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*Original Article*

# Congenital cystic lung lesions: a clinical analysis of 28 newborns

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**Abstract:** Objective: To discuss the clinical features of congenital cystic lung lesions (CCLL) in newborns. Method: From January 2008 to June 2014, 28 newborns treated at Department of Neonatology, Guangzhou Women and Children's Medical Center for CCLL, were retrospectively analyzed. The baseline information, clinical manifestations, imaging findings, diagnosis, treatment and prognosis were analyzed with literature review. Results: There were 20 males and 8 females with CCLL. By the type of lesions, there were 16 cases (57.14%) with congenital lobar emphysema, 7 cases (25.00%) with pulmonary sequestration, 4 cases (14.29%) with congenital cystic adenomatoid malformation, and 1 case (3.75%) with bronchogenic cyst. Clinical manifestations included shortness of breath (78.57%), cyanosis (39.29%), cough and gasp (17.86%), feeding intolerance (14.29%), and fever (10.71%); asymptomatic cases accounted for 21.43%. Two cases were combined with congenital heart disease and four were combined with other deformities (diaphragmatocele, laryngeal cartilage dysplasia, funnel chest and polycystic kidney disease). Chest CT revealed lesions in all cases. Four cases received pulmonary lobectomy, and 2 of these 4 cases received emergency surgeries, while the remaining cases received conservative treatment. Among all 28 cases, 17 cases were improved and discharged from hospital; 8 cases were discharged against medical advice, and 3 cases died. Conclusion: Congenital lobar emphysema is the most common type of CCLL in newborns, mainly presented as shortness of breath and cyanosis. The suspected cases of CCLL should receive chest CT or MRI as early as possible. Doppler echocardiography and other ultrasonic examinations should be performed as well to exclude deformities. Good outcomes usually occur for CCLL patients and long-term follow-up is necessary.

**Keywords:** Newborn, congenital lobar emphysema, pulmonary sequestration, bronchogenic cyst, congenital cystic adenomatoid malformation

## Introduction

With the advances and popularization of prenatal diagnostic techniques and prenatal ultrasonography, more and more congenital malformations are diagnosed prenatally. Congenital cystic lung lesion (CCLL), a less common congenital lung abnormality, is derived from the abnormal germination or branching of embryonic trachea and bronchi. The cystic lesions are filled with either gas or liquid with the cystic space-occupying lesions containing liquid and gas. CCLL can occur at any position of the bronchial tree and at any stage of lung development. CCLL is generally divided into 4 types, congenital cystic adenomatoid malformation (CCAM), bronchogenic cyst, pulmonary sequestration and congenital lobar emphysema. This article presents a retrospective analysis of 28 newborns with CCLL treated at Department of Neonatology, Guangzhou Women and Children's Medical Center from January 2008 to June 2014. The purpose is to provide new understanding of the clinical features of CCLL.

## Materials and method

### *Subjects*

From January 2008 to June 2014, 28 newborns treated at Department of Neonatology, Guangzhou Women and Children's Medical Center for CCLL, were included.

### *Diagnostic criteria*

CCLL was diagnosed based on the following criteria [1]: Combined with clinical manifestations and imaging findings; Surgical or pathological

**Table 1.** Baseline data

| Type of disease (case) | Gender | | Gestational age | | | Body weight at birth | | | Age of onset | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | Female | ~34 w | ~37 w | ≥37 w | ~1000 | ~1500 g | ~2500 g ≥2500 g | 0 ~7 d | ~28 d | |
| Congenital lobar emphysema | 12 | 4 | 3 | 2 | 11 | 1 | 1 | 3 | 11 | 10 | 6 |
| Pulmonary sequestration | 5 | 2 | 0 | 1 | 6 | 0 | 0 | 2 | 5 | 6 | 1 |
| CCAM | 3 | 1 | 0 | 1 | 3 | 0 | 0 | 0 | 4 | 4 | 0 |
| Bronchogenic | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 |
| Total | 20 | 8 | 3 | 4 | 21 | 1 | 1 | 5 | 21 | 21 | 7 |

