Difficulties in tracheal extubation due to phrenic nerve injury during massive mediastinal tumor resection
A case report
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Abstract
Rationale: Massive mediastinal tumors present a major challenge for surgery and anesthesia management due to possible perioperative circulation and respiratory dysfunction.

Patient concerns: A 36-year-old female underwent difficulty with tracheal extubation and required mechanical ventilation for 3 months after resection of a massive mediastinal tumor.

Diagnoses: Postoperative B-ultrasound examination of diaphragmatic motor weakness and electrophysiological examination indicated respiratory failure due to phrenic nerve injury.

Interventions: The patient failed tracheal extubation several times after the operation and finally a tracheotomy was performed. Mechanical ventilation, anti-infective treatment, and systemic supportive treatment were provided.

Outcomes: The patient recovered well after tracheotomy and approximately 3 months of ventilation support.

Lessons: Weaning difficulty caused by phrenic nerve injury seriously affected patient postoperative rehabilitation. To reduce the occurrence of similar problems, intraoperative phrenic nerve electrophysiological monitoring should be conducted.

Abbreviations: CMAPs = compound motor action potentials, CT = computed tomography, ICU = intensive care unit.

Keywords: mediastinal tumor, phrenic nerve electrophysiological monitoring, phrenic nerve injury, tracheal extubation

1. Introduction
Mediastinal tumors are anatomically adjacent to the phrenic nerve and may cause damage to the phrenic nerve during massive mediastinal tumor surgery. At present, the monitoring of phrenic nerve function is not perfect, and injury is often difficult to detect in good time,1,2 which may result in blind extubation after surgery and complications from long-term intubation. Here, we report a case of difficult extubation in a 36-year-old female patient due to intraoperative phrenic nerve injury. We believe that this case highlights the importance of good intraoperative monitoring and appropriate postsurgery extubation time to reduce the occurrence of these complications.

2. Case report
Approval was obtained from the Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University for reporting of this case.

A 36-year-old female patient presented at the hospital complaining of “cough and chest tightness.” The patient had no history of severe systemic disease or surgery. No abnormalities were noted on physical examination. Pulmonary function tests showed mild obstructive and restricted ventilation dysfunction.

Laboratory data were predominantly normal. Chest-enhanced CT showed a soft tissue mass in the anterior mediastinal space (Fig. 1A; approximately 12.3 × 5.8 cm), which was diagnosed as a tumor. Thymoma was considered, and chest X-ray showed that the upper mediastinum was significantly wider than normal (Fig. 1B).

Pathological examination of mediastinal puncture specimens indicated that type B1 thymoma should be considered, and T lymphoblastoma was not excluded.

Following an evaluation of anesthesia, routine monitoring was organized for the patient in the operating theatre. Left radial artery and femoral vein catheterizations were performed under B-ultrasound guidance. Anesthesia was induced using rapid induction intubation after intravenous administration of

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Medicine (2019) 98:26(e16252)

Received: 4 January 2019 / Received in final form: 1 May 2019 / Accepted: 7 June 2019
http://dx.doi.org/10.1097/MD.0000000000016252
etomidate (20 mg), fentanyl (0.3 mg), and rocuronium (50 mg). We used visual laryngoscope exposure to intubate with a steel wire tracheal tube (internal diameter, 8 mm). Fiberoptic bronchoscopy examination revealed that the trachea and both bronchi were unobstructed.

We hypothesized that the mass might be attached to the right lung; therefore, the right bronchus was inserted into an occluded tube, under the guidance of a fiberoptic bronchoscope, to facilitate separation of the right lung during the procedure.

Anesthesia was maintained with a continuous intravenous injection of propofol (4–6 mg/kg/h) and remifentanil (8–10 μg/kg/h), and a bolus of cis-atracurium (5 mg/30 min). Medial adhesion of the thoracic cavity was observed during the operation. The focus of the anterior mediastinum invaded the pericardium and blood vessels, and was wrapped around the aortic arch and its 3 branches. Anterior mediastinal mass resection was performed, followed by reconstruction of the superior vena cava and ligation of the thoracic duct, pericardectomy, and separation of the bilateral phrenic nerves.

The operation lasted for approximately 7 hours. The patient was transferred to the intensive care unit (ICU) with tracheal intubation immediately after the operation due to separation of the bilateral phrenic nerves and extended operation time.

