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Alveolar haemorrhage after epileptic seizures: A case report

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Abstract

We describe a case in which a child with epilepsy developed dyspnoea and a continuous decrease in blood oxygen saturation after convulsion. The child's symptoms were relieved after oxygen was provided. A complete chest CT revealed diffuse pulmonary infiltration. Bronchoscopy revealed that the lavage fluid was bloody, and pathology revealed haemosiderin cells in the BALF; thus, pulmonary haemorrhage was considered. Two weeks later, the abnormal findings on chest CT disappeared without treatment. After pulmonary haemorrhage caused by other diseases was excluded, the relationship between pulmonary haemorrhage and epilepsy in children was considered.

Introduction

Aspiration pneumonia after epileptic seizures is common, but what we described in a child with epilepsy who developed dyspnoea and a continuous decrease in blood oxygen saturation after convulsion was not aspiration pneumonia. After pulmonary haemorrhage caused by other diseases was excluded, the relationship between pulmonary haemorrhage and epilepsy in children was considered. Epilepsy may lead to increased pulmonary vascular permeability and structural damage to the Blood Gas Barrier (BGB), which can lead to pulmonary haemorrhage. In epilepsy patients with increased respiratory rates after convulsion and diffuse pulmonary interstitial changes visible on lung CT, the possibility of pulmonary haemorrhage should be considered. Although pulmonary haemorrhage caused by epilepsy can be alleviated by itself, in view of the potential risk of Neurogenic Pulmonary Oedema (NPE), when considering whether children with epilepsy need to use antiepileptic drugs, the risks and benefits caused by pulmonary haemorrhage in children with epilepsy should also be considered.

Case report

A 8-year-old female was admitted to the hospital in September 2022 due to shortness of breath and wheezing for one day. One day before admission, the child had a convulsion for which there was no obvious inducement, which manifested as sudden falling to the ground, limb stiffness, eye turning, blue lips, and mouth foaming, which were relieved after 12 minutes. Later, she went to the emergency department. At that time, the patient was accompanied by dyspnoea, and her blood oxygen saturation was 88% without an oxygen supply. With a nasal tube oxygen supply (2 L/min), the percutaneous blood oxygen saturation was maintained at approximately 91%. Blood gas analysis revealed a pH of 7.309, PCO_2 of 32.3 mmHg, PO_2 of 81.1 mmHg, HCO_{3-} of 15.8 mmol/L, BE of -9.3 mmol/L, and lactic acid of 1.8 mmol/L. A routine blood examination revealed the following: white blood cell count, 16.9 x 10^9/L; neutrophil count, 0.880; haemoglobin, 11.9 g/dL; platelet count, 284 x 10^9/L; and C-reactive protein <1 mg/L. A chest CT scan revealed a diffuse patch and cloud flocculent shadow in both lungs. The upper lung was marked, and a fine grid shadow could be seen. Diffuse lesions in both lungs were considered (Figure 1A). Alkaline liquid infusion was used for acid correction, and no other treatment was given on the day of admission; the patient's respiration gradually improved, and her transcutaneous oxygen saturation returned to normal. Epilepsy was diagnosed when the patient was 6 months old, and it occurred once every six months and resolved after a few minutes. Because the seizure attacks were few and short,

