

[CASE REPORT]

Enlargement of Intrathoracic Goiter with Unilateral Phrenic Nerve Paralysis Leading to Cardiopulmonary Arrest

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Abstract:

As an intrathoracic goiter expands, it causes airway stenosis and phrenic nerve paralysis, and slight respiratory stimuli can trigger sudden life-threatening hypoventilation. A 78-year-old obese woman with a large intrathoracic goiter was found unconscious with agonal breathing in her room early in the morning. Cardiopulmonary resuscitation restored spontaneous circulation. She underwent surgical removal of the goiter; however, she required long-term mechanical ventilation because of atelectasis due to phrenic nerve paralysis. In patients with large intrathoracic goiters, difficulty breathing on exertion and diaphragm elevation on chest X-ray may be significant findings predicting future respiratory failure.

Key words: cardiopulmonary arrest, intrathoracic goiter, phrenic nerve paralysis

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Introduction

Intrathoracic goiters are benign tumors and occur within the mediastinum or thoracic cavity. A large intrathoracic goiter, due to its mass effects, may cause life-threatening complications if it compresses cardiorespiratory structures, such as the tracheobronchial airway, the main pulmonary artery, the atrium, and the superior vena cava (1). In particular, the effects of compression on the airways are serious problems. It has been reported that airway obstruction due to increased intratumoral hemorrhaging causes cardiopulmonary arrest (CPA) (2, 3). A combination of tumor-related tracheal stenosis and unilateral phrenic nerve palsy, obesity, and sleep posture can lead to life-threatening hypoventilation, even if there is no apparent obstruction, such as massive intratumoral hemorrhaging.

We herein report a case in which respiratory failure was exacerbated due to some kind of trivial respiratory stimuli, such as sputum or cough, in the course of a precarious res-

piratory condition associated with tumor enlargement.

Case Report

The patient was a 78-year-old woman who had been diagnosed with a large intrathoracic goiter at another hospital. Eighteen months later, she was referred to our hospital, underwent some preoperative examinations, and then went home. The respiratory function tests revealed severe restrictive lung disorder (Table 1). Chest X-ray depicted a large mass in the upper mediastinum that was compressing the trachea to the left, and the right side of the diaphragm was elevated (Fig. 1A). Early the next morning, her family found her lying in bed, unconscious, and they called an ambulance immediately. Bystander cardiopulmonary resuscitation was not performed. When emergency personnel arrived at the scene, she had agonal breathing and pulseless electrical activity according to a medical monitor. Chest compressions and laryngeal tube insertion were subsequently performed by an emergency medical technician. Spontaneous circula-

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Table 1. A Respiratory Function Test on the Day before Hospitalization.

VC	0.53 L	FVC	0.56 L
%VC	25.4 %	FEV _{1.0}	0.47 L
ERV	0.12 L	FEV _{1.0%}	83.93 %
IRV	0.24 L	PEF	1.74 L/s
TV	0.17 L	MMF	0.54 L/s
IC	0.41 L		

VC: vital capacity, %VC: % vital capacity, ERV: expiratory reserve volume, IRV: inspiratory reserve volume, TV: tidal volume, IC: inspiratory capacity, FVC: forced vital capacity, FEV_{1.0}: forced expiratory volume in one second, FEV_{1.0%}: forced expiratory volume % in one second, PEF: expiratory peak flow, MMF: maximal mid-expiratory flow

tion returned after cardiopulmonary resuscitation and the administration of a total of 2 mg of epinephrine.

On arrival at our hospital, she was afebrile (34.9°C), with a blood pressure of 119/74 mmHg, a regular pulse of 93 bpm, no spontaneous breathing, and an oxygen saturation of 93% under bag valve mask ventilation with 10 L/min oxygen flow. The patient did not require continued chest compressions or catecholamine administration but did need ventilator management because she had no spontaneous breathing. An arterial blood gas analysis at this time showed severe respiratory acidosis (Table 2). She did not have an obvious airway obstruction due to expectorated sputum or foreign bodies. Tracing her medical history, according to her family members, she had complained of mild dyspnea and

