Case Report

Rare cause of chronic cough in a young healthcare worker - A case of exogenous lipoid pneumonia!

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Abstract

Exogenous lipoid pneumonia (ELP) is a rarely reported entity caused by aspirating or inhaling fat or oil-containing substances. Clinically, patients present with subacute to chronic-onset non-specific symptoms such as cough, fever, breathlessness, and general malaise. In addition, lobar or multifocal interstitial and parenchymal infiltrates on chest imaging can mimic any other infectious etiology. Diagnosis of lipoid pneumonia is often missed or delayed in many cases and requires a high index of clinical suspicion. We report a case of a 36-year-old nursing officer who presented with a cough and right-sided pneumonia on chest imaging. She was being treated empirically with antitubercular therapy without any clinical response to the treatment. ELP was diagnosed after carefully evaluating the radiological findings, reviewing the clinical history, and finding supportive evidence of lipid-laden alveolar macrophages in her broncho-alveolar lavage fluid. It is vital to uphold a heightened clinical suspicion for non-infectious etiologies in non-resolving pneumonia and investigate the patient thoroughly before resorting to empirical treatments.

Keywords: Chronic cough, exogenous lipoid pneumonia, non-resolving pneumonia

Introduction

Lipoid pneumonia (cholesterol or lipid pneumonia) is uncommon pneumonia characterized by the accumulation of fatty substances in the alveolar sacs, resulting in an inflammatory response and alveolar-interstitial edema.[1,2] It is misdiagnosed chiefly as infectious pneumonia,[3] treated with unnecessary empirical treatments, or even remains undiagnosed in many patients. Therefore, its precise incidence is unknown but is reported to be around 1%–2.5% in previous studies.[4] It is majorly a diagnosis of exclusion as no clinical manifestations are specific to it.[2-4] It generally has a subacute to chronic course and rarely presents acutely. The diagnosis relies on keeping an index of clinical suspicion. It is primarily based on chest computed tomography (CT) findings supported by the characteristic history of inhalation of fatty or oil-containing substances.[2-4] We report an interesting case of exogenous lipoid pneumonia (ELP) as a cause of persistent cough in a young nursing officer who was misdiagnosed with pulmonary tuberculosis (PTB).

Case History

A 36-year-old female nursing officer presented to her primary healthcare center with a 1-month history of low-grade fever, general malaise, and cough with scant expectoration for over 3 weeks. There were no notable findings on the physical examination; however, her chest X-ray revealed infiltrates in the right middle and lower zones [Figure 1a]. As she was a healthcare worker, her primary physician kept a very high suspicion of PTB. Her Mantoux test was also positive, showing an induration of 12 mm. The sputum workup was non-yielding due to scant expectoration. After being treated with antibiotics for

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Received: 18-07-2024 **Revised:** 11-09-2024
Accepted: 16-09-2024 **Published:** 13-01-2025

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1233_24

How to cite this article: Dikshit N, Gupta M, Nigam N, Nath A. Rare cause of chronic cough in a young healthcare worker - A case of exogenous lipoid pneumonia! J Family Med Prim Care 2025;14:487-90.

community-acquired pneumonia (CAP) with no clinical response, her physician started her on antitubercular therapy (ATT) empirically. However, she had no clinical or radiological response to it and developed ATT-induced adverse drug effects such as nausea, transaminitis, and generalized itching in the body. Her ATT had to be withheld, and she was referred to us for further management.