**Table 2.** Clinical presentations of CCLL

| Type of disease (case) | Clinical presentation | | | | | | Abnormal physical signs | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | No | Fever | Shortness of breath | Cyanosis | Cough and gasp | Feeding intolerance | No | Moist rales | Three depression sign | Asymmetrical breath sound | Thoracic local eminence |
| Congenital lobar emphysema | 0 | 2 | 16 | 6 | 5 | 1 | 0 | 6 | 5 | 5 | 1 |
| Pulmonary sequestration | 3 | 1 | 4 | 3 | 0 | 2 | 4 | 1 | 0 | 2 | 1 |
| CCAM | 2 | 0 | 2 | 2 | 0 | 1 | 3 | 0 | 1 | 1 | 1 |
| Bronchogenic cyst | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Total | 6 | 3 | 22 | 11 | 5 | 4 | 8 | 7 | 6 | 8 | 3 |

confirmation of CCLL. Either of the two could be used for the diagnosis of CCLL.

*Methods*

The medical records of the cases were reviewed. The baseline data of the included cases with CCLL (congenital lobar emphysema, pulmonary sequestration, congenital cystic adenomatoid malformation, bronchogenic cyst) were collected, including gender, age of onset, symptoms, findings of chest X-ray or chest CT, treatment method and prognosis. Literature review was also performed.

## Results

*Baseline information*

There were 20 males (71.43%) and 8 females (28.57%). The gestational age was ~34 weeks in 3 cases (10.71%), ~37 weeks in 4 cases (14.29%) and ≥37 weeks in 21 cases (75.00%). The body weight at birth was ~1000 g in 1 case (3.57%), ~1500 g in 1 case (3.57%), ~2500 g in 5 cases (17.86%) and ≥2500 g in 21 cases (75.00%). The average age of onset was 4.68 d, including 21 early newborns (0-7 d) (75.00%) and 7 late newborns (~28 d) (25.00%). Congenital abnormalities were found by prenatal ultrasonography in 4 cases (14.29%), among which 3 cases were diagnosed as pulmonary sequestration and 1 as CCAM. Two cases had history of birth asphysia (7.14%) (**Table 1**).

In terms of the type of CCLL, 16 cases had congenital lobar emphysema (57.14%), 7 cases had pulmonary sequestration (25%), 4 cases had CCAM (14.29%) and 1 case had bronchogenic cyst (3.57%).

*Clinical presentations*

Six cases (21.43%) were asymptomatic. Among those presenting with symptoms, 3 cases (10.71%) had fever, 22 cases (78.57%) had shortness of breath, 11 cases had cyanosis (39.29%), 5 cases had cough and gasp (17.86%) and 4 cases had feeding intolerance (14.29%). Eight cases (28.57%) had no abnormal physical signs; 7 cases had rough breathing sound and moist rales (25%), 6 cases (21.43%) had three depression sign, 8 cases (28.57%) had asymmetrical breathing sound and 3 cases (10.71%) had thoracic local eminence (**Table 2**).

*Site of lesions*

The sites of lesions and the corresponding number of the cases were summarized as follows: 12 cases (42.86%) had lesions in the right upper lobe, 3 cases (10.71%) had lesions in the right lower lobe, 7 cases (25.00%) had lesions in the left upper lobe, 10 cases (35.71%) had lesions in the right lower lobe and 4 cases (14.29%) had lesions straddling the lobes. Six cases had pulmonary sequestration in the left lower lobe and 1 in the right lower lobe; 2 cases