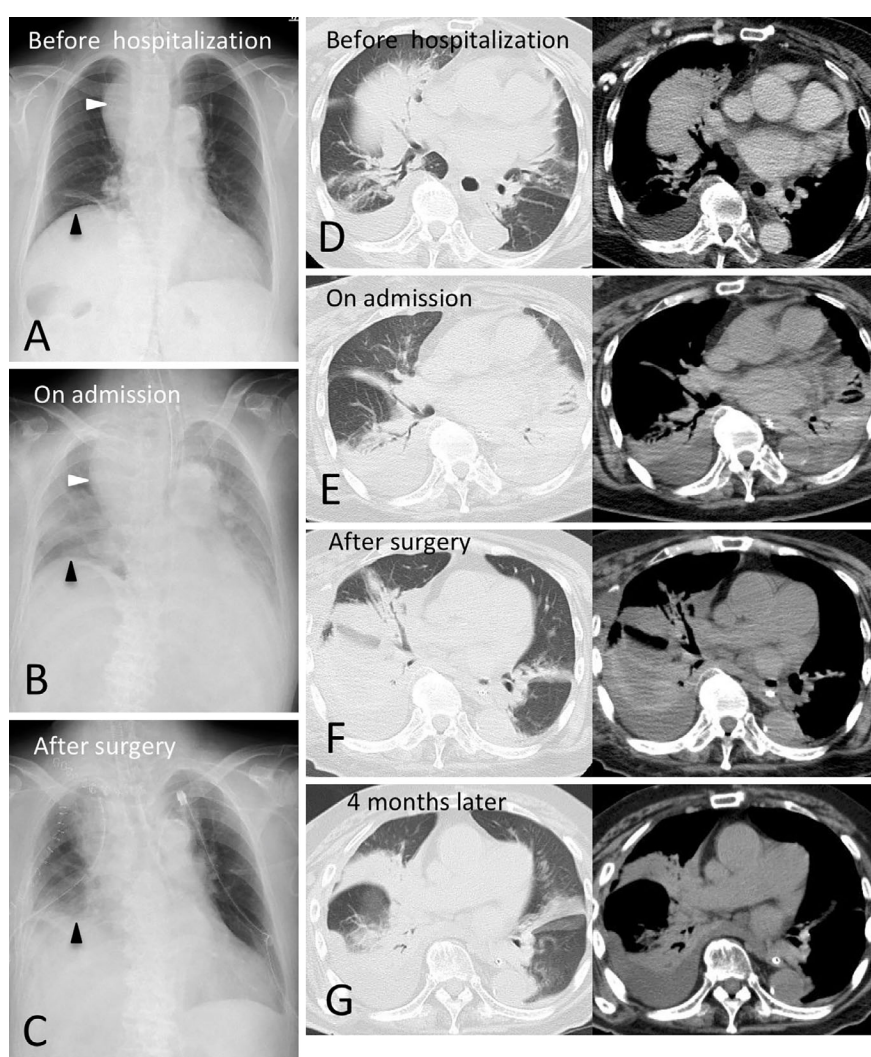


Figure 1. A, D: Chest X-ray and chest CT on the day before hospitalization. X-ray demonstrated a large thyroid mass (white arrowheads) with retrosternal extension and deviation of the trachea to the right. The right side of the hemidiaphragm was elevated (black arrowheads). In contrast, the left side was not elevated (A). Chest CT showed small pleural effusion and atelectasis on the right lung (D). B, E: Chest X-ray and chest CT on admission. On X-ray, the left diaphragmatic shadow was not clear (B), and on CT, the atelectasis areas on both sides were enlarged (E). C, F: Chest X-ray and chest CT after surgery. X-ray showed improvement in tracheal deviation. The level of the right diaphragm was unchanged (C). On CT, the left atelectasis disappeared; however, the right atelectasis was further enlarged (F). G: CT after four months did not reveal any improvement in atelectasis.

Table 2. Blood Test Results of Our Case on Admission.

