Journal of Investigative Medicine High Impact Case Reports
Volume 10: 1–4

DOI: 10.1177/23247096211055334
journals.sagepub.com/home/hic
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A 66-Year-Old Man With Subacute Cough and Worsening Dyspnea Previously Diagnosed With COVID-19 Pneumonia

Michelle A. Quan, MD[1], Joshua L. Hoerger, MD, MPH[1,2], Elizabeth H. Mullins, MD[1], and Brooks T. Kuhn, MD, MAS[1,2]

Abstract

A 66-year-old man presented with subacute cough and worsening dyspnea. Labs were notable for moderate peripheral eosinophilia, and computed tomography (CT) scan demonstrated extensive crazy-paving throughout bilateral upper lung fields. Bronchoalveolar lavage (BAL) revealed macrophages with lipid-filled vacuoles and negative periodic acid-Schiff (PAS) stain. Further history obtained from the patient and family was notable for daily application of commercially available vapor rub to nares and intentional deep inhalation of nebulized fluids containing scented oils. The patient was diagnosed with exogenous lipoid pneumonia through an unusual route of lipid administration.

Keywords

pulmonary critical care, lipoid pneumonia, COVID-19

Introduction

Exogenous lipoid pneumonia is a rare disease, first described in a 1925 autopsy series. Alveolar filling by vacuolated mononuclear cells was seen among children receiving topical menthol and alboline oils to their nares and throat as treatment for respiratory symptoms.[1] Aspiration of even small quantities of animal, vegetable, or mineral oil-containing materials can lead to accumulation in distal airways and alveoli. They may then generate slow giant cell aggregation and fibrosis or undergo phagocytosis by macrophages and deposit in interlobular septa.[2,3] Historically seen in high aspiration-risk patients (usually children and the elderly) using oil-based nose drops or mineral oil laxatives, present-day cases may be found among healthy adults with a broader (and often subtler) array of exposures to oil- and petroleum-based products.[3,4] The mainstay of treatment is removal of the offending agent and providing supportive therapy such as supplemental oxygen and respiratory care. Systemic corticosteroids may be used in severe cases, but high-quality evidence for the efficacy of this intervention is lacking.[5-7]

We describe the case of a patient with exogenous lipoid pneumonia after longstanding, daily intranasal application of commercial oil-containing compounds (Vicks VapoRub), as well as inhalation of nebulized oils from a home humidifier.

Case Description

A 66-year-old diabetic man presented to an outside hospital with subacute progressive cough and dyspnea. During that admission, he had 5 negative SARS-CoV-2 PCR (severe acute respiratory syndrome coronavirus 2 polymerization chain reaction) nasal swab tests and ultimately underwent bronchoscopy revealing a positive SARS-CoV-2 PCR on bronchial wash. He was diagnosed with COVID-19 pneumonia and discharged on prednisone 20 mg per day for a total of 4 days, but he experienced worsening symptoms and hypoxemia measured on home pulse oximeter, prompting him to present to our hospital.

On presentation, he was afebrile, mildly tachycardic, and tachypneic with an oxygen saturation of 70% on room air. Physical examination was notable for diffuse rhonchi throughout all lung fields. Chest X-ray showed low lung

[1]University of California Davis School of Medicine, Sacramento, USA
[2]VA Northern California Health Care System, Mather, CA, USA

Received September 3, 2021. Accepted September 30, 2021.

Corresponding Author:
Michelle A. Quan, MD, Department of Internal Medicine, University of California Davis School of Medicine, 4150 V Street, Sacramento, CA 95817-2201, USA.
Email: mquan@ucdavis.edu

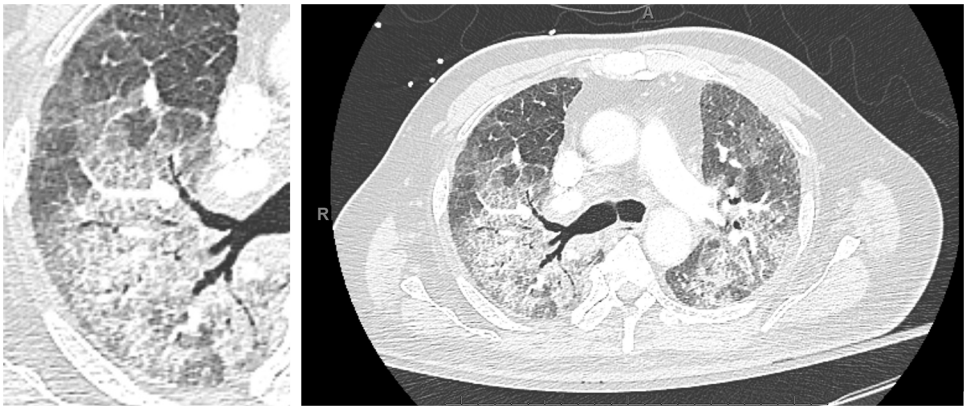

Figure 1. CT chest findings of crazy-paving pattern throughout all lung fields.
Abbreviation: CT, computed tomography.

