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Gorham Syndrome with Post-operative Respiratory Failure and Requiring Prolonged Mechanical Ventilation

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ABSTRACT

Gorham syndrome is a rare disease that presents as progressive osteolysis and may affect any part of the skeleton. The pathologic process involves the replacement of normal bone by aggressively expanding but non-neoplastic vascular tissue resulting in massive osteolysis of the adjacent bone. If the spine and ribs are affected, the subsequent kyphosis and chest wall deformity may cause severe restrictive ventilatory impairment.

Here is a report of a 34-year-old male with Gorham syndrome presenting as progressive kyphosis with severe back pain and unstable gait. He also had exertional dyspnea. Pulmonary function test revealed severe restrictive ventilatory impairment. He underwent spinal operation but could not be extubated after surgery. Post-operative pulmonary complications of left lower lung pneumonia and respiratory failure required prolonged mechanical ventilation. After a weaning program of pressure support ventilation and T-piece trials, the patient was successfully weaned from mechanical ventilation.

Key words: Gorham syndrome; prolonged mechanical ventilation; respiratory failure; restrictive lung disease

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INTRODUCTION

Gorham syndrome is a rare chronic disorder that is characterized by the abnormal proliferation of thin-walled capillaries and small lymphatic vessels resulting in the massive osteolysis of the adjacent bone.[1-3] It may affect any part of the skeleton, but most commonly involves the skull, shoulders and pelvis.[1-3] The vertebrae, ribs and scapulae are other common sites.[4] When the spine and ribs are involved, Gorham syndrome can lead to severe kyphosis and chest wall deformity.[4, 5] These changes further lead to severe restrictive ventilatory impairment. The disease can occur at any age, but is common in adolescents and young adults.[2]

Here is a report of a 34-year-old male with Gorham syndrome. He suffered from progressive kyphosis with unstable gait and exertional dyspnea. Pulmonary function test revealed severe restrictive ventilatory impairment. Spinal surgery was done but respiratory failure happened with prolonged mechanical ventilation after operation. After a gradual weaning program, successful extubation and weaning from mechanical ventilation was performed in this case.

CASE SUMMARY

A 34-year-old male presented with lower back pain since 6 years ago. He was of normal intelligence and had no other clinical abnormalities. Family and medical

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histories were unremarkable. He consulted at the Department of Orthopedics where x-ray and computed tomography (CT) scan of the thoracolumbar (T-L) spine revealed T-L junctional kyphosis and multiple osteolytic lesions. From CT-guided biopsy via L3 vertebral body, there was granulation tissue with distinct vascularization. Gorham syndrome was diagnosed based on clinical, radiologic and histopathologic features. The patient then received radiotherapy and interferon–α treatment.

Two years ago, he developed left-sided pleural effusion. Thoracentesis revealed chylothorax. He received pig-tail catheter insertion for drainage of the effusion. Subsequent pleurodesis with minocycline (400 mg in 30 ml normal saline) was successful and no recurrent chylothorax was noted since then. The patient continued to follow-up at the Department of Orthopedics.

Recently, the patient experienced progressive kyphosis with severe back pain and unstable gait. Reconstructed CT scan of the T-L spine and chest revealed severe kyphosis and bony destruction over T12-L1 level (Fig. 1) and left lower ribs (Fig. 2). On physical examination, he had pronounced retraction of the left hemithorax and no palpable left lower ribs. He also had exertional dyspnea. Pulmonary function test of spirometry revealed severe restrictive ventilatory impairment with forced expiratory volume in one second (FEV1) of 0.91 L (25% of predicted value), forced

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vital capacity (FVC) 0.94 L (21% of predicted value), FEV1/FVC ratio 0.97. Lung volume test using body plethysmography documented total lung capacity (TLC) of 2.32 L (40% of predicted value), residual volume (RV) 1.2 L (88% of predicted value), functional residual capacity (FRC) 1.69 L (53% of predicted value), and RV/TLC ratio 52%.