Complete blood cell count and biochemical tests			
WBC	12,800 / μ L	BUN	32.4 mg/dL
RBC	4.33×10^6 / μ L	Creatinine	1.59 mg/dL
PLT	16.3×10^4 / μ L	CRP	0.3 mg/dL
AST	702 IU/L	TSH	0.4 μ IU/mL
ALT	520 IU/L	F-T3	3.0 pg/mL
LDH	1,757 IU/L	F-T4	1.1 ng/dL
CK-MB	15 IU/L		
cTnI	0.08 ng/mL		
Arterial blood gas analysis (using Bag valve mask with 10 L/min O ₂ flow)			
pH	6.98		
PO ₂	63.7 mmHg		
PCO ₂	176.0 mmHg		
HCO ₃	25.7 mmol/L		

WBC: white blood cell count, RBC: red blood cell count, PLT: platelet count, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, CK-MB: creatine kinase-MB fraction, cTnI: cardiac specific troponin I, BUN: blood urea nitrogen, TSH: thyroid-stimulating hormone, F-T4: free thyroxine, F-T3: free triiodothyronine, PaO₂: partial pressure of arterial oxygen, PaCO₂: partial pressure of arterial carbon dioxide, HCO₃: bicarbonate

fatiguability on exertion but gone about her daily life. She had not undergone polysomnography during her clinical course and had no diagnosis of sleep-related breathing disorders.

Chest computed tomography (CT) demonstrated a large mass in the upper mediastinum (Fig. 2A). The trachea was compressed to the left (Fig. 2B, C), and the narrowest part had a diameter of 8 mm. Her height was 147 cm, her body weight was 58.4 kg, and her body mass index (BMI) was 27. She had a short neck and a relatively small jaw. On hospital day 2, her consciousness improved, and her circulation became stable. On day 14 of hospitalization, the tumor was successfully removed via a cervical collar incision combined with thoracotomy. During the operation, there was no adhesion between the goiter and the phrenic nerve. A pathological analysis confirmed the diagnosis of an adenomatous goiter (Fig. 3A, B).

Microscopic findings showed scattered fresh hemorrhaging in the tumor (Fig. 4). However, the amount of bleeding was not enough to cause airway obstruction. On hospital day 28, the right diaphragmatic elevation did not improve, and right atelectasis appeared on follow-up chest radiography (Fig. 1B, F). A nerve conduction velocity test revealed right phrenic nerve paralysis (Fig. 5). As a result, she received respiratory rehabilitation and prone position therapy for atelectasis. However, on hospital day 29, tracheostomy was performed because long-term airway management was considered necessary. Right phrenic nerve paralysis and atelectasis did not improve seven days after surgery (Fig. 1C, F). Because of the above, the patient was unable to be withdrawn from mechanical ventilator management,

and we performed a tracheotomy 15 days post-surgery. On day 69 of hospitalization, further long-term rehabilitation was considered necessary, and she was transferred to another hospital. Four months later, chest CT showed that the right diaphragm was still elevated, and atelectasis remained (Fig. 1G).

Discussion

Intrathoracic goiters are benign tumors that can cause life-threatening complications if they compress cardiorespiratory structures. In addition, as reported in the literature, airway obstruction due to massive intratumoral hemorrhaging may result in CPA (2, 3). Enlarged tumors can also compress the phrenic nerve. Phrenic nerve paralysis is considered a very unusual feature of intrathoracic goiter enlargement. The co-existence of phrenic nerve palsy, obesity, and a supine position during sleep may further promote hypoventilation. Chest X-ray findings of diaphragmatic paralysis indicated that the tumor had grown to compress the phrenic nerve. If patients have dyspnea on exertion, they are considered at risk of developing respiratory failure. To avoid respiratory failure, it is necessary to prevent the reduction of the ventilation volume. To this end, patients should be placed in a lateral position, with the affected side up, and their bowel movements should be controlled so as not to increase the abdominal pressure.

