Generalized Convulsion Complicating Acute Diffuse Pulmonary Hemorrhage: The Report of a Rare Case

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Abstract

Purpose: The immediate complications associated with a generalized tonic-clonic (GTC) seizure usually involve injuries such as aspiration pneumonia, head injury, skull or vertebral fracture and orolingual biting injury. Here we present a young man who suffered from GTC that was followed by a rare complication, acute diffuse pulmonary hemorrhage, which presented with massive hemoptysis and subsequent respiratory failure.

Case Report: An 18-year-old boy developed a GTC convulsion that lasted for about two minutes and then regained consciousness 15 minutes later. Another GTC convulsion occurred four hours later for about two minutes. Upon admission, coughing with blood clots was noted and was initially imputed to a bite wound affecting the tongue. However, massive hemoptysis developed soon after. A chest X-ray showed diffuse consolidation of the bilateral lungs. He was transferred to the intensive care unit and was intubated immediately owing to acute respiratory failure. A further chest CT also showed extensive consolidation of the bilateral lungs, mainly in the central and posterior portions. Bronchoscopy showed diffuse tracheal and bronchial erythematous mucosa and post-hemorrhage changes. Laboratory surveys for autoimmune disease, infectious disease, tuberculosis and intoxication gave normal results. After treatment with anticonvulsants, antibiotics and corticosteroids, he was stabilized and extubated on the 5th day of hospitalization.

Conclusion: The disease entity of acute diffuse pulmonary hemorrhage is similar to neurogenic pulmonary edema. Physicians should be aware of this extremely rare but life-threatening complication, namely seizure-related acute diffuse pulmonary hemorrhage. The patient's response to respiratory support and corticosteroid is usually quite satisfactory.

Key Words: generalized tonic-clonic convulsion, seizure, epilepsy, acute diffuse pulmonary hemorrhage, neurogenic pulmonary edema

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INTRODUCTION

The complications associated with epilepsy depend on the type and severity of the seizure. The immediate complications that are associated with generalized tonic-clonic (GTC) seizure usually involve injury and include aspiration pneumonia, head injury, skull or vertebral fracture, and orolingual bite injury. Neurogenic pulmonary edema (NPE) is an unusual but a serious complication of seizure. The clinical findings may be confused with alternate conditions, such as cardiogenic pulmonary edema, acute respiratory distress syndrome, or diffuse pulmonary hemorrhage[1]. Hemoptysis and infiltrating lesions of the bilateral lungs are the common features of NPE. However, massive hemoptysis with chest pain, but without tachypnea or dyspnea, is not a typical presentation of NPE. Here we present a young man who suffered from recurrent GTC followed by massive hemoptysis and chest pain.

CASE REPORT

This 18-year-old boy without any medical disease and who lacks a past history of head injury or drug abuse developed a GTC convulsion while at school and was brought to our emergency room. The convulsion lasted for about two minutes and he regained his consciousness 15 minutes later. Another GTC convulsion occurred four hours later and lasted for about 3 minutes. Valproic acid was given for seizure control. A brain computed tomography (CT) showed no any abnormality. Some blood was found in the mouth due to lip and tongue bites having occurred during the seizure. According to his parent's description, he had undergone an episode of sudden upward gaze with a dull response for several minutes three months prior to this episode. A cough with blood clots was noted upon admission. The blood was initially imputed to the bite wound that had affected the tongue. However, subsequent episodes of massive hemoptysis with fresh blood and chest pain arouse the suspicion of a pulmonary lesion. The patient did not complain of tachypnea or dyspnea. Pulmonary auscultation revealed the presence of bilateral coarse breathing sounds without wheezing. An emergency chest X-ray found diffuse consolidation of the bilateral lungs with multiple airspace-filling that was radio-opaque; this is suggestive of acute diffuse pulmonary hemorrhage (Fig 1A). He was transferred to the intensive care unit and was intubated immediately due to subsequent acute respiratory failure. No pink frothy sputum from trachea was observed during intubation. Low dose intravenous midazolam was given to aid ventilator synchronization.