She was evaluated in our outpatient clinic for her persistent cough, chest discomfort, and general malaise. Her vital signs were normal, and her oxygen saturation (SpO2) was maintained at 95% in room air. Her chest examination showed no clinical findings except occasional crepitations on the right lower chest. She underwent a CT-thorax, which revealed multifocal areas of ground glassing with interlobular and intralobular septal thickening involving the right middle and lower lobes, indicative of a typical crazy paving pattern [Figure 1b]. The mediastinal window of the CT scan was non-contributory for any significant findings. As the CT-thorax findings were suggestive of non-resolving symptomatic pneumonia with an alveolo-interstitial pattern in a previously healthy young female, we kept a possibility of lipoid pneumonia. We decided to review the clinical history again. Upon probing for a detailed personal history, she reluctantly confessed to regularly applying and sniffing mustard (organic) oil into her nostrils to prevent dryness for the last few months and inadvertently aspirating a small quantity of the oil. With a supporting history and clinical-radiological presentation, a video bronchoscopy-guided broncho-alveolar lavage (BAL) was performed on her. BAL fluid was milky white in gross appearance [Figure 2a], with a characteristic yellowish lipid layer on the top. BAL fluid came out negative for infections (such as TB, bacterial, and fungal). However, it revealed enlarged foamy vacuolated pulmonary alveolar macrophages on May-Grunwald-Giemsa stain [Figure 2b] and lipid-laden alveolar macrophages (LLAMs) in Sudan-B staining [Figure 2c]. Finally, a diagnosis of ELP was established in this case. The patient reported improved chest discomfort immediately after the BAL procedure. She was advised to refrain from intranasal application of the offending agent (i.e. mustard oil) and to keep under close follow-up. She underwent repeat therapeutic multisegmental bronchoscopic lavage under local anesthesia after a week. The patient showed marked improvement clinically as well as radiologically. She became asymptomatic with the disappearance of infiltrates from the affected areas over the next 3 months [Figure 3].

Discussion

ELP is a rare clinical entity caused by aspiration or inhalation of fatty substances. Laughlen GF first described the occurrence of

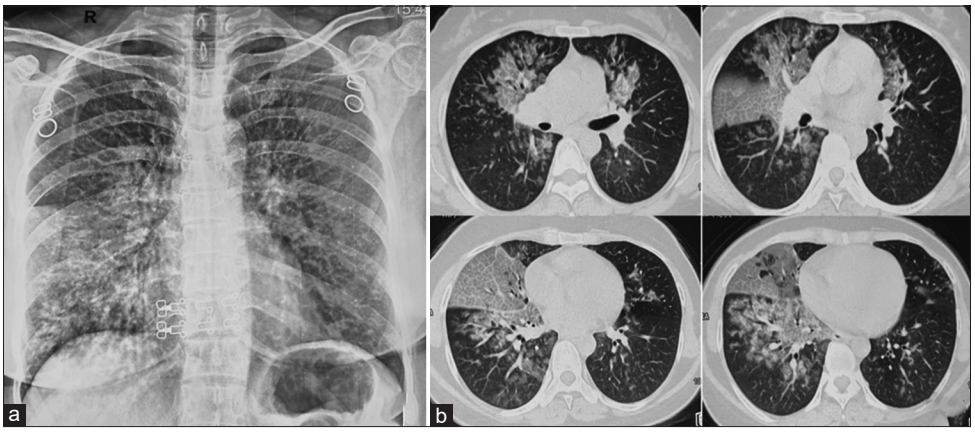

Figure 1: (a): Non-homogenous patchy Infiltrates (nodules, reticulations, and ground glassing) in the right middle and lower zones on chest X-ray. (b): Right middle and lower lobe ground glassing with inter and intralobular septal thickening suggestive of typical "crazy paving pattern" on high-resolution CT imaging

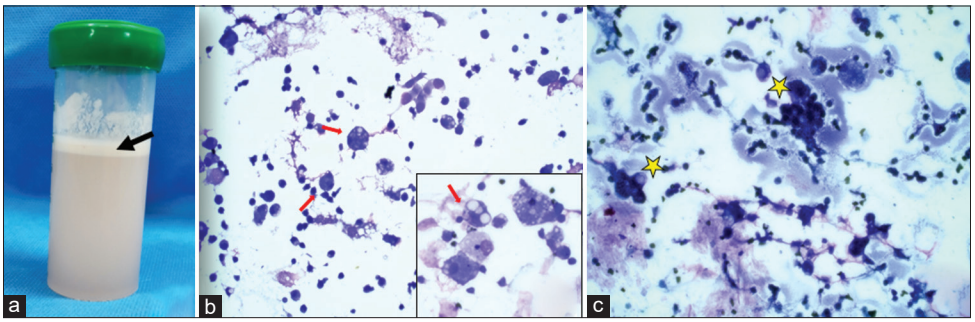

Figure 2: (a) Milky white appearance of broncho-alveolar lavage (BAL) fluid with a yellowish lipid layer on top (marked with the black arrow). (b, c) Cytology smears from BAL fluid show alveolar macrophages with prominent cytoplasmic fat vacuolations (marked with the red arrow (b) May Grunwald Giemsa stain; 200 × and (c) Sudan Black stain for fat; 200×; marked with the yellow star)

