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CASE REPORT

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Treatment of electronic cigarette or vaping product use-associated lung injury (EVALI) by corticosteroid and low-dose pirfenidone: Report of a case

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Abstract

Electronic (e)-cigarette or vaping product use-associated lung injury (EVALI) is a novel and potentially lethal disease first reported in the United States. We report the case of a 56-year-old man who presented to our hospital with dyspnoea and cough lasting for 2 months after using an e-cigarette for approximately 50 puffs over 2 weeks. Physical examination revealed crackles in the left lower lung. High-resolution computed tomography (HRCT) showed consolidation and ground-glass opacities in both lungs. The baseline forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO) were 65.7% and 63.9% of the predicted, respectively. Lung biopsy revealed organizing pneumonia with focal fibrosis. In addition to prednisolone, he was treated with a low-dose pirfenidone (200 mg three times per day) due to the persistence of a mild cough, exertional dyspnoea and basal crackles after discharge. His symptoms and FVC significantly improved, but the recovery of the DLCO was slow. The follow-up HRCT demonstrated only minimal fibrotic changes. To our knowledge, this was the first reported case of EVALI successfully treated with a combination of corticosteroid and antifibrotic agents.

KEYWORDS

corticosteroid, e-cigarette or vaping product use associated lung injury (EVALI), organizing pneumonia, pirfenidone

INTRODUCTION

Electronic (e)-cigarette or vaping product use-associated lung injury (EVALI) is a novel disease defined by the US Centers of Disease Control and Prevention in response to a multi-state outbreak of severe lung illness, first identified in August 2019.[1] Patients with EVALI may present with non-specific symptoms, such as dyspnoea or cough, and their imaging results also vary, making it difficult to detect and diagnose.[2,3]

The optimal treatment strategies of EVALI are yet to be established. Pirfenidone is an antifibrotic agent which has been widely used in the treatment of idiopathic pulmonary fibrosis (IPF) and other interstitial lung diseases.[4–6] Recently, several studies suggested that it may be of benefit in the management of fibrotic complications after acute lung injuries.[7,8] Herein, we report the long-term clinical outcomes of an adult patient with EVALI who was treated with corticosteroids and a low-dose pirfenidone.

CASE REPORT

A 56-year-old man presented to our hospital with exertional dyspnoea and cough lasting for 2 months after using an e-cigarette for approximately 50 puffs over 2 weeks, which he stopped thereafter. His e-cigarettes were purchased abroad and had unknown ingredients, and he denied adding additional organic compounds. His past history was notable for a smoking history of 50 pack-years, but he had been previously asymptomatic.

Upon admission, the patient's consciousness was clear. His vitals were as follows: body temperature, 36.5°C; blood pressure, 116/69 mmHg; respiratory rate, 19 per minute; and heart rate, 90 beats per minute. The resting oxygen saturation was 94%. Chest auscultation revealed crackles in the left lower lung. Laboratory data showed a haemoglobin level of 12.3 g/dl and a leucocyte count of 8370 cells/L. All autoimmune profile parameters were within normal limits.

