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Case Report: a Young Women with Infected Polycystic Lung Disease that Affects the Quality of Life

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Abstract

Introduction: Polycystic lung disease (PLD) is a group of diseases with heterogeneous pathophysiological processes. The demographics and clinical symptoms vary widely. The etiology of PLD is related to neoplasms, genetics, lymphoproliferative disorders, infections, interstitial diseases, smoking, and developmental disorders. In HRCT, cystic, nodular, ground glass opacities and pneumothorax can be found. Tissue biopsy and immunohistochemistry are needed to determine the type of PLD. Age is very influential towards the survival rates, rapid decline in lung function often occurs at a young age, thus, causing long-term complications in the cardiovascular system

Case Description: A 14-years-old woman complained of shortness of breath and cough was diagnosed with Poly cystic lung disease with Lung TB as secondary infection. CT Scan Thorax showed multiple cavities with consolidation, abdominal ultrasound of the ovary found a simple cystic lesion. The patient underwent TB treatment. After evaluation, clinical symptoms improved, but the patient is often absent from school, thus, indicating disruption in quality of life. Spirometry data showed decreased pulmonary function ad modum restriction, and moderate obstruction. The patient is planned to undergo several examinations such as Bodypletysmography, Bronchoscopy, and VATS to obtain tissue samples, so a diagnosis can be made. Considering the age of the patient—who is still young—definitive therapy as a continuation is expected to improve the patient's quality of life.

Conclusion: The diagnosis of PLD in the patient still requires further examination. Other tests, such as biopsy followed by immunohistochemical examination, can be used to confirm the type of PLD. Currently, the patient is undergoing TB treatment and routine control to the clinic. Ater treatment, the clinical symptoms alleviated, but shortness of breath is still present, especially felt after walking fast and carrying heavy loads. Spirometry was done as an evaluation of pulmonary function, showing moderate restriction and obstruction. It is clear that PLD affects the quality of life in this patient.

Keywords: Polycystic Lung Disease, Multiple Cysts, HRCT, Quality of Life

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1. Background

Cystic lung disease (CLD) is a group of diseases with a pathophysiological process being the presence of several round or irregular, thin-walled, air-filled spaces in the pulmonary parenchyma. The underlying etiology of CLD is caused by neoplasm, polyclonal or monoclonal lymphoproliferative disorders, infection, interstitial lung disease, smoking, and congenital or developmental disabilities.[1]

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Table 1. The Classification of Cystic Lung Disease.[2]

Classification	Description
1. Neoplastic	Lymphangioleiomyomatosis—sporadic as well as associated with tuberous sclerosis Pulmonary Langerhans cell histiocytosis, and non–Langerhans cell histiocytoses, including Erdheim Chester disease Other primