의 병리조직학적 소견과 고해상 CT 소견을 비교하였다. Squalene 흡인성 폐렴은 3예에서는 조직생검 소견에 따라서, 4는 기관지 폐포세척소견으로, 2예는 객담검사와 임상증상에 의하여 진단하였다. 모든 환자에서 squalene을 복용한 병력이 있었다.

결과 : 고해상 CT에서 소엽내(intralobular) 간유리상 혼탁(ground-glass opacity)(8예), 폐혈관 음영을 소실시키는 경결(consolidation)(4예), 산재되어 있는 중심소엽성 경결(2예)과, 세엽간 격막의 비후(6예)를 볼 수 있었다. 병변은 모든 환자에서 기하학적인 소엽성분포를 보였다. 조직병리학적 소견과의 비교에서 소엽내 간유리상 혼탁은 지방 함유 대식세포(lipid-laden macrophage)의 폐포내 침윤과 폐포내의 삼출액에 의한 것이었으며, 소엽간 격막의 비후는 경도의 섬유화와 type II 폐세포(pneumonocyte)의 증식에 의한 것이었다.

결론 : 이러한 결과를 바탕으로 squalene을 복용한 병력이 있는 환자에서 위와 같은 고해상 CT소견을 보일 때 squalene 흡인성 폐렴을 진단할 수 있으며, 이러한 고해상 CT소견은 병리조직학적 소견을 잘 반영한다.