Fatal e-cigarette or vaping associated lung injury (EVALI): a first case report in Europe

To the Editor:

Numerous cases of e-cigarette, or vaping, associated lung injury (EVALI) have recently prompted an investigation of the outbreak in the USA [1]. Only two non-fatal cases have been reported so far in Europe: one case of hypersensitivity pneumonia in the UK after the use of flavoured e-cigarette liquid by a young adolescent [2], and one US imported case recently described in Spain [3]. To our knowledge, this is the first report of a fatal EVALI case in Europe.

An 18-year-old previously healthy man was admitted to the infectious diseases ward presenting with haemoptysis, coughing and progressive dyspnoea evolving for 5 days. He reported regular tobacco and cannabis smoking for the past 6 months and the use of e-cigarette containing nicotine and cannabidiol (CBD; 5 $mg{\cdot}mL^{-1}$) for three consecutive days in the three weeks prior to the onset of symptoms. The e-liquid used had been bought over the counter in a Belgian shop, but its country of production is unknown. On admission, lung computed tomography images showed bilateral poorly defined centrilobular nodular infiltrates with bronchial wall thickening. Blood tests showed neutrophilic leukocytosis (13 890 neutrophils per µL) and moderate elevation of C-reactive protein levels (86·3 $mg{\cdot}L^{-1}$). Extensive infectious workup performed early during hospitalisation (blood, sputum and bronchoalveolar lavage (BAL) cultures, urinary *Streptococcus pneumoniae* and *Legionella* antigens, multiplex PCR assay for bacterial, fungal and viral pathogens on BAL) was unrevealing. The BAL was not well tolerated by the patient and had to be rapidly interrupted due to severe oxygen desaturation. Priority was thus given to the microbiology and virology samples. Analyses of bronchial lavage showed 45% of macrophages, 42% of neutrophils, 7% of lymphocytes and 6% of eosinophils. The pathologist did not see any giant cells nor foamy, iron- or haemosiderin-laden macrophages, and *Pneumocystis jirovecii* was not detected by microscopy with staining. HIV and autoimmune serologic testing (antinuclear antibodies, antineutrophil cytoplasmic autoantibodies, rheumatoid factor) were negative and the cardiac ultrasound was normal. After a 5-day course of empirical antibiotic therapy, the patient presented respiratory failure and was transferred to the intensive care unit. He underwent intubation, mechanical ventilation and finally veno-venous extracorporeal membrane oxygenation (ECMO). At that time, a lung biopsy was performed, immediately followed by the initiation of glucocorticoids (methylprednisolone 3 $mg{\cdot}kg^{-1}$ for 3 days followed by tapering doses over 14 days). Biopsy samples showed acute diffuse alveolar damage with fibrosis (figure 1). Despite a slight transient improvement, the patient developed ECMO bleeding complications and ventilator-associated pneumonia, requiring the conversion of veno-venous ECMO to central veno-arterial ECMO. He improved slightly under piperacillin-tazobactam but shortly after presented *Wautersia paucula* bacteraemia. Despite adequate antibiotic coverage, he developed refractory septic shock and died 4 weeks after admission from multiple organ failure. The consumption of e-cigarettes containing nicotine and CBD 3 weeks before the onset of symptoms appears to be the most probable cause of lung injury developed by this patient.

This patient meets the criteria proposed by Layden *et al.* [4] for confirmed cases of EVALI: the use of an e-cigarette within the 90 days preceding onset of symptoms, a compatible radiological picture [5] and the exclusion of alternative diagnoses. The pathological [6] pattern was also consistent with this diagnosis. Of interest, vitamin E (alpha tocopherol) and vitamin E acetate were not detected in the vaping fluid by

@ERSpublications
Numerous cases of e-cigarette or vaping associated lung injury (EVALI) have been described, mainly in the US and Canada. However, public health and medical communities need to be aware that this deadly disease may occur outside North America. https://bit.ly/2UzZJpI

Cite this article as: Marlière C, De Greef J, Gohy S, *et al*. Fatal e-cigarette or vaping associated lung injury (EVALI): a first case report in Europe. *Eur Respir J* 2020; 56: 2000077 [https://doi.org/10.1183/13993003.00077-2020].

