

CLINICAL VIGNETTE

Seizure-Associated Diffuse Alveolar Hemorrhage

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Introduction

Diffuse alveolar hemorrhage (DAH) is a medical emergency involving bleeding into the alveolar spaces of the lungs and is typically caused by systemic autoimmune disease, cardiac disease, coagulation disorders, inhalational injury, infection, or malignancy causing injury or inflammation of the arterioles, venules, or alveolar septal capillaries. We report a 15-year-old male with epilepsy and recurrent hemoptysis following tonic-clonic seizure episodes. DAH secondary to neurogenic pulmonary edema in the setting of recent seizure activity is a potential diagnosis of exclusion. While the pathophysiology behind neurogenic pulmonary edema is incompletely understood, theories suggest neuro-hemodynamic mechanisms and intrathoracic pressure abnormalities.

Case Description

A 15-year-old male with epilepsy unresponsive to multiple anti-epileptics and on a ketogenic diet presented to the Emergency Department with dyspnea after a 15-second generalized tonic-clonic seizure followed by small volume hemoptysis. He had a prior history of hemoptysis in the setting of seizure activity, and a chest film from that episode was concerning for pulmonary hemorrhage. While in the Emergency Department, he was noted to be tachycardic and hypoxic, with 85% O₂ saturation while breathing ambient air. He was subsequently stabilized on 4 liters of oxygen via nasal cannula. Physical exam demonstrated no evidence of oropharyngeal trauma. Workup for vasculitis, infection, and malignancy was unrevealing. Complete blood count, complete metabolic panel, and iron studies were unremarkable. Computed tomography pulmonary angiogram revealed diffuse pneumomediastinum extending from the neck to the level of the left atrium with bilateral pulmonary patchy ground glass opacities consistent with possible alveolar hemorrhage versus aspiration. There was no evidence of pulmonary embolism (Figure 1). Esophogram was negative for esophageal perforation. He was observed in the intensive care unit overnight. The following day, dyspnea resolved, and the patient was breathing comfortably on ambient air. Further invasive work-up was deferred. He was discharged on a ketogenic diet with close Neurology outpatient follow-up. Five days later, he was seen by his pulmonologist. The patient was asymptomatic and his repeat chest film demonstrated resolution of his airspace disease, so bronchoscopy was deferred (Figures 2 and 3). Over the next year, he was hospitalized three more times for

tonic-clonic seizure-associated hemoptysis and dyspnea with similar radiographic findings followed by prompt resolution.

Discussion

Diffuse alveolar hemorrhage is recognized clinically by hemoptysis, anemia, diffuse radiographic pulmonary infiltrates, and hypoxemic respiratory failure. The etiologies of DAH are divided into pulmonary capillaritis, bland pulmonary hemorrhage, and diffuse alveolar damage. Pulmonary capillaritis involves inflammation and destruction of the blood vessel walls in the pulmonary vasculature and is attributable to numerous vasculitides and rheumatic diseases, collagen vascular disease, and anti-glomerular basement membrane disease. Bland pulmonary hemorrhage in comparison does not involve destruction or inflammation of alveolar structures and is more associated with bleeding disorders and anticoagulant therapy along with elevated left ventricular end diastolic pressures. Lastly, diffuse alveolar damage is caused by edema of the alveolar septa and formation of hyaline membranes lining alveolar spaces as seen in acute respiratory distress syndrome. Because the most common etiologies are inflammatory in nature, corticosteroids to achieve immunosuppression and supportive respiratory care remain mainstays of treatment in the vast majority of clinical situations.¹

Seizure activity leading to neurogenic pulmonary edema is infrequently implicated as an etiology of DAH outside of case reports and autopsy series, and the pathophysiology remains under debate. During seizure activity or other neurologic insults that cause abrupt, rapid, and extreme elevations in intracranial pressure, it has been hypothesized that neuronal compression and ischemia results in massive catecholamine release, producing significant lability in autonomic nervous system function.² These perturbations produce transient pulmonary hypertension and increased capillary pressure followed by structural damage to the blood-gas barrier, resulting in pulmonary hemorrhage and subsequent hemoptysis.^{3,4} The catecholamine surge has been recorded in animal models to cause rapid increases in aortic pressures as well, overwhelming the capacity of the left ventricle to pump blood to systemic circulation. As such, backup of blood flow into the left atrium, pulmonary veins, and pulmonary circuit contributes to pulmonary edema.⁵

