Respiratory Medicine Case Reports 31 (2020) 101143

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: http://www.elsevier.com/locate/rmcr

Case report

Acute eosinophilic pneumonia following inhalation of turpentine oil: A case report

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ARTICLE INFO

Keywords:
Acute eosinophilic pneumonia
Turpentine oil
Inhalation

ABSTRACT

Acute eosinophilic pneumonia (AEP) is an eosinophilic lung disease associated with environmental substances including smoking. Although the etiology of AEP has not been fully elucidated, it has been hypothesized that IL-33 plays a central role in the pathogenesis of AEP. Turpentine oil, from resins of pine trees, is not only used in paints, but also utilized in experimental animal models of inflammation because it leads to the production of inflammatory cytokines including IL-33. Here, we report the first case of AEP following turpentine oil inhalation. A 67-year-old woman reported using urushiol with turpentine oil to repair home goods. She had fever and persistent cough after turpentine inhalation over a very short period of time. The chest X-ray image showed consolidation in the upper right lung field. Laboratory findings indicated that there was no evidence of infection, collagen vascular diseases, and other allergic diseases that cause pneumonia, but analysis of the bronchoalveolar lavage fluid revealed 29% eosinophils with a small number of lipid-laden macrophages. With these findings, the diagnostic criteria of AEP was met. We rendered a diagnosis of AEP by inhalation of turpentine because no other cause for AEP was identified even with a structured questionnaire survey. The manifestations resolved immediately after steroid therapy. This is the first report of a case of AEP caused by the inhalation of turpentine oil.

1. Introduction

Acute eosinophilic pneumonia (AEP) is characterized by acute onset, severe dyspnea, diffuse consolidation on chest radiographs, or symptomatic and radiographic resolution of pneumonia following steroid treatment [1]. It was first proposed by Allen et al., in 1989 [2], and a modified diagnostic criteria is currently used to diagnose AEP [3]. Elevated eosinophil counts in bronchoalveolar lavage (BAL) can assist with the diagnosis of AEP [4]. Turpentine oil is a pine wood distillate that belongs to a separate class of hydrocarbons called the terpene derivatives. Hydrocarbons, including turpentine, can induce pneumonia and lung injury. To our knowledge, this is the first reported case of AEP caused by the inhalation of turpentine oil.

2. Case presentation

A 67-year-old Japanese woman, who had never smoked, reported repairing ceramics using urushiol with turpentine oil; however, she stopped work immediately due to the sense of foul smell. At this time, only the turpentine oil container had been opened, and the urushiol container had remained unopened. The working time consisted of a few minutes. She reported having fever and dry cough 2 days after inhalation and visited a primary care office for a follow-up from a cerebral hemorrhage. Her past history included cerebral hemorrhage but no sequelae and no allergies, asthma, or atopic illness. She denied being exposed to animals, including birds. She used no prescription medications or healthcare supplements. In the primary care office, the chest X-ray image showed consolidation in upper right lung field, and she was

Abbreviations: AEP, acute eosinophilic pneumonia; BAL, bronchoalveolar lavage; CRP, C-reactive protein; GGO, ground-grass opacity; BALF, bronchoalveolar lavage fluid; ELP, Exogenous lipoid pneumonia; ILC2, Group2 innate lymphoid cells; Th2, T helper 2.

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https://doi.org/10.1016/j.rmcr.2020.101143
Received 1 March 2020; Received in revised form 21 June 2020; Accepted 24 June 2020
Available online 2 July 2020
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Table 1
Results of vital sign measurements, laboratory tests, and BALF analysis.