A chest CT showed extensive consolidation within the bilateral lungs, mainly in the central and posterior portions (Fig 1B, C). Bronchoscopy found diffuse tracheal and bronchial erythematous swelling and post-hemorrhage changes to the mucosa without active bleeding. Electroencephalography did not detect the presence of epileptiform discharge. All laboratory studies were normal including biochemistry, a hemogram, cardiac enzymes, seromarkers of autoimmune antibodies (antinuclear, C3, C4, rheumatic factor, immunoglobins, anti-nDNA, anti-glomerular membrane, cardiolipin, anti-ribonucleoprotein, anti-Smith, antineurophil cytoplasmic, myloperoxidase, and proteinase 3), a sputum tuberculosis examination, a urine toxicology screening study and a cerebrospinal fluid analysis. Valproic acid was continued to the patient for seizure control. Parenteral tranexamic acid and empirical antibiotics combined with steroid treatment were given for the pulmonary hemorrhage. An echocardiography showed normal cardiac chambers with preserved ventricular systolic function. Further brain magnetic resonance angiography did not disclose any abnormality. A follow-up chest X-ray 4 days later demonstrated the consolidated lung lesions were much improved (Fig 1D). The hemoptysis improved gradually. He was successfully extubated on day 5 and was discharged on the 10th day after admission without any sequelae.

No more seizures occurred during hospitalization and therefore he did not wish to take any anticonvulsion medication after discharge despite our recommendation that it should be prescribed. Unfortunately, another episode of tongue biting with oral bleeding occurred during morning wakening two weeks later and he was sent to the emergency room again. There was neither hemoptysis nor chest pain this time and a chest X-ray study was normal. We prescribed valproic acid and suggested to him that he continue this anticonvulsive in order to ensure seizure control. He has received regular anticonvulsant treatment since then and no more seizures have been observed over

a period of one year follow-up.

DISCUSSION

This patient developed acute diffuse pulmonary hemorrhage presenting as massive hemoptysis and chest pain without tachypnea or dyspnea several hours after two episodes of GTC convulsions. No other known cause of the pulmonary hemorrhage other than the seizures was found when a range of examinations and laboratory studies were carried out. The pulmonary hemorrhage improved rapidly after intubation and corticosteroid treatment over a period of one week.

Hemoptysis may occur in association with both NPE and pulmonary hemorrhage. In this patient, however, there was a moderate amount of blood expectoration with chest pain, but without tachypnea and dyspnea, which is atypical feature of NPE. Neither was any pink frothy sputum found during intubation. Diffuse consolidation of the bilateral lungs was found on chest X-ray and CT and such findings are usually indistinguishable when NPE, diffuse pulmonary hemorrhage and acute respiratory distress syndrome are considered. The lung condition improved rapidly after corticosteroid treatment but without diuretics. We proposed that the diffuse pulmonary hemorrhage was the main pathological change affecting the lungs together with a certain degree of NPE.

Aspiration pneumonia comprises the majority of pulmonary complications associated with seizure. NPE is an uncommon complication related to seizure[2,3]. Acute diffuse pulmonary hemorrhage is even rarer after seizure[4,5]. NPE is a clinical syndrome characterized by the