For the severe kyphosis with unstable gait, the patient underwent surgery for T12 vertebral column resection, L1 pedical subtraction osteotomy with strut allografting, posterior instrumentation and infusion of T5~L4 and posterior decompression of T11~L1. The patient received pre-operative education of triflow incentive spirometry, directed cough, forced expiration, postural drainage and chest percussion to prevent post-operative complications. However, post-operatively, he became tachypneic, so extubation was not performed. He was then transferred to the intensive care unit (ICU) with pressure control ventilation (PCV) support at pressure control (PC) level 20 cmH_2O, positive end-expiratory pressure (PEEP) 5 cmH_2O, fraction of inspired oxygen (FiO_2) 30%, and tidal volume (V_T) around 450ml.

He received fentanyl infusion (0.15 mg/hr) continuously for his surgical wound pain. While at the ICU, mechanical ventilation was gradually tapered from PCV to synchronized intermittent mandatory ventilation (SIMV) and pressure support ventilation (PSV). T-piece trial was done after pressure support (PS) level was

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reduced to 8 cmH_2O. On day 6 post-operation, he could tolerate 30 min of T-piece trial and his weaning profile was V_T 248ml, RR 23, rapid shallow breathing index (RSBI) 92.7, and maximal inspiratory pressure (MIP) -18 cmH_2O. Extubation was then performed.

However, the patient continued to cough with much sputum after extubation. Fever was then noted and left lower lung pneumonia and bilateral pleural effusions were found by chest x-ray (Fig. 3). Diagnostic thoracentesis via left pleural effusion revealed an exudate with protein of 6.8 g/dl, glucose 123 mg/dl, and lactate dehydrogenase 288 IU/L. Left lower lung pneumonia with parapneumonic effusions was diagnosed. The right thoracentesis revealed clear fluid and further analysis revealed transudate. His serum albumin was 1.9 g/dL and the cause of right sided pleural effusion was hypoalbuminemia. Parental antibiotics with Subacillin 1.5 gm (ampicillin sodium 1gm + sulbactam sodium 0.5 gm /vial) every six hours was prescribed for his sputum culture revealed *Acinetobacter baumannii complex*. To manage the progressive tachypnea and shallow breathing, he was given non-invasive positive pressure ventilation (NIPPV) support. Because of progressive dyspnea with paradoxical respiration, use of accessory muscles, and desaturation (SpO_2 90%) under NIPPV, the patient was re-intubated for mechanical ventilation support on day 8 post-operation.

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He then received PCV with PC 24 cmH_2O, PEEP 6 cmH_2O, FiO_2 35%, and V_T around 500 ml. Arterial blood gases showed pH 7.48, PaO_2 105 mmHg, $PaCO_2$ 53 mmHg, HCO_3^- 35 mmol/L. Central venous pressure was 14 cmH_2O (PEEP 6 cmH_2O). After re-intubation, mechanical ventilation was gradually tapered to PSV. For the prolonged mechanical ventilation (PMV) and difficult weaning of more than two weeks, he was transferred to the respiratory care center (RCC).

At the RCC, he was afebrile but mildly tachycardic with heart rate (HR) of 110 beats/min, and tachypneic with respiratory rate (RR) of 25-30 breaths/min under PSV mode of mechanical ventilation. He was alert but nervous. Laboratory examinations revealed hemoglobin level of 11.1 g/dL, white blood cell count 9.4 x 10^9/L, neutrophils 69%, and lymphocyte 15%. Liver and renal function tests, and electrolytes levels were all within normal range. The patient received exercise training with hand cycle ergometer for 30-40 min once daily. As he became clinically stable, with $SaO_2 \geq 90\%$ on $FiO_2 \leq 40\%$, PEEP $\leq$ 8 cmH_2O and no respiratory distress, the PS level was gradually tapered. Pressure level was titrated to achieve RR <25 breaths/minute and $V_T \geq 5$ ml/kg. When the PS level was tapered to 8 cmH_2O, the patient started to receive T-piece trial. The clinical assessment during T-piece trial was performed by continuously monitoring of his consciousness level, respiratory pattern, SpO_2, HR, RR, and blood pressure (BP). If there was agitation,

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depressed mental status, diaphoresis, cyanosis, increased accessory muscle activity, SpO_2 < 90%, severe dyspnea, RR> 35 breaths/min or a 50% increase, HR > 140 beats/min or a 20% increase, systolic BP (SBP) > 180 mmHg or a 20% increase, SBP < 90 mmHg, or cardiac arrhythmias, the T-piece trial was terminated.