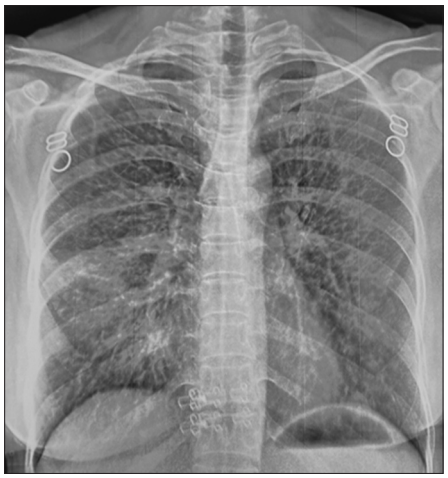

Figure 3: Chest X-ray at follow-up (6 weeks) suggested marked radiological improvement with resolution of the infiltrates

lipoid pneumonia in the early twentieth century, caused by the inhalation of nasopharyngeal oil droplets.[5] Lipoid pneumonia has since been reported worldwide across all age groups.[6-11] It has been classified into endogenous, exogenous, or idiopathic types, depending on the mode of lipid acquisition. The exogenous type is more common and is associated with using mineral oil to treat constipation with laxatives. The endogenous type, on the contrary, is secondary to bronchial obstruction or caused by pulmonary fat embolism, alveolar proteinosis, and lipid deposition diseases. The idiopathic form is a rare occurrence described in smokers.[2-4] Here, we have presented a case of ELP in a young healthcare worker, which was misdiagnosed initially and treated as a case of CAP and later as pulmonary TB. The case highlights physicians' lack of awareness about this entity. These cases are often missed and even misdiagnosed. Many are treated empirically as TB in endemic countries such as India based on clinical symptoms and Mantoux positivity, which can very commonly be seen in people living in a TB-endemic country and specifically in healthcare workers as in this case.[12,13]

ELP, an uncommon pneumonia, can mimic infectious pneumonia and even a neoplastic process due to the absence of specific clinical features and imaging characteristics. The clinical presentation and the extent of radiological manifestations depend upon the type of exposure, amount, frequency, and chronicity. Mineral oils, the most common offending agents, fail to get metabolized by the enzymes and accumulate in the macrophages as LLAMs. LLAMs may remain dormant for some time and release the lipid contents into the alveoli upon their lysis, invoking an inflammatory reaction. Chronic exposure leads to eventual coalescence in the alveoli, interstitial fibrosis, and sometimes encapsulation to form nodular masses. Vegetable oils, animal oils, and other inhalants such as nasal ointments/drops and occupation-related substances have also been implicated. Lung lipases hydrolyze these agents into free fatty acids that trigger alveolo-interstitial inflammatory reactions.[14] Although seen across all ages, ELP occurs more frequently in the elderly and pediatric population, especially with anatomic or functional swallowing abnormalities, and a history of exposure should be carefully sought. Some of the predisposing risk factors include developmental disabilities, anatomical anomalies such as Zenker's diverticulum and hiatal hernia, loss of consciousness, gastroesophageal reflux, dysphagia, neurologic disease, alcohol abuse, cerebral infarction, tracheal stoma, and illicit drug dependence.[2,4,15] Patients may remain asymptomatic after the exposure or have an acute onset of symptoms such as fever, cough, and chest pain or present with chronic cough, breathlessness, and malaise, rarely associated with low-grade fever, weight loss, chest pain, and hemoptysis.[1-4,11,15] Radiologically, it may appear as consolidation, ground-glass opacities (GGO), "crazy-paving" pattern (i.e., thickened interlobular septa superimposed on a GGO reminiscent of irregular paving stones), interstitial thickening, or a mass.[2-4,11] These findings can be bilateral, multifocal, or segmental in distribution and commonly involve the middle and lower lobes, as seen in this case. Other uncommon findings include poorly marginated nodules, pneumatoceles, and rarely pneumomediastinum, pneumothorax, and pleural effusions. The mediastinal or soft tissue window in the CT-thorax can reveal areas of fat attenuation (as low as − 30 Hounsfield Units within the consolidative opacities and nodules, a finding pathognomic of lipoid pneumonia.[4,11] However, even though the attenuation of the opacities or nodules can be low at initial presentation, the presence of superimposed inflammation can be a confounding factor by increasing the attenuation so that the fat component becomes less conspicuous or obscured. In our case, the CT-thorax did not demarcate attenuation similar to fat in the affected areas, most likely due to secondary inflammation, which can be seen in the parenchymal cuts in the form of ground glassing and interlobular septal thickening and consolidation.

