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Case report

Pneumomediastinum while using mechanical insufflation-exsufflation after recovery from riluzole-induced interstitial lung disease

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ABSTRACT

We, herein, report a 61-year-old male patient with amyotrophic lateral sclerosis (ALS) complicated pneumomediastinum while using mechanical insufflation-exsufflation (MI-E) after recovery from riluzole (RZ)-induced interstitial lung disease (RZ-ILD). After the treatment of RZ-ILD, he required non-invasive mechanical ventilation (NIV) at minimal pressure settings and MI-E to manage ALS-related breathing and airway-clearance issues, respectively. After a while, he developed progressive worsening dyspnoea, and chest computed tomography revealed extensive pneumomediastinum that had spread to the area surrounding the oesophagus, the retrosternal space, and the pericardial space. He was treated with immediate discontinuation of MI-E; however, he had to keep using NIV to support his severe respiratory muscle involvement. Pneumomediastinum gradually reduced in size and no recurrence of pneumomediastinum occurred. The clinical course of our patient suggests that excessive coughing associated with MI-E combined with his previous RZ-ILD, which potentially renders his lungs vulnerable to airway pressure, may have been the aetiological factors for secondary pneumomediastinum, i.e. barotrauma. Clinicians should be aware of the risk of pneumomediastinum while using MI-E in patients with ALS, who have other pre-existing risk factors for pneumomediastinum, such as drug-induced ILD in our case.

1. Introduction

Pneumomediastinum is defined as the presence of air in the mediastinum and commonly occurs as a result of alveolar rupture. Secondary pneumomediastinum generally has an identifiable cause, such as trauma, or predisposing intrinsic lung and airway pathologies including chronic obstructive pulmonary disease (COPD), excessive coughing due to asthma, or interstitial lung disease (ILD) [1]. Pneumomediastinum is typically self-resolving and requires only conservative management, without requiring prolonged hospitalisation; however, tension pneumomediastinum obstructs the great vessels of the heart and causes cardiac tamponade, which necessitates invasive intervention [2].

Riluzole (RZ) is the first the United States Food and Drug Administration approved drug used to treat amyotrophic lateral sclerosis (ALS) and its tolerability is generally good and adverse events due to RZ are acceptable in clinical practice; however, patients with ALS treated with RZ have possibly presented with rare but potentially life-threatening RZ-induced ILD (RZ-ILD), which could render the lungs vulnerable.

We, herein, report an instructive case of pneumomediastinum while using mechanical insufflation-exsufflation (MI-E), which produces adequate coughing by mechanical pressure supports, after recovery from RZ-ILD in a patient with ALS.

2. Case report

A 61-year-old male developed, who presented to the emergency department with a 6-day history of progressively worsening dyspnoea, had developed potentially life-threatening pneumomediastinum after recovery from RZ-ILD.

He developed progressive muscle weakness in his left limbs, dysarthria, dysphagia, exertion dyspnoea and body weight loss 8 months before the current presentation [3]. Then, he was diagnosed with clinically definite ALS according to the revised El Escorial criteria 5 months prior to the current presentation [4]. Then, 6 weeks after initiating

Abbreviations: ALS, amyotrophic lateral sclerosis; COPD, chronic obstructive pulmonary disease; CT, computed tomography; GGO, ground-glass opacities; ILD, interstitial lung disease; KL-6, Krebs von den Lungen-6; MI-E, mechanical insufflation-exsufflation; NIV, non-invasive mechanical ventilation; RZ, riluzole; RZ-ILD, riluzole-induced interstitial lung disease.

