Clinical Analysis of Atelectasis Caused by Influenza A in Xiamen Children's Hospital Between 2017 and 2019

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Research article

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Abstract

Background: We aimed to analyze the clinical characteristics of pediatric patients with atelectasis caused by influenza A to provide a reference for reasonable clinical diagnosis and treatment.

Methods: We included 79 pediatric patients with atelectasis caused by influenza A diagnosed at Xiamen Children's Hospital between January 1, 2017 and December 31, 2019. We analyzed their epidemiological characteristics, clinical manifestations, imaging changes, diagnosis, treatment process, and outcomes.

Results: Among the 79 included patients (males: 52; females: 27), 70 (88.61%) were > 6 years-old and 54 (68.35%) had atelectasis onset during winter. A majority experienced fever and cough. Among them, 44, 16, 21, 14, and 12 had normal/decreased white blood cells, elevated procalcitonin, abnormal hepatic function, abnormal myocardial enzyme spectrum, *Mycoplasma pneumoniae* infection, and *Streptococcus pneumoniae* infection, respectively. Seventy-nine patients presented different atelectasis degrees, including 16 and 29 with atelectasis in the right and left lung, respectively, while 34 had multiple consolidations and atelectasis lesions in both lungs. Fiberoptic bronchoscopy examination of 57 cases revealed mucus plug blockage in 6 cases; among them, 2 cases underwent bronchial cast removal. All patients received oseltamivir or peramivir for antiviral treatment and antibacterial treatment for complicated bacterial infection. All the patients recovered and were eventually discharged. Post-discharge follow-up showed that 77 cases were cured while 2 experienced recurrent respiratory tract infections and post-activity shortness of breath with chest computer tomography showing mosaic perfusion.

Conclusion There is a high incidence of atelectasis caused by influenza A during winter among children aged < 6 years. The main manifestations are fever (mostly hyperpyrexia) and cough. Chest imaging shows consolidation and atelectasis occurring in any lung lobe. Some patients present multiple consolidations and atelectasis lesions complicated by mucus plugs or bronchial casts. Timely fiberoptic bronchoscopy and alveolar lavage could shorten the disease course and improve the prognosis.

Background

Influenza is an acute respiratory tract infectious disease that is caused by influenza viruses. Based on the antigenicity of the viral matrix protein and nucleoprotein, influenza viruses are classified into type A, B, and C (or influenza A, B, and C). Influenza A has high antigenic variability and strong infectivity, which causes a sudden start and rapid disease progression with subsequent adverse effects on human health. Children, who are at a high risk of influenza A, should receive particular attention. Atelectasis refers to a condition characterized by reduced capacity/air content in one or more lung segments/lobes. It is not an independent disease; rather, it often occurs as a complication of various chest diseases. Infective atelectasis is most prevalent among children. It may cause recurrent infections if not promptly diagnosed and treated. Moreover, if long-term treatment is not effective, the pulmonary function may be affected and respiratory failure may occur. Therefore, given the high possibility of influenza A causing atelectasis, pediatricians should be highly vigilant. However, there have been few clinical studies on atelectasis

caused by influenza A. Consequently, we aimed to analyze the clinical data from pediatric patients with atelectasis caused by influenza A. We believe that this study could improve doctors' understanding of this disease.

Methods

Participants

In this retrospective study, we included 79 pediatric patients with atelectasis caused by influenza A who were hospitalized in Xiamen Children's Hospital from January 1, 2017 to December 31, 2019. This study was approved by the Ethics Committee of Xiamen Children's Hospital. We obtained informed consent from the families of all the pediatric patients.

Diagnostic basis

According to the *Diagnosis and Treatment Plan for Influenza (2018 Edition)* [1] issued by the National Health Commission, respiratory tract specimens (including nasopharyngeal swabs and sputum) were collected from the pediatric patients upon hospital admission. Alveolar lavage fluid was collected from some pediatric patients and a definitive influenza A diagnosis was made via immunofluorescence detection. Atelectasis was confirmed using pulmonary imaging (chest X-ray and/or chest computed tomography [CT]) for all patients.