This case exemplifies classic ELP, with supporting clinico-radiological features that were initially overlooked. Therefore, thorough history-taking and careful consideration of radiological findings are essential before arriving at a final diagnosis. As reported in previous studies, a history of oil aspiration (or other inhalant) use is rarely provided at the initial presentation. Confirmation of the diagnosis may be pursued with broncho-alveolar cytology sampling (BAL) or fine-needle aspiration (FNA) or a biopsy. BALs and FNAs of ELP have the characteristic large vacuolated foamy cells containing lipids. However, these are frequently overlooked in routine cytopathological examination, and the diagnosis is typically confirmed by additional measures such as lipid-specific staining (Oil red-O and Sudan) or lung biopsy depicting extracellular lipid material, intracytoplasmic vacuoles (cholesterol clefts) in alveolar macrophages, distribution of macrophages in the lung tissue, and physicochemical characteristics of the oil. There may be a giant cell granulomatous reaction (lipid granulomatosis), chronic inflammation, and alveolo-interstitial fibrosis.[4,11,15] The management of ELP has not been well-studied, and it remains mainly supportive. The primary step is to avoid ongoing exposure to the offending agent.[16] ELP has been successfully treated with corticosteroids, immunoglobulins, and whole-lung lavage (WLL) in symptomatic cases.[17-20] As performed in this case, therapeutic segmental or lobar

bronchoscopic lavages using local anesthesia seem to be a great alternative to WLL in mild cases.[16,20]

The case report particularly emphasizes the need for primary care physicians to keep a high level of clinical suspicion for ELP. A diagnosis of ELP should be considered in cases of pneumonia with non-specific clinical features and focal or bilateral interstitial pneumonitis with GGOs or "crazy paving" patterns on the CT-thorax. It underscores the fact that not all instances of chronic cough and malaise, even in healthcare workers, are attributable to tuberculosis. Primary care physicians may have to elicit a detailed history of the patient's personal and occupational habits to obtain a history suggestive of oil aspiration/inhalation, as seen in this case. Recognizing and diagnosing ELP is essential to identify the offending agent and prevent associated complications such as pulmonary fibrosis, superimposed infection, and cor pulmonale.

Learning points

1. Lipoid pneumonia is a rarely reported entity, and being diagnosed with exclusion requires a high index of clinical suspicion.
2. Primary care physicians should specifically re-evaluate patients for ELP when the patient presents with infiltrates on chest imaging but is only mildly symptomatic.
3. Radiological findings on high-resolution CT can differ from case to case; however, it still plays a crucial role in diagnosing lipoid pneumonia.
4. Air space consolidation, ground glassing, nodules, and localized crazy paving patterns are the most commonly seen radiological manifestations.
5. ELP should be kept as a differential in cases of non-resolving pneumonia after excluding active infections.
6. Exposure cessation remains the mainstay of treatment. Most patients improve with avoidance of further exposure, and for patients with more severe diseases, a trial of systemic glucocorticoids is a reasonable option.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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