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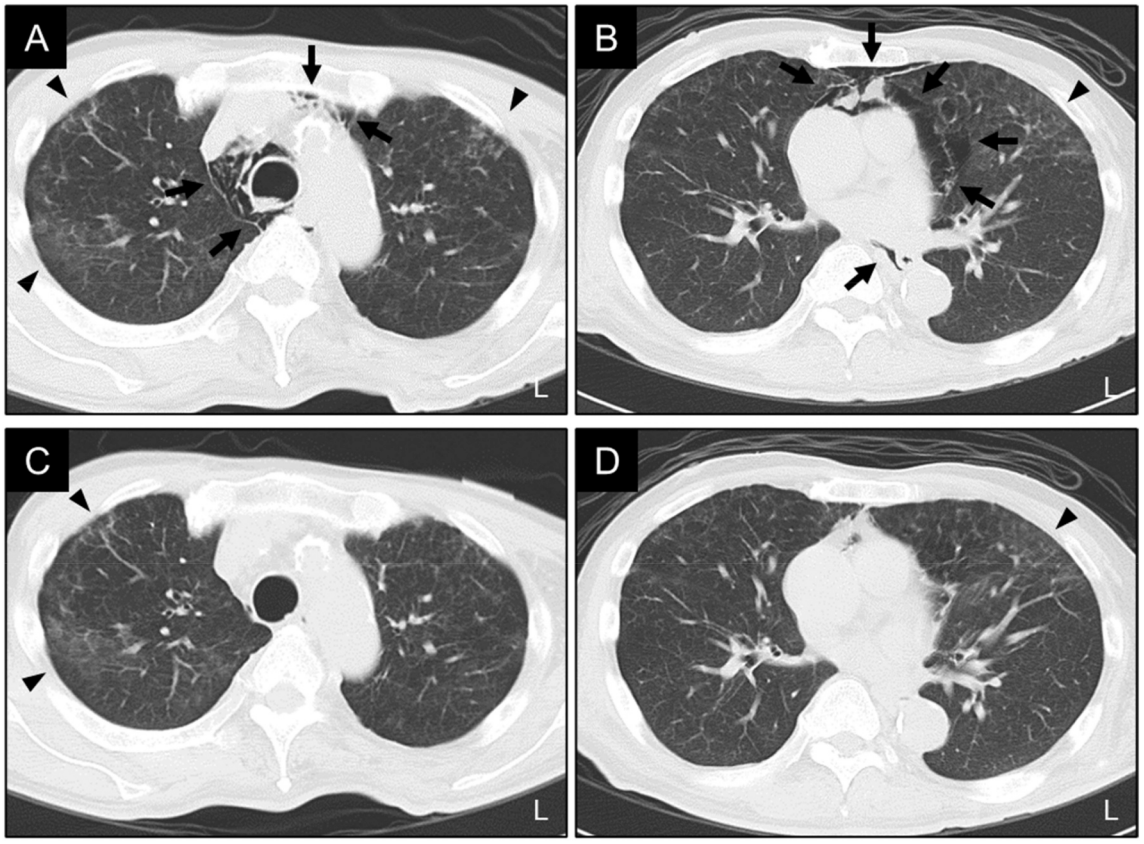

Fig. 1. Series of chest computed tomography images of a patient with amyotrophic lateral sclerosis with pneumomediastinum while using mechanical insufflation-exsufflation after recovery from riluzole-induced interstitial lung disease.
(A, B) Chest computed tomography (CT) images performed at current admission revealed an extensive pneumomediastinum that had spread around the oesophagus, the retrosternal space, and the pericardial space (i.e. pneumopericardium) (arrows). Despite high-dose steroid therapy, presence of residual ground-glass opacities (GGO) from riluzole-induced interstitial lung disease (RZ-ILD) was observed in both lungs (arrowheads). (C, D) After a 2-week conservative treatment including immediate discontinuation of mechanical insufflation-exsufflation, pneumomediastinum almost disappeared on chest CT. Residual GGO from the RZ-ILD was still observed in both lungs (arrowheads).

treatment of RZ 100 mg daily, and 3 months before the current presentation, he developed dyspnoea at rest together with exertional dyspnoea. Physical examination disclosed fine crackles in both lung bases, and chest computed tomography (CT) revealed dorsal dominant ground-glass opacities (GGO) in his bilateral lobes. Blood laboratory analyses showed elevated white blood cell count 9200/μL, C-reactive protein 5.68 mg/dl, and lactate dehydrogenase 403 IU/l. Although Krebs von den Lungen-6 (KL-6), which is a serological biomarker for ILD, was within normal limits in early-stage, follow up evaluation showed an elevation of KL-6. Auto-antibodies and infectious agents were not detected upon serological analysis. Considering the possibility of RZ-ILD for his ILD, RZ was withdrawn and he received non-invasive mechanical ventilation (NIV) to support his respiration. However, his hypoxemia and findings of GGO on chest CT worsened. Therefore, he was additionally treated with high-dose intravenous methylprednisolone 1 g daily over 2 weeks, resulting in a marked improvement in dyspnoea, chest CT findings of GGO and laboratory findings. According to the clinical characteristics of his ILD, including duration of RZ exposure until ILD onset and good response to the treatment in our patient were compatible with previous cases of RZ-ILD, he was finally diagnosed with RZ-ILD.