Nonetheless, his RR was 35 breaths/min and HR was 130 beats/min after 15 min of the first T-piece trial. The duration of the T-piece trial was gradually increased as the patient tolerated it. Finally, when he could tolerate a T-piece trial of 30 min to 2 hours, he was screened daily to determine if he could be extubated. Initially, his weaning profile was V_T 228ml, RR 28, RSBI 122.8, and MIP -15 cmH_2O. After 10 days of exercise and T-piece training, his weaning profile passed the criteria for extubation (V_T 268ml, RR 27, RSBI 100.7, and MIP -24 cmH_2O), the patient was then extubated and weaned from mechanical ventilation (day 26 post-operation). His chest x-ray on the day of extubation was displayed in Figure 4. After successful extubation, he was transferred to an ordinary ward for further care.

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DISCUSSION

In 1955, Gorham and Stout defined a specific disease entity with idiopathic resorption of multiple bones.[1] Gorham syndrome is a rare disease presenting as progressive osteolysis that it may affect any part of the skeletal system, but most commonly the skull, shoulders, pelvis, vertebrae, ribs, and scapulae.[1-4] It has a slow, irregular, local progress with concentric shrinkage of the shaft of bones, and tapering of the involved end, giving the appearance of 'sucked candy'.[2, 3] Chylous pleural effusion is also a common presentation.[4] The disease can occur at any age, but is common in adolescents and young adults. There is also no sex or racial predilection. The pathologic process is the replacement of normal bone by an aggressively expanding but non-neoplastic vascular tissue that results in the massive osteolysis of the adjacent bone.[1-3] Its etiology and pathogenesis remains unknown.

Diagnosis is essentially one of exclusion and based on combined clinical, radiologic, and histo-pathologic findings. During the acute phase, localized bone pain, swelling, progressive deformity and contractures are common features. Spontaneous fractures are likewise frequent. The end result is severe deformity and functional disability.[1-3] Biochemical and hematologic tests are usually unremarkable and serve only to exclude other diagnosis.[6] Various treatment modalities include radiation therapy, anti-osteoclastic medication, and interferon.[7, 8] If the disease

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becomes progressive, surgical treatment by resection of the lesion, with or without replacement by a prosthesis and bone graft, radiotherapy and even amputation may be considered.[7, 8]

This case report has the typical presentations of Gorham syndrome of multiple osteolysis (radiologic features), bone destruction with granulation tissue, prominent vascularization (pathologic features), and chylothorax. Based on these, the diagnosis was made and the patient was given radiotherapy, interferon, and surgical treatment.

Literature regarding the influence of Gorham syndrome on respiratory systems is limited. Since Gorham syndrome often involves thoracic and spinal deformities, it is rational to conclude that Gorham syndrome influences respiratory mechanics with restrictive ventilatory impairment. Spinal surgery is sometimes necessary for various indications such as pain, deformity, and fracture. Because of impaired ventilation, such patients may be at risk of post-operative complications, particularly after vertebral reconstructive surgery.[9] Moreover, impairment of chest wall mechanics is related to post-operative respiratory failure,[10] which is related to increased chest wall work and respiratory energy expenditure.[10, 11] Thus, some patients may require intensive care after undergoing spine surgery.[12] A previous study reveals that FVC < 40% of predicted value is a sign of severe respiratory compromise after surgery.[13]

The severe restrictive disease is not just a challenge to anesthesia and surgical

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personnel. Respiratory complications are a major concern of spinal surgery and include pneumonia, respiratory failure, prolonged post-operative intubation, and thrombo-embolic disease, among others.[12] In the post-operative period, there are factors that may increase the risk of developing post-operative pulmonary complications. These are drugs, pain, trauma of the operation, decreased lung capacity, and decreased mobility.[13] Thus, the prevention of complications is essential. Pre-operative management and education of directed cough, forced expirations, postural drainage and chest percussion are critical in preventing post-operative complications.[14] Post-operative ventilatory problem lead to re-intubation and PMV is described in this case report. Therefore, extubation must be planned carefully.

