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# Negative pressure pulmonary edema: a case report

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**Case Report**

**Keywords:** Negative pressure pulmonary edema, hypocortisolism, hypothyroidea, obstructive sleep apnea

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# Abstract

**Background:** The negative pressure pulmonary edema is rare clinical situation which caused mainly by upper airway obstruction. However the present case was without obvious upper airway obstruction, so we suspected there were other culprits combined with the mild upper airway obstruction to produce the negative pressure pulmonary edema.

**Case presentation:** This case was a 5-year-old girl with tumor on saddle area, her hormones level were abnormal preoperatively, such as cortison, adrenocorticotrophic hormone, free T4 and total T4. During the stage of induction, negative pressure pulmonary edema took place due to the mild upper airway obstruction. And the instant chest Computer tomography proved the diagnosis. After intensive care, mostly lung field of the girl recovered to the normal within 48 hours.

**Conclusion:** The patient with abnormal hormone levels is vulnerable to pulmonary edema, although there is no obvious upper airway obstruction. Thus pre-operation hormones supplement is as important as keeping the upper airway unobstructed.



**Keywords:** Negative pressure pulmonary edema, hypocortisolism, hypothyroidea, obstructive sleep apnea.


# Background

Negative pressure pulmonary edema (NPPE) is an uncommon and life threatening complication of general anesthesia. Its incidence is 0.1% of general anesthesia with tracheal intubation, which is mostly caused by the laryngospasm [1]. In other words, although patients may be with labored breathing caused by upper airway obstruction, they rarely develop NPPE in clinical [2]. We report a case of instant pulmonary edema following elective general anesthesia using sevoflurane inhalation induction, whose signs of laryngospasm and other causes of upper airway obstruction were not obvious peri-induction. We explore the possibility of pulmonary edema was exactly unapparent negative pressure generation, but also ask whether the other agents should be considered as culprits.

# Case Presentation

A 5-year-old female child was admitted for intracranial tumor on 29th March 2018. Her chief complaint was polydipsia and polyuria for 3 years. The MRI image of December 2015 in local hospital showed tumor on saddle area, with characteristics of T1 hypointensity, T2 hyperintensity and homogenous enhancement. Recent 2 months, she presented with symptoms of intermittent body seizure and unconsciousness. The reexamination MRI in March 2018 revealed the tumor enlarged [Figure 1]. The length of girl was 95 centimeters and body weight 32 kilogram, the body mass index was 35.5. Her previous history was negative. Body examination indicated no obvious signs except obstructive sleep apnea (OSA) and short neck. The scale of ASA was II and Mallampati III. The results of blood routine, coagulation function and D-dimer tests were normal. But the blood electrolytic, such as serum $Na^+$ (154.8mmol/L) and $Cl^-$ (119mmol/L) were significantly higher than the reference. In the meanwhile, some

blood hormone results were also abnormal. For example, free T4 (0.56ng/ml) and total T4 (3.27ug/ml) were slightly lower than the reference, but cortisol (1.41ug/dl) and adrenocorticotropin (<5.0pg/ml) were significantly reduced. These changes of hormone demonstrated the pituitary dysfunction and might cause the electrolytic and distribution of body fluids abnormal. The electrocardiogram and echocardiogram tests were normal too. The serious fatty liver was detected by abdominal ultrasound. Thus, for exact diagnosis and treatment in progress, the operation under general anesthesia should be taken to draw the tumor tissue for pathological examination.

After admission, sodium valproate 0.5g/bid and levothyroxine 25ug/qn were administered. The blood electrolytic was monitored and regulated daily. The chest computer tomography (CT) on 30th March indicated clear lung field, and her preoperative chest examination was normal [Figure 2]. $Na^+$ 146.6mmol/L and $Cl^-$ 111.6mmol/L, which re-examined on 3rd April, closed to the normal range.

On 4th April, the girl was sent to the operating-room by stretcher. It was difficult to establish venous access because she was obese and incompatible, so the sevoflurane inhalation induction was given with 3%~8% sevoflurane and $O_2$ 6L/min. She struggled at the beginning of inhalation a few seconds. The monitor showed $SpO_2$ was about 92%~96%. Although she was keeping spontaneous breathe, the tidal volume was very low, just 70~100ml. Meanwhile, the breathe movement was not as same as the normal, because there was very mild collapse of suprasternal fossa on inhalation stage, albeit it was not apparent. On the other hand, jaw-thrust was difficult, thus another anesthesiologist was called for more assistance. By squeezing breather bag, support ventilation following her spontaneous breathe was tried, but the situation was not improved and jaw-thrust was still difficult.