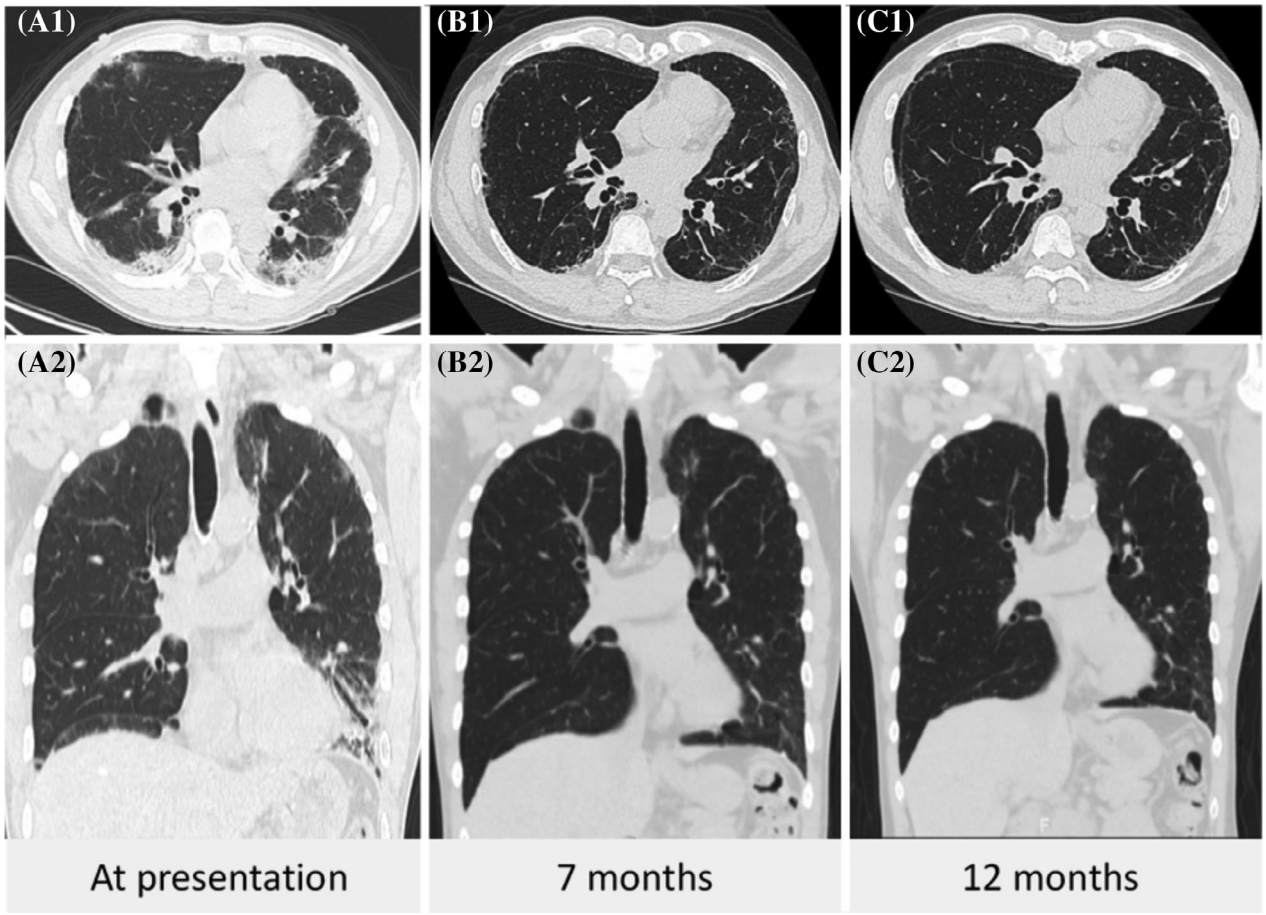

FIGURE 1 Serial axial (A1, B1, C1) and coronal (A2, B2, C2) images of chest computed tomography at presentation, 7 months and 12 months, respectively