Data collection

Epidemiological survey: We analyzed 79 pediatric patients with atelectasis caused by influenza A with respect to the onset season, sex, age, etc.

Clinical analysis: We analyzed the clinical manifestations, laboratory examinations, imaging data, treatment plans, efficacy, outcomes, and other characteristics of the included patients.

Statistical analysis

We used SPSS 22.0 statistical software for data processing. We expressed normally and non-normally distributed measurement data as mean ± standard deviation (x ± s) and median (quartile distance), respectively. Enumeration data were expressed as a percentage.

Results

Epidemiological Characteristics

Between January 1, 2017 and December 31, 2019, 79 pediatric cases of atelectasis caused by influenza A were definitively diagnosed in the Xiamen Children's Hospital. These patients included 52 males and 27 females with a male-to-female ratio of 1.94:1.00. The mean age at onset was 4.4 (1.1,5.8) years (0.6–12.5 years). Specifically, 43.04% (34/79), 45.57% (36/79), and 11.39% (9/79) of the patients had an age

at onset of < 3 years, 4–6 years, and > 6 years, respectively. Table 1 presents the specific age distribution of the included patients. During the three years between 2017 and 2019, the disease onset mainly occurred between November and February, which corresponded to the winter season. Figure 1 shows the specific time (seasonal) distribution of the onset of atelectasis caused by influenza A.

Table 1
Age distribution of pediatric patients with atelectasis caused by influenza A in Xiamen Children's Hospital from 2017 to 2019

Year	0–3 years	4–6 years	¬ 6 years	Total
2017	5	9	2	16
2018	13	8	4	25
2019	16	19	3	38
Total	34	36	9	79

Clinical Features

Clinical Manifestations:

All the included pediatric patients had acute onset with a majority (78/79, accounting for 98.73%) presenting fever with a course of 4–12 days. Moreover, 52 (65.82%) presented a maximum temperature ≥ 40°C. All the included pediatric patients experienced different cough degrees; specifically, 13 (16.46%), 11 (13.92%), and 21 (26.58%) experienced wheezing, convulsions, and gastrointestinal reactions (nausea and vomiting), respectively.

Laboratory examinations:

Peripheral blood tests revealed normal, decreased, and increased leukocytes in 21 (26.58%), 23 (29.11%), and 35 (44.31%) cases, respectively. Moreover, 31 (39.24%), 16 (20.25%), 21 (26.58%), 10 (12.66%), and 9 (11.39%) cases presented with increased procalcitonin, abnormal hepatic dysfunction, abnormal myocardial enzyme, increased D-dimer levels, and increased fibrin degradation product (FDP), respectively.

Etiological examination:

Etiological examination of respiratory tract samples revealed a positive result for influenza A virus. This included 66 (83.54%) cases with positive nasopharyngeal swabs and 13 (16.46%) cases being positive for at least one of the seven common respiratory viruses in alveolar lavage fluid. There were 42 (53.16%) cases with mixed infections; among them, 14, 12, 7, 6, 2, and 1 cases were complicated by *Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Adenoviridae*, and respiratory syncytial virus infection, respectively.

Imaging examination: All the pediatric patients underwent chest X-ray and/or CT examination, which revealed different atelectasis degrees (see Figs. 2 and 3). Among them, 34 (43.04%) cases showed multiple consolidations and atelectasis lesions in both lungs while 29 (36.71%) and 16 (20.25%) cases showed segmental consolidation and atelectasis in the left and right lung, respectively. There were 51 (64.56%) cases with ≥ 2 lung segments involved. Subsequent follow-up revealed mosaic perfusion and small airway lesions on lung CT in two (2.53%) cases.

