



Early View

Research letter

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

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

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Numerous cases of e-cigarette, or vaping, associated lung injury (EVALI) have recently prompted an investigation of the outbreak in the US (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 hemoptysis, coughing and progressive dyspnea 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, 5mg/ml) 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 (13890 neutrophil/ μ l) and moderate elevation of C-reactive protein levels (CRP 86.3mg/L). Extensive infectious workup performed early during hospitalization (blood, sputum and broncho-alveolar lavage (BAL) cultures, urinary *Streptococcus pneumoniae* and *Legionella* antigens, multiplex polymerase-chain-reaction 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 didn't see any giant cells nor foamy, iron- or hemosiderin-laden macrophages, and *Pneumocystis jirovecii* was not detected by microscopy with staining. HIV and auto-immune 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/kg 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* bacteremia. 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 proposed criteria by Layden and colleagues (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 on the vaping fluid by 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 US (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 etiology and the biological mechanisms of this new and deadly disease.

We declare no competing interests.

Contributors

CM, JDG, DH, LMJ, SG and LB were involved in the patient's care. PW performed the e-liquid analysis.

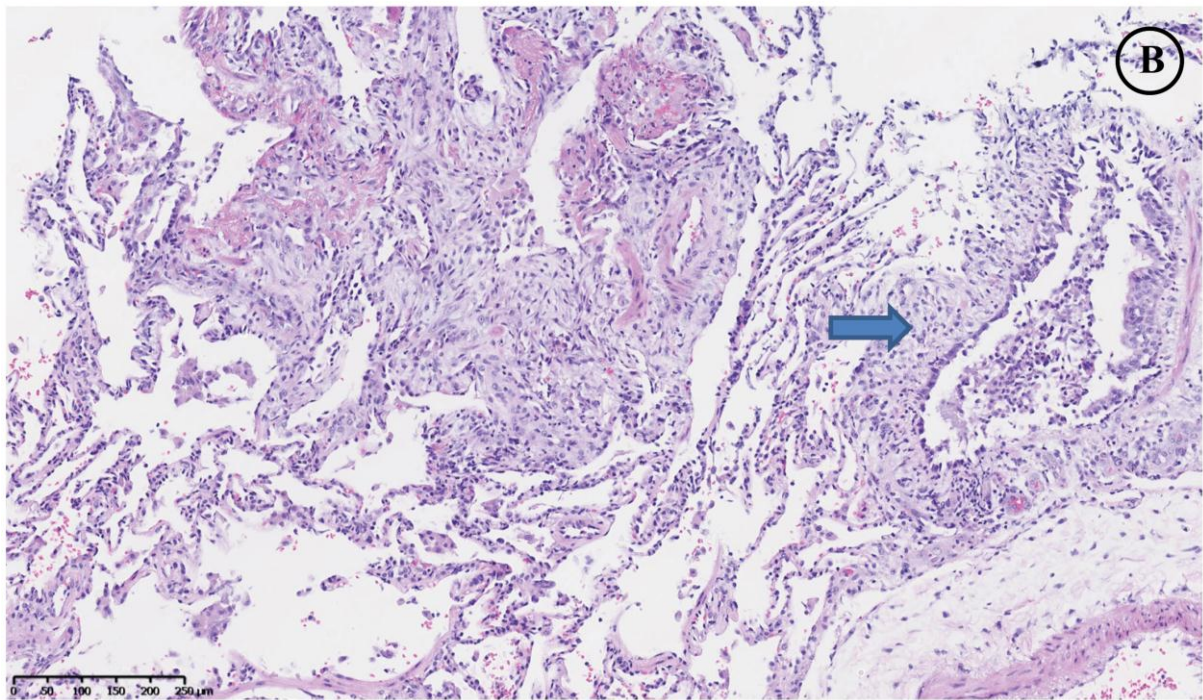
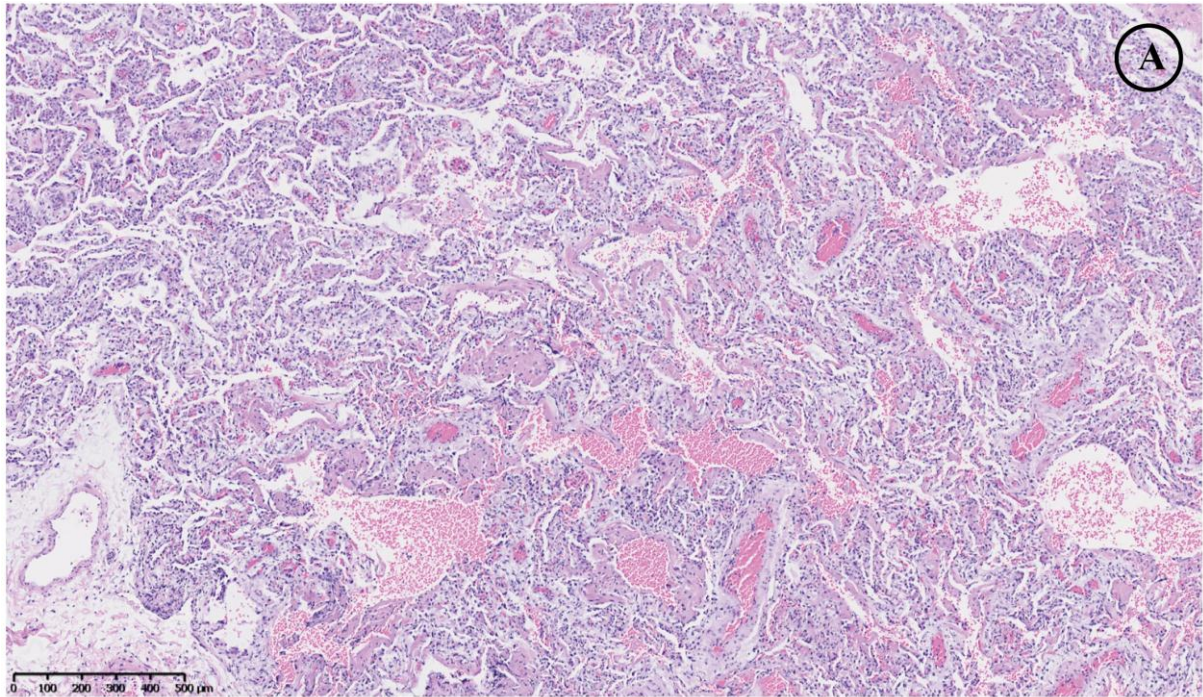
CM and JDG wrote the draft. DH sent and commented the illustration. DH, PW, LMJ, SG and LB revised, commented and corrected this manuscript with their individual expertise. All authors approved the final version.

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A. Diffuse alveolar damage characterized by hyaline membranes, capillary congestion and edema. Inflammation is sparse.

B. Alveolar septal thickening due to organizing fibrosis and remnants of hyaline membranes. Note the peribronchiolar predominant organisation (arrow).