Twenty minutes later, venous access was build. Thus propofol 50mg, sulfentanil 15ug and rocuronium 40mg were administered. Endotracheal intubation with 4.5-intensive-tube was successful by the routine laryngoscope, because it was easy to expose and visualize the larynx and glottis. There was no secretion in her mouth, and her tonsilla and vocal cords were normal. During the induction phase, although heart rate and blood pressure waved normally, low tidal volume, low $SpO_2$ and mild airway blocking sustained, the $SpO_2$ was only 91%~95% with $FiO_2$ 100%.

After endotracheal intubation, mechanical ventilation setting was as follows: tidal volume 200ml, I:E=1:2, f 20, $FiO_2$ 100%. The serious high peak pressure sustained at 36~39cm$H_2O$. In the meanwhile the $SpO_2$ was only 90%~92% and EtCO2 more than 55mmHg. The obvious blistering sound and coarse crackles presented in all lung fields by chest auscultation. Airway was aspirated immediately with only little secretion in the tracheal, and the ventilation was still not ameliorated. After changing volume controlling model into pressure controlling model, the situation was too bad as well. So the general anesthesia was enhanced by increasing the concentration of sevoflurane and administering sulfentanil 10ug and rocuronim 20mg. At the same time, methylpredisolone 40mg and furosemide 10mg were administered. Unfortunately, the ventilation situation was not better than before, such as seriously high airway peak pressure and low $SpO_2$. The operation had to be given up. And the girl was sent to ICU after taking chest CT scan [Figure 3]. It was astonished that chest CT showed bilateral pulmonary consolidation

accompanied by air bronchogram and the ground-glass opacity lesions, although echocardiography demonstrated a preserved left ventricular ejection fraction 65%.

In ICU, positive pressure mechanical ventilation was initiated. Methylpredisolone 40mg and levothyroxine 25ug for one dose were administered. Although there was no bacterial organisms in sputum culture, meropenem was administered for anti-infection. Several hours later, breathe sound was obviously better except the bottoms of bilateral lung with tiny rale. After 48 hours of supportive care in ICU, the pulmonary edema resolved rapidly, reexamined chest CT demonstrated the most of lung field was normal except the bilateral lower lobe alveolar infiltrates and consolidation [Figure 4].

# Discussion And Conclusions

NPPE, also known as postobstructive pulmonary edema, develops in patients with spontaneous respiratory effort who have upper airway obstruction and generate very negative intrathoracic pressure leading to sever hypoxemia and pulmonary edema [3].

Most children cases of NPPE have been caused by glottis or subglottic obstruction [4]. But causes of adult NPPE are not as same as that of children. The most often reported reason is post-extubation laryngospasm [5], even the incidence of NPPE is more than 50% among men following laryngospasm [6]. In this case, although there were no apparent causes discussed above, mild collapse of suprasternal fossa and the difficult jaw-thrust during induction phases predicted the possibility of upper airway obstruction. In fact, when unexplained pulmonary edema takes place, NPPE should be considered in the different diagnosis, albeit it is uncommon [3]. In the meanwhile, this case included other similar aspects of NPPE, for example, rapid onset of pulmonary edema after efforts at inspiration against the obstructive airway [3] and rapid resolves within 12 to 24 hours [7]. In addition, the normal ejection fraction also led us from cardiogenic pulmonary edema to non-cardiogenic pulmonary edema.