Further animal model studies have suggested upper airway obstruction as an additional source of pulmonary edema following seizure activity. Dyssynchronous glottis movement during an active seizure and postictal laryngospasm may result in both excess negative and positive intrathoracic pressure from deep inspiratory and expiratory efforts against a closed glottis, respectively.⁶ An increase in negative intrathoracic pressure results in increased pulmonary vasculature blood volume and increased pulmonary arterial pressure, thereby causing significant fluid transudation from pulmonary capillaries to the interstitium.⁷ Additionally, further positive intrathoracic pressure against a closed glottis has been described as capable of increasing intraalveolar pressures to the point of barotrauma and rupture, producing escape of air into the mediastinum and pleural space.^{8,9}

Current treatment for DAH precipitated by neurologic insults remain focused on resolution of the underlying neurologic condition along with respiratory support. In addition to cutting off sympathetic discharge from neurologic pathologies, case reports have attempted pharmacologic intervention with anti- α -adrenergic agents to achieve hemodynamic control with success.^{10,11} Given the rarity of this condition, however, comprehensive studies of these agents to abort hemodynamic instability have not been performed.

Conclusion

This case illustrates the evaluation and differential for DAH and demonstrates the need to consider significant hemodynamic changes along with extreme intraalveolar and intrathoracic pressures following a central nervous system insult as a potential cause of DAH.

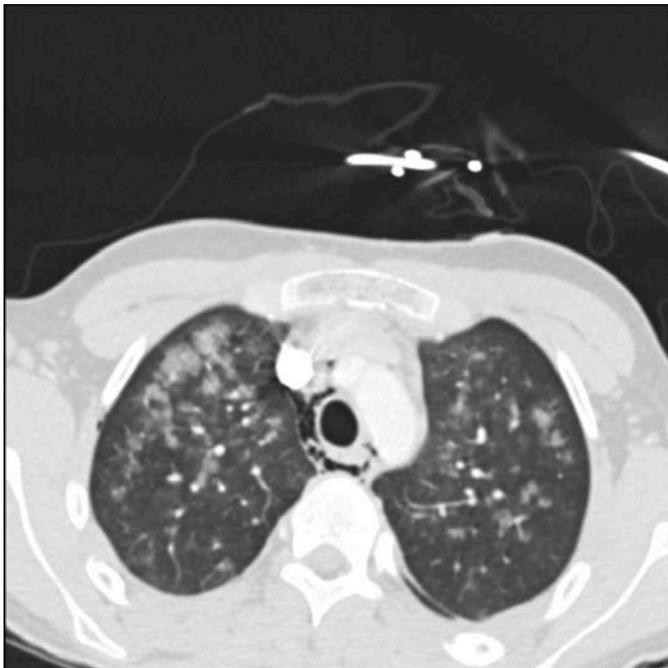


Figure 1. CT pulmonary angiogram demonstrating significant pneumomediastinum and bilateral pulmonary patchy ground glass opacities, likely secondary to alveolar hemorrhage.



Figure 2. PA chest radiograph obtained during hospital admission demonstrating multifocal airspace opacities in the right greater than left lung consistent with pulmonary hemorrhage versus aspiration.

