

Case Report: Microembolic Thrombi in a patient with Vaping Related Lung Injury

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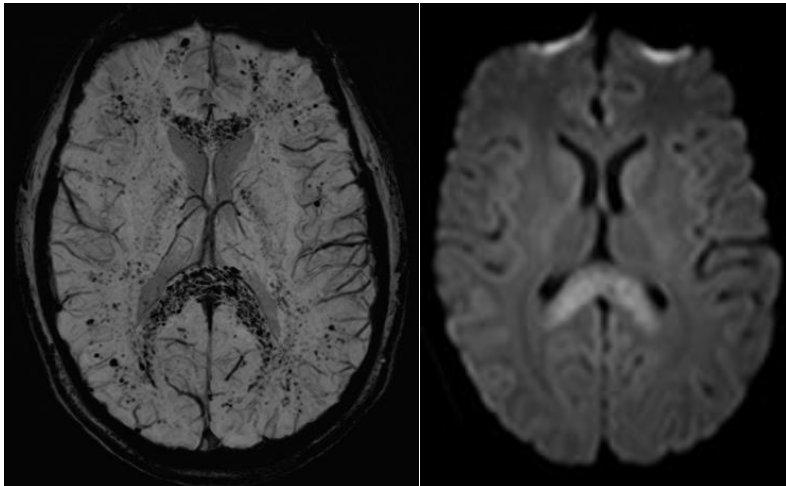
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A 17-year-old, previously healthy male was admitted to the hospital with respiratory distress and malaise. He presented with a history of fever, body aches, chest pain, shortness of breath and cyanosis after failing outpatient flu treatment with Tamiflu. He was hypoxic (SpO₂ 49% on room air) and had bilateral reticulonodular opacities on chest X-ray. His infectious workup included testing for common bacterial and viral pathogens was negative. He had a 7-month history of vaping and urine toxicology screen was positive for Carboxy-delta 9-THC Glucuronide (THC), naproxen and opiates (given in ED). He was diagnosed with E-cigarette or vaping product use-associated lung injury (EVALI) and admitted to the ICU on positive pressure ventilation. He progressed to acute respiratory distress syndrome (ARDS) requiring intubation and mechanical ventilation. He developed microvascular and left ventricular thrombi with splenic and nephric infarcts requiring anticoagulation. He was started on an unfractionated Heparin drip and was then transitioned to Enoxaparin. Despite a normal neurologic exam, a brain MRI/MRA obtained 12 days after initiation of anticoagulation was notable with microembolic disease. MRA was normal.

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MRI Brain: Widespread microembolic thrombi with areas of restricted diffusion and signal voids on susceptibility-weighted imaging (SWI) throughout the brain, greatest in the splenium of corpus callosum and watershed regions.



Left: Axial SWI demonstrates diffuse foci of gradient susceptibility throughout the white matter, most concentrated in the corpus callosum.

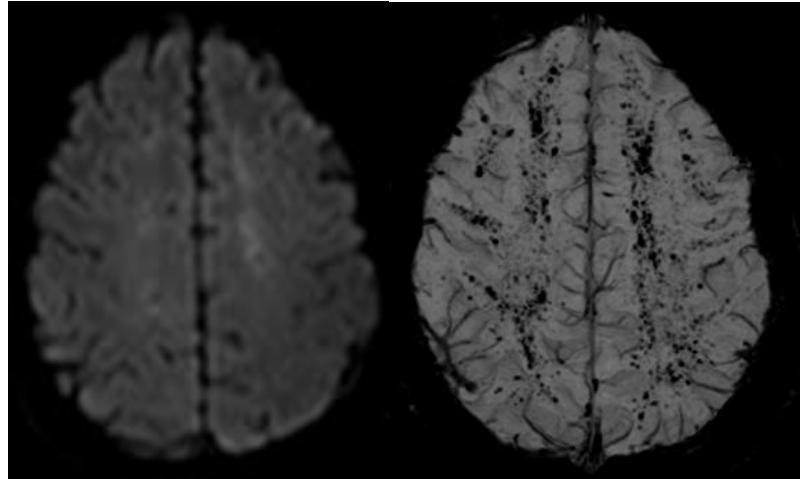
Right: Axial diffusion weighted image shows associated diffusion restriction in the splenium of the corpus callosum.

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Left: Axial SWI reveals innumerable foci of gradient susceptibility throughout the white matter, greatest throughout the centrum semiovale.

Right: Axial diffusion weighted image depicts associated diffusion restriction which is less pronounced than the susceptibility abnormalities.



Discussion

This patient has findings of diffuse cerebral microhemorrhages in the setting of EVALI-related respiratory failure. It remains unclear if imaging findings are related to thromboembolic events, severe lung injury, or is a manifestation of vaping-related toxicity. Notably, there was no apparent neurological deficit on bedside exam. Because he is at risk of deficits in cognitive functioning such as processing speed, memory, or executive function, he will undergo a neuropsychological evaluation.

Our patient's story is similar to the case reported by Messina et al. in the Journal of Pediatric Radiology which involved a teen found to have restricted diffusion in the corpus callosum,

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which the authors noted was consistent with a cytotoxic lesion of the corpus callosum (CLOCC)¹. There was, however, no mention of susceptibility weighted imaging and/or microhemorrhages related to the lesion in this case. Our case, then, adds to the variety of imaging findings possible with EVALI and reinforces the need for brain imaging in this population. Some have suggested that the involvement of the splenium of the corpus callosum in CLOCC may be due to loss of autoregulation and hypoxic vasodilation due to lack of adrenergic tone leading to overperfusion, which in turn, could contribute to the appearance of microhemorrhages².