In this case, there are other agents to prompt the development of NPPE, such as abnormal hormones and OSA. Because the tumor disturbed the function of pituitary endocrine, so the serum levels of free T4, total T4, cortisol and adrenocorticotropin were abnormal. It has been well known that edema is the most obvious sign of patients with hypothyroidism. If hypothyroidism was severe, cardiogenic pulmonary edema would happen because of the loss of inotropic and chronotropic effects of thyroid hormone [8]. Even non-cardiogenic pulmonary edema could be caused indirectly because hypothyroidism results in the leakage of plasma protein and increases capillary permeability [9]. Meanwhile, hypothyroidism is considered as one potential cause of upper airway obstruction [10]. A variety of factors may be involved, such as alteration in ventilator drive, obesity, and so on [11]. If a patient was with hypothyroidism complication with obesity and OSA, just like this case, there is more probability to develop non-cardiogenic pulmonary edema [12]. In the present case, this girl’s status of OSA was obvious and serious, and her BMI was greater than 35. When the chest CT before operation was reviewed, especially compared to the CT after ICU therapy, it looked as if effusion of both lung fields was more than normal level. If there is unexplained postoperative pulmonary edema in patients without the history of laryngospasm, OSA

should be considered as one of culprit [3, 13]. The trait of OSA is frequent episodes of intermittent hypoxia, which leads to pulmonary vascular dysfunction by damaging vascular endothelial cells [14]. On the basis of pulmonary vascular dysfunction, the girl was susceptible to the leaky lung syndrome, which increased the permeability of lung capillaries leading more fluids into the pulmonary interstitium. This might be the reason of increased oxygen and pressure dependency. In fact, these signs predicted severe lung leaking syndrome.

In this case, except hypothyroidism and OSA, serum cortisol and adrenocorticotropin were also significantly lower than the normal level, which are considered as the stress hormone. Its abnormity is a signal of dysfunction of axis of hippocampus-pituitary-adrenal. Patients with hypocortisolism may be more vulnerable to develop lung leaking syndrome. Vice versa, pulmonary edema could be a symptom of adrenal insufficiency. Therefore glucocorticoids have been widely used to treat the syndrome. Clinically, hydrocortisone reduces tracheal aspirate fluid volume and oxygen dependency effectively. And hydrocortisone may improve capillary permeability as well as the inflammation of lung [15].

In ICU, positive pressure ventilation, diuretics and other treatment were administered. The positive pressure ventilation alleviated negative airway pressure in chest. Diuretics were used for the aim of conservative fluid strategy. Hormone supplementary therapy protected alveolar and vessel endothelial intact. Although the girl recovered as soon as the most cases of NPPE, she had been confronted with severe hypoxemia due to the massive pulmonary edema and shunt. After 5 days of actively supportive care, she was discharged from the ICU.

In current case, although there was no apparent laryngospasm, on the base of mild upper airway obstruction, all other causes, for example hypothyroidism, OSA and hypocortisolism, worked tighter to trigger and accelerate NPPE. So we speculated the pathophysiology of this case was that, the tumor on saddle area damaged pituitary endocrine function to produce body hormones disorder. The abnormity caused body fluid distribution disorder and increased pulmonary capillary permeability. In other words, the tumor made the girl vulnerable to pulmonary edema. At last, the mild upper airway obstruction triggered the cascade of NPPE.

In the present case, there was the biggest regret that the family of the girl rejected second opportunity of operation. But for us, there were some apocalypses. Firstly, we should open mind to look for a pathology that would explain the whole clinical scenario. If second operation had to be taken, the supplement of hormones should be sufficient to sustain electronic at the normal range before the operation. During the process of anesthesia induction, the upper airway should be kept smoothly. The normal ventilation may be the most important to avoid NPPE.

# Abbreviations

computer tomography (CT)

negative pressure pulmonary edema (NPPE)

obstructive sleep apnea (OSA)

# Declarations

**Ethics approval and consent to participate:** This is a case report, not clinical research. But we informed the ethics committee of Sanbo Brain Hospital, Capital Medical University, and got its approval.

**Consent to publish:** Because this case was a 5-year-old girl, so a written informed consent was obtained from the patients' parents for publication of this case report and any accompanying images.

**Availability of data and materials:** The images of chest CT of this case are available from the corresponding author. The email address of the corresponding author is B2008194@126.com.

**Competing interests:** Not applicable.

**Funding:** Not applicable.

**Authors' contributions:** Jun Xiong is the first author and the anesthesiologist who was responsible for the case. Yongxing Sun is the corresponding author.