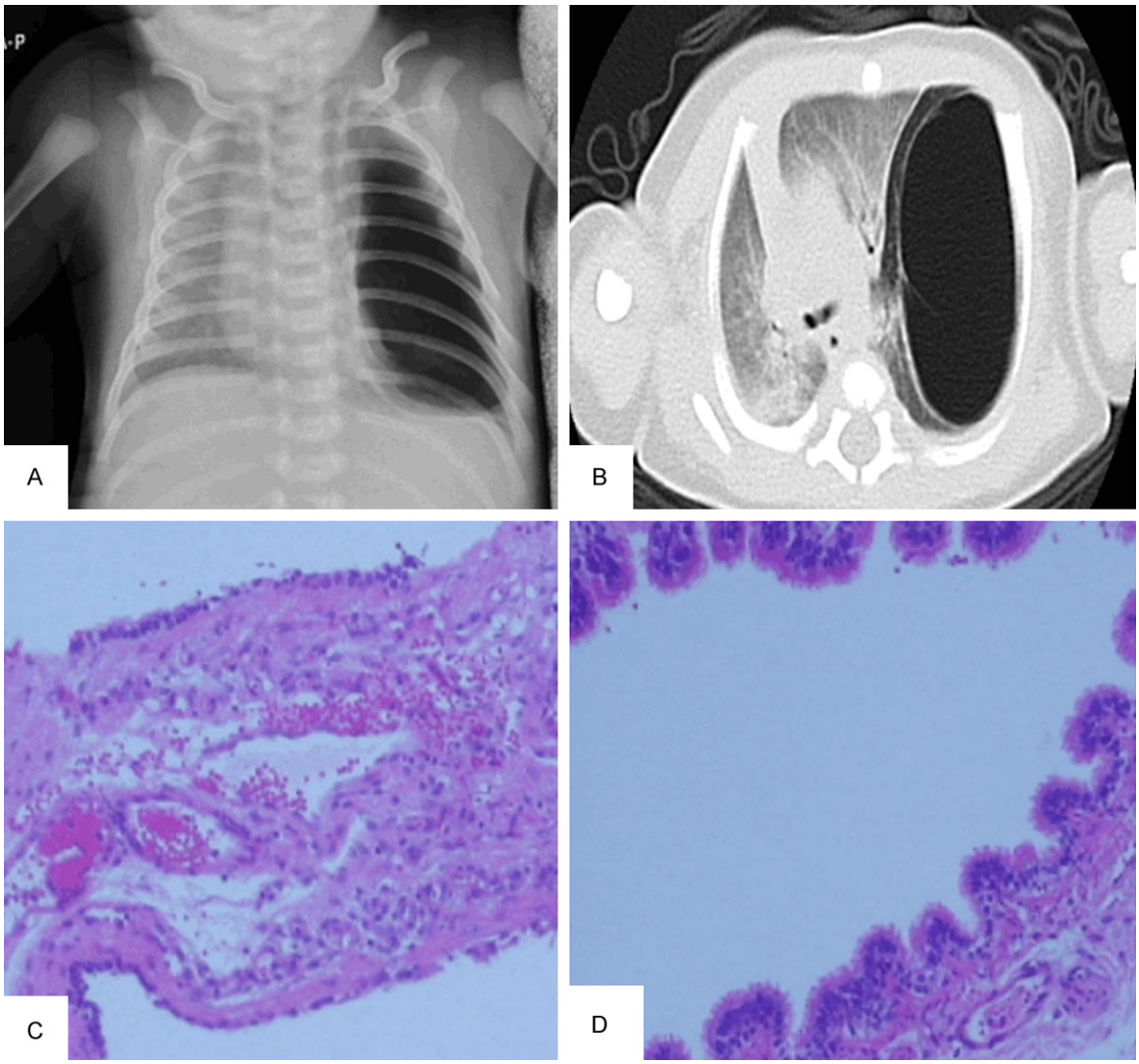


**Figure 1.** Clinical, imaging and pathological findings of congenital lobar emphysema. A female case with onset on the day of birth; shortness of breath, cyanosis, cough and gasp, and feeding intolerance; three depression sign, asymmetrical breath sound, thoracic local eminence, combined with polycystic kidney disease. Imaging findings: solitary cysts; this case was finally cured. A. Chest X-rays reveal huge transparent area without lung markings in the left lung; B. Chest CT reveals huge cystic lesion measuring about 3.0×6.7 cm in the left lower lobe, with slightly thickened wall and bullae in the left lower lobe; C and D. Extensive bleeding in the cyst wall under the light microscope, with single layer of flattened cells being covered on the inner wall and inflammatory cell infiltration in the cyst wall (HE staining 100×).

had CCAM in the left lung and 2 in the right lung. Bronchogenic cyst affected the left lower lobe in 1 case.

*Imaging findings*

Seventeen cases (60.71%) had solitary cysts, among which 15 cases had solitary gas-containing cysts and 2 had solitary liquid-containing cysts. Four cases (14.29%) had multiple cysts, among which 2 had multiple gas-containing cysts and 2 had multiple liquid-containing cysts. Chest X-rays showed dense shadows in seven cases (25.00%), all of which were pulmonary sequestration. All 16 cases of congenital lobar emphysema had solitary gas-containing cysts with mediastinal shift.