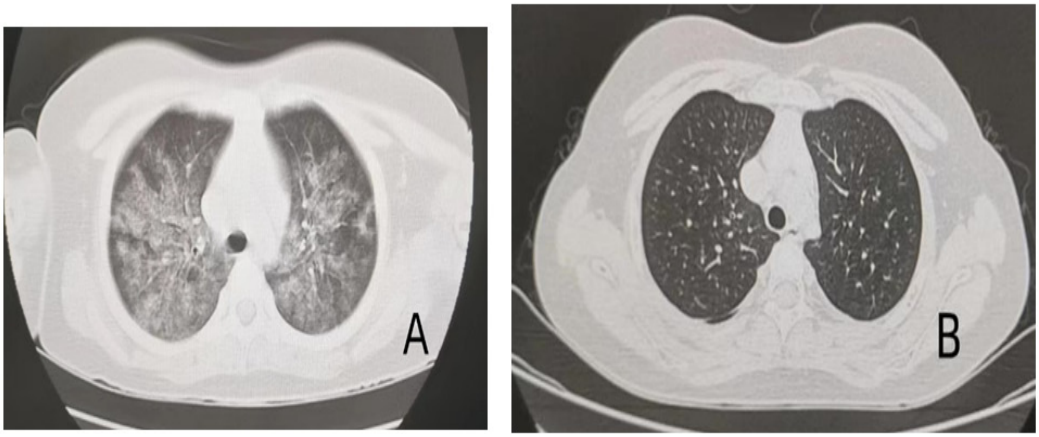

Figure 1: (A) The patient's lung CT on the day of convulsion revealed a diffuse patch and cloud flocculent and fine grid shadow in both lungs. **(B)** Fourteen days after convulsion, the patient's lungs were rechecked with CT, and no obvious abnormalities were found in either lung.

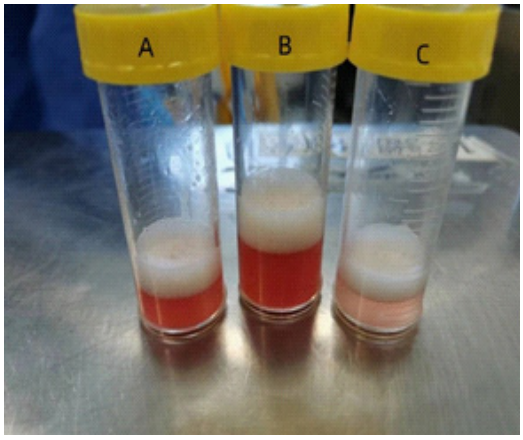

Figure 2: BALF from the patient. **(A)** from the left upper lobe; **(B)** from the right middle lobe; **(C)** from the right upper lobe.

Table 1: The causes of pulmonary haemorrhage.

Classification	Disease
Respiratory system	Trachea, bronchus, and lung diseases, such as infectious diseases, including acute and chronic bronchitis, pneumonia, pulmonary tuberculosis, and invasive fungal infection of the lung; bronchial and lung structural abnormalities, such as pulmonary sequestration and cystadenoma malformation of the lung; bronchiectasis, cystic fibrosis, and idiopathic pulmonary hemosiderosis; and other conditions, such as trauma, tumours, and bronchial foreign bodies
Circulatory system	Congenital heart disease, pulmonary hypertension, pulmonary embolism, pulmonary vascular malformation
Systemic diseases	Bleeding and coagulation dysfunction and connective tissue disease
Others	Medication intake, radiotherapy