Measurements	Primary care office	Our Hospital
Vital signs		
Body temperature (°C)	38.7	38.6
Blood pressure (mmHg)	100/76	134/83
Pulse rate (beats/min)	110	93
Respiratory rate (breaths/min)	14	13
Oxygen saturation in ambient air (%)	95	95
Laboratory findings		
Hematology		
WBC (/μL)	5840	4840
Neut (%)	71	75
Lymp (%)	20	15
Eos (%)	1.5	2.6
Biochemistry		
AST (U/L)	35	29
ALT (U/L)	52	43
Cr (mg/dL)	0.58	0.48
LDL (mg/dL)	NA	116
HDL (mg/dL)	NA	80
TG (mg/dL)	NA	49
Serology		
CRP (mg/dL)	10.8	11.8
IgE (mEq/L)	NA	8
ANA (index)	NA	negative
PR3-ANCA (EU)	NA	negative
MPO-ANCA (EU)	NA	negative
Beta-D-glucan (pg/mL)	NA	negative
BALF		
cell count (/mL)	NA	4.39 × 106
Neut (%)	NA	2
Lymp (%)	NA	45
Eos (%)	NA	29

Increase in body temperature and CRP at the primary care office and our hospital. BALF analysis shows elevated eosinophil ratio.

diagnosed with bacterial pneumonia. Treatment with tazobactam/piperacillin was initiated for 3 days; however, the fever did not resolve, and the pulmonary opacity of the chest X-ray image in the upper right lung field was enlarged. BAL was deemed necessary for diagnosis, and she was referred to our hospital. Vital signs noted at our hospital are described in Table 1. Her systemic examination was unremarkable, except for a reduction in respiratory sounds on the right back. There was no rash or lymphadenopathy. Laboratory findings revealed elevated levels of C-reactive protein (CRP), but negative auto-immune antibodies, normal low density and high density lipoproteins, and normal IgE (Table 1). Computed tomography of the chest revealed consolidation with ground-glass opacity (GGO) in the posterior segment of the right upper lobe and patchy GGO in segment 6, with slight pleural effusions (Fig. 1). The pulmonary opacity was present in the right lung only. Bronchoalveolar lavage fluid (BALF) was obtained from the B^2 bronchus. Analysis revealed 4.39×10^6 nucleated cells per mL, of which 2% were neutrophils, 45% were lymphocytes, and 29% were eosinophils (Table 1). We found that macrophages were phagocytosing lipids (Fig. 2). Gram stain and cultures of infectious agents, including bacterial, fungal, mycobacterial, and viral pathogens, were negative. We used a structured questionnaire to identify other causes of AEP; e.g. Eosinophilic pneumonia caused by other chemicals including prescription medications and healthcare supplements was excluded, however, evidence of other causes was not found; therefore, we suspected that the patient had developed AEP from inhalation of turpentine oil. High-dose (1 g) methylprednisolone pulse therapy was initiated, which was transitioned to oral prednisolone (30–10 mg, daily). Tazobactam/piperacillin was discontinued by day 1. Her fever improved (36.3 °C) and oxygen saturation (ambient air) was 97% by hospital day 3; the chest X-ray image showed an improvement in the shadow of the upper right lung field (Fig. 3). The patient had been on corticosteroids for 9 days and tapered off prednisolone on hospital day 10. The rate of peripheral eosinophil count was 0.5% on hospital day 3, 0.3% on hospital day 6, and 1.9% on hospital day 9. She did not have any recurrence after discontinuing prednisolone and was discharged on hospital day 11. The lungs showed improvement without shadow on the chest X-ray image; therefore, we believed that lung damage was absent.