*Complications*

The occurrence of complications and the corresponding number of cases were as follows: pneumonia in 13 cases (46.43%), congenital heart disease in 2 cases (7.14%, abnormality of

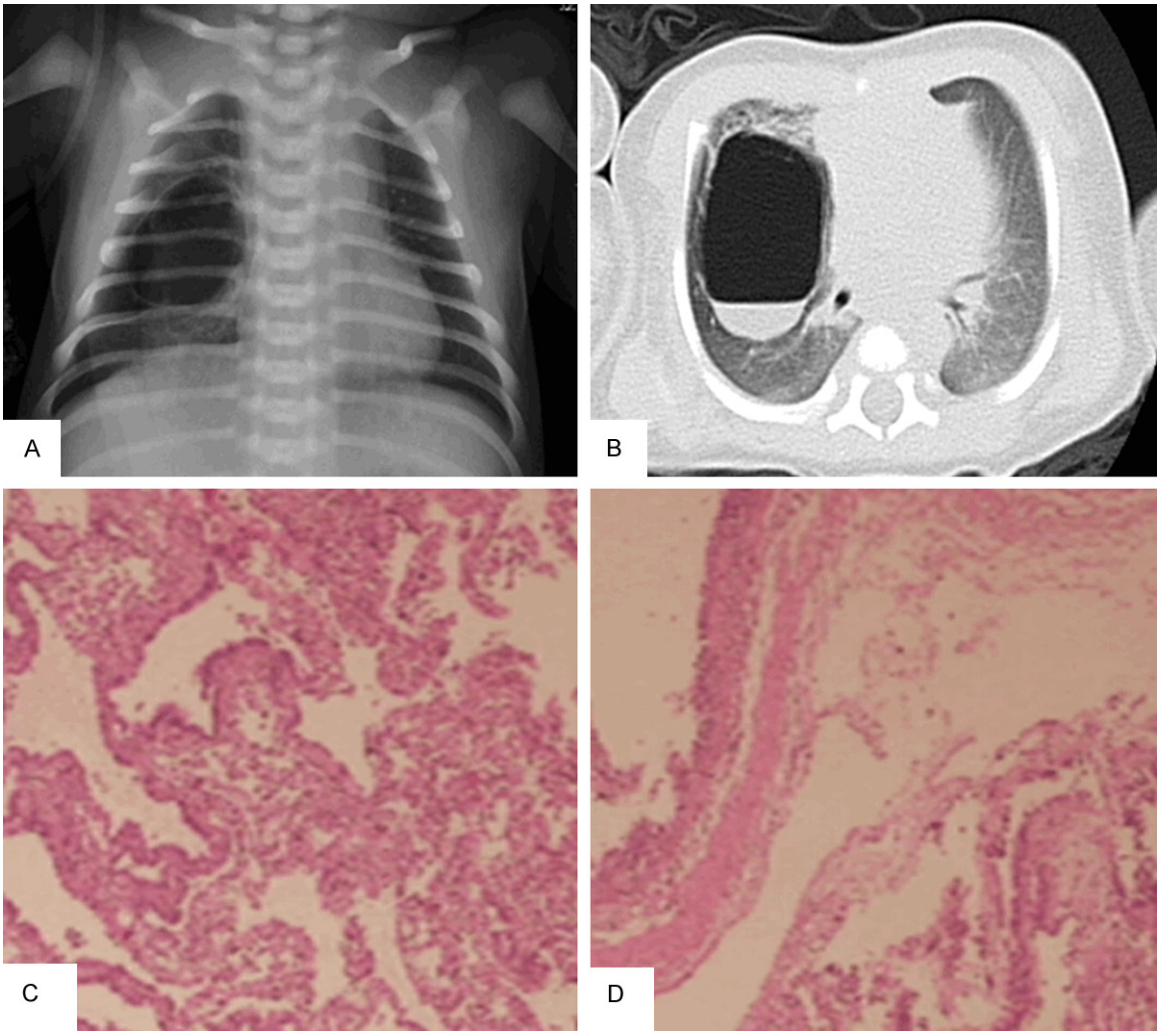


**Figure 2.** Clinical, imaging and pathological features of CCAM. A male case with onset on the day of birth; shortness of breath, cyanosis, and dyspnea three depression sign, asymmetrical breath sound, thoracic local eminence; multiple liquid-containing cysts; this case was finally cured. A. Chest X-rays reveal a cystic transparent area in the right lung field measuring about 2.8 cm×3 cm, with thin cyst wall, no obvious septa in the cysts but the presence of space-occupying cystic lesion in the right lung. B. Chest CT reveals a quasi-round transparent area in the right middle lobe measuring about 3.2×2.5 cm, with unclear boundary. A few patchy shadows are seen in the periphery, with thin cyst wall and gas-liquid interface in the cyst. C and D. The cyst wall is lined with pseudostratified ciliated columnar epithelium. Many small cystic spaces separated by septa and composed of simple ciliated columnar epithelium are seen in the surrounding lung tissues, with alveolar dilation and focal hemorrhage (HE staining 100×).