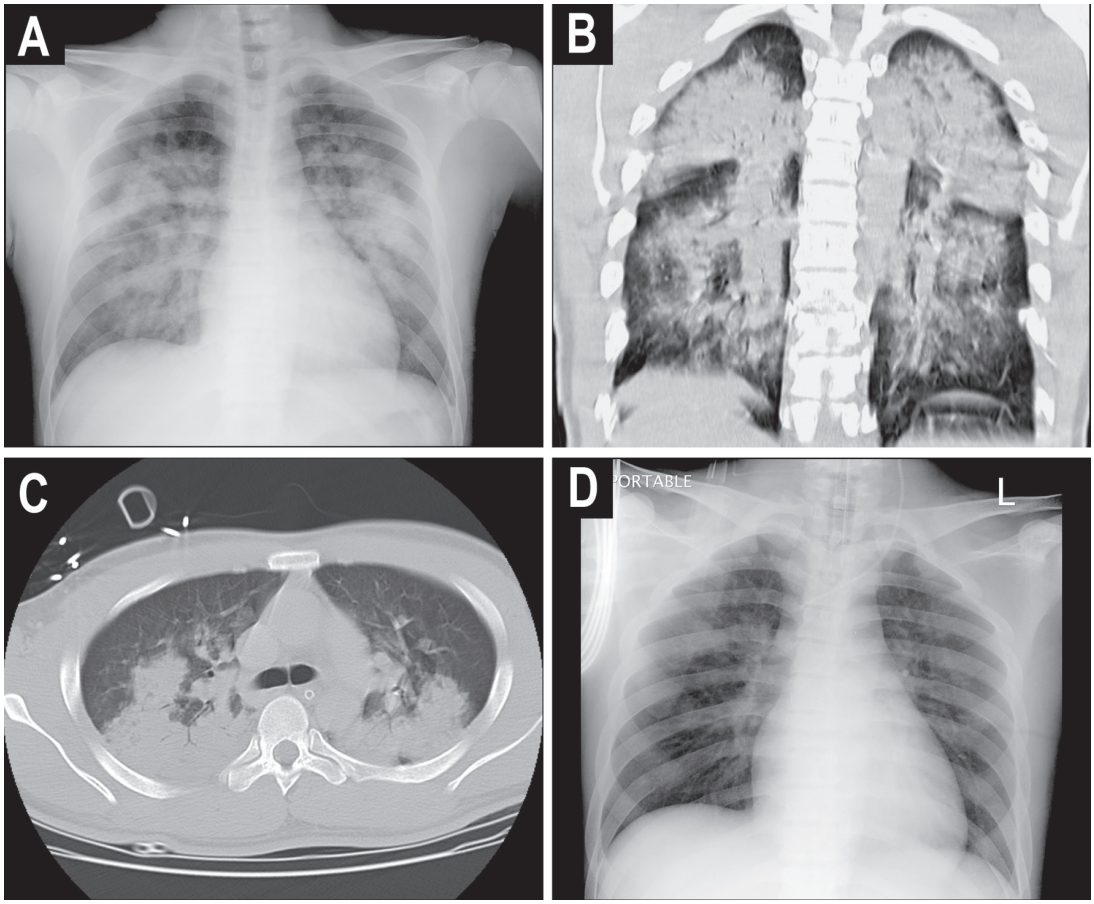

Figure 1: (A) Initial chest X-ray discloses diffuse airspace consolidation of the bilateral lungs. (B, C) The chest CT demonstrates extensive consolidation in the bilateral lungs, mainly in central and posterior portions. (D) A follow-up chest X-ray carried out 4 days later shows that the consolidated lung lesions have undergone much improvement.

acute onset of pulmonary edema following a significant insult from the central nervous system. It occurs within minutes to hours after the insult and resolves within a few days. Possible causes of NPE include traumatic head injury, subarachnoid hemorrhage, intracranial hemorrhage, brain tumor, meningitis, and a grand mal seizure, particularly status epilepticus[6,7]. An abrupt increase in intracranial pressure might activate the sympathetic nervous system, mostly the hypothalamus and the medulla, and this can induce the release of catecholamines. Four clinicopathological paradigms have been proposed for NPE: the neuro-cardiac paradigm, the neuro-hemodynamic paradigm, the blast theory paradigm, and the pulmonary venule adrenergic hypersensitivity paradigm[7]. The typical clinical presentations of NPE are acute tachypnea, dyspnea, hypoxia, and respiratory failure. Pink frothy sputum is commonly seen and bilateral crackles with rales are usually audible on auscultation.