Bronchoscopic examination and treatment:

A total of 57 (72.15%) cases were treated via fiberoptic bronchoscopic examination and alveolar lavage. The main manifestations of bronchoscopic examination were mucosal hyperemia and edema; moreover, inflammatory secretions and various sputum volumes were visible. There was significant mucus plug blockage in 6 patients (see Fig. 4) who subsequently underwent fiberoptic bronchoscopic lavage 2–3 times. Among them, 2 patients underwent bronchial cast removal via the bronchoscope (see Fig. 5).

Treatment and outcome:

All the pediatric patients received antiviral (oseltamivir/peramivir) treatment after definitive diagnosis. Patients with bacterial or *Mycoplasma pneumoniae* infections received anti-infective treatment. Among them, 9 and 13 patients received gamma globulin for immunity regulation and short-term methylprednisolone for anti-inflammatory treatment, respectively. Moreover, 2 patients were under mechanical ventilation during treatment. Patients with hepatic dysfunction and abnormal myocardial enzyme spectrum underwent liver protective and myocardial nutritional treatments, respectively. The length of hospital stay ranged from 7 to 21 days. All the included pediatric patients fully recovered and were discharged. During the 6-month post-discharge follow-up period, 2 pediatric patients presented with recurrent respiratory tract infections and post-activity shortness of breath. Chest CT showed mosaic perfusion and small airway lesions.

Discussion

Influenza A virus is among the important viral pathogens that cause respiratory tract infections among children. Moreover, atelectasis caused by influenza A is clinically common. Influenza A is highly prevalent during winter and spring with children being at high risk. Atelectasis caused by influenza A has similar epidemiological characteristics to those of influenza A. We observed a 68.35% (54/79) incidence rate of atelectasis caused by influenza during winter (December to February) in our hospital between 2017 and 2019; moreover, 88.61% (70/79) of the confirmed cases were aged < 6 years. This is consistent with previous epidemiological studies on pediatric influenza in China and other countries [2, 3]. Young children are at a high risk of influenza A and subsequent atelectasis, which could be attributed to the immature immune function, decreased anti-infection ability, and insufficient ability of the body to inhibit post-infection virus replication. Our findings indicated that the incidence of atelectasis caused by influenza A was higher in males than in females (with a male-to-female ratio of 1.94:1). However, this study has a relatively small sample size; moreover, related previous studies in China and other countries lacked a

large sample size. Therefore, the exact gender characteristics of atelectasis caused by influenza A remain unclear.

Atelectasis is characterized by absent or reduced lung gas volume resulting from various causes, which is accompanied by collapsed lung tissue and reduced lung volume. Infections are an important cause of pediatric atelectasis. After a child is infected with influenza A virus, a strong inflammatory response could cause accumulation and release of many inflammatory cells, sputum congestion, reduced airway mucociliary clearance ability, and other pathophysiological changes, leading to atelectasis. The clinical atelectasis symptoms caused by influenza A range in severity. They are mostly characterized by acute onset with similar typical symptoms as to those of atelectasis caused by infections with other pathogens [4, 5]. Fever and cough with expectoration of different degrees are the main manifestations with fever being the initial symptom in most cases. Children with persistent hyperpyrexia could present with complicated febrile convulsion. Laboratory examinations may present with increased D-dimer, FDP, creatine kinase isoenzyme, and transaminase levels, as well as electrolyte disturbance. Notably, the proportion of patients with maximum temperature > 40°C was high (65.82%) with the longest duration being 12 days. Therefore, persistent hyperpyrexia could be an important indicator of pediatric influenza A progressing to atelectasis. Prolonged hyperpyrexia indicates ineffectively controlled inflammation, which causes congestion, edema, necrosis, and shedding of the bronchial mucosa, as well as lumen blocking and compression, which results in atelectasis.

