

## Exogenous lipid pneumonia caused by herbicide inhalation

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### Keywords

Gas chromatography, herbicide, lipid pneumonia, morpholine, respiratory failure.

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### Abstract

Exogenous lipid pneumonia is caused by aspiration or inhalation of oily substances. Generally, lipid pneumonia has non-specific clinical and radiological presentations and may be misdiagnosed as bacterial pneumonia. Our patient, a 68-year-old man who had been diagnosed with pneumonia on three previous occasions, was admitted to our hospital with a fourth similar episode. Computed tomography of the chest revealed extensive consolidations with air bronchograms in lung fields on the right side. The bronchoalveolar lavage fluid (BALF) increased *ghost*-like macrophages that stained positive for lipid. Our patient reported that he had sprayed herbicide in large quantities without wearing a mask. We analysed the BALF and herbicide by gas chromatography and diagnosed exogenous lipid pneumonia caused by inhalation of herbicide. Clinicians should be aware of lipid pneumonia, which may present as infectious pneumonia.

### Introduction

Exogenous lipid pneumonia is caused by aspiration or inhalation of oily substances. Although it may be an easy diagnosis if there is a history of oil-based ingestion, 25% of adult cases of lipid pneumonia occur in individuals without any predisposing factors [1]. This is the first report of lipid pneumonia caused by inhalation of herbicide. We identified the causative agent by gas chromatography.

### Case Report

A 68-year-old man, who had been complaining of dyspnoea on exertion and fever for five days, presented to a community hospital. A chest X-ray showed right lobe infiltrations. He was admitted with a diagnosis of community-acquired pneumonia and started on antimicrobial therapy. A chest X-ray taken three days later showed worsening of infiltrations in the right lung (Fig. 1A). He was referred to our hospital.

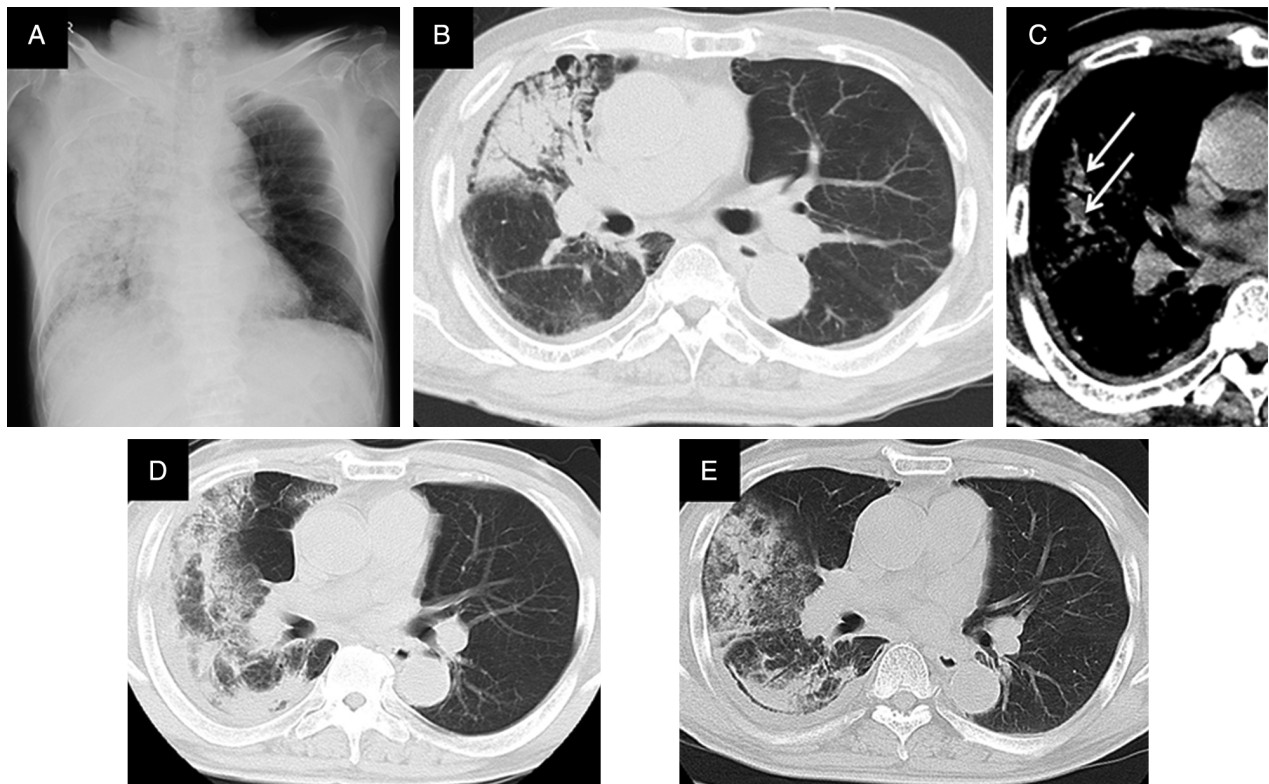
Right pleural thickening and upper lobe predominance consolidations with air bronchograms were revealed by computed tomography (CT) of the chest (Fig. 1B). His past medical history included well-controlled type 2 diabetes and three episodes of pneumonia. CT images