The patient was ventilated using a pressure control mode, with a set pressure of 25 cmH₂O after the operation. On postoperative day 1, the patient’s respiratory frequency increased rapidly in the breathing exercise before attempting to extubate, tidal volume was low, and sweating appeared. The motion displacement of the right and left diaphragm was approximately 5 and 4 mm, respectively, as measured on B ultrasound (normal range, 14 ± 4 mm under calm breathing), which indicated that the motion amplitude of the bilateral diaphragm was decreased. These results suggested that, except for thoracotomy, phrenic nerve injury could not be ruled out. The anti-acetylcholine antibody test was negative on postoperative day 2. Postoperative pathology revealed a diagnosis of T lymphoblastic lymphoma, which ruled out thymoma; therefore, the neuromuscular junction lesion was not implicated in any postoperative respiratory insufficiency.

The patient was extubated on postoperative day 3; however, this led to shortness of breath, rapid heart rate, and elevated blood pressure with no improvement after high flow oxygen inhalation and noninvasive ventilator-assisted respiration. Therefore, intubation was done again. The motion displacement of the right and left diaphragm was approximately 7.9 and 10 mm, respectively, which indicated recovery of bilateral diaphragm movement. However, the right diaphragm movement remained weak. Electromyography revealed that motor fiber conduction latency of the right phrenic nerve was over 2 times longer than the left phrenic nerve. Further, the motor wave amplitude decreased to one-third of the left phrenic nerve. There was no increase in amplitude during high-frequency stimulation, suggesting that the right phrenic nerve myelin sheath and axonal cord were damaged.

Next, the patient was treated with cefuroxime to prevent infection; ambroxol hydrochloride to eliminate phlegm; and methycobal and other nerve growth factors to support nerve nutrition. She remained ventilated in a pressure control mode. Ten days after the operation, chest CT (Fig. 2A) and airway reconstruction (Fig. 2B, C) showed no obvious infection or stenosis of the airway. Extubation was attempted 14 days after the operation; however, 1 h after extubation, the respiratory rate increased and was accompanied with dyspnea. Secondary intubation was performed and the laryngoscope showed obvious glottic edema. A tracheotomy was carried out the next day.

The patient was obviously anxious after operation and treated with citalopram to reduce anxiety. The dyspnea of the patient improved gradually and almost recovered 3 months after the operation. At that time, fiberoptic bronchoscopy examination showed that the main bronchus was unobstructed. A chest X-ray examination only showed a small amount of pleural effusion on the left side (Fig. 3). Following this, the tracheal cannula was removed and the patient was transferred to the general ward. After 1 week, the patient was discharged from the hospital.

3. Discussion

Tracheal extubation has high risk for anesthesia. At the end of certain surgeries, the pathophysiology of patients may have changed significantly; therefore, tracheal extubation is a reversal of the intubation process, but also a greater challenge to postoperative success.

In this case, the difficulty of extubation following surgery to remove a mediastinal tumor may be related to phrenic nerve injury caused by the separation of phrenic nerves during the operation. On postoperative day 1, the patient was obviously anxious after operation and treated with citalopram to reduce anxiety. The dyspnea of the patient improved gradually and almost recovered 3 months after the operation. At that time, fiberoptic bronchoscopy examination showed that the main bronchus was unobstructed. A chest X-ray examination only showed a small amount of pleural effusion on the left side (Fig. 3). Following this, the tracheal cannula was removed and the patient was transferred to the general ward. After 1 week, the patient was discharged from the hospital.

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operation. Our hypothesis is related to the following details: the postoperative anti-acetylcholine antibody test was negative; CT airway 3D reconstruction suggested airway patency; and B-mode ultrasound and electromyography suggested that diaphragm movement and phrenic nerve conduction were weakened.

The phrenic nerve is a branch of the cervical plexus, which is composed of the 3 to 5 anterior branch of the cervical plexus that descends obliquely with the internal jugular vein across the anterior scalene, deep to the prevertebral layer of deep cervical fascia, and the transverse cervical and suprascapular arteries. The phrenic nerve runs posterior to the subclavian vein as it joins the thorax, where it runs anterior to the root of the lung and between the pericardium and mediastinal face of the parietal pleura. It supplies the motor fibers to the diaphragm and sensory fibers to the pericardium, mediastinal pleura, and diaphragmatic peritoneum.\(^4\)

Its special anatomy and adjacent relationship mean that mediastinal tumors, especially those in excess of 10 cm, can easily invade the phrenic nerve and are highly susceptible to be injured during the operation for resection of these tumors. Injury of the phrenic nerve most commonly occurs in surgical or therapeutic procedures, such as cardiac and thoracic surgery, radio frequency ablation, and nerve block.\(^5\) The clinical manifestations of phrenic nerve injury are not specific; unilateral injury may show no obvious symptoms. Conversely, diaphragmatic elevation, gastrointestinal displacement, intestinal paralysis, acute cardiac tamponade, and acute respiratory distress syndrome have been shown in severe cases.\(^9\) The diagnosis of phrenic nerve injury includes B ultrasound, X-ray examination, and electromyography; however, electrophysiological examination remains the gold standard.\(^10\)

In this case, B-mode ultrasound in the patient showed weakened movement of the double-side phrenic muscle; however, the cause was not clear. Electromyogram examination showed the phrenic nerve conduction function more objectively, which enabled a more efficient diagnosis.