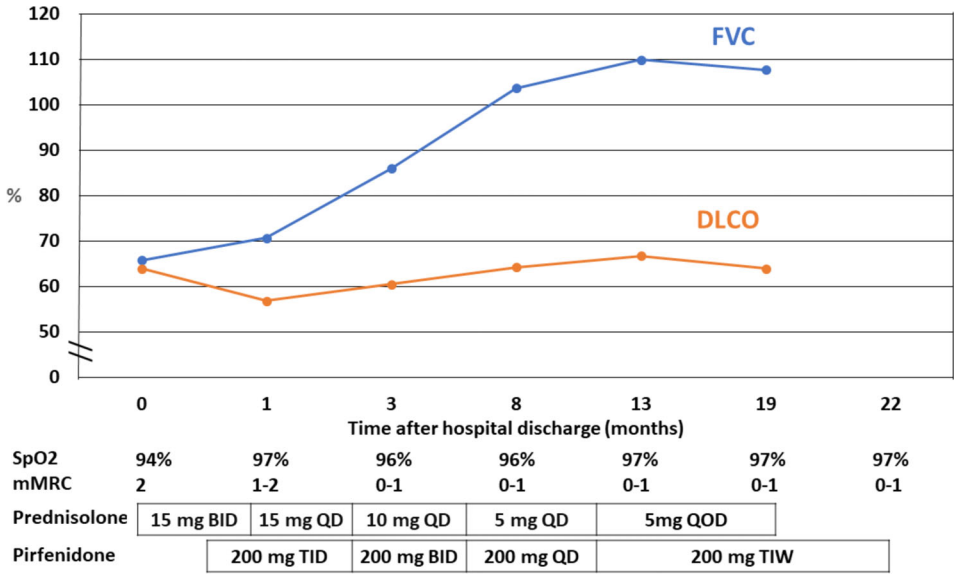

FIGURE 2 Serial pulmonary function testing results (% of predicted) with corresponding dosage of prednisolone and pirfenidone below. Blue line, forced vital capacity; orange line, diffusing capacity for carbon monoxide. BID, twice a day; mMRC, modified Medical Research Council dyspnoea scale; QD, once a day; QOD, every other day; TID, three times a day; TIW, three times a week

Neither blood nor sputum cultures showed significant growth. The immunoglobulin E level was 127 IU/ml, but the serum screening test result for common allergens was negative. High-resolution computed tomography (HRCT) revealed patchy consolidation, ground-glass opacification and traction bronchiectasis in the bilateral lower lungs (Figure 1). At baseline, the pulmonary function test showed that his forced vital capacity (FVC) was 65.7% of the predicted value, while the forced expiratory volume in the first second (FEV1) was 76.3% of the predicted value, leading to an FEV1 to FVC ratio (FEV1/FVC) of 94.9. Lastly, the diffusion capacity for carbon monoxide (DLCO) was 63.9% of the predicted value. Bronchoscopy did not reveal gross pathological abnormalities, and microbiological studies of the bronchoalveolar lavage fluid yielded no significant findings. He underwent biopsy of the left lower lobe through a video-assisted thoracoscopic surgery, and the pathology revealed organizing pneumonia with focal fibrosis but without honeycombing. EVALI was diagnosed based on the CDC's criteria.[9]

Oral prednisolone was administered at an initial dose of 15 mg twice daily, and his respiratory symptoms and oxygen saturation gradually improved. Two weeks after hospital discharge, pirfenidone therapy was initiated due to a residual mild cough, exertional dyspnoea and bibasilar crackles noted in the outpatient clinic. The initial dose of pirfenidone was 200 mg three times per day and his cough subsided 1 week later. Pulmonary function tests showed gradual improvement in the FVC and FEV1, but the recovery of the DLCO was slow (Figure 2). The doses of both oral prednisolone and pirfenidone were gradually tapered. The follow-up HRCT demonstrated only minimal fibrotic changes in the lower lobes (Figure 1). The total duration of prednisolone treatment was 19 months. The course of pirfenidone therapy was prolonged due to persistence of bibasilar crackles and slow recovery of DLCO during follow-up. Pirfenidone was finally discontinued 22 months after discharge because of no exertional dyspnoea and the DLCO value had reached a plateau. No adverse effects from either drug were observed throughout the course of treatment.

DISCUSSION

In this report, we describe the first adult case of EVALI in Taiwan. This patient showed notable long-term clinical improvements following a combination therapy with corticosteroid and a low-dose pirfenidone. To our knowledge, such a treatment strategy for EVALI has not been reported in the literature.

The natural history and optimal management of EVALI remain unclear and few previous studies have addressed the long-term impact of current therapies on its long-term outcomes. In the largest survey of 2807 patients according to the CDC, as of 18 February 2020, the mortality rate was 2.42%.[10] The risk factors included older age (>35 years), history of asthma, obesity, cardiac disease and a mental health condition.[11] Nevertheless, few previous studies have addressed its long-term impacts on lung function, exercise performance and quality of life.