confirmed the past episodes of pneumonia, which were very similar to this occurrence (Fig. 1D,E). We doubted a diagnosis of bacterial pneumonia because the shadow was too similar to past episodes and worsened in spite of adequate antimicrobial therapy.

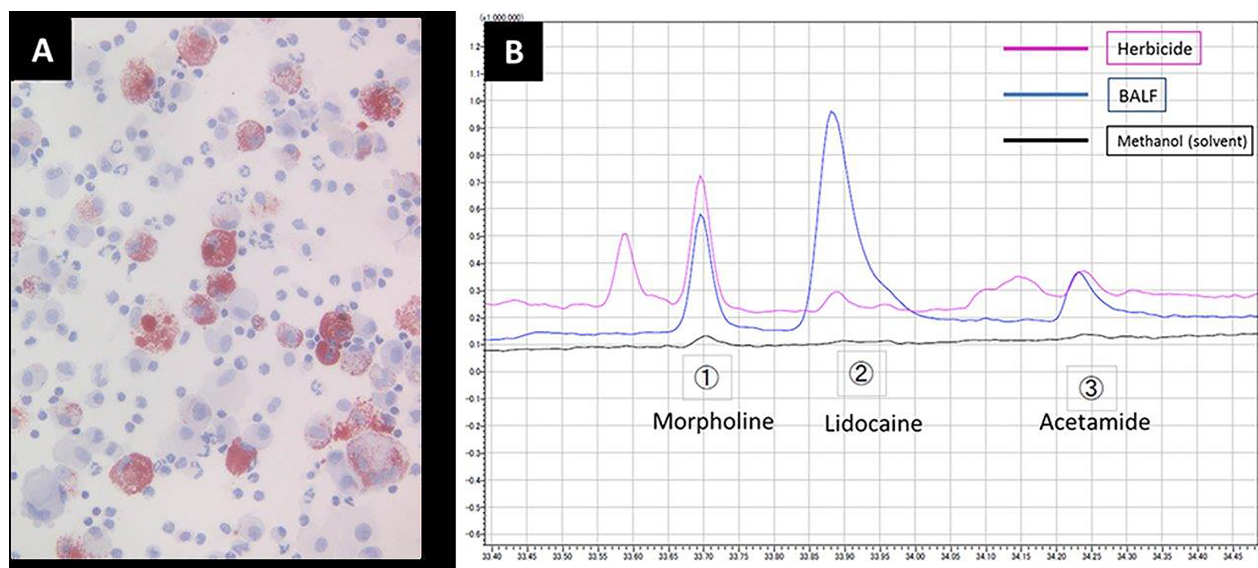
A bronchoscopy was performed. Bronchoalveolar lavage fluid (BALF) showed increased numbers of ghost-like macrophages (53.8%) that stained positive for Oil-Red-O, consistent with lipid-laden macrophages (Fig. 2A). Further history revealed that he had sprayed herbicide in large quantities without a mask before hospitalization but had not taken oil.

To identify the causative agent, we analysed BALF and the herbicide used by the patient using gas chromatography (Fig. 2B). When analysed, BALF and herbicide both showed a peak component of morpholine. The morpholine was used in the herbicidal product as a surfactant ingredient. We diagnosed lipid pneumonia caused by inhalation of herbicide.