3. Discussion

In this report, we describe a case of AEP induced by the inhalation of turpentine oil. AEP is a severe and rapidly progressive lung disease that can cause fatal respiratory failure. In many cases, the cause of AEP in patients cannot be identified (idiopathic AEP), while some cases are caused by smoking and inhalation of dust or drugs [1,5]. Briefly, the

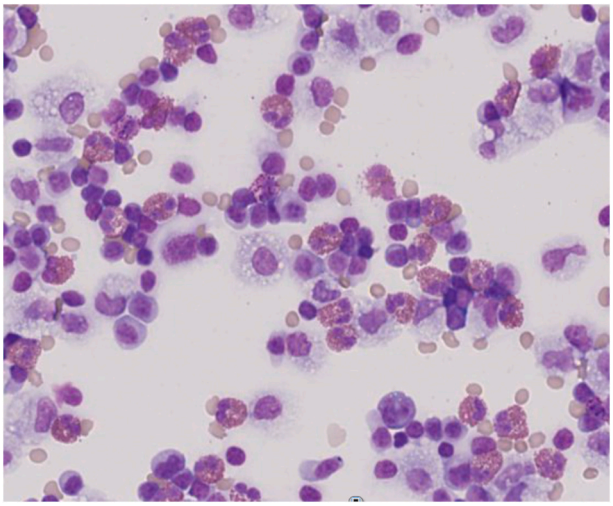

Fig. 2. Giemsa stain of the bronchoalveolar lavage fluid. Representative image showing many eosinophils and lipid-laden macrophages. Original magnification, × 800.

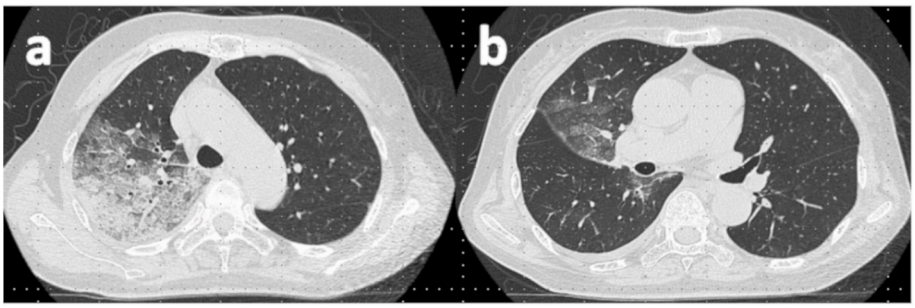

Fig. 1. Computed tomography of the chest at hospitalization. (A) Consolidation with ground-glass opacity (GGO) in posterior segment of right upper lobe. (B) Patchy GGO in segment 6 with slight pleural effusions.