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# References

1. Tebay Aay, Bouti K, Tebay N. Negative pressure pulmonary edema following a cholecystectomy-A case report. Rev Pneumol Clin 2017; 73: 267-71. https://doi.org/10.1016/j.pneumo.2017.08.006.
2. Arita Y, Yamamoto S, Eda Y, Haseqawas S. Negative pressure pulmonary edema. Intern Med 2018; 57: 3673-4. https://doi.org/10.2169/internalmedicine.1286-18.
3. Bhattacharya M, Kallet RH, Ware LB, Matthay MA. Negative-pressure pulmonary edema. Chest 2016; 150: 927-33. https://doi.org/10.1016/j.chest.2016.03.043.
4. Berdai AM, Labib S, Harandou M. Postobstructive pulmonary edema following accidental near-hanging. Am J Case Rep 2013; 14: 350-3. https://doi.org/10.12659/AJCR.889415.
5. Chen Y, Zhang X. Acute postobstructive pulmonary edema following laryngospasm in elderly patients: A case report. J Perianesth Nurs 2018. https://doi.org/10.1016/j.jopan.2018.05.010.
6. Lee JH, Lee JH, Lee MH, Cho HO, Park SE. Postoperative negative pressure pulmonary edema following repetitive laryngospasm even after reversal of neuromuscular blockade by sugammadex: a case report. Korean J Anesthesiol 2017; 70: 95-9. https://doi.org/10.4097/kjae.2017.70.1.95.
7. Mehta KK, Ahmad SQ, Shah V, Lee H. Postobstrucive pulmonary edema after biopsy of a nasopharyngeal mass. Respir Med Case Rep 2015; 16: 166-8. https://doi.org/10.1016/j.rmcr.2015.10.007.

8. Klein l, Danzi S. Thyroid disease and the heart. Circulation. 2007; 116(15): 1725-35. https://doi.org/10.1161/CIRCULATIONAHA.106.678326.
9. Lange K. Capillary permeability in myxedema. American Journal of Medical Sciences. 1944; 2005-15. https://doi.org/10.1097/00000441-194407000-00002.
10. Lopez A, Lorente JA, Jerez V, Julia JA. Sleep apnea, hypothyroidism and pulmonary edema. Chest 1990; 97: 763-4. PMID: 2306985.
11. Kittle WM, Chaudhary BA. Sleep apnea and hypothyroidism. South Med. 1988; 81(11): 1421-25. PMID: 3055327.
12. Al-Sofiani M, Nikolla D, Metta VV. Hypothyroidism and non-cardiogenic pulmonary edema: are we missing something here? Endocrinol Diabetes Metab Case Rep. 2015; 2015: 150014. https://doi.org/10.1530/EDM-15-0014. PMID: 25866647.
13. Medford ARL. Negative pressure pulmonary edema: consider undiagnosed obstructive sleep apnea too. Chest 2012; 141: 1365. https://doi.org/10.1378/chest.11-3089.
14. Sharma P, Dong Y, Somers VK, Peterson TE, Zhang Y, Wang S, et al. Intermittent hypoxia regulates vasoactive molecules and alters insulin-signaling in vascular endothelial cells. Sci Rep 2018; 8:14110. https://doi.org/10.1038/s41598-018-32490-3.
15. Mizobuchi M, Iwatani S, Sakai H, Yoshimoto S, Nakao H. Effect of hydrocortisone therapy on severe leaky lung syndrome in ventilated preterm infants. Pediatr Int 2012; 54: 639-45. https://doi.org/10.1111/j.1442-200X.2012.03636.x.