they could be relieved quickly, and no special treatment was given. At age 4, she was admitted to the hospital for "unwilling to look at each other, communicate with others and be pleased to recite the whole book" and was diagnosed with "high-functioning autism". She did not have a history of fever, cough, wheezing, kidney disease or anaemia. Physical examination at admission revealed the following: body temperature, 36.2°C, respiration, 20 breaths/minute; heart rate, 96 beats/minute; percutaneous oxygen saturation (without an oxygen supply), 98%; and blood pressure, 96-62 mmHg. She was conscious and appeared comfortable, presented with ruddy complexion, stable breathing, and no nasal fan or chest wall concave signs. The breathing sounds in both lungs were rough, without rales. The heart sounds were powerful and regular, and no murmur was heard. No abnormalities were found in the abdomen or nervous system. The extremities were warm, with a capillary refilling time of 1 s. The patient was admitted to the hospital because a chest CT scan revealed bilateral lung infiltrates. Because the CT image was similar to a pulmonary haemorrhage, flexible bronchoscope and other related examinations were performed on the second day after admission and epilepsy. The results of routine blood examination revealed the following: white blood cell count, 8.76 x 10^9/L; neutrophil count, 0.479; haemoglobin, 12.6 g/dL; platelet count, 308 x 10^9/L; and C-reactive protein, 3.8 mg/L. Biochemistry and blood coagulation results were generally normal, and procalcitonin levels were normal. Under bronchoscopy, bright red liquid was drawn from the left upper lobe, right middle lobe and right upper lobe after lavage, and alveolar haemorrhage was considered (Figure 2). Lung haemosiderin cells were positive, and Periodic Acid-Schiff (PAS) staining was negative according to BALF pathology. No infectious pathogens were detected via metagenomics next-generation sequencing (NGS) of the BALF. Antinuclear Antibody (ANA) and Antineutrophil Cytoplasmic Antibody (ANCA) levels were negative. Antirenal membrane basement membrane antibody levels were negative. No abnormality was found on head MRI. On the third day of admission, the child's parents signed for discharge for personal reasons. At the outpatient follow-up visit two weeks after discharge, chest CT re-examination revealed no obvious abnormalities in either lung (Figure 1B).

Discussion

When "epilepsy" and "pulmonary haemorrhage" were used as the search words, a foreign report was extracted from the Wan fang and CNKI databases (expanded in Chinese and English) from the establishment of the databases to October 2022, which included an adult with pulmonary haemorrhage after convulsion. No relevant literature was found by the PubMed database search (also to October 2022) with the keywords "pulmonary haemorrhage" and "epilepsy" or with the keywords "alveolar haemorrhage" and "epilepsy". With "haemoptysis"

and "epilepsy" as the key words, four articles were retrieved through the PubMed database, including one article of epilepsy with haemoptysis. A 49-year-old female patient with a history of epilepsy was reported. After 15 minutes of tonic-clonic seizures, she developed chest pain, cough and hypoxemia. In the absence of oxygen inhalation, the patient's percutaneous oxygen saturation was 88%. The patient's lung CT revealed bilateral diffuse mixed alveolar filling. The upper lobe was dominant, but there was no pulmonary embolism. The alveolar lavage fluid was red. A diagnosis of diffuse alveolar haemorrhage was made [1], which is very similar to the pulmonary CT of our patient. Although patients in the other three articles all had epilepsy and pulmonary haemorrhage, the latter was considered caused by other factors (lung cancer, pulmonary embolism, etc.). Although the patient had no haemoptysis, bright red fluid could be observed in the BALF, and the pathology of the BALF indicated that haemosiderin cells were positive. No mucosal haemorrhage was detected via bronchoscopy, so the diagnosis of pulmonary haemorrhage was clear. The causes of pulmonary haemorrhage in children vary (Table 1) [2]. This patient had no recent infection history. NGS examination of alveolar lavage fluid revealed no infectious pathogens, except for pulmonary haemorrhage caused by infectious diseases. In addition, ANA and ANCA were negative in this patient, and there was no fever, rash, arthralgia, renal involvement or other manifestations, which excluded ANCA-related vasculitis and systemic lupus erythematosus and other diseases. Echocardiography revealed no evidence of valvular disease or heart failure. There was no abnormality in blood coagulation, which does not support diseases related to bleeding or coagulation dysfunction. No vasodilation was found in the skin, and cranial MRI did not support telangiectasia. The measurement of pulmonary Diffusion Capacity (DLCO) holds certain value in the differential diagnosis of pulmonary hemorrhage, pulmonary edema, and aspiration pneumonia. An elevated DLCO is an important indicator of pulmonary hemorrhage, especially when there are no significant imaging findings. However, performing DLCO testing in children has significant limitations. Standard DLCO testing equipment is typically designed for adults and may not be suitable for children's smaller facial structures or lower lung volumes, potentially affecting the accuracy of the test. Additionally, children's lung function and the surface area of the alveolar-capillary membrane change with age, making it difficult to standardize normal DLCO ranges. Currently, normal DLCO reference values are primarily based on adult data, with limited reference values available for children, which may lead to inaccurate interpretation of results. Specifically, in the case of classification disease respiratory system trachea, bronchus, and lung diseases, such as infectious diseases, including acute and chronic bronchitis, pneumonia, pulmonary tuberculosis, and invasive fungal infection of the lung; bronchial and lung structural abnormalities, such as pulmonary sequestration and cystadenoma malformation of the lung; bronchiectasis, cystic fibrosis, and idiopathic pulmonary hemosiderosis; and other conditions, such as trauma, tumours, and bronchial foreign bodies circulatory system congenital heart disease, pulmonary hypertension, pulmonary embolism, pulmonary vascular malformation Systemic diseases bleeding and coagulation dysfunction and connective tissue disease Others medication intake, radiotherapy this child, who has autism, DLCO testing could not be completed.