We found that 42 (53.16%) cases with atelectasis caused by influenza A that presented with mixed infections. The main pathogens include *Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, etc. A prospective observational study on influenza virus by Casalino et al. [6] reported that only 5.6% and 28.6% of influenza-negative and influenza-positive patients, respectively, had complicated bacterial infections. This indicates a similar incidence as that observed in this study. Influenza A virus can destroy host epithelial cells, which reduces the host's resistance to external pathogens and contributes toward secondary mixed infections. Influenza virus has been shown to remove sialic acid residues of glycoproteins on the surface of the host cell membrane through neuraminidase. This exposes receptors that bind bacteria bind to cells, which facilitates bacterial colonization and subsequent infections [7]. Wu et al. [8] reported that influenza A virus significantly reduced the response-ability of host macrophages and neutrophils to *Streptococcus pneumoniae*, as well as the levels of influenza virus-specific antibody. This results in an increased probability of mixed infections among patients with influenza A. There is currently no definite conclusion regarding the pathogen most likely to cause concurrent infection with influenza. Although we observed a high mixed infection rate in atelectasis caused by influenza A, there were different proportions of patients infected with *Mycoplasma pneumoniae* and different bacteria (*Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*). Therefore, we could not determine the pathogen most likely to cause complicated infections. Moreover, we employed a limited sample size; therefore, there is a need for future studies with larger studies to perform more detailed assessments.

Regarding influenza A treatment, various guidelines in China and other countries have indicated that antiviral treatment application at the early disease stage (within 48 hours of onset) could reduce influenza complications, minimize mortality, and shorten hospital stay [1, 9]. It remains difficult to clinically diagnose influenza within 48 hours. We found that most pediatric patients with atelectasis caused by influenza A did not have an early-stage diagnosis. However, a majority of the patients showed relatively good responses to treatment with neuraminidase inhibitors oseltamivir or peramivir at 48 hours after disease onset. For those who did not, glucocorticoid and/or gamma globulin treatment had a good response. During the follow-up period, two pediatric patients presented recurrent respiratory tract infections and post-activity shortness of breath; further, mosaic perfusion images were observed on lung CT. Occlusive bronchiolitis should be carefully considered and doctors should pay attention to the long-term complications of influenza virus infection.

The effect and status of bronchoscopic lavage in the treatment of infectious atelectasis remain unclear in China and other countries. Previous studies have suggested that infection-induced atelectasis could subside spontaneously after anti-infective treatment and that bronchoscopic treatment could be excessive [10]. We believe that the advantages of bronchoscopy outweigh its disadvantages. Bronchoscopic alveolar lavage removes pathogens adhered to the airway surface by inflammatory media, effectively reduces direct and indirect pathogen-induced damages to bronchial mucosa, improves lung expansion ability, facilitates lung inflation and pulmonary circulation restructuring, effectively improves clinical pediatric atelectasis symptoms, shortens the disease course, and reduces complications. Among our included patients, 57 were treated with bronchoscopy, which showed sufficient efficacy in all of them. Bronchoscopic examination can also be used for differential diagnosis and identifying other complications. In our study, bronchoscopy revealed significant mucus plug blockage in 6 pediatric patients; among them, 2 underwent bronchial cast removal through the bronchoscope. This blockage could be attributed to increased airway mucus secretion and decreased clearance ability after cilia damage caused by post-infection continuous inflammatory stimulation. Pulmonary atelectasis complicated by mucus plugs or bronchial casts is a serious complication of influenza A virus infection. In these cases, tracheoscopy is indicated and bronchial cast removal via bronchoscopy is the most direct and effective diagnosis and treatment method [11, 12].

Conclusions

In conclusion, atelectasis caused by influenza A mainly occurs during winter and among children aged < 6 years. Its main manifestations are recurrent hyperpyrexia and cough with chest imaging showing consolidation and atelectasis. Moreover, mixed infections may occur. Based on conventional antiviral treatment, timely fiberoptic bronchoscopic examination and alveolar lavage could shorten the disease course, as well as improve clinical symptoms and prognosis.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Capital Institute of Xiamen Children's Hospital (no. Xmetyy-2016-03). All data collected were stripped of patient identifiers, with no possibility to track the data to an individual person's identity.

Consent for publication

Not applicable.

Availability of data and materials

Datasets analyzed in this study can be obtained from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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No funding was secured for this study.