# Figures

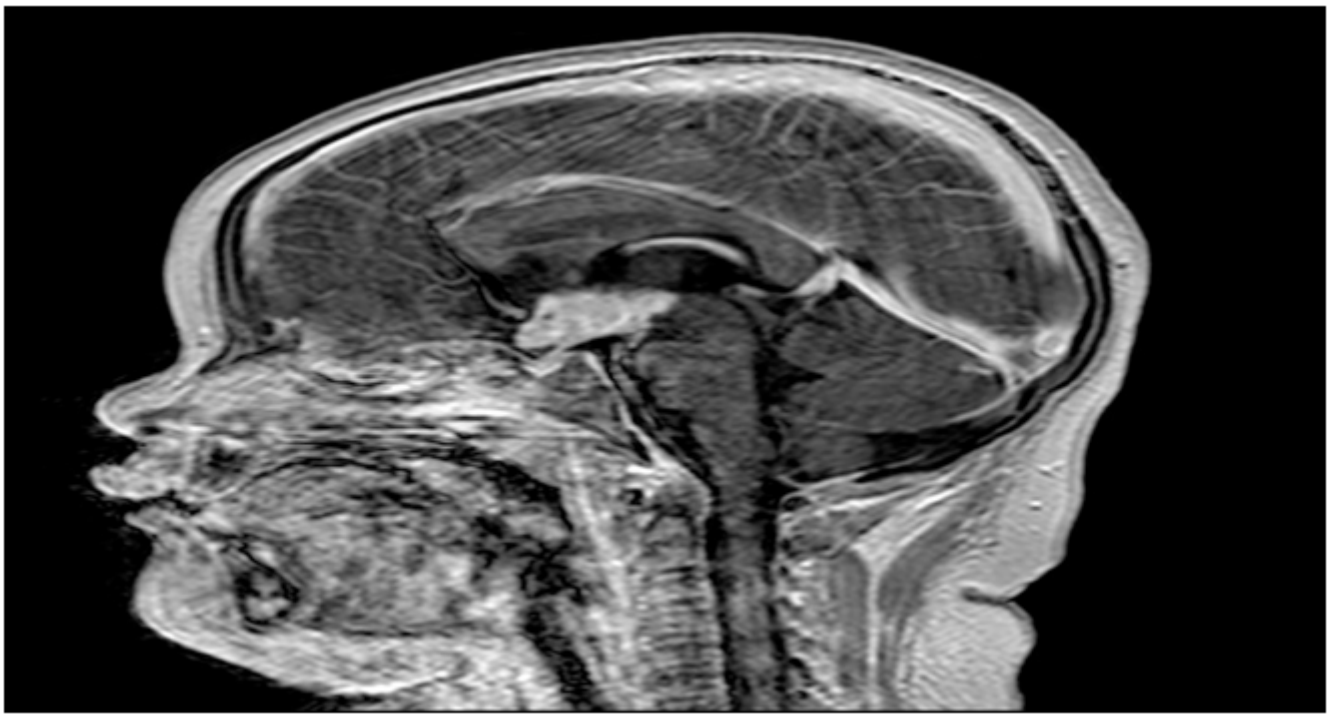


**Figure 1**

Tumor on saddle area. The tumor is T1 hypointensity, T2 hyperintensity and homogenous enhancement.