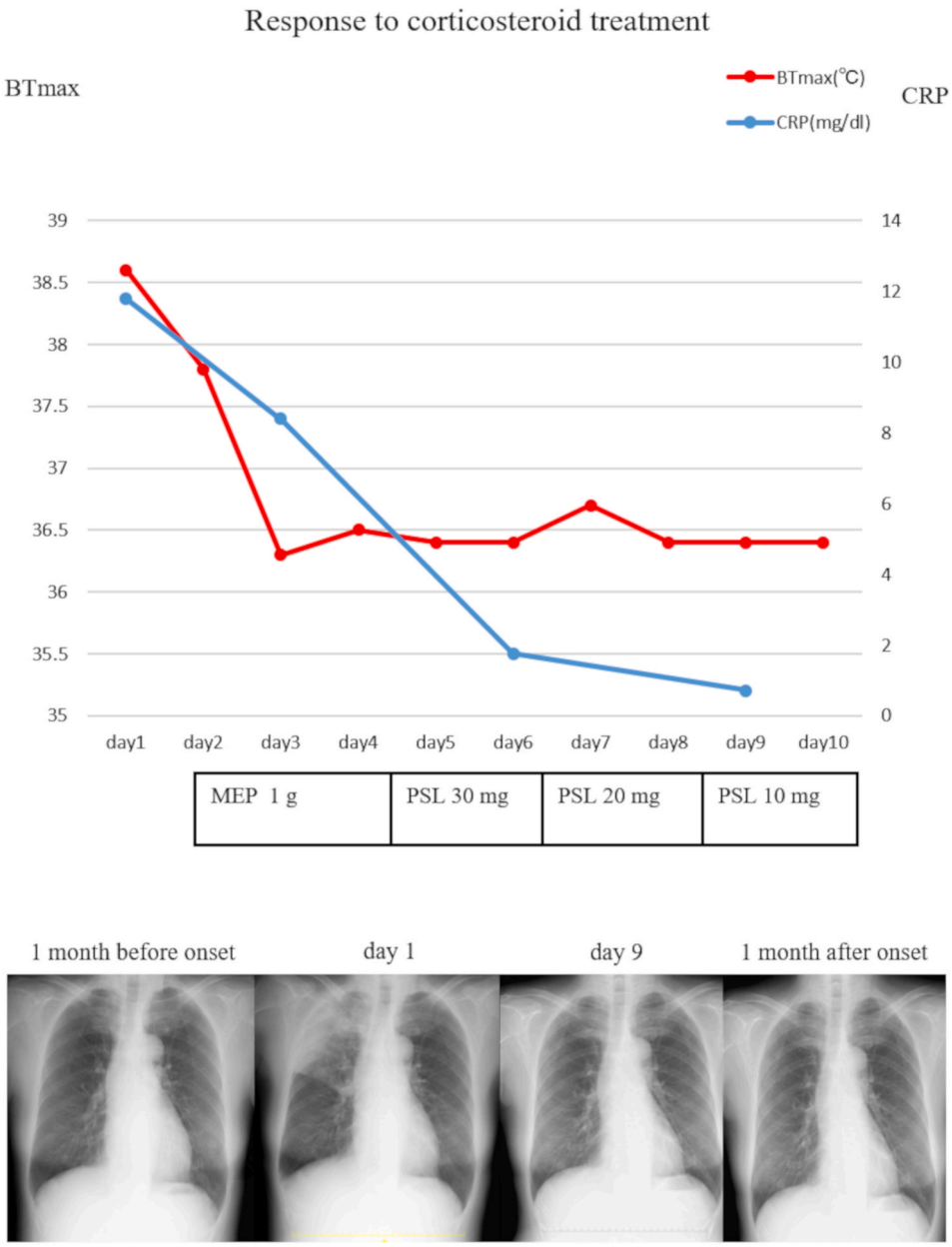

Fig. 3. Response to corticosteroid treatment. Body temperature and CRP levels were measured daily for 9 days of corticosteroid treatment. Body temperature was stable in the normal range on day 10. Chest X-ray imaging was performed 1 month before onset, 1 month after onset, and on days 1 and 9 of corticosteroid treatment. BTmax, temperature maximum; CRP, C-reactive protein; MEP, methylprednisolone; PSL, prednisolone.

commonly used criteria for diagnosis of AEP is as follows: acute onset of respiratory disease, pulmonary infiltrates on chest radiography, lung eosinophilia with >25% eosinophils on BAL or eosinophilic pneumonia on lung biopsy and absence of eosinophilic lung disease [3]. Diagnosis can be established using BAL and treatment with corticosteroids shows rapid and drastic treatment efficacy without recurrence [4]. Our patient met all criteria, and her symptoms improved drastically following corticosteroid treatment, with no recurrence.

Although the pathogenesis of AEP remains incompletely clarified, it has been hypothesized that alveolar epithelial injury following exposure to inhaled antigens or drugs can activate inflammatory pathways, leading to secretion of IL-25 and IL-33, which subsequently simulate group 2 innate lymphoid cells (ILC2) and facilitate T helper 2 (Th2) immune response [3,6]. Indeed, increased levels of the cytokines, IL-5 and IL-33, have been reported in BALF and in peripheral blood of patients with AEP [7–9]. Most importantly, it has been postulated that IL-33 plays a central role in the pathogenesis of AEP since epithelial cell injury can induce robust IL-33 production and activate ILC2 [3]. Turpentine oil is pine wood distillate that belongs to a separate class of volatile hydrocarbons called terpenes. Terpenes are classified into monoterpenes, sesquiterpenes, and diterpenes, depending on the carbon units. The main components of turpentine oil are the monoterpenes ($C_{10}H_{16}$), dimers of isoprene, e.g., alpha-pinene, beta-pinene, or 3-carene found in nature [10]. Sesquiterpenes are found in latex-producing plants, and diterpenes are used as an anticancer drug such as paclitaxel and its derivatives [11]. Turpentine oil is used a tool for painting, but is known as an inducer of experimental inflammation and tissue injury. Of note, an *in vivo study* has shown that gene expression of IL-33 was increased in injured tissue after injection of turpentine oil in mice and that the IL-33/ST2 pathway plays a key role in the pathogenesis of acute inflammation induced by turpentine oil [12]. Given that IL-33 is significantly associated with the pathogenesis of AEP,