the right aortic arch in 1 case, and dextrocardia and ventricular septal defect in 1 case), diaphragmatocele in 1 case (3.57%), laryngeal cartilage dysplasia in 1 case (3.57%), funnel chest in 1 case (3.57%) and polycystic kidney disease in 1 case (3.57%).

*Treatment and prognosis*

The treatments used and the corresponding number of cases were as follows: mechanical ventilation in 11 cases (39.29%), constant-pressure oxygen inhalation therapy in 16 cases (57.14%), antibiotics therapy in 23 cases (82.14%). Four cases received surgical treatment, and 2 of these 4 cases had congenital lobar emphysema, 1 had pulmonary sequestration, and 1 had CCAM. The age of onset in all 4 cases was shortly after birth with the presentations of shortness of breath, cyanosis, three depression sign, asymmetrical breath sound and thoracic local eminence. CCLL was confirmed by imaging findings for all of them (**Figures 1**-**3**). They were followed up until 2 years old with no repeated respiratory tract

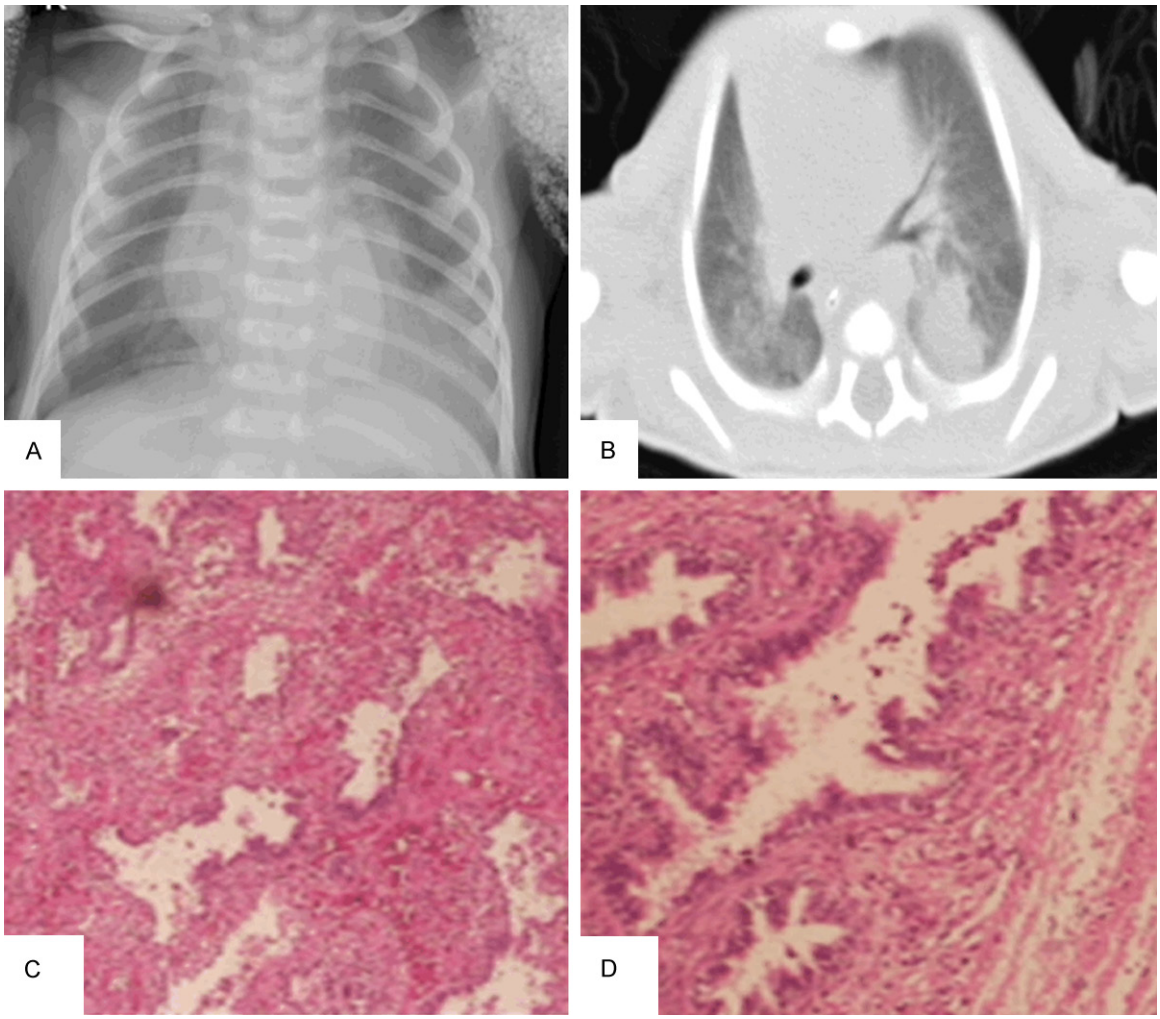


**Figure 3.** Clinical, imaging and pathological features of pulmonary sequestration. A female case with onset on the day of birth; shortness of breath, cyanosis, and feeding intolerance; asymmetrical breath sound, thoracic local eminence, combined with diaphragmatocele. Imaging findings: dense shadow; this case was finally cured. A. Chest X-rays indicate reduced transparency in the left lower lung, with massive, flaky, obscure shadow. B. Chest CT reveals soft tissue shadow in the left lower lobe measuring about 4.0×3.3 cm. Tortuous blood vessels stemming from the abdominal aorta supply the blood, and pulmonary sequestration is diagnosed in the left lower lobe. C and D. Mixed distribution of alveoli and bronchioles under the light microscope, with dysplasia and bleeding (HE staining 100×).

infections or neurological complications. There were 3 deaths among the 28 cases, including 2 cases of congenital lobar emphysema and 1 case of pulmonary sequestration. 17 cases were improved after treatment and discharged and 8 cases were discharged against the medical advice.

## Discussion

The incidence of CCLL in newborns is 1:10000 to 1:35000 [2]. The studies 15-20 years ago suggested intrauterine deaths in 40% of CCLL cases, and abortion was usually recommended. However, recent studies showed that most CCLL cases had good prognosis [1].