The spontaneous hemorrhaging of cervical goiters resulting in tracheal compression is well known. Three cases of cardiopulmonary arrest caused by severe airway obstruction associated with increased intratumoral hemorrhaging or excretion deficiency of sputum have been reported (Table 3) (2-4). In our patient, evidence of massive intratumoral hemorrhaging or an obvious airway foreign body was unclear. Evidence suggesting acute respiratory distress was suggested by blood gas findings that the partial pressure of carbon dioxide level was extremely high and the bicarbonate value was within the normal range along with elevated liver function enzyme levels (Table 2). In the present case, the serum creatine kinase and cardiac specific troponin I levels were not elevated, and the elevation of liver enzymes was considered to indicate hypoxia due to respiratory failure. Yokoyama et al. reported that elevated serum lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels were frequently observed as hepatic dysfunction (5). Kuriyama et al. noted that severe respiratory failure with hypoxemia presents ischemic hepatopathy with high levels of serum AST, ALT, and LDH (6). The cause of hypoventilation in the present patient was considered to be a combination of the following factors: i) airway narrowing due to giant goiter, ii) diaphragmatic paralysis evident from chest X-ray findings, and iii) obesity and sleep posture. In addition to these characteristics, dynamic airway collapse associated with sputum and cough was considered to have triggered the hypoventilation. Given the course of the right phrenic nerve, we considered it to

