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Case Report
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Exogenous Lipoid Pneumonia Complicated with Drug Fever in a Patient with Ileus: A Case Report

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Abstract

Introduction: Exogenous Lipoid Pneumonia (ELP) is a rare kind of pneumonia whose pathogenesis constitutes the inhalation or aspiration of a fatty substance. It often manifests as a chronic respiratory illness like interstitial lung diseases. As can be seen from this patient, patients with ELP still need to be alert to the possibility of complicated with other diseases when they have fever symptoms.

Case Report: We make a case report of a 76-year-old female who presented with fever and cough. Chest radiograph revealed findings bilateral consolidation in the lower lobes. Pathology micrograph of the bilateral consolidation showing lipid-filled vacuoles. On further questioning, the patient received a total amount of 500 ml paraffin oil due to intestinal obstruction one month before admission. After anti-infective and anti-inflammatory treatment, the symptom of fever did not improve. However, the patient's temperature returned to normal after intravenous fluids were discontinued.

Conclusion: Our case illustrates an unusual ELP presenting with drug fever that makes differential diagnosis more complicated. Clinicians should be aware of ELP pneumonia, which may manifest as infectious pneumonia.

Keywords: Lipoid pneumonia; Drug fever; Bronchoalveolar lavage fluid

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Introduction

Exogenous Lipoid Pneumonia (ELP) is a rare lung condition because of the inflammatory reaction caused by the presence of foreign fatty substances in the alveoli, its imaging findings are easily misdiagnosed as interstitial pneumonia or lung cancer. Diagnosis confirmation necessitates special staining of the Bronchoalveolar Lavage Fluid (BALF) or lung biopsies [1,2]. Drug fever is particularly problematic whenever it occurs among patients with non-infection, and drug fever can result in overutilization of anti-infectives and other agents trying to treat non-existing infections, possibly resulting in an increase in the risk of complications. By comparison and summary, Baron “et al”. found that all individuals with acute ELP had fever for several days to weeks "while all the patients with chronic ELP had no fever". However, this study did not describe in detail the patients' fever type and peak body temperature [3]. The clinical manifestations of ELP vary, patients mainly presenting chronic cough, and a small number of patients will have chest pain, hemoptysis, weight loss, intermittent fever and so on [4]. The diversity observed with cases of drug fever makes it difficult to form general conclusions. No study has shown a pathogenetic correlation between ELP and drug-induced fever, the complicated with drug fever in present case remind us that fever in ELP patients may not be associated with ELP.

Case Presentation

A 76-year-old never smoking female, was admitted with fever and slight cough for 3 weeks. Fever symptoms occurred on December 06th, 2020 with a thermal peak of 39.5^{o}C. Cough slightly with white foamy phlegm. Chest CT on December 09th, 2020 indicated diffuse inflammation in both lungs. One week after anti-infection treatment with cefoperazone/sulbactam and levofloxacin, reexamination on chest CT showed no improvement in the lung lesions. Then treatment with fluconazole and meropenem for 10 days, the patient's fever did not ease. Her past medical history consisted of Gastroesophageal Reflux Disease (GERD) and cerebral infarction for many years. On December 25th, 2020, the subject was transferred to our hospital for further treatment. Her WBC (White Blood Cell) count was 6.07 × 10^{9} cells/L, N% 84.7%, C-reactive protein was 120 mg/L. Procalcitonin was 0.08 ng/ml. Body temperature was 38.2^{o}C. To rule out infectious fever,