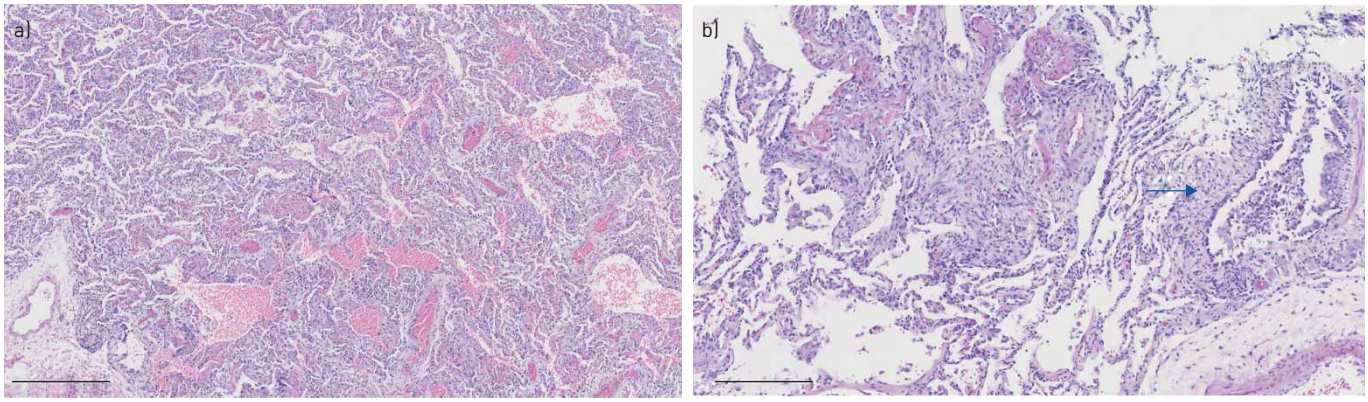

FIGURE 1 a) Diffuse alveolar damage characterised by hyaline membranes, capillary congestion and oedema. Inflammation is sparse. Scale bar 500 μm. b). Alveolar septal thickening due to organising fibrosis and remnants of hyaline membranes. Note the peribronchiolar predominant organisation (arrow). Scale bar 250 μm.

ultraperformance liquid chromatography coupled with UV detection (Waters Acquity, Milford, MA, USA). Vitamin E acetate, a substance used as diluent in e-liquids, has recently been suggested as a potential cause of EVALI in the USA [7].

The EVALI outbreak may now be affecting Europe and public health and medical communities need to be aware of this finding. We urge European clinicians to report suspected cases to local health authorities. Moreover, we suggest a coordinated European effort to register EVALI cases across different countries. The absence of vitamin E acetate in vaping fluid used by our patient is intriguing and highlights the need for further research, as different substances may play a role in triggering EVALI. The creation of a European registry would enable quick and coordinated research on the aetiology and the biological mechanisms of this new and deadly disease.

Camille Marlière[1,7], Julien De Greef[1,2,7], Sophie Gohy[3], Delphine Hoton[4], Pierre Wallemacq[2,5], Luc-Marie Jacquet[6] and Leïla Belkhir[1,2]

[1]Dept of Internal Medicine and Infectious Diseases, Cliniques universitaires Saint Luc, Brussels, Belgium. [2]Louvain Centre for Toxicology and Applied Pharmacology (LTAP), Institut de recherche expérimentale et clinique (IREC), UCLouvain, Brussels, Belgium. [3]Pneumology Dept, Cliniques universitaires Saint Luc, Brussels, Belgium. [4]Pathology Dept, Cliniques universitaires Saint Luc, Brussels, Belgium. [5]Clinical Chemistry Dept, Cliniques universitaires St Luc, Brussels, Belgium. [6]Cardiac ICU Dept, Cliniques universitaires Saint Luc, Brussels, Belgium. [7]These authors have contributed equally to this work.

Correspondence: Julien De Greef, Dept of Internal Medicine and Infectious Diseases, Cliniques universitaires Saint Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium. E-mail: julien.degreef@uclouvain.be

Received: 14 Jan 2020 | Accepted after revision: 17 March 2020

Acknowledgements: We thank Mariana Andrade who provided writing and editorial assistance. No commercial funding was received for this purpose.

Author contributors: C. Marlière, J. De Greef, D. Hoton, L-M. Jacquet, S. Gohy and L. Belkhir were involved in the patient's care. P. Wallemacq performed the e-liquid analysis. C. Marlière and J. De Greef wrote the draft. D. Hoton sent and commented on the illustration. D. Hoton, P. Wallemacq, L-M. Jacquet, S. Gohy and L. Belkhir revised, commented on and corrected this manuscript with their individual expertise. All authors approved the final version.

Conflict of interest: None declared.

References

1 Lozier MJ, Wallace B, Anderson K, *et al.* Update: demographic, product, and substance-use characteristics of hospitalized patients in a nationwide outbreak of E-cigarette, or vaping, product use-associated lung injuries — United States, December 2019. *MMWR Morb Mortal Wkly Rep* 2019; 68: 1142–1148.
2 Nair N, Hurley M, Gates S, *et al.* Life-threatening hypersensitivity pneumonitis secondary to e-cigarettes. *Arch Dis Child* 2019; in press [https://doi.org/10.1136/archdischild-2019-317889].
3 Casanova GS, Amaro R, Soler N, *et al.* An imported case of e-cigarette or vaping associated lung injury in Barcelona. *Eur Respir J* 2020; 55: 1902076.
4 Layden JE, Ghinai I, Pray I, *et al.* Pulmonary illness related to E-cigarette use in Illinois and Wisconsin — preliminary report. *N Engl J Med* 2019; 382: 903–916.
5 Henry TS, Kanne JP, Kligerman SJ. Imaging of vaping-associated lung disease. *N Engl J Med* 2019; 381: 1486–1487.

6 Butt YM, Smith ML, Tazelaar HD, *et al.* Pathology of vaping-associated lung injury. *N Engl J Med* 2019; 381: 1780–1781.
7 Blount BC, Karwowski MP, Morel-Espinosa M, *et al.* Evaluation of bronchoalveolar lavage fluid from patients in an outbreak of E-cigarette, or vaping, product use-associated lung injury — 10 states, August–October 2019. *MMWR Morb Mortal Wkly Rep* 2019; 68: 1040–1041.