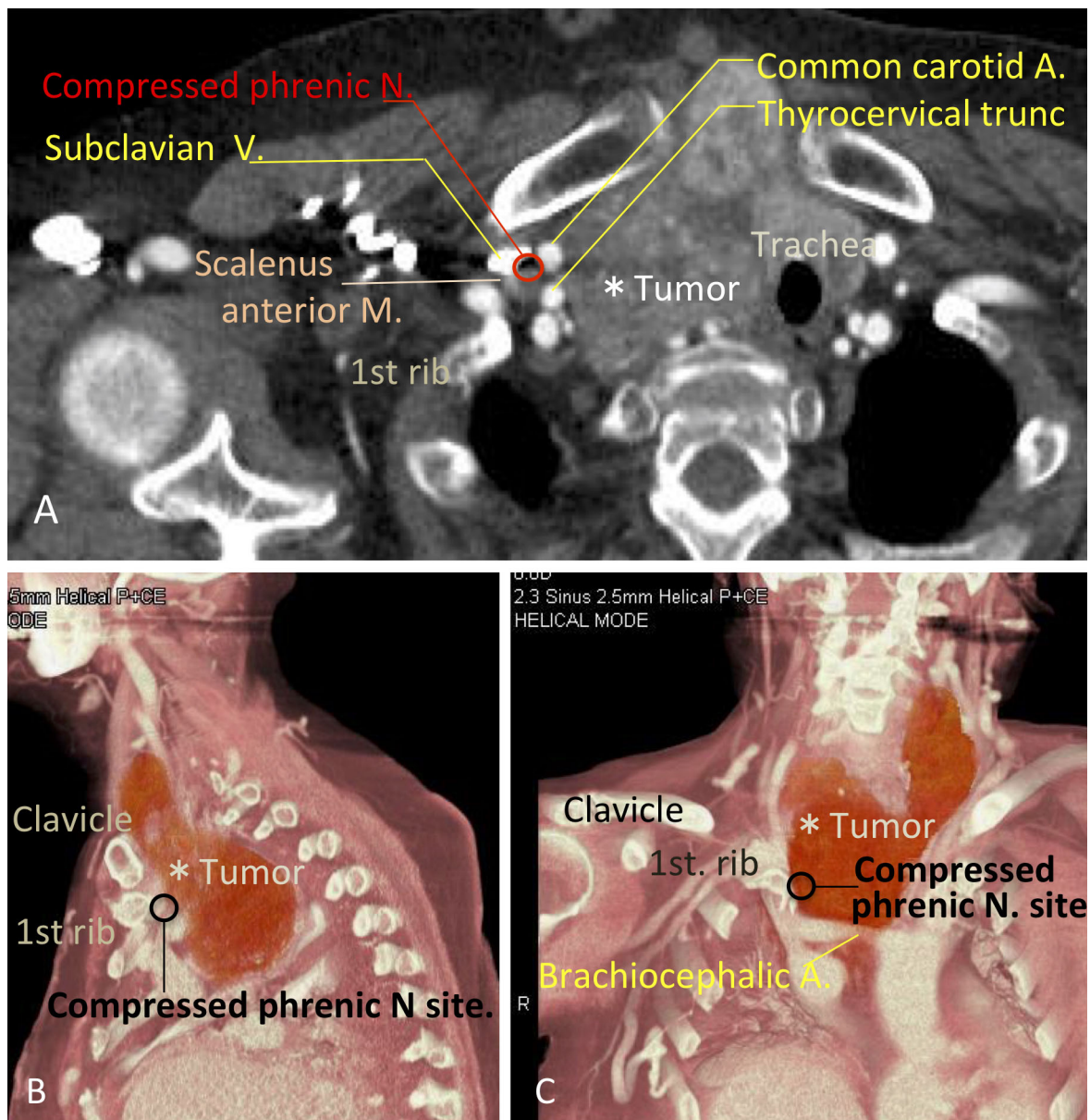


Figure 2. CT at the level of the clavicle revealed a large tumor causing significant deviation and compression of the trachea and the esophagus to the left side (A). Direct visualization of the nerve was difficult on CT. Axial, sagittal, and coronal CT sections revealed the expected location of the right phrenic nerve (red and white circle). The right phrenic nerve passed between the subclavian artery and the subclavian vein. The large tumor compressed the subclavian artery and vein to the right (A, C), and the right phrenic nerve was expected to be compressed at the level of the first rib (A, B).

have been compressed at the thoracic inlet near the first rib (Fig. 2). This can be explained anatomically by the positional relationship with the giant tumor. The right phrenic nerve runs vertically downward and across the front of the scalenus anterior muscle (Fig. 2A), passing over the brachiocephalic artery posterior to the subclavian vein (Fig. 2A, C). Even after tumor removal, phrenic nerve paralysis caused atelectasis (Fig. 1C, F), making it difficult to wean the patient from respiratory management.

Chest X-ray findings of diaphragmatic paralysis indicated that the tumor had grown to compress the phrenic nerve, suggesting a likelihood to progress to respiratory failure. The patient showed restrictive ventilatory impairment on a

respiratory function test the day before hospitalization, including anomalies with the vital capacity (VC) and expiratory reserve volume (ERV) (Table 1). Our patient had an airway diameter of 8 mm and no severe obstruction. However, new bilateral atelectasis was confirmed on CT (Fig. 1E), and it cannot be denied that airway clearance was not sufficient. She may have suffered excessive collapse of the trachea during cough and forced expiration.

As Ernst found, the symptoms of airway obstruction become dyspnea on exertion when the diameter has narrowed to less than 8 mm. When the diameter is less than 5 mm, the symptoms become severe, and patients experience dyspnea at rest (7). According to Murgu, the tracheobronchial lu-

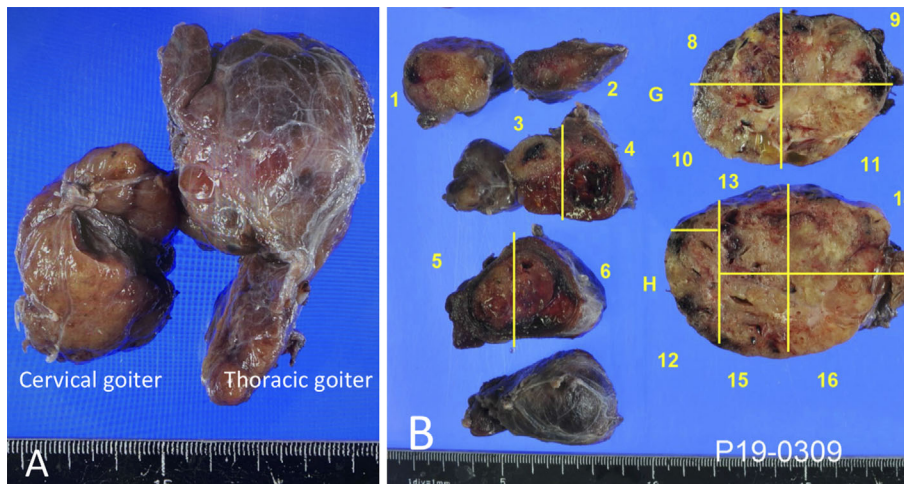


Figure 3. Excised intrathoracic goiter. The two lobes were enucleated and delivered from the cervical region completely intact. The size of the cervical tumor was 8.5×6.5×3.5 cm, and the size of the thoracic tumor was 12×8.0×5.0 cm (A). The gross picture of the resected specimen showed cystic degeneration with intra-thyroidal hemorrhaging and hematoma formation. (B).