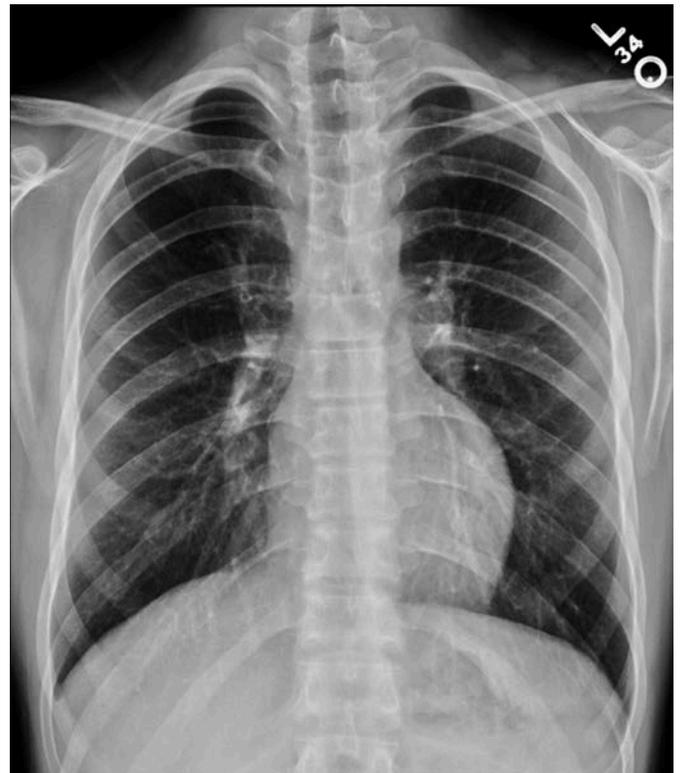


Figure 3. PA chest radiograph at 5-day Pulmonologist follow-up demonstrating resolution of multifocal airspace disease.

REFERENCES

1. **Lara AR, Schwarz MI.** Diffuse alveolar hemorrhage. *Chest.* 2010 May;137(5):1164-71. doi: 10.1378/chest.08-2084. Review. PubMed PMID: 20442117.
2. **Davison DL, Terek M, Chawla LS.** Neurogenic pulmonary edema. *Crit Care.* 2012 Dec 12;16(2):212. doi: 10.1186/cc11226. Review. PubMed PMID: 22429697; PubMed Central PMCID: PMC3681357.
3. **Sedý J, Zicha J, Kunes J, Jendelová P, Syková E.** Mechanisms of neurogenic pulmonary edema development. *Physiol Res.* 2008;57(4):499-506. Epub 2007 Nov 30. Review. PubMed PMID: 18052674.
4. **Kennedy JD, Hardin KA, Parikh P, Li CS, Seyal M.** Pulmonary edema following generalized tonic clonic seizures is directly associated with seizure duration. *Seizure.* 2015 Apr;27:19-24. PubMed PMID: 25844030; PubMed Central PMCID: PMC4383169.
5. **Sarnoff SJ, Sarnoff LC.** Neurohemodynamics of pulmonary edema. II. The role of sympathetic pathways in the elevation of pulmonary and systemic vascular pressures following the intracisternal injection of fibrin. *Circulation.* 1952 Jul;6(1):51-62. PubMed PMID: 14936200.
6. **Lorch DG, Sahn SA.** Post-extubation pulmonary edema following anesthesia induced by upper airway obstruction. Are certain patients at increased risk? *Chest.* 1986 Dec;90(6):802-5. PubMed PMID: 3780326.
7. **Tavee J, Morris H 3rd.** Severe postictal laryngospasm as a potential mechanism for sudden unexpected death in epilepsy: a near-miss in an EMU. *Epilepsia.* 2008 Dec;49(12):2113-7. doi: 10.1111/j.1528-1167.2008.01781.x. Epub 2008 Sep 17. PubMed PMID: 18801039.
8. **Curran H, Ross J.** Bilateral pneumothoraces and pneumomediastinum complicating a generalized tonic-clonic seizure. *CJEM.* 2008 Mar;10(2):176-8. PubMed PMID: 18371255.
9. **Dechant A, Johannson K.** Diffuse alveolar haemorrhage and pneumomediastinum after hypoglycaemic seizure. *ERS.* 2013; 42 (57): P2178.
10. **Loughnan PM, Brown TC, Edis B, Klug GL.** Neurogenic pulmonary oedema in man: aetiology and management with vasodilators based on haemodynamic studies. *Anaesth Intensive Care.* 1980 Feb;8(1):65-71. PubMed PMID: 6992637.
11. **Wohns RN, Tamas L, Pierce KR, Howe JF.** Chlorpromazine treatment for neurogenic pulmonary edema. *Crit Care Med.* 1985 Mar;13(3):210-1. PubMed PMID: 2857630.