He did not develop relapse of RZ-ILD in the absence of continuous oral steroid therapy. However, he continued to require NIV at minimal pressure settings (inspiratory and expiratory airway pressures of 8 and 4 cm H_2O, respectively) to manage ALS-related breathing issues and MI-E with inspiratory and expiratory pressures of +30 and − 30 cm H_2O, respectively, to help with airway-clearance issues. No findings indicated pneumomediastinum or subcutaneous emphysema, despite the presence of residual ground-glass opacities from RZ-ILD in both lungs on chest X-rays and CT.

A physical examination during his current hospital admission revealed low-grade fever and tachycardia. Abnormal breath sounds and subcutaneous emphysema were not observed. Although chest X-ray showed no abnormalities in the lung fields, chest CT revealed extensive pneumomediastinum that had spread to the area surrounding the oesophagus, the retrosternal space, and the pericardial space (i.e. pneumopericardium) (Fig. 1A, B). Potentially life-threatening causes of pneumomediastinum, such as laryngeal, tracheobronchial, and oesophageal rupture, were excluded through endoscopy and CT assessments, whereas the mild symptoms observed in the current patient suggested that these were not the cause of his pneumomediastinum. He was managed conservatively with immediate discontinuation of MI-E and intravenous administration of prophylactic antibiotics; however, he had to keep using NIV to support his severe respiratory muscle involvement. Pneumomediastinum gradually reduced in size and he was discharged 18 days after presentation, with no recurrence of pneumomediastinum (Fig. 1C, D).

3. Discussion

In patients with ALS, the generation of adequate coughing for airway-clearance becomes ineffective due to the respiratory and bulbar muscle involvement. Mechanical insufflation-exsufflation, which delivers rapid positive inspiratory pressure followed by negative pressure

and supports to produce adequate coughing, is considered being beneficial for airway-clearance [5,6]. Although transpulmonary pressure that distends the alveoli is not usually enough to cause alveolar rupture during physiological coughing, additional pressure induced by MI-E could superimpose transpulmonary pressure on the injured lung, resulting in alveolar rupture in our patient. Alveolar rupture is followed by air dissection along bronchovascular sheaths and the spread of this pulmonary interstitial emphysema into the mediastinum, eventually leading to pneumomediastinum [7]. This pathophysiological mechanism, otherwise known as the "Macklin effect", has been considered to be involved in blunt traumatic pneumomediastinum [8]. Greater than 95% of pneumomediastinum cases result from alveolar rupture, whereas tracheobronchial ruptures or oesophageal tears are minor causes of pneumomediastinum [9,10]. Indeed, immediate discontinuation of MI-E alone led to a complete resolution of pneumomediastinum in our patient, even with continued NIV. This result suggests that excessive coughing associated with MI-E combined with his previous RZ-ILD, which potentially renders his lungs vulnerable to airway pressure, may have been the aetiological factors for secondary pneumomediastinum, i.e. barotrauma.

In conclusion, pneumomediastinum could occur while using MI-E in ALS patients who recovered from RZ-ILD, as a result of barotrauma. In acute respiratory symptoms in patients with ALS after recovery from RZ-ILD, pneumomediastinum should be taken into consideration as differential diagnoses, as well as ventilation failure and aspiration pneumonia due to the involvement of respiratory muscle and bulbar palsy, respectively. Although our case report does not conclude a direct causative link between MI-E use and pneumomediastinum, clinicians should be aware of the risk of pneumomediastinum while using MI-E in patients with ALS, who have other pre-existing risk factors for pneumomediastinum, such as a history of ILD, use of NIV, or COPD.

Author contributions

1) Conception and design of the study.
Yuji Saitoh.
2) Primary patient care and analysis of data.
Yuji Saitoh, Masayuki Miyazaki, Nobuaki Arai, Yuji Takahashi.
3) Drafting a significant portion of the manuscript or figure/table.
Yuji Saitoh.
4) Reviewing and approving the final manuscript.
Yuji Saitoh, Masayuki Miyazaki, Nobuaki Arai, Yuji Takahashi.

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Informed consent

The authors have obtained written informed consent for publication from the next-of-kin of patient.

Declaration of Competing Interest

All authors declare that there is no conflict of interest to disclose.

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