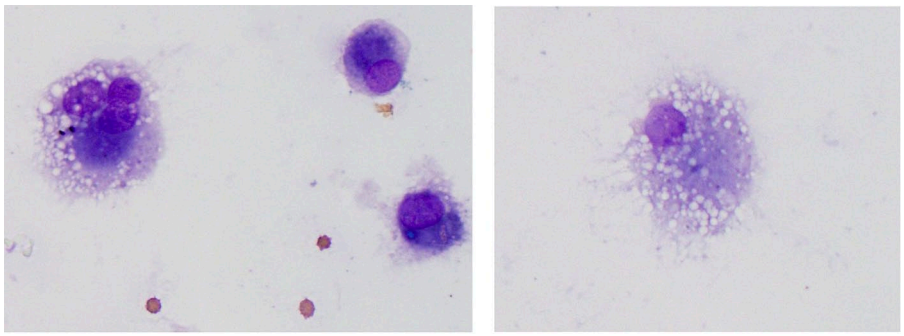

Figure 2. Lipid-laden alveolar macrophages.

volumes with bilateral airspace opacities, and subsequent computed tomography (CT) scan revealed extensive bilateral consolidations and ground-glass with thickened interlobular septa in crazy-paving pattern (Figure 1). Density measured by Hounsfield units in the areas of consolidation ranged from −60 to −112. Laboratory testing showed leukocytosis to 13 100/mm^3 (normal 4.5-11k/mm^3) with absolute eosinophil count of 1200/mm^3 (normal 0-500/mm^3). Both rapid SARS-CoV-2 RNA PCR via nasal swab and serum immunoglobulin G (IgG) testing were negative.

Bronchoscopy with bronchoalveolar lavage (BAL) of the right lower lobe yielded a white blood cell count of 337 cells/mm^3 with 10% eosinophils and 43% macrophages and negative bacterial, fungal, and mycobacterial cultures, as well as ova and parasites examination. Cytology revealed 10% to 15% of alveolar macrophages featuring lipid-laden vacuoles, which were identified by Oil Red O stain (a fat-soluble dye that stains neutral triglycerides and lipids) and negative periodic acid-Schiff (PAS) staining (Figures 2 and 3). *Histoplasma*, *Coccidioides*, *Strongyloides*, *Toxoplasma*, beta-D-glucan, and *Aspergillus* galactomannan serologies were negative. Further history was obtained revealing that for years, patient had treated sinus congestion through copious application of commercially available vapor rub to his nares, as well as using a home humidifier with liquid additive–containing eucalyptus, menthol, and cedar oils. The patient's family also reported he had recently started using the humidifier more frequently by placing his head close to the machine and draping a towel around his head and the humidifier to further concentrate the inhaled vapors.

The patient was diagnosed with exogenous lipoid pneumonia and started on moderate dose corticosteroids, followed by a prolonged taper with gradual improvement in respiratory status over subsequent 6 weeks. Interval imaging showed improved crazy-paving pattern and consolidations.

Discussion

The diagnosis of lipoid pneumonia can be challenging, requiring consistent clinical and cytological findings and a positive exposure history. A history of exposure is imperative to the diagnosis, as clinical features are nonspecific.[8]

Symptoms typically include dyspnea and cough, and presentation may be acute in cases of large volume aspiration or

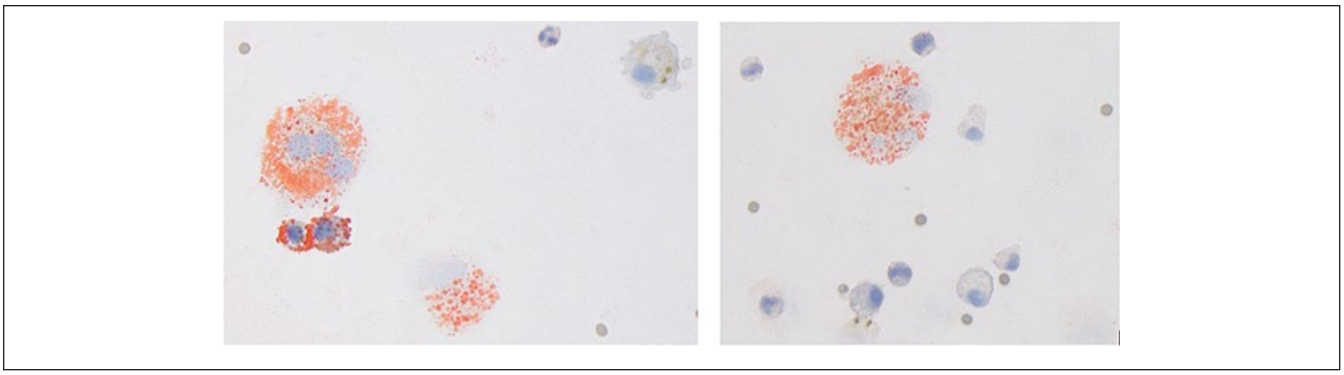

Figure 3. Positive Oil Red O staining.