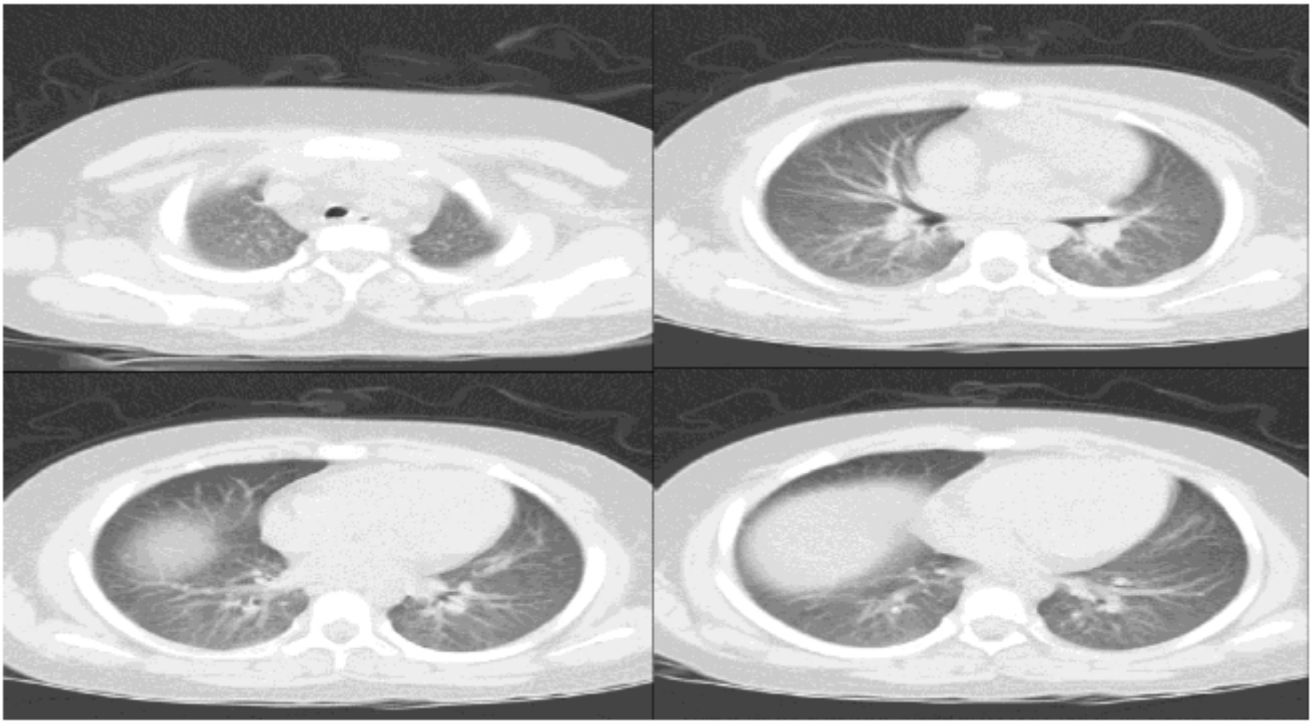
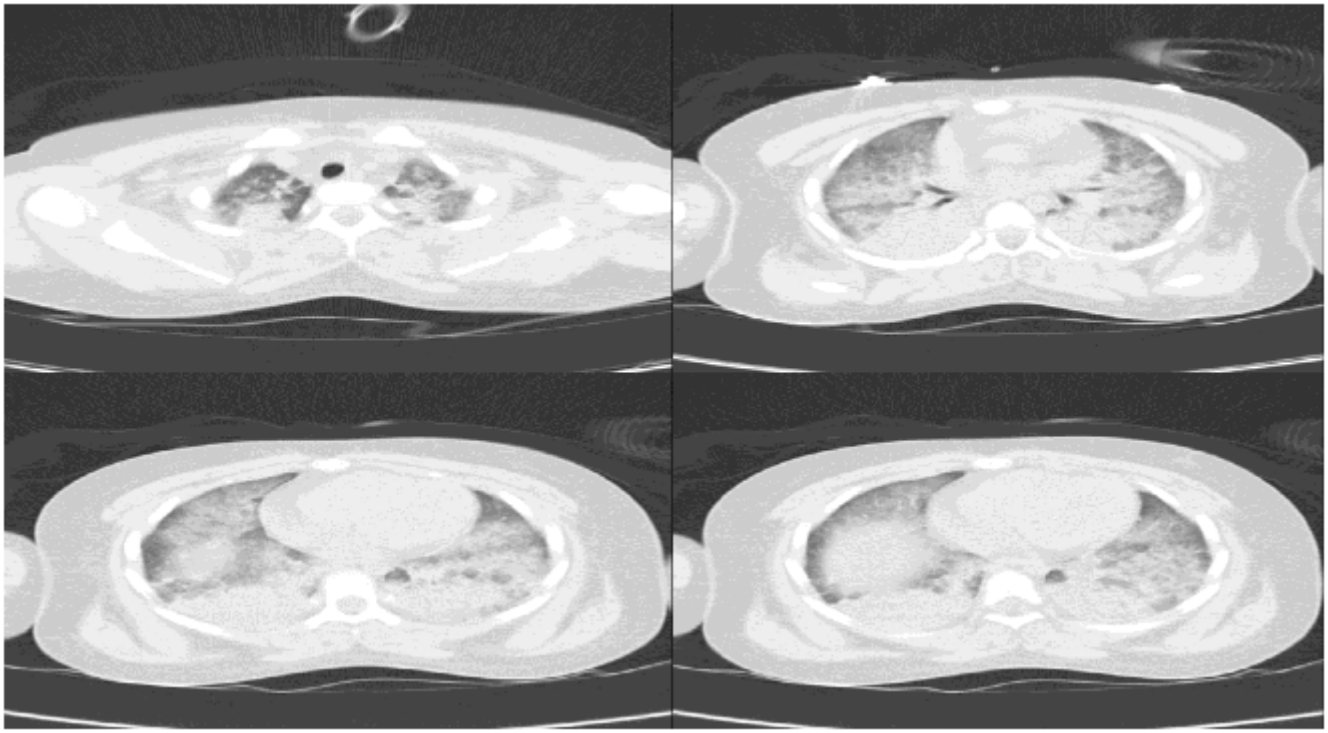