Although aspiration pneumonia is a common complication after seizures, there was no evidence of infection in this patient. The alveolar lavage fluid is bloody and improves without anti-infection treatment, which does not support aspiration pneumonia. In this case, Neurogenic Pulmonary Oedema (NPE) associated with seizures may have been the cause of pulmonary haemorrhage. A series of nervous system diseases can lead to NPE. In adults, the most common causes of NPE are subarachnoid haemorrhage and seizures; the most common diseases of NPE in children are craniocerebral trauma and EV71 infection, which are also observed in simple febrile convulsion, subdural haematoma, hydrocephalus, multiple sclerosis, spontaneous cerebellar haemorrhage and cryptococcal meningitis. An increase in intracranial pressure and injury to the trigger area of NPE located in the hypothalamus, brain stem and medulla oblongata are the basis of NPE [3]. Most NPE patients have a sharp onset, which occurs within hours or days after the injury. In mild cases, restlessness, increased heart rate, conscious chest tightness, and fine moist rales can be heard in the middle and lower fields of both lungs. Severe cases may present with shortness of breath, cough with white foam sputum, bloody foam sputum, haemoptysis, or spitting out coffee-like substances. Dyspnoea and cyanosis may occur when they are limited to interstitial pulmonary oedema. Severe children may have pale, damp and cold skin and a sense of dying. Both lungs are full of moist rales and become progressively worse, which can lead to congestive atelectasis, respiratory failure and manifestations similar to acute respiratory distress syndrome [4]. Our patient had a similar clinical course, so it is speculated that the same mechanism may exist. In addition, increasing transpulmonary pressure during epileptic seizures is also one of the causes of pulmonary hemorrhage. We also considered the possibility of another mechanism. Severe exercise reportedly leads to pulmonary haemorrhage and haemoptysis to different degrees [5-7], among which structural dysfunction of the Blood Gas Barrier (BGB) is considered the cause. Inflammation and pulmonary oedema can damage the BGB, leading to pulmonary haemorrhage and haemoptysis.

Conclusion

This paper describes a case of pulmonary haemorrhage caused by epilepsy. Epilepsy may lead to increased pulmonary vascular permeability and structural damage caused by the BGB, which can lead to pulmonary haemorrhage. Epilepsy patients with increased respiratory rates after convulsion and diffuse pulmonary interstitial changes visible on lung CT should consider the possibility of pulmonary haemorrhage. Although pulmonary haemorrhage caused by epilepsy can be alleviated by itself, in view of the potential risk of NPE, when considering whether children with epilepsy need to use antiepileptic drugs, the risks and benefits caused by pulmonary haemorrhage in children with epilepsy should also be considered.

Declarations

Ethics statement: The legal guardian was informed that their consent and participation in the publication of this case report was entirely voluntary.

Author contribution statement: All the authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement: Data will be made available upon request.

Declaration of interest statement: The authors declare that they have no conflicts of interest.

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