CCLL can be discovered at about 18-20 w of gestational age. Ultrasound scan at late stage of gestation may indicate abnormal echoes in the fetal thoracic cavity. In that case, the mother will need prenatal diagnosis and consultation. If the type of CCLL cannot be determined with conventional prenatal ultrasonography, MRI will be used to diagnose pulmonary sequestration, CCAM and congenital lobar emphysema, but not bronchogenic cyst generally [3]. Thus the newborns suspected of lung lesions by prenatal ultrasonography should receive chest X-rays and chest CT immediately after birth. In the present study, only 4 newborns (14.29%) were found to have space-

occupying lesions in the chest by prenatal ultrasonography, indicating low prenatal detection rate. However, according to foreign reports, CCLL is mostly diagnosed prenatally [4]. The goals of prenatal diagnosis of CCLL are to determine the size of the lesions and its adverse impact, decide the best time for surgery and predict prognosis (instead of the histological subtype). Ehrenberg-Buchner [5] believed that prenatal MRI can predict fetal lung lesions based on congenital pulmonary airway malformation volume ratio (CVR). If CVR >1.6, fetal hydrops can be predicted; if CVR <1.0, there may be no respiratory symptoms; if CVR >1.0, the symptoms of the respiratory system may present with the need for surgical treatment.

CCLL may be either symptomatic or asymptomatic with the manifestations of pulmonary infection and lung and tracheal compression. If the lesions are small, CCLL is usually asymptomatic. In the present study, 21.43% of the newborns were asymptomatic and 28.57% had no abnormal physical signs. If the lesions are small and connected with the bronchi, secondary cysts and (or) pulmonary infection may occur. Comparatively, infections are more common than compression. In this study 46.43% of the newborns were combined with pneumonia. If the lesions are aggravated with large volume or rupture, pneumothorax and hydropneumothorax may happen, leading to compression or even respiratory distress. For cases responding poorly to the treatment for cough and gasp, chest CT or MRI is necessary to exclude CCLL.