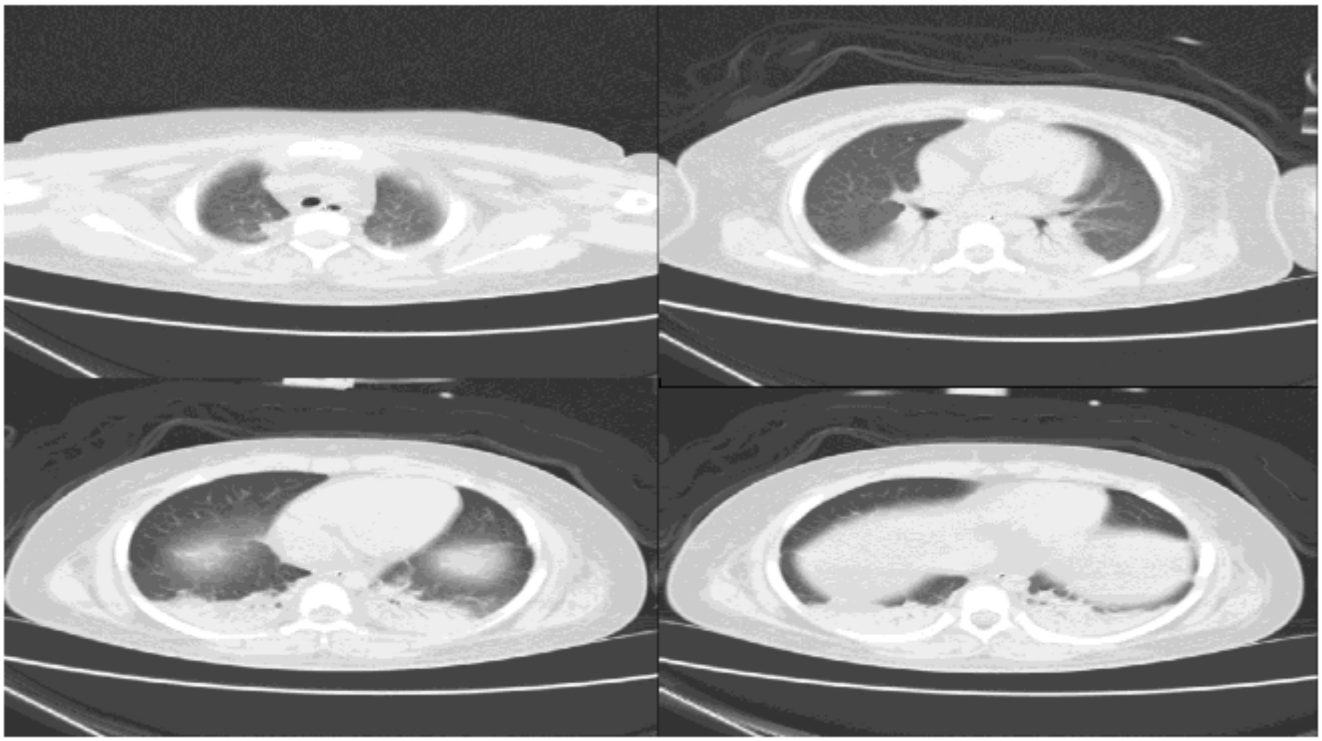
**Figure 2**

Chest CT of 30th March (Before the operation). This CT examination showed all lung fields were clean.



## Figure 3

Chest CT of 4th April (The day of operation). These images demonstrated bilateral pulmonary consolidation accompanied by air bronchogram and the ground-glass opacity lesions.



## Figure 4

Chest CT of 6th April (after 48 hours of ICU supportive care). This revealed the most of lung field was normal except the bilateral lower lobe alveolar infiltrates and consolidation.

## Supplementary Files

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- supplement1.doc