Other explanations for the findings on imaging were also considered. Cerebral fat embolism syndrome can have similar findings on imaging when droplets of marrow fat can embolize to the brain after a long bone or pelvic fracture via right-to-left shunting at the cardiac or pulmonary level. Similar to our patient, the fat emboli target the white matter and may be associated with confluent cytotoxic edema and petechial hemorrhage^{3,4}. The pattern is also similar to prior reports from severe lung injury and high altitude lung injury^{5,6,7}. In three ARDS survivors, brain MRI revealed multiple microhemorrhages, predominantly in the splenium of the corpus callosum, similar to our patient⁵. Possible mechanisms of injury include disruption of the blood-

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brain barrier due to a cytokine storm that allows for leakage of blood into the parenchyma, impaired venous return due to positive pressure ventilation, and hypoxia⁷. The widespread nature of the MRI findings on SWI in our patient are less consistent with clinically occult micro emboli from the cardiac thrombus.

The pathophysiology by which e-cigarette use results in brain damage remains elusive. One hypothesis is that the carrier agents used in these devices, such as Vitamin E acetate, may play a role. A synthetic form of Vitamin E acetate serves as a thickening agent embedded with THC-containing products⁸. Isotope dilution mass spectrometry methods developed by the CDC to analyze specific toxicants in fluid obtained from bronchoalveolar lavages (BAL) in 29 patients with EVALI showed Vitamin E acetate in all patient BAL samples providing direct evidence of vitamin E acetate at the primary site of injury and possibly the inciting agent⁸. Though causation has not been established, the MR findings observed in our patient may relate to subclinical cerebral micro emboli of the vitamin E acetate or other lipids used in vaping products. Further studies are needed to explore this relationship.

Here we describe a report of diffuse cerebral microhemorrhages found in the setting of severe lung injury in EVALI. The pattern of multiple microhemorrhages focused in the splenium of the corpus callosum is atypical and should be investigated as a potential biomarker in similar cases. Our case demonstrates the importance of neuroimaging in this population and the need for detailed neurologic and cognitive evaluation after EVALI.

References

1. Messina MD, Levin TL, Blumfield E. Cytotoxic lesion of the splenium of the corpus callosum in a patient with EVALI. *Clin Imaging*. 2020;66:73-76. doi:10.1016/j.clinimag.2020.05.009
2. Garcia-Monco JC, Cortina IE, Ferreira E, et al. Reversible splenial lesion syndrome (RESLES): what's in a name?. *J Neuroimaging*. 2011;21(2):e1-e14. doi:10.1111/j.1552-6569.2008.00279.x
3. Kuo KH, Pan YJ, Lai YJ, Cheung WK, Chang FC, Jarosz J. Dynamic MR imaging patterns of cerebral fat embolism: a systematic review with illustrative cases. *AJNR Am J Neuroradiol*. 2014;35(6):1052-1057. doi:10.3174/ajnr.A3605

4. Yeap P, Kanodia AK, Main G, Yong A. Role of susceptibility-weighted imaging in demonstration of cerebral fat embolism. *BMJ Case Rep.* 2015;2015.
5. Riech S, Kallenberg K, Moerer O, et al. The Pattern of Brain Microhemorrhages After Severe Lung Failure Resembles the One Seen in High-Altitude Cerebral Edema. *Crit Care Med.* 2015;43(9):e386-e389. doi:10.1097/CCM.0000000000001150
6. Hall JP, Minhas P, Kontzialis M, Jhaveri MD. Teaching NeuroImages: Distinct brain microhemorrhage pattern in critical illness associated with respiratory failure. *Neurology.* 2018;90(22):e2011. doi:10.1212/WNL.0000000000005609
7. Hackett PH, Yarnell PR, Weiland DA, Reynard KB. Acute and Evolving MRI of High-Altitude Cerebral Edema: Microbleeds, Edema, and Pathophysiology. *AJNR Am J Neuroradiology.* 2019;40(3):464-469. doi:10.3174/ajnr.A5897
8. Blount BC, Karwowski MP, Shields PG, et al. Vitamin E Acetate in Bronchoalveolar-Lavage Fluid Associated with EVALI. *N Engl J Med.* 2020;382(8):697-705. doi:10.1056/NEJMoa1916433
9. Liebeskind DS, Sanossian N, Sapo ML, Saver JL. Cerebral microbleeds after use of extracorporeal membrane oxygenation in children. *J Neuroimaging.* 2013;23(1):75-78. doi:10.1111/j.1552-6569.2012.00723.x

10. Jackson JC, Hopkins RO, Miller RR, Gordon SM, Wheeler AP, Ely EW. Acute respiratory distress syndrome, sepsis, and cognitive decline: a review and case study. *South Med J*. 2009;102(11):1150-1157.
11. Kamenar E, Burger PC. Cerebral fat embolism: a neuropathological study of a microembolic state. *Stroke*. 1980;11(5):477-484. doi:10.1161/01.str.11.5.477
12. Messina MD, Levin TL, Conrad LA, Bidiwala A. Vaping associated lung injury: A potentially life-threatening epidemic in US youth. *Pediatric Pulmonology*. 2020;55(7):1705-1711. doi:10.1002/ppul.24755