insidious with chronic, smaller aspirations. Fever, chest pain, hemoptysis, and weight loss have also been described, although are less common.[4] Risk factors include esophageal dysfunction, reflux, altered level of consciousness, and immunocompromised status.[9]

Chest imaging findings may include airspace consolidations, ground-glass opacities with or without interlobular septal thickening (crazy-paving), and nodules or mass-like consolidations.[4,8] Classically, consolidations demonstrate density of −30 to −150 Hounsfield units consistent with fat. The presence of denser aggregates of inflammatory cells or heterogenous involvement of oils with interspersed lower-density, air-filled alveoli renders using measured lung density neither sensitive nor specific.[10]

BAL cytology typically shows lipid-laden macrophages, which may be suggestive of the diagnosis. Lipid-laden macrophages are not specific to lipoid pneumonia; they are commonly found to be elevated in inhalation and aspiration-based diseases, including gastroesophageal reflux disease (GERD) with aspiration pneumonitis, E-cigarette or vaping-associated lung injury (EVALI), cigarette smoking, silicosis, and others. However, the presence of lipid-laden macrophages may prompt gathering of additional associated history.[11-13]

This is an unusual case in which aerosolization of lipids by nasal application of commercially available vapor rub and subsequent home humidifier use is implicated in exogenous lipoid pneumonia. However, identification of a novel route of lipid administration is unfortunately a too common occurrence in the developing understanding of lipoid pneumonia and highlights the difficulties that health care providers face in establishing the exposure and diagnosis. In addition to the commonly identified aspiration of oil-based products intended for enteral consumption (eg, mineral oil laxatives), regular application of oil- or petroleum-based products to the face, including lip glosses and balms, as well as topical decongestants and antitussives, may lead to chronic, asymptomatic aspiration.[8,14] Aspiration of clinically relevant quantities of these products may occur even when used as directed by manufacturers and among those who lack identifiable risk factors for aspiration. Occupational exposures to aerosolized oils may occur among spray painters and those in industrial environments where lipid-containing liquids are used as lubricants, sealants, solvents, coolants, and other applications that lead to aerosolization under high heat or pressure. Notorious cases have arisen among people siphoning automotive fuels and performance fire-eaters, who draw petroleum-based hydrocarbons into their mouths and accidentally aspirate contents prior to expelling.[8,15-17]

Because chronic aspiration of lipid-containing compounds may be asymptomatic and incurred during common, everyday activities, patient histories must be broad enough to capture the relevant exposure while remaining detail-oriented to elicit recall of innocuous-appearing events by patients. We propose the following framework for gathering patient histories based on potential routes of exposure:

1. Use of topical creams, lotions, medications, or cosmetics applied to face, lips, or nares.
2. Oral intake of nonfood substances intended to be either gargled/spit or swallowed, including laxatives, mouthwashes, and prescription, over-the-counter, or traditional medications.
3. In-home or occupational environmental exposures to aerosolized sprays, mists, or other airborne particulate matter.

Exposure to industrial environments and recurrent aspiration symptoms may be identified in a more general pulmonary history and should raise suspicion for lipoid pneumonia, although their absence is unfortunately nonreassuring. Mineral oils in particular are weak triggers of cough and gag reflex and decrease ciliary motility, leading to decreased awareness of aspiration on the part of the patient.[16]

Several other aspects of our patient's case are noteworthy. Mild to moderate pulmonary eosinophilia on BAL and presence of eosinophilic structures on pathology may be seen in patients with lipoid pneumonia. Typically, these levels are below those seen in acute or chronic eosinophilic pneumonia, and a more indolent clinical response to glucocorticoids suggests an alternative diagnosis to atopic or rheumatologic

disease.[9,17-21] The patient's positive SARS-CoV-2 PCR on BAL at the outside hospital likely represents a false positive, in the context of multiple negative nasal swab PCRs, a repeat negative BAL PCR, and negative SARS-CoV-2 antibody testing. The gradual progression of respiratory symptoms and hypoxemia over the course of 4 weeks also suggests an alternate diagnosis.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

ORCID iD

Joshua L. Hoerger https://orcid.org/0000-0001-9261-5886
Brooks T. Kuhn https://orcid.org/0000-0003-0036-1300

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