Authors' contributions

Lin Yuan and Ding-zhen Bai were responsible for conception and design and drafted the initial manuscript.

Lin Yuan and Zhi-qiang Zhuo conducted part of the figure, operated bronchoscopy and reviewed and revised the manuscript.

Lin Yuan operated bronchoscopy and reviewed and revised the manuscript.

Xing-dong Wu participated in conception and design, supervised data collection and analyses, and critically reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Not applicable.

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13. Appendices.

Figures

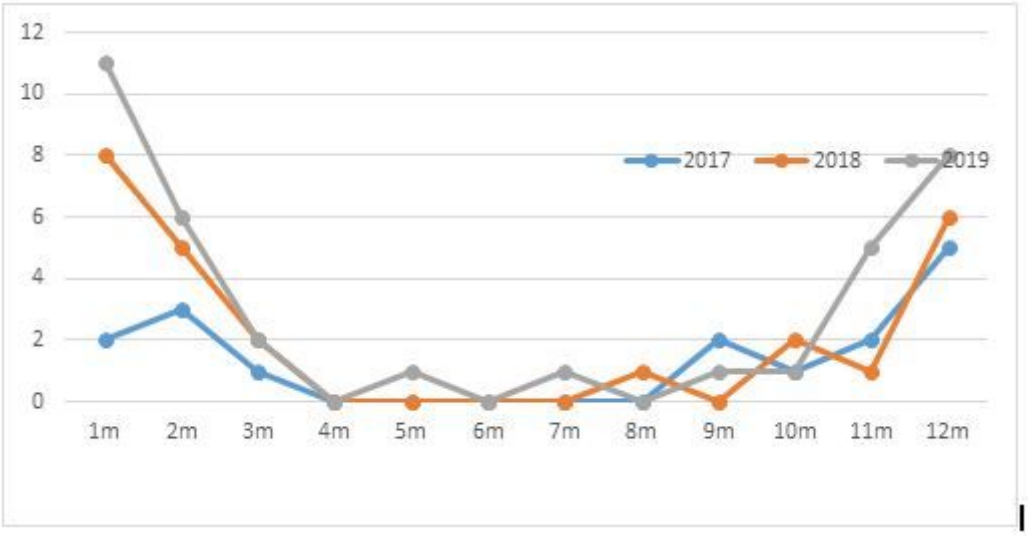

Figure 1

Time distribution proportion chart of atelectasis cases caused by influenza A in Xiamen Children's Hospital from 2017 to 2019