The recovery time of phrenic nerve injury varies from days to years after the injury; however, the range is commonly between 6 and 12 months.\(^11\) If the symptoms of unilateral phrenic nerve injury are mild, patients can recover spontaneously after treatment, such as respiratory exercise. In addition, diaphragm plication surgery can relieve dyspnea caused by severe bilateral phrenic nerve injury.

The clinical manifestation of this injury is not specific, recovery time can be lengthy, and the postoperative rehabilitation of patients can be severely affected; therefore, it is important to find a method to effectively monitor phrenic nerve function during surgery to injury. The traditional method enables physicians to assess diaphragm muscle movement directly under the costal margin, and use X-ray to observe the mobility of the diaphragm and angiography positioning before surgery. However, these methods are rarely used.\(^14\) Recent studies have shown that 3D reconstruction modeling of the heart and blood vessels can be obtained using 3D electroanatomic mapping in radiofrequency ablation. Furthermore, pacing is used to locate the phrenic nerves in the superior vena cava, subclavian vein, or hepatic vein. This can effectively reduce the incidence of phrenic nerve injury.\(^12,13\)

Previous studies have placed a phrenic nerve pacing catheter in the superior vena cava and electrocardiogram lead electrodes in the right and left arms 5 cm above the xiphoid and 16 cm along the right rib from the xiphoid, to form a modified electrocardiogram lead 1.\(^14,15\) During the operation, diaphragmatic com-

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**Figure 2.** Chest computed tomography (A) and airway reconstruction (B) of the patient 10 days after the operation. The mass in the anterior mediastinum was removed; there was no obvious infection (A), and the airway is unobstructed (B).

**Figure 3.** Chest X-ray of the patient 3 months after the operation.
pound motor action potentials (CMAPs) were continuously monitored, and injury was considered when these fell 30 to 35% below baseline. In addition, Ghosh et al[16] have indirectly predicted the occurrence of phrenic nerve injury by monitoring changes in femoral vein pressure waveform during radiofrequency ablation. However, these new technologies are rarely used in other surgical procedures and limited application in thoracotomy, indicating that their stability and application value require further study.

Duque et al[17] have used the nerve monitoring system (NIM 2.0 or 3.0; Medtronic, Jacksonville, FL) to ensure phrenic nerve integrity for the first time during neck dissection for advanced thyroid cancer. The procedures were done with a phrenic nerve stimulation current of 0.5 or 0.3 mA on the triangle area of clavicle and the trapezius muscle. Surgeon and anesthesiologist observations of the contraction of the diaphragm or the rising of the thoracic wall determined the integrity of the phrenic nerve. However, an electrode remains necessary in the downstream intercostal muscle or diaphragm to record the contraction of diaphragm, but it is not widely used because of its invasiveness and high cost. This method performs nerve stimulation in the supraclavicular region and makes it possible for use in thoracotomy.

In this case, the mediastinal tumor was huge and had invaded the surrounding blood vessels and nerves. The phrenic nerve was isolated during the operation, but its function was not effectively monitored, which caused a delay in diagnosis and a tracheotomy was performed after multiple extubations. The patient experienced glottic edema, lung infection, and severe anxiety during hospitalization, which seriously affected the rapid recovery after surgery. If the phrenic nerve injury was detected early by the monitoring system or electrophysiology, clinicians may have extended the time of extubation or proceed with a tracheotomy immediately after surgery. This may shorten the recovery time and reduce any postoperative complications.

4. Conclusions

The difficulty of weaning caused by phrenic nerve injury seriously affects the postoperative rehabilitation of patients. Therefore, in cardiac and thoracic surgery, surgeons and anesthesiologists should fully recognize the possibility of its occurrence. Phrenic nerve function should be continuously monitored during surgical procedures in which the phrenic nerve is at risk of injury. Furthermore, any difficulty in extubation should be predicted, ensuring the appropriate time of extubation is chosen, and relevant rescue measures are performed.

Author contributions

K-RW and F-FL collected clinical data, F-FL wrote the original manuscript, Y-FZ reviewed and revised the manuscript. All authors gave final approval of the version to be published.

Data curation: Kui-Rong Wang, Fan-Fan Liu.
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