A 66-Year-Old Man With Subacute Cough and Worsening Dyspnea Previously Diagnosed With COVID-19 Pneumonia

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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.4,5 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...
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/mm³ (normal 4.5-11k/mm³) with absolute eosinophil count of 1200/mm³ (normal 0-500/mm³). 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/mm³ 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.\(^9\)

Symptoms typically include dyspnea and cough, and presentation may be acute in cases of large volume aspiration or...
insidious with chronic, smaller aspirations. Fever, chest
pain, hemoptyisis, and weight loss have also been described,
although are less common. Risk factors include esophageal
dysfunction, reflux, altered level of consciousness, and
immunocompromised status.

Chest imaging findings may include airspace consolida-
tions, ground-glass opacities with or without interlobular
septal thickening (crazy-paving), and nodules or mass-like
consolidations. 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 den-
sity neither sensitive nor specific.

BAL cytology typically shows lipid-laden macrophages,
which may be suggestive of the diagnosis. Lipid-laden mac-
rophages are not specific to lipoid pneumonia; they are com-
monly 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.

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 occur-
rence 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
dehcongestants and antitussives, may lead to chronic, asymp-
tomatic aspiration. Aspiration of clinically relevant quan-
tities 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 applica-
tions that lead to aerosolization under high heat or pressure.
Notorious cases have arisen among people siphoning auto-
 motive fuels and performance fire-eaters, who draw petro-
 leum-based hydrocarbons into their mouths and accidentally
aspire contents prior to expelling.

Because chronic aspiration of lipid-containing com-
 pounds 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 cos-
metics 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 particu-
late 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.

Several other aspects of our patient’s case are noteworthy.
Mild to moderate pulmonary eosinophilia on BAL and pres-
ence 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 pneumo-
nia, and a more indolent clinical response to glucocorticoids
suggests an alternative diagnosis to atopic or rheumatologic

Figure 3. Positive Oil Red O staining.
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.

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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.

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