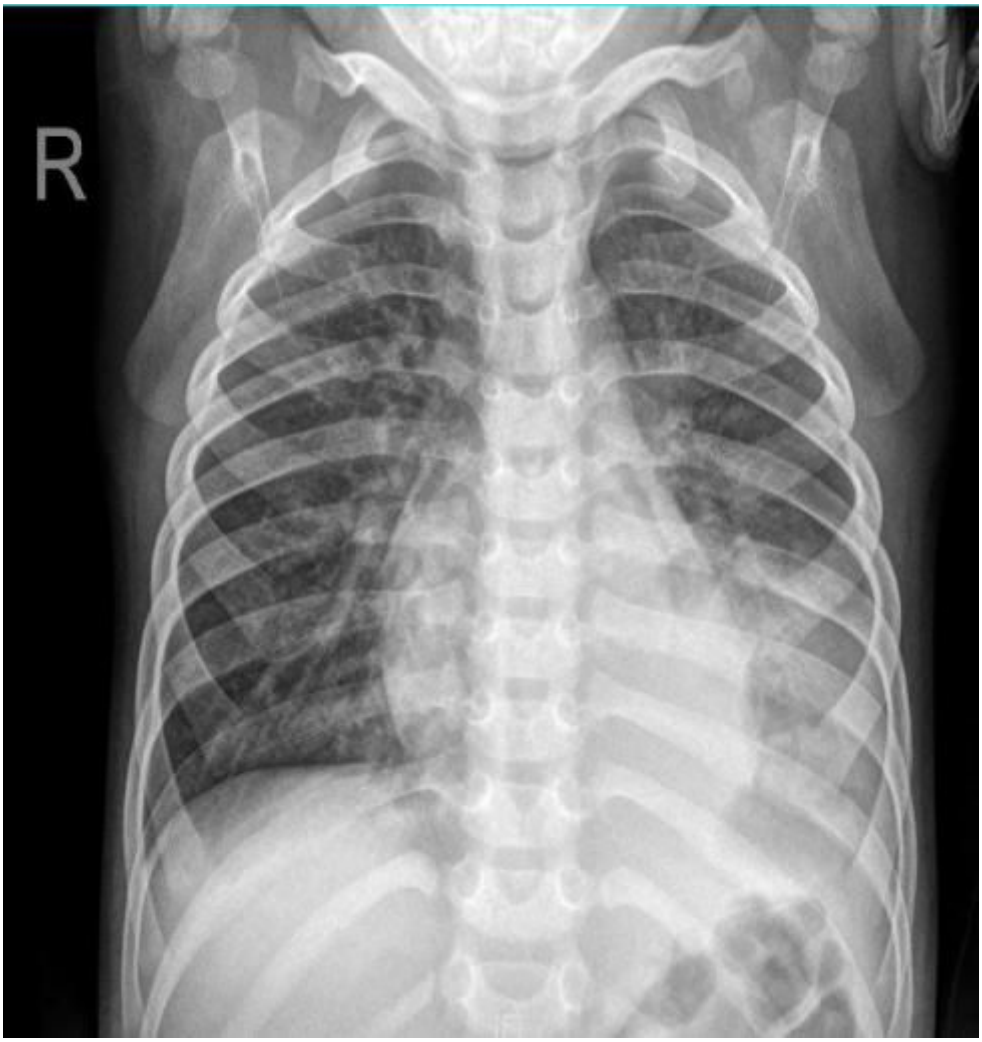

Figure 2

Consolidation and atelectasis of the lower left lung lobe.