Weaning difficult-to-wean patients requires great skill and expertise.[15] Clinical assessments are required to determine whether the patient is ready for reduction or removal of the ventilatory support.[16] There are no specific weaning programs for patients with thoracic deformities and the patient was weaned using general weaning protocols. There are two weaning protocols typically used: the progressive reduction of ventilator support or the progressively longer periods of spontaneous breathing trials.[15] The patient reported here initially had a weaning program by PSV, which is useful for overcoming the extra work of breathing imposed by the endotracheal tube, inspiratory valve, and circuit of the ventilator.[17] As such, PSV improves the efficacy

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of spontaneous breathing and reduces external respiratory work and oxygen consumption by respiratory muscles during weaning [17]

The initial PS level that should be adjusted to begin weaning is usually determined by allowing the patient to breathe in a comfortable way.[17] The suggested optimal initial PS level is the level that provides a RR 25-30 breaths/min and V_T 10ml/kg.[17] During the course of weaning, the PS level is decreased according to the patient's tolerance, usually by steps of 2-4 cmH_2O twice a day.[17] In general, an adequate tolerance to PS $\leq$ 8 cmH_2O is required before attempting extubation.[17]

In the present case, when the patient tolerated a PS level of 8 cmH_2O, he was started on a T-piece trial. Tolerance to a T-piece is a good test to evaluate a patient's capacity to maintain autonomous spontaneous breathing.[15] Its optimal duration has not been well established and 30 min to 2 hours appears to be a good balance between optimal extubation rate and low reintubation rate.[15] The evaluation of clinical tolerance to spontaneous breathing during a T-piece trial should take into account signs of increased patient effort, such as an increased RR, accessory muscle recruitment, paradoxical motion of the rib cage and abdomen, inappropriate recruitment of expiratory muscles, recession of suprasternal and intercostal spaces, diaphoresis, cardiovascular instability, and abnormal mental status.[15]

This patient was weaned twice but with different results. Although the weaning

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protocols used were similar, the weaning conditions were different. The first time, mechanical ventilation was weaned rapidly after surgery. But the patient had operative wound pain and still received continuous intravenous fentanyl infusion. He also had poor cough function. After extubation, he developed pneumonia that required re-intubation and invasive mechanical ventilator. On the second attempt at extubation, the patient was weaned gradually by tapering the mechanical ventilation to PSV and by gradually lowering the PS level. His pneumonia was under control with parental antibiotics. However, after long-term mechanical ventilation and inactivity, his respiratory muscle strength and V_T decreased compared to his initial measurements. Thus, he received daily exercise and T-piece training. His MIP, V_T, and cough function improved and after passing the weaning profile, he was successfully weaned from mechanical ventilation.

The benefits of exercise training in ventilated patients should be addressed. Critical illness has many devastating sequelae, including neuromuscular weakness, psychological and cognitive disturbances that frequently result in functional impairment.[18] The inactivity of ventilated patients further leads to impaired skeletal muscle, cardiovascular and respiratory functions.[19] Pulmonary rehabilitation for ventilated patients is emerging as an important strategy for preventing and treating acquired weakness.[18] Greenleaf et al. have demonstrated the feasibility of exercise

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training in patients with bed-rest de-conditioning syndrome, and have shown that exercise training induces significant improvement in muscular endurance.[20] Chen et al. also found that exercise training results in significant improvement in pulmonary mechanics (V_T and RSBI) and functional status in subjects with PMV.[21] Clini et al. demonstrated that exercise training leads to decreased RR, improved respiratory muscle strength, and increased lung volume.[22] The mechanisms of improvement after pulmonary rehabilitation are not precisely known. With increasing hyperinflation during exercise training, inspiratory muscle predominance may shift from the diaphragm to the accessory inspiratory muscles.[23] Costi et al. suggested improving physiologic factors like increased aerobic capacity or enhanced ventilatory and peripheral muscle function after pulmonary rehabilitation.[24]

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In conclusion, this report describes a case of Gorham syndrome with severe restrictive ventilator impairment due to a significant deformity of the spine and chest wall. The patient underwent spinal surgery but had prolonged mechanical ventilation due to post-operative complications. After respiratory training by weaning program and upper limbs exercise training, the patient was subsequently successfully weaned from mechanical ventilation.

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Figure Legend

Fig 1. Reconstructed computed tomography (CT) scan of the thoraco-lumbar spine revealed severe kyphosis and bony destruction over the T12-L1 level.