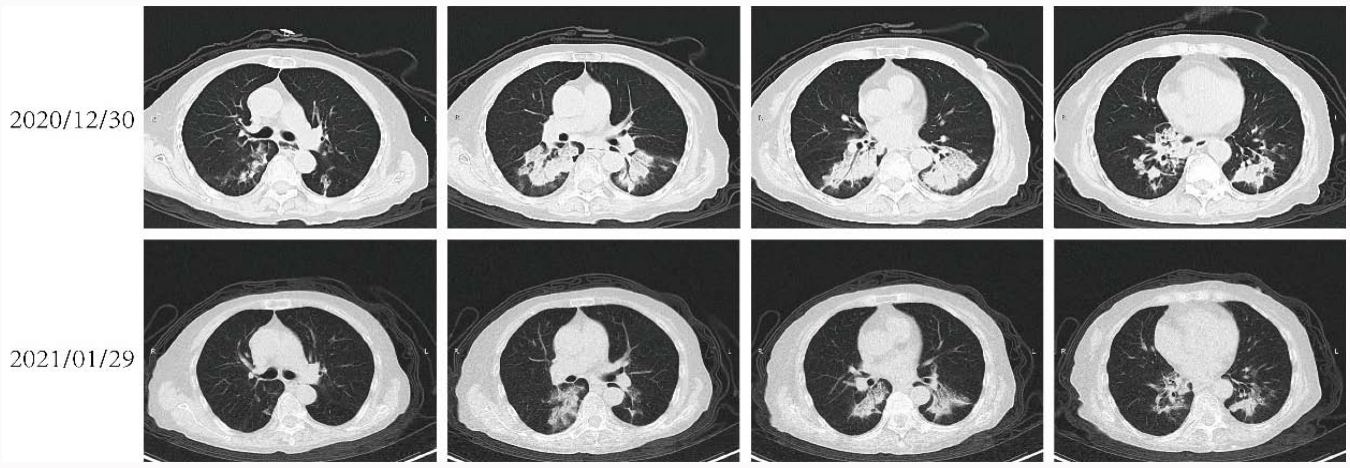

Figure 1: Chest computed tomography scan on admission and three weeks after the initiation of corticosteroid treatment, shows improvement of bilateral consolidation in the lower lobes.

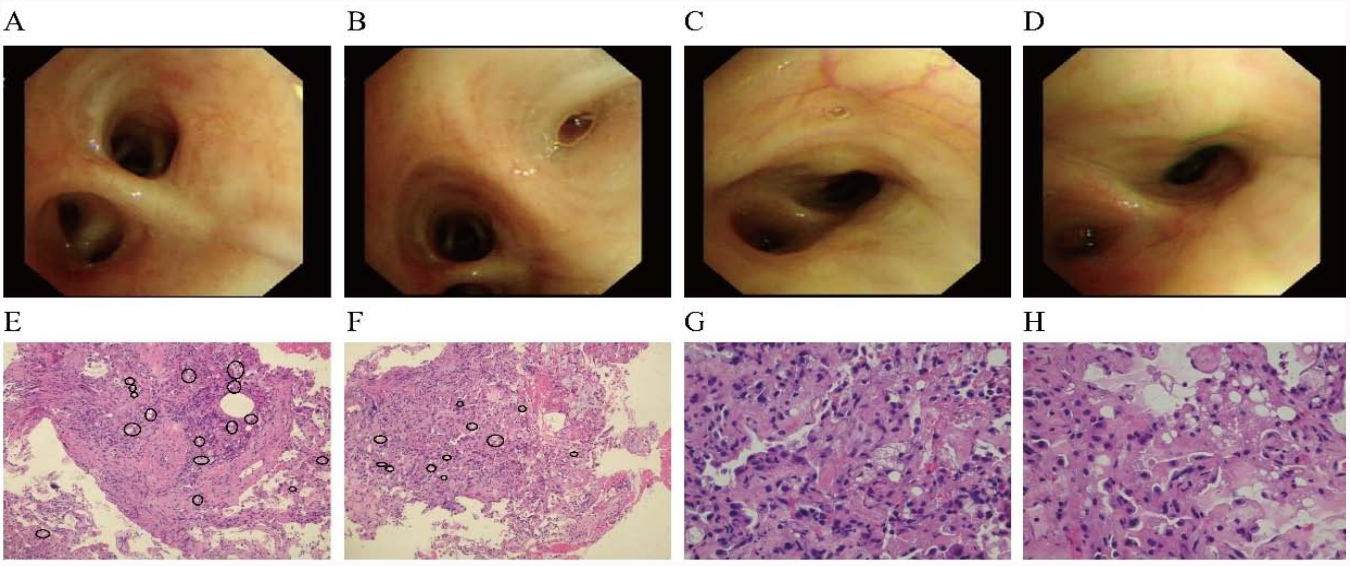

Figure 2: Bronchoscopy showed that the wall of the air tube was mild edematous in the lower lobes (A-D). Hematoxylin and eosin-stained slides with both low (x10, E and F) and high power (x40, G and H) microscopic view of alveolar septum and alveolar lumen with lipid-laden macrophages (indicated by elliptical circle).