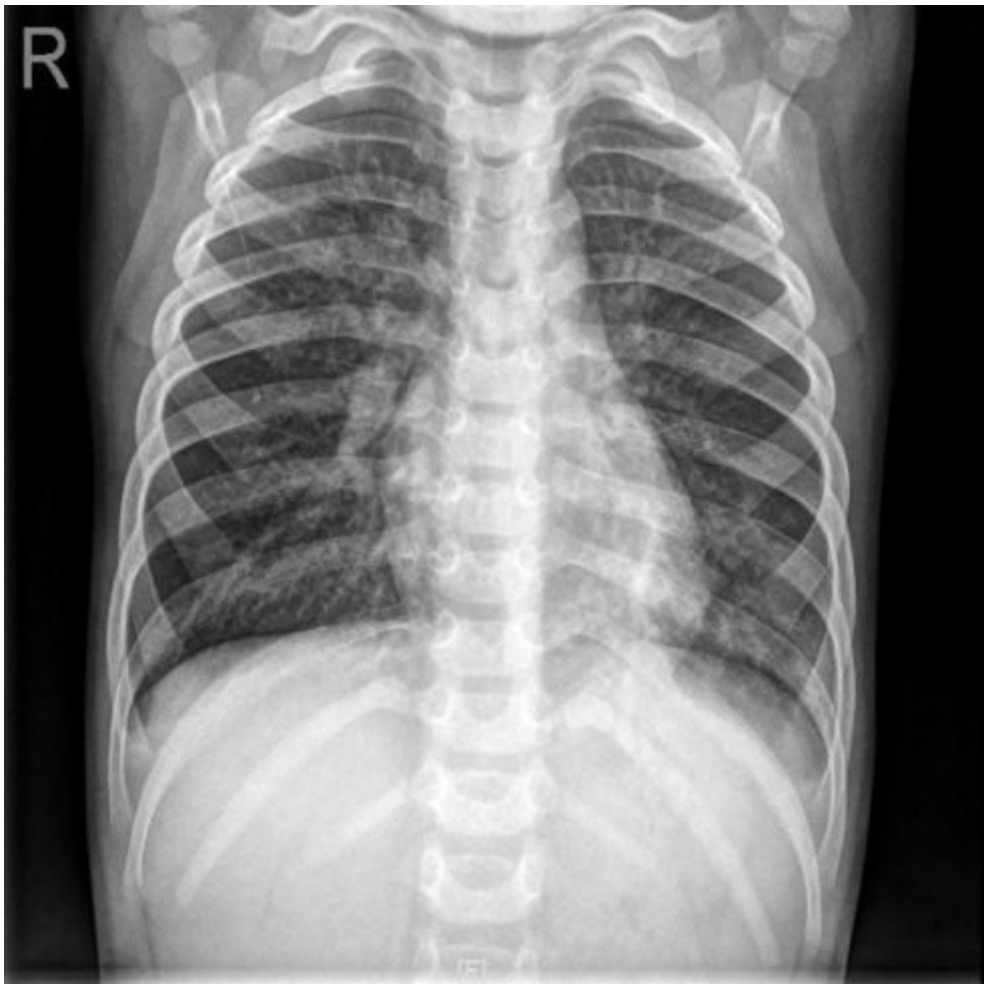

Figure 3

Re-expansion of the lower left lung lobe after treatment.