Fig 2. Reconstructed CT scan of the chest demonstrated bony destruction of the left lower ribs.

Fig 3. Chest x-ray after the first attempt at extubation (day 6 post-operation) showed left lower lung pneumonia, bilateral pleural effusion, and left lower ribs deformity. The endotracheal tube was in proper position.

Fig 4. Chest x-ray before the second attempt at extubation (day 26 post-operation) demonstrated left lower lung infiltration, bilateral pleural effusion, and left lower rib deformity.

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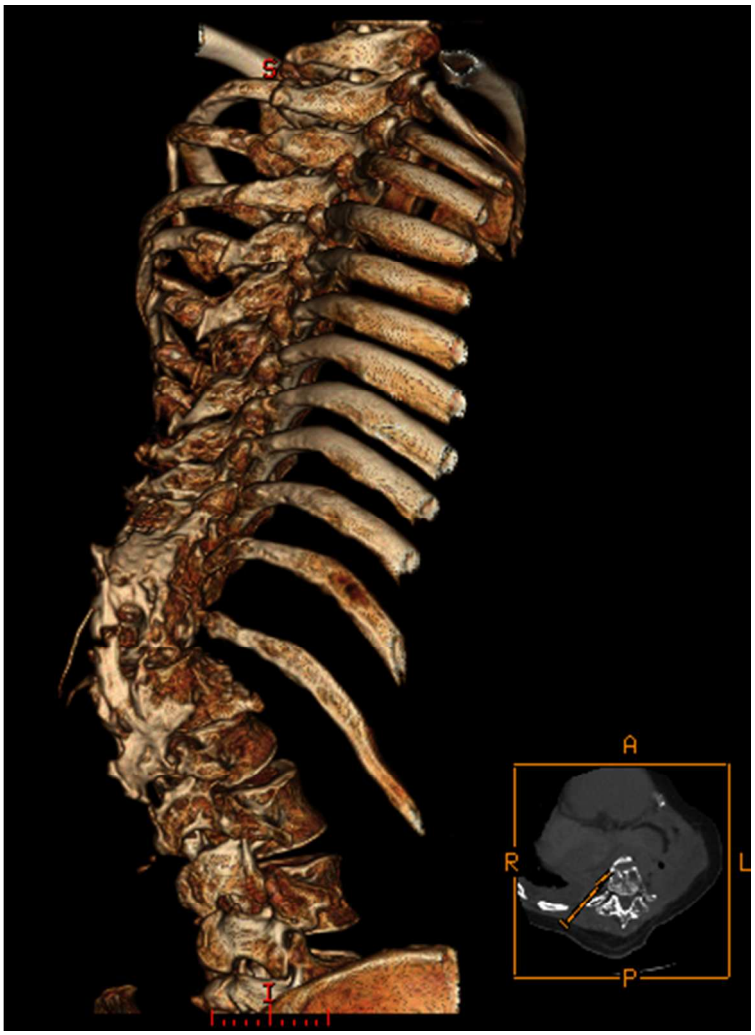

Fig 1. Reconstructed computed tomography (CT) scan of the thoraco-lumbar spine revealed severe kyphosis and bony destruction over the T12-L1 level.
131x180mm (72 x 72 DPI)