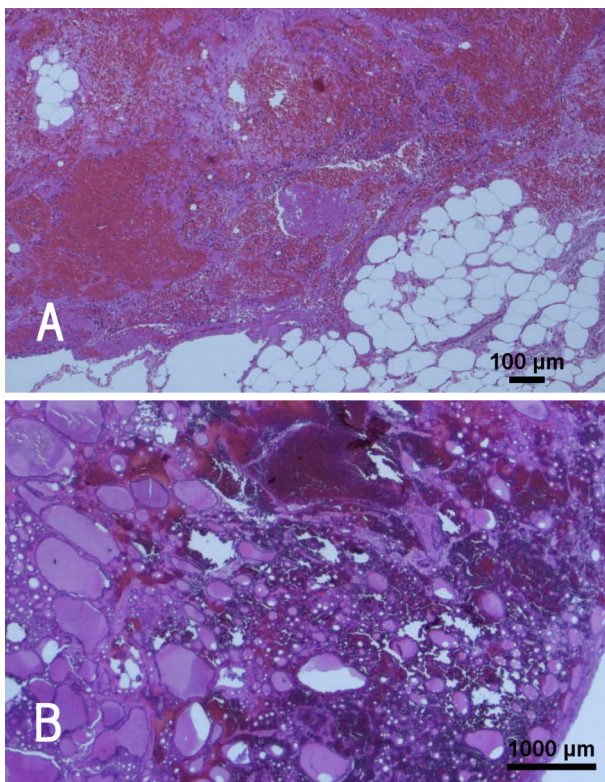


Figure 4. Microscopic findings showed hyperplastic follicles of varying sizes on a background of fibrosis and fresh hemorrhaging with partial calcification and hyalinization. (A) Hematoxylin and Eosin (H&E) staining, 40×, (B) H&E staining, 200×.

men during coughing was 18-39% narrower than the maximal inspiratory lumen observed during restful respiration. In healthy people, some degree of dynamic airway collapse is physiological and probably enhances expectoration and secretion clearance (8). Simon et al. reported that a 320-slice dynamic CT scan has the ability to capture such dynamic

airway stenosis (9), but the 64-slice CT at our facility failed to clarify such findings.

Although unilateral phrenic nerve paralysis is often asymptomatic, it should be noted that abdominal pressure and postural changes can reduce ventilation volume. Gould showed a 21% reduction in VC in a right phrenic nerve palsy group (8). According to Hino et al., a postoperative patient with right phrenic paralysis showed decreased oxygenation due to oral ingestion, abdominal distention, and sleep; however, oxygenation was improved by enemas and the adoption of a lateral position with the affected side up (10). The rapid shallow breathing index (RSBI) is defined as the ratio of the respiratory frequency to the tidal volume (f/V_T) and is usually an indicator of ventilator weaning (11). An RSBI of greater than 105 breaths/min/L is highly predictive of weaning failure (11, 12), and a high RSBI suggests that respiratory muscle weakness may be present (13). Noninvasive positive-pressure ventilation (NPPV) can be expected to produce upper respiratory tract patency, improve ventilation, and reduce respiratory muscle fatigue. The introduction of NPPV may be effective in patients spending increased effort to breath (14) and who have local atelectasis and lung volume reduction sites (15).

In the present case, the patient's respiratory rate was not measured on the previous day; however, she showed an extremely low V_T . Understanding the RSBI's variability will likely help predict the extent of respiratory muscle fatigue. Bowel management to relieve abdominal pressure and the adoption of a lateral position with the affected side up can be effective for preventing decreased ventilation. The worst-case scenario may be avoided by promptly using NPPV as well.