The patient was ventilated after bronchoalveolar lavage (BAL). We started intravenous prednisolone 60 mg (1 mg/kg). Extubation was six days after BAL. One month after the intervention, the patient was asymptomatic. Oxygen saturation was 95% in ambient air. The chest CT showed significant decrease of alveolar opacity. By avoiding the use of herbicide, he has not had a relapse.



**Figure 1.** Representative images from the chest X-ray scan (A) and chest computed tomography (CT) scan at the level of the middle lobe (B) performed at the time of admission to our hospital. Mediastinal window (C) showed consolidation with superimposed areas of low attenuation (ranging from  $-73$  to  $20$  HU) in the right upper lobe (arrows). Panels (D) and (E) are CT images from previous episodes of pneumonia in this patient at the level of the middle lobe (D; nine years previously, E; six years previously).



**Figure 2.** (A) The bronchoalveolar lavage fluid (BALF) revealed increased ghost-like macrophages that stained positive for lipid. Lipid-laden alveolar macrophages were dyed red (Oil-Red-O stain,  $\times 200$ ). (B) Analysis of BALF, herbicide, and methanol (solvent) by gas chromatography. Peak components of BALF were morpholine, lidocaine, and acetamide. Both BALF and herbicide showed a peak component of morpholine.

## Discussion

Exogenous lipoid pneumonia results from the pulmonary accumulation of fat-like compounds of animal, vegetable, or mineral origin. Most cases result from oil-based laxatives such as paraffin oil in adults. Factors that increase the risk of exogenous lipoid pneumonia include extremes of age and anatomical or structural abnormalities of the pharynx and oesophagus [2]. Its clinical presentation is non-specific; lipoid pneumonia may mimic bacterial pneumonia, presenting with fever and cough [3]. Unless linked to a specific episode, diagnosis is considered to be difficult.

The diagnosis of lipoid pneumonia is based on a history of exposure to oil and the presence of lipid-laden macrophages in sputum or BALF. However, lipid-laden macrophages can also be present in lung tissue damaged by malignant tumours or purulent lesions. Fat embolism, thromboembolism, Wegener granulomatosis, or pulmonary alveolar proteinosis are known as endogenous-causing factors of lipoid pneumonia. BALF findings alone are not diagnostic of exogenous lipoid pneumonia.

Radiological findings are varied, for example, airspace consolidations, crazy paving pattern, interlobular septal thickening, and nodules. Mediastinal lymph node enlargement or pleural thickening has also been reported. The most characteristic finding in lipoid pneumonia is the presence of consolidation with areas of fat attenuation (−150 and −30 HU) [2]. The mediastinal window of this case (Fig. 1C) showed consolidation with low attenuation areas. CT values ranged from −73 to 20 HU.

Herbicide is used all over the world, and the sole circumstance of having been used in large quantities without a mask was not enough to confirm it as the causative agent when the patient was referred to our hospital. The gas chromatography analysis revealed a matching peak in the BALF and the herbicide and demonstrated the presence of morpholine, which does not exist *in vivo*. Morpholine fatty acid salts are used as a surfactant in herbicide, therefore representing the offending agent in the herbicide and justifying how the herbicide exposure caused lipoid pneumonia. However, an initial suspicion of lipoid pneumonia from the clinicians was essential as the diagnosis is difficult.

Tissue reaction of exogenous lipoid pneumonia is defined by quality and amount of oil, time course, or host

side conditions [3,4]. In many cases, there is no predisposing condition, and the excessive use of oily substances is the presumed cause. This patient had developed three previous episodes of pneumonia, and host susceptibility was considered the most significant contributor. Due to repeated exposure, sensitivity was probably enhanced.

With regard to the treatment of lipoid pneumonia, the most important point is identifying and discontinuing exposure to the offending oil [1]. There are no other established strategies of treatment. As infection is the main differential diagnosis, there are strong arguments for using an antimicrobial agent. The use of steroids was often reported in the literature [5]. However, steroid therapy remains controversial and should be reserved for severe cases. In addition, whole lung lavage may also be therapeutic [2].

In conclusion, we report a case of repeated lipoid pneumonia due to herbicide. To the best of our knowledge, it is the first reported case in the world. Diagnosis of exogenous lipoid pneumonia depends on suspicion of exposure. Gas chromatography was useful for the diagnosis of this case.

## Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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