Diagnosis of EVALI in the COVID-19 era

Nobeastsofierce/SPL

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As of Feb 18, 2020, a total of 2807 cases of e-cigarette, or vaping, product use-associated lung injury (EVALI) and 68 attributed deaths have been reported to the US Centers for Disease Control and Prevention.[1] Diagnostic criteria for EVALI consists of a mixture of non-specific systemic symptoms (eg, fever, chills, and vomiting) and respiratory symptoms (eg, shortness of breath, cough, chest pain, pnoea, and hypoxia), along with detection of lung opacities on imaging. Diagnosis also depends on identifying a history of vaping and careful exclusion of alternative conditions.[2] A urine drug screen positive for tetrahydrocannabinol, although non-specific for the disease, might be helpful in this aspect by identifying marijuana-containing electronic cigarettes and vape use. Patient laboratory findings show elevated inflammatory markers and are suggestive of an active non-specific inflammatory process. Radiological diagnosis of EVALI is often challenging because of a large overlap in its radiological features with other disease processes, particularly viral lung infections. Computer tomography of the chest might provide diagnostic clues, as patients with EVALI often showcase a specific airway-centred acute inhalation injury, presenting as a combination of bilateral symmetric ground glass opacities and lung consolidation with subpleural sparing.[3] In 2019, the bronchoscopy results of 19 patients with EVALI were described in *The Lancet*.[4] The findings suggested that while bronchoalveolar lavage (BAL) outcomes were non-specific, they were helpful in excluding alternative infectious processes via bacterial, fungal, viral, and acid-fast bacilli testing. Qualitative presence of lipid-laden macrophages in BAL was shown to have poor specificity and cannot be suggested as a laboratory marker for EVALI.[5] A more promising alternative might be testing for vitamin E acetate in BAL fluid, which was found in 48 of 51 patients with EVALI in a 2020 study.[6] The test was negative in 52 non-users of electronic cigarettes, and even more importantly, in 18 electronic cigarette users without obvious lung disease. These findings make a strong case for detection of vitamin E acetate in BAL as the laboratory standard for diagnosis of EVALI.[6]

Histological findings in EVALI often present a form of airway-centred chemical pneumonitis with various patterns of acute lung injury, such as acute fibrinous pneumonitis, diffuse alveolar damage, or organising pneumonia. Foamy macrophages and pneumocyte vacuolisation have been reported in many cases and are considered to be more specific for diagnosis in the clinical context.[7] Considering the presence of vast areas of affected lung parenchyma in most patients, transbronchial lung biopsy with or without endobronchial ultrasound guidance seems to be a reasonable addition to the bronchoscopic investigation.

Despite a legal age requirement of 18 years for purchasing electronic cigarettes, use of vaping products has been increasing among teenagers. As a result, cases of EVALI have been reported in children, who also might present with severe respiratory failure requiring intensive therapy. In one study of 98 patients with EVALI, Layden and colleagues reported 26% were aged younger than 18 years.[2]

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has made differential diagnosis of EVALI even more challenging due to the high rate of SARS-CoV-2 diagnosis in e-cigarette smokers (5 times more likely among daily users[8]) and large overlap of clinical and radiological features of the two conditions.[9] Adding another level of difficulty is the recent emergence of multisystem inflammatory syndrome in children (MIS-C) with COVID-19. Similar to EVALI, MIS-C is clinically characterised by non-specific systemic symptoms and high concentrations of inflammatory markers. At least 18% of children with MIS-C present with shortness of breath and other respiratory symptoms,[10] not unlike those of EVALI. Unfortunately, BAL characteristics and lung pathology of MIS-C are not well described and diagnosis relies heavily on a history of recent SARS-CoV-2 infection or exposure, which is common for children and young adults residing in COVID-19 hotspots, and more common still in those who use vape products.[8] The overlap of similar clinical features, use of vape products, and probable SARS-CoV-2 exposure make distinguishing the differential diagnosis of EVALI from MIS-C challenging in both children and adults, particularly when MIS-C presents with respiratory symptoms.

In summary, clinical presentation of EVALI is fairly non-specific and differential diagnosis is challenging, particularly in the SARS-CoV-2 pandemic era.

Nevertheless, radiological detection of airway-centred acute inhalation lung injury, along with the presence of vacuolisation of macrophages and pneumocytes, and most importantly the detection of vitamin E acetate in BAL fluid, provide important diagnostic clues for this condition.

We declare no competing interests.

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