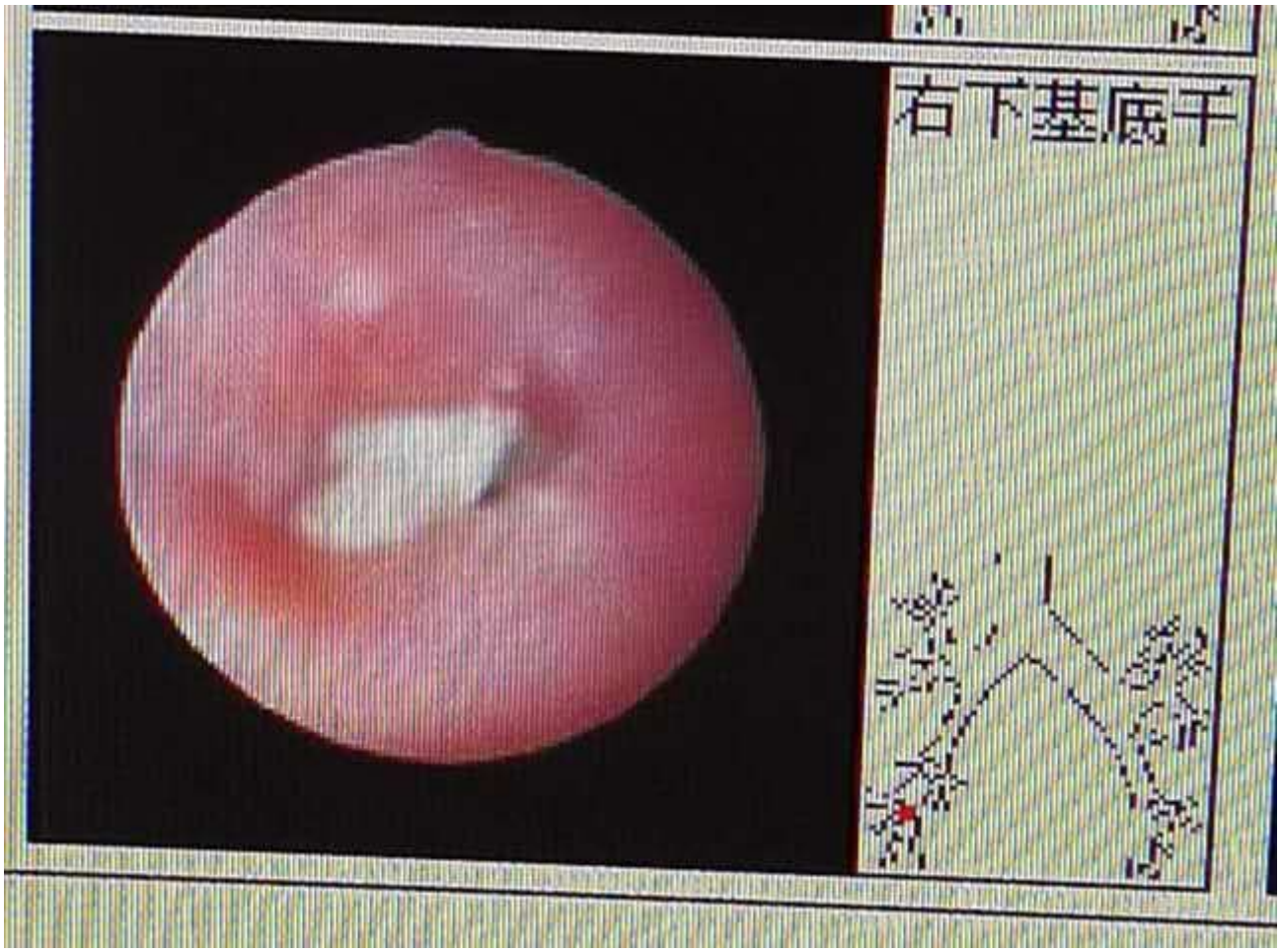

Figure 4

Mucus plug blockage under the bronchoscope

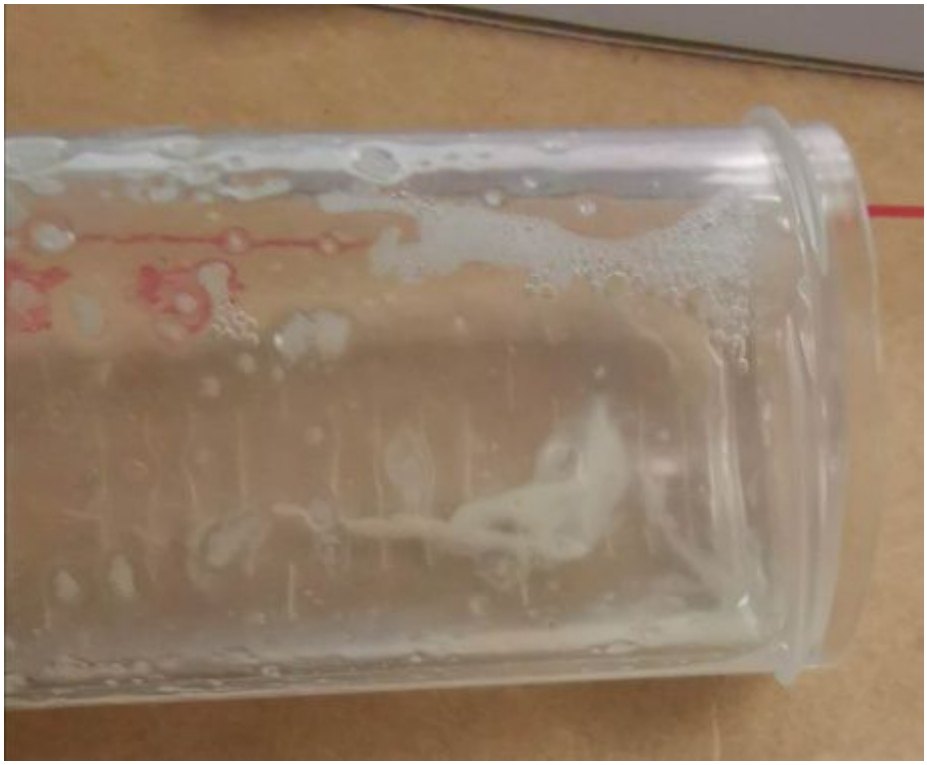

Figure 5

Bronchial casts removed through the bronchoscope