on December 28th, 2020, high throughput sequencing of the blood samples was detected, and test results showed that 36 sequences of Epstein-Barr virus and 4 sequences of cytomegalovirus. On December 29th, 2020, blood samples were negative for aspergillus antigen test and cryptococcus gel qualitative test. Chest computed tomography scan on December 30th, 2020, which shows bilateral consolidation in the lower lobes (Figure 1). Ultrasonic bronchoscope examination was performed on December 30th, 2020, reveals that the wall of the air tube was mildly edematous, without of pus or necrosis (Figure 2). Cell classification results of BALF showed that neutrophils were 50%, lymphocytes 20%, histological cells 10%, columnar epithelial cells 20%, and tumor cells were not found. Then the patient continued to be treated with antibiotics for an extra week, nevertheless the patient's fever persisted.

On January 06th, 2021, pathological results of dorsal segment of the lower lobes reported that lipid-filled vacuoles associated with lipid-laden macrophages in alveolar septum and alveolar lumen (Figure 2). On further questioning the patient was hospitalized for intestinal obstruction 1 month before admission, she received a total amount of 500 ml paraffin oil, and aspiration occurred for 3 times. Therefore, the diagnosis of ELP was made. Then, from January 06th, 2021, the patients were given methylprednisolone 60 mg/day for 6 days. From January 12th, 2021, prednisone dose was reduced to 40 mg/day. The puzzle was that the patient still had fever symptoms after anti-infective and anti-inflammatory treatment. After excluding other factors, the possibility of drug fever was considered. Intravenous medication was stopped on January 08th, 2021, and oral medication was retained. The patient's body temperature returned to normal on January 10th, 2021. On January 15th, 2021, the patient had stable vital signs, without fever symptoms, and was discharged with prednisone 30 mg/day oral administration. The patient feels well and without adverse or unanticipated events during prednisone oral administration. The reexamination of chest CT on January 29th, 2021 indicated that the lesion in the lung was improved (Figure 1).

Discussion

ELP is an uncommon type of pneumonitis, resulting from

exogenous lipids of mineral, vegetal, or animal origin [4], which reach the alveoli by inhalation of volatile hydrocarbons [5], or by aspiration of oil-based substances. Most ELP cases originate from mineral oil aspiration present in laxatives and oily nose drops [6]. The typical clinical manifestation of ELP constitutes a chronic cough manifesting with or without dyspnea along with the presence of diffuse interstitials infiltrates on imaging assessment of chest [7]. While, the patient in this case presented with persistent fever as the main clinical feature.

The clinical manifestations of ELP depend on the type, dosage, and frequency of lipids inhaled. Acute heavy inhalation can lead to fever, cough and dyspnea while chronic long-term inhalation may not show symptoms or only mild cough, expectoration, weight loss and other non-specific symptoms [8]. Hemoptysis is uncommon, with only one reported case in English language literature [7]. The symptoms of this patient in present report are insidious onset of cough, as well as fever, without dyspnea, similar to infectious pneumonia. We initially considered infectious fever according to the patient's lung lesions, so we gave adequate anti-infective therapy. However, chest CT reexamination 1 week after anti-infective treatment indicated that the patient's pulmonary lesions had not improved and fever was still present. After the patient's lung lesions were pathologically confirmed to be ELP, we adjusted the treatment plan and added methylprednisolone, but the patient's body temperature was still not well controlled. After excluding other factors, we considered that the patient might have a drug-induced fever. Due to the poor physical condition of the patient and the long duration of fever, there was not enough time to stop intravenous drugs successively to observe the changes in the patient's body temperature, so we chose to stop all intravenous drugs of the patient. The patient had no fever after discontinuation of intravenous drugs. Although we do not know exactly what medication caused the patient's fever, the patient's body temperature returned to normal after the intravenous medication was discontinued, so the diagnosis of drug-induced fever in this patient should be confirmed.