turpentine oil may induce AEP though induction of IL-33.

On the other hand, aspiration or inhalation of hydrocarbons typically causes chemical pneumonitis; the mechanisms are direct injury to the pulmonary parenchyma, disruption of the lipid surfactant layer, and destruction of alveolar and capillary membranes, leading to increased vascular permeability as well as edema and collapse of distal airways and alveoli. However, oil containing hydrocarbons can cause lipoid pneumonia [13]. Additionally, Takamizawa et al. have reported acute eosinophilic pneumonia induced by inhalation of acetylene, classified as a hydrocarbon, in a 17-year-old man, who developed respiratory symptoms 12 hours after inhalation of acetylene over a few seconds [14]. Thus, hydrocarbons can cause not only chemical pneumonitis but also AEP. To date, two cases of chemical pneumonitis due to inhalation of turpentine have been reported [15,16]. It should be noted that a case of asthma caused by turpentine during art painting has been reported, wherein asthma symptoms tended to appear after 30–60 minutes of turpentine exposure [17]. In the patient, an increased proportion of eosinophils in sputum was found 24 hours after the turpentine inhalation. Over all, we postulated that inhaled volatile turpentine caused alveolar epithelial injury in this case and Th2 immune response was activated through IL-33 production.

In the present case, allergy tests for turpentine oil were not performed; the specific test is only performed by a limited number of laboratories. We were hesitant to administer a challenge test to our patient due to ethical considerations. Instead, we used a structured questionnaire to exclude other causes for the AEP, and found no other cause in this case. A differential diagnosis was exogenous lipoid pneumonia (ELP) because lipid-laden macrophages were observed. ELP typically results from episodes of aspiration or inhalation of animal fat, minerals, or vegetable oils, while endogenous lipoid pneumonia can be caused by hyperlipidemia [18]. In our case, there was no evidence of hyperlipidemia. The percentage of neutrophils in BALF is increased in patients with lipoid pneumonia [19]; however, there was no increase in the percentage of neutrophils on BALF in our case. The eosinophil ratio in BALF samples was >25%; therefore, we presumed that the turpentine oil had caused an allergic reaction in the lung, instead of lipoid pneumonia. This speculation is concordant with the excellent response to steroid therapy that we observed, with an improvement of AEP without persistent lung damage; although treatment failure can occur in patients with AEP and with an initial normal peripheral eosinophil count, the patient had a favorable response and did not have any recurrence after discontinuing prednisolone [20].

To the best of our knowledge, we believe that this is the first report of a case of AEP caused by the inhalation of turpentine oil. Further, differences in exposure limit our comparability across the three cases. We conclude that inhalation by turpentine can cause alveolar epithelial injury and allergic inflammation.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent for publication of clinical details and clinical images was obtained from the patient.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed.

Funding

Not applicable as no funds were procured or used for the purpose of any research or manuscript writing related to this case report.

Authors' contributions

YU and SO contributed to decision of treatment, collecting clinical data, data analysis, and writing the manuscript. TT, YK, YM, TS, and YO contributed to discussions about the patient. NH, KD, and YY were responsible for writing. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

Not applicable.

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