The optimal treatments for EVALI are still yet to be established. Several recent studies suggested that corticosteroids may be beneficial for these patients,[12–14] but it is also possible for patients to recover without corticosteroids or by avoiding vaping. Moreover, the dosage and duration of corticosteroid use varied widely in previous reports.[12–14] In a case series of hospitalized EVALI cases, the most typical steroid regimen was methylprednisolone 40 mg every 6–12 h.[13] The patients were discharged on a prednisone taper, with a median steroid use of 24.5 days. In that study, all patients had complete resolution of symptoms and ground-glass opacities on HRCT within 3 weeks.[13] In another study of 98 patients, systemic corticosteroids were administered to 84% of patients for at least 7 days, but clinical improvement was attributed to the use of glucocorticoids in only half of them.[14] It is still unknown whether corticosteroid can have an impact on mortality and long-term outcomes of EVALI.

In the acute stage of EVALI, both obstructive and restrictive spirometry patterns have been reported, and often accompanied by a reduced DLCO.[15–19] Improvements in these parameters after corticosteroid treatment, however, varied widely between previous studies.[15,16] In our case, the DLCO was still abnormal 19 months after discharge despite significant improvements in symptoms and spirometry. Neither evidence of previous lung disease nor pulmonary hypertension was observed in our patient. The slow recovery of his DLCO may suggest some residual lung fibrosis and irreversible damage to the blood gas barrier by EVALI, although the possibility of subclinical lung diseases due to long-term smoking cannot be totally excluded.

Patients with organizing pneumonia generally respond well to corticosteroid therapy, with a 5-year survival of 73%.[20] About a quarter of these patients, however, presented with progressive fibrosis.[21] These patients had a poorer outcome[22] and might benefit from immunosuppressants therapies including azathioprine, cyclophosphamide and mycophenolic acid.[20]

No previous studies have used antifibrotic agents (nintedanib and pirfenidone) in the treatment of EVALI. Pirfenidone has been considered as a potential therapeutic option for acute lung injury and acute respiratory distress syndrome (ARDS) because of its antifibrotic and anti-inflammatory actions.[23,24] In animal studies, e-cigarette vapour has been shown to alter fibroblast viability and further promote lung fibrosis by increasing the expression of connective tissue growth factor and tumour growth factor-beta 1 in fibroblasts.[25,26] Therapeutic benefits of combined glucocorticoid and pirfenidone have been reported in lung fibrosis due to H1N1-related ARDS,[7] and in two Chinese patients suffering from severe inhalation lung injury due to burning smoke bomb.[8] The encouraging experience from our case provides insights into the potential benefits of pirfenidone for EVALI and other lung injuries with incomplete or poor responses to corticosteroid therapy.

The main limitation of our report was the lack of a control group, as the improvements in our case might be attributed to the natural course of EVALI. Second, no results of pulmonary function were available before EVALI, although our patient was previously asymptomatic. In addition, the effects of pirfenidone at higher dose were not evaluated. The main reason for using a low-dose pirfenidone was that the patient could not afford the cost of higher doses, as this was an off-label use. In a post-marketing surveillance of pirfenidone in Japan, 24.8% of patients with IPF were on a dose ≤600 mg per day.[27] A recent real-world study revealed no difference in its effectiveness between patients treated with daily doses higher and less than 1200 mg.[28] On the other hand, the body mass index of our patient was only 21.2 (kg/m^2), which might also contribute to the clinical benefits as well as the good tolerance of this regimen.

In conclusion, EVALI is a novel and potentially lethal disease. Experience from this case suggests that combined therapy with corticosteroid and an antifibrotic agent may confer a therapeutic benefit for moderate to severe EVALI. The addition of pirfenidone may be indicated for EVALI patients with persistent symptoms or evidence of lung fibrosis after corticosteroid therapy. Our results, however, should be confirmed by prospective clinical trials. Further studies are also required to investigate the therapeutic implications of histopathology EVALI, and the efficacy of this novel strategy in patients with other lung injuries.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

Chia-Hao Wu contributed to the literature search and drafting of the manuscript. Ting-Yu Liao and Yung-Hsuan Chen contributed to the concept of work. Ping-Hung Kuo provided a substantial contribution to the concept of the work and revision of the manuscript. All authors have reviewed and approved the final version of the manuscript.

ETHICS STATEMENT

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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