According to Shen, thyroid hormone or radioiodine ablation as a non-surgical treatment is usually not successful, and radiofrequency ablation can cause dyspnea, especially in elderly individuals (16). Most reviews strongly recommend

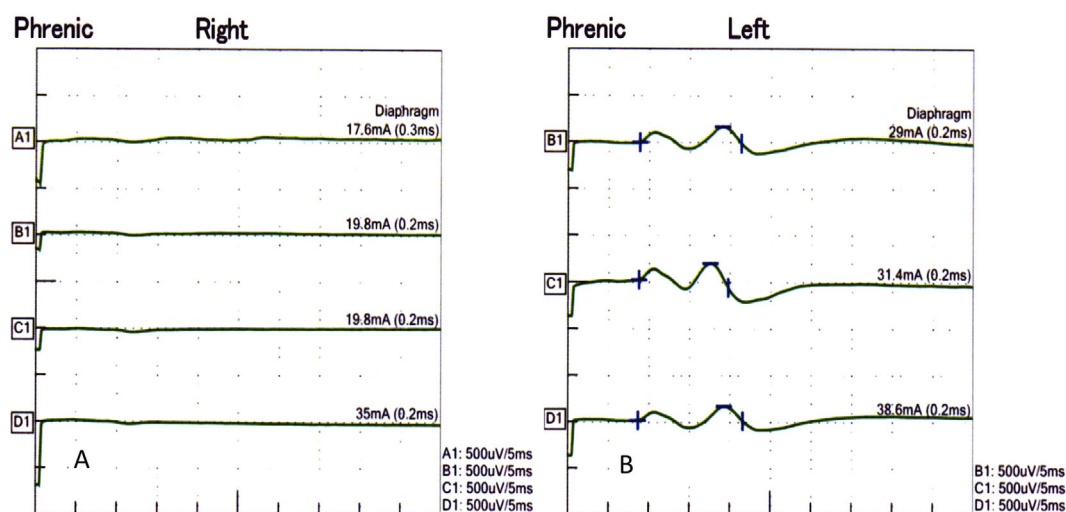


Figure 5. A motor nerve conduction study showed the absence of the right phrenic nerve; (A) compound motor action potential compared with the normal left side (B).

Table 3. Three Cases of Cardiopulmonary Arrest for Intrathoracic Goiter in the Literature.

Case	Reference	Age and gender	Cause of CPA	Intrathoracic goiter		Operation date	Outcome
				Size (cm)	Pathology		
1	2)	77 woman	choking on a candy (OHCA)	13.5×6.0×4.0	Thyroid nodule	no listed	survival
2	3)	64 woman	suspected sputum (OHCA)	5.2×3.3×4.3	Follicular adenoma	5th day	survival
3	4)	70 woman	suspected cough and sputum (IHCA)	no listed	no listed	emergency	survival

CPA: cardiopulmonary arrest, OHCA: out of hospital cardiac arrest, IHCA: in-hospital cardiac arrest

early surgery for patients with tracheoesophageal compression due to an enlarged intrathoracic tumor (16-18). Of the three cases of cardiopulmonary arrest, in Hirotsu's case, it was difficult to secure the airway, and emergency surgical tracheotomy including volume resection for the tumor was required due to severe airway obstruction (4). Airway management and oxygenation maintenance will likely become more severe after cardiopulmonary arrest. The procedure can usually be performed using the cervical approach, but at times, sternotomy or thoracotomy is necessary, depending on the size and location of the tumor. However, it has been reported that sternotomy leads to increased surgical stress of the patient, and the risk of mediastinitis is a severe problem, especially in cases with tracheotomy (17, 18). Our patient underwent surgery on day 14 of hospitalization, and tracheotomy was performed 15 days after the operation. No further complication of mediastinitis was noted.

In conclusion, the presence of phrenic nerve paralysis means that the intrathoracic tumor has expanded considerably, and respiratory failure may develop in the near future. Chest X-ray findings of diaphragmatic elevation and dyspnea on exertion suggest a high likelihood of future severe respiratory failure. Bowel management to relieve abdominal pressure, adoption of a lateral position with the affected side up, and the temporary use of NPPV until surgery may help prevent the further reduction of the ventilation capacity.

The authors state that they have no Conflict of Interest (COI).

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