Massive hemoptysis is defined as expectoration of a large amount of blood and/or a rapid rate of bleeding (usually > 100 mL) over 24 hours[8]. Common causes of massive hemoptysis include tuberculosis, bronchiectasis, abscess, and malignancy. Nevertheless, acute diffuse pulmonary hemorrhage usually does not occur in above mentioned diseases. Diffuse pulmonary hemorrhage is a syndrome characterized by widespread hemorrhage from the pulmonary microvasculature that leads to hemoptysis, iron deficiency anemia, and a chest radiograph showing bilateral airspace consolidation[9]. However, each of these features is nonspecific and may be absent or variable. If the bleeding is into the alveolar spaces, this syndrome can be classified as diffuse alveolar hemorrhage. Diffuse pulmonary hemorrhage is associated with a variety of diseases, such as collagen diseases, systemic vasculitis and mitral stenosis. A sudden increase in capillary pressure may destroy the blood-gas barrier of the lungs and thus induce pulmonary hemorrhage and varying amounts of hemoptysis[5]. This mechanism is similar to the "pulmonary venule adrenergic hypersensitivity" theory in NPE. Ueno et al found that the plasma level of angiotensin II is increased in the pulmonary circulation and then pulmonary hypertension proceeds to systemic hypertension without any increase in catecholamine during the seizure[10]. In the present case, a systematic serological test did not find any autoimmunity-related problems. The only possible precipitating condition in relation to the diffuse pulmonary hemorrhage was the GTC convulsions.

Although uncommon, most reported seizure related acute lung injury events involve NPE. Patients who present with tachypnea, dyspnea, with or without small amount of hemoptysis, and who are responsive to diuretic treatment are considered to be suffering from NPE. Acute diffuse pulmonary hemorrhage is an extremely rare complication of seizure. Most of the hemoptysis due to pulmonary hemorrhage that is associated with seizure is part of the clinical presentations of an autoimmune syndrome disease such as systemic lupus erythematosus or Goodpasture's syndrome[11,12]. Hemoptysis with seizure has also been reported in patients with tuberous sclerosis from progressive lymphangioleiomyomatosis of the lung[13,14]. Ryu et al reported the first case of recurrent massive pulmonary hemorrhage without any other systemic disease after seizure[4]. Azuma et al reported a second case of pulmonary hemorrhage induced by epileptic seizure[5]. Collander et at reported a patient with diffuse alveolar hemorrhage secondary to GTC[15]. We have not been able to find another case report that describes a seizure-related non-autoimmune "pure pulmonary hemorrhage" such as the one presented here in the English medical literature.

Valproic acid has been reported to induce diffuse alveolar hemorrhage through the unusual side effect of thrombocytopenia or platelet dysfunction[16-18]. Diffuse alveolar hemorrhage induced by valproic acid secondary to a combination of hemostatic disorders including intrinsic and extrinsic coagulation systems has been proposed by Inzirillo et al[18]. This patient received valproic acid treatment while in the emergency room and during hospitalization in order to bring about seizure control. Valproic acid-associated pulmonary hemorrhage can be excluded based on the patient's normal serial hemogram studies without thrombocytopenia and the fact that there was rapid improvement to the lung lesions without discontinuation of the valproic acid.

Sudden unexplained death in epilepsy accounts for 15% of all deaths in people with epilepsy and 50% of deaths among refractory epilepsy patients. Possible causes are ictal or postictal cardiac arrhythmias, central hypoventilation or apnea, and NPE[19,20]. Acute diffuse pulmonary hemorrhage is a disease entity similar to NPE but is a more challenging clinical problem. Physicians

should be aware of this rare and life-threatening complication of seizure-related acute diffuse pulmonary hemorrhage.

CONCLUSIONS

Acute diffuse pulmonary hemorrhage may occur as a rare cause of massive hemoptysis after epileptic seizure. The response to respiratory support and corticosteroid therapy is usually satisfactory. Acute diffuse pulmonary hemorrhage is an important differential diagnosis for patients with seizure and hemoptysis.

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