Physical exam findings of ELP are those of interstitial lung disease. The lungs can be clear or have fine rales. As seen in our patient, we could hear distinct rales in the lower lobes of both lungs, which was consistent with the radiographic findings of the patient.

Due to its association with aspiration, the CT scan of ELP is usually patchy ground glass with thickening of intralobular septa and consolidation in both lower lungs along the bronchial vascular bundle [8]. In addition, it can also be shown as isolated nodules with lobes and burrs, or mass shadow [9], and these lesions may have high uptake during PET-CT and are difficult to distinguish from lung cancer.

ELP diagnosis is often a challenge because the symptoms, signs, along with the radiographic results are all a bit nonspecific. Although aspiration is the most common cause of ELP, patients may not be aware of inhaling irritating drugs because repeated small amounts of the fatty substance might not cause a significant cough-stimulating reflex [10]. Notably, not all ELP cases originate from aspiration; some cases result from inhalation and nasal drop. Case reports have demonstrated that ELP can develop among vaper. Chronic inhalation of e-cigarette which contain of vegetable glycerin caused the patient to manifest with insidious onset cough, night sweats, progressive dyspnea on exertion along with fever, and was in respiratory failure on admission to hospital [11]. While, the clinical use of mineral oils is even more widespread. Thus, the history of exposure to exogenous lipids substances is a remarkable clue to the diagnosis of ELP. Histopathological examination is the gold standard for the diagnosis of ELP. Microscopically, foamy lymphocytes in the alveolar space can be seen. Floating oily foamy substance and fat globules are found in BALF, which are also of high diagnostic value for this disease.

It is evident in our case that the patient's diagnosis was delayed for several reasons. First of all, the patient was an elderly woman with fever, so the pulmonary lesions were primitively considered infectious disease. Secondly, there is a lack of detailed inquiry on the specific treatment of intestinal obstruction, causing the omission of a history of chemical irritants inhalation. In addition, the patient had no respiratory symptoms other than a cough, nonspecific clinical features. What's more, this patient had a clear history of cerebral infarction and GERD. A multicenter review revealed an incidence of 80% ELP caused by aspiration in patients with intestinal obstruction and chronic constipation accompanied by GERD while using liquid paraffin and Vaseline as a laxative [6]. This reminds us that patients with a history of chemical irritants aspiration, especially those with GERD or cerebral infarction, should be highly suspicious of ELP.

To date, ELP standardized treatment regimens have not been established. Recommendations for treating ELP are on the basis of clinical experience and not long-term observational studies. Because ELP is often associated with aspiration, prevention is important. Avoiding ongoing exposure, as well as providing supportive care constitutes the main stay of treatment. Antibiotic therapy alone is usually ineffective. Systemic corticosteroid treatment has been utilized successfully in some cases to dampen inflammatory response [12,13]. Nonetheless, corticosteroids might not be applied routinely on account of the severe side effects, and could be utilized if the lung injury is severe and ongoing. It has been reported that corticosteroid therapy on kerosene aspiration was ineffective [14]. In this case our patient responded well to corticosteroids and CT assessments were improved after a month of treatment with corticosteroids. Bronchoscopic Alveolar Lavage (BAL) has treatment implications in some cases. Numerous case reports documented the effectiveness of treatment lung lavage for lipoid pneumonia, which washed away lipids directly, as well as improved lung opacities [15-17]. However, in patients with respiratory failure or severe complications, BAL cannot be performed. Localized lobectomy may also be considered if medical treatment fails. In present case, two BAL were performed on the patient, but the results were not satisfactory.

Conclusion

In conclusion, we report an exogenous lipoid pneumonia case associated with liquefied petrolatum that was complicated with drug fever. To the best of our knowledge, it is the first case which report that ELP complicated by drug fever. The clinical manifestations of ELP vary greatly, ranging from asymptomatic to severe life-threatening. As can be seen from this patient, patients with ELP still need to be alert to the possibility of complicated with other diseases when they have fever symptoms.

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