Pulmonary sequestration is most common in the left lung, and less common between a lower lobe and the diaphragm, below or in the diaphragm or in the mediastinum. It is most rarely in the right lung. Among our cases, 85.71% of the cases with pulmonary sequestration were affected in the left lower lobe and 12.5% in the right lower lobe. Congenital lobar emphysema was the most common in the upper lobes, and CCAM mostly affected unilateral lobes, with left and right CCAM accounting for 50%, respectively. This agrees with the published statistics [6].

Congenital lobar emphysema and bullous emphysema are more common types of CCLL in newborns and small infants, usually causing dyspnea [7]. Bronchogenic cyst may present as repeated pulmonary infection, and this is exactly how bronchogenic cyst is discovered in childhood. Among our cases, congenital lobar emphysema accounted for 57.14%. The clinical features of congenital lobar emphysema include tension pneumothorax, shortness of breath, cyanosis or dyspnea. Physical examination may show shift of the trachea to the opposite site with tympanic percussion resonance and reduced or no breath sound in the affected side. Chest X-rays may reveal atelectasis and shift of the mediastinum and trachea caused by lung cystic lesions. The patients may be combined with mediastinal hernia and atelectasis on the ipsilateral side, which are very critical conditions. If left untreated, the newborns may die of respiratory failure. Among 3 deaths in this study, 2 deaths were due to congenital lobar emphysema. Bronchogenic cysts may present as repeated pulmonary infections, fever and cough, which are atypical symptoms. Some newborns may be asymptomatic and therefore miss their diagnoses. Bronchogenic cysts rank the first in terms of incidence among all types of CCLL [6].

CCLL may be concurrent with other deformities. For example, congenital lobar emphysema is usually concurrent with cardiovascular malformations, funnel chest, anterior mediastinal defect, diaphragmatocele, hiatal hernia, dyschondroplasia and renal hypoplasia. In this study, 1 newborn of pulmonary sequestration was combined with diaphragmatocele and 2 newborns of congenital lobar emphysema were combined with congenital heart disease. One of these 2 newborns was combined with congenital laryngeal cartilage dysplasia, funnel chest and polycystic kidney disease. Thus, for those with CCLL, Doppler echocardiography, ultrasound examinations and larynx and airway examination are needed to exclude concurrent deformities.

Pulmonary sequestration and CCAM are more likely to be associated with infections, tension cysts and pyopneumothorax. Congenital lobar emphysema at early stage may present respiratory symptoms. The patients unresponsive to conservative treatments can resort to surgical treatments which usually achieve good outcomes. Bronchogenic cysts may be discovered due to repeated cough and gasp in childhood and receive surgical treatment. Considering the risk of long-term infections and malignancy, more and more researchers agree that asymptomatic CCAM and pulmonary sequestration

can be treated by elective surgery [8]. Study shows that for asymptomatic CCLL, early-stage surgery and elective surgery do not differ significantly in complications, length of hospital stay and the risk of malignancy. However, the surgical time is still disputable [9]. Surgery for asymptomatic CCAM may be justified as follows: to prevent repeated infections, extensive pleural adhesions, pneumothorax and hemorrhage; to prevent malignancy, typically pleuropulmonary blastoma; to facilitate alveolar regeneration and respiratory compensation; to reduce the risk associated with emergency surgery [10]. According to the literature reports, the best surgical time for asymptomatic CCAM is 3-6 months [11]. Among newborns with asymptomatic CCLL, many would develop respiratory symptoms at the age of 2, and 10% of them would suffer from infections at the age of 1. So elective surgery can be performed at the age of 1 [12]. All newborns receiving the surgical treatment presented symptoms of shortness of breath and cyanosis. However, the surgical time for asymptomatic newborns has to be determined by long-term follow-up. CCLL newborns are usually combined with pneumonia and 82.14% of the newborns in our study received antibiotics therapy. Antibiotics can greatly reduce the risk associated with surgical treatment and preserve the normal lung tissues as much as possible.

Prenatal ultrasound examinations for CCLL can help understand the natural history of diseases and determine the treatment strategies. This is of great significance for prenatal and postnatal disease management. With advances in genetic diagnostic testing, CCLL can be diagnosed or treated prenatally, thereby reducing the risk of CCLL and improving the life quality of the newborns.

## Disclosure of conflict of interest

None.

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