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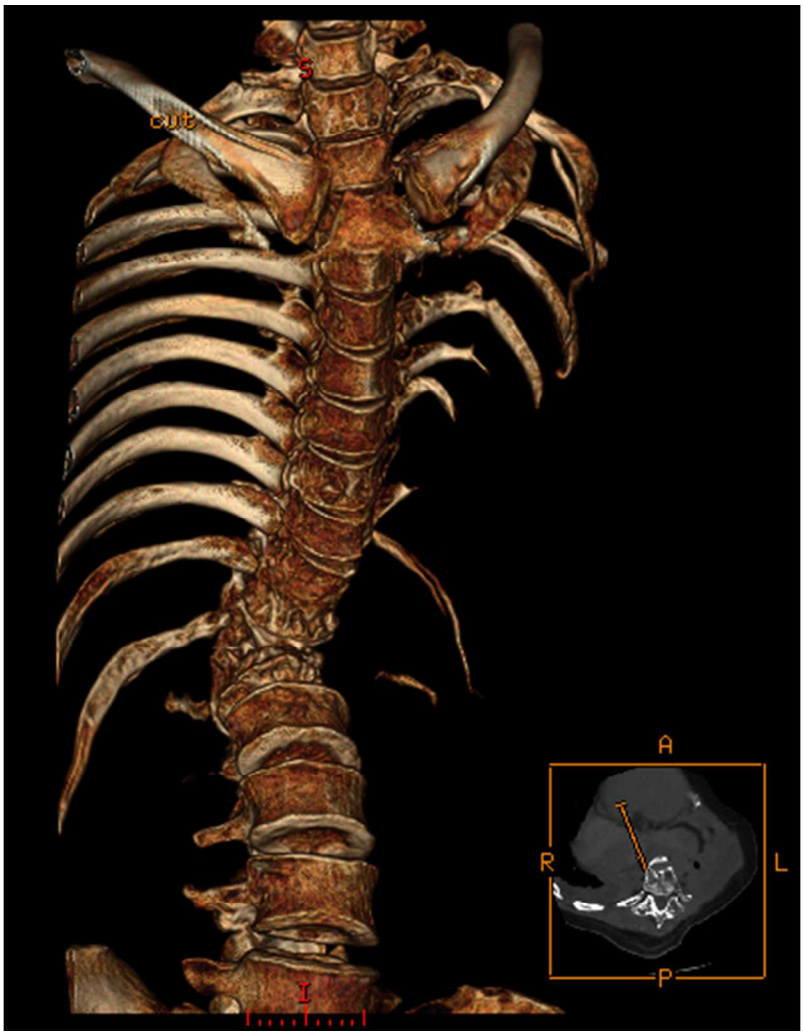

Fig 2. Reconstructed CT scan of the chest demonstrated bony destruction of the left lower ribs.
140x180mm (72 x 72 DPI)

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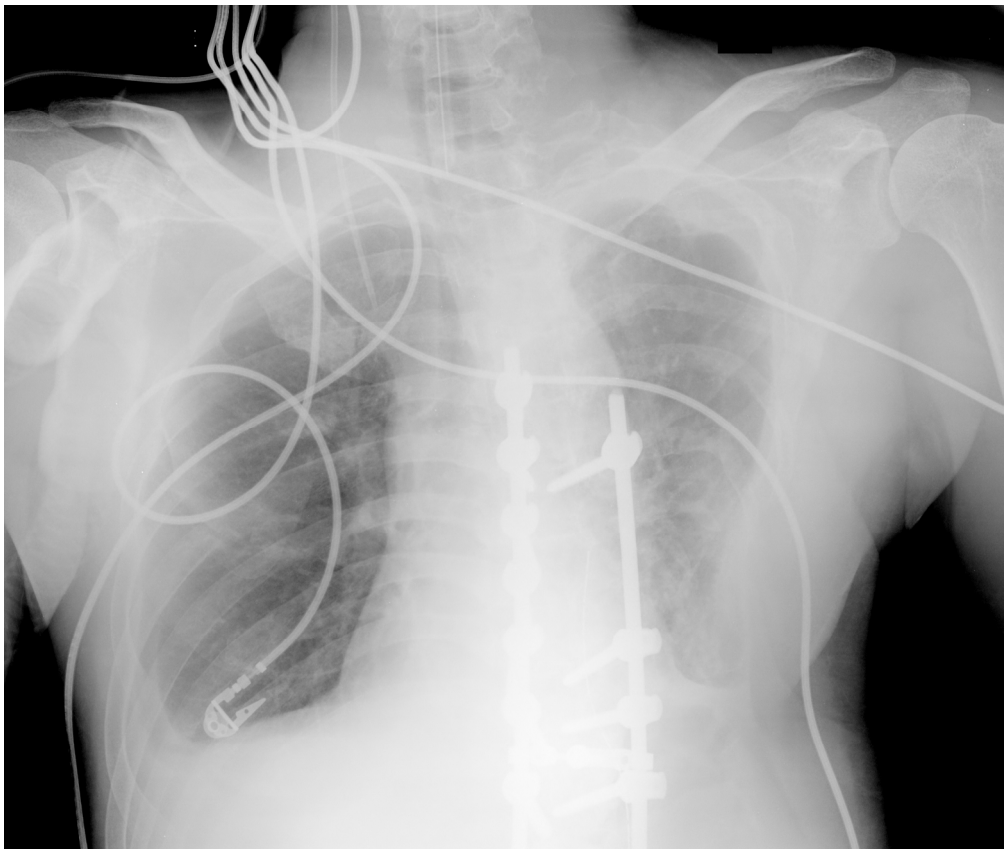

Fig 3. Chest x-ray after the first attempt at extubation (day 6 post-operation) showed left lower lung pneumonia with bilateral pleural effusion, and left lower ribs deformity. The endotracheal tube was in proper position.
919x775mm (72 x 72 DPI)

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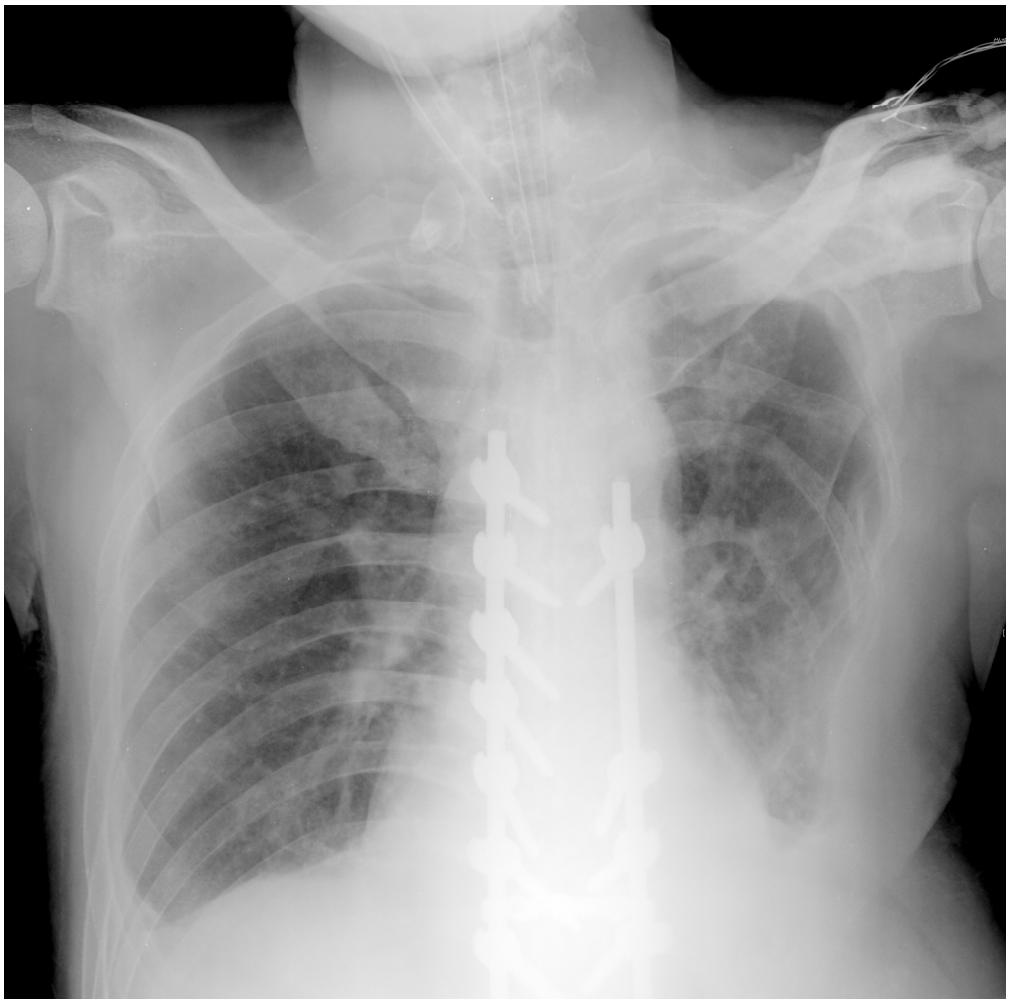

Fig 4. Chest x-ray before the second attempt at extubation (day 26 post-operation) demonstrated left lower lung infiltration, bilateral pleural effusion, and left lower rib deformity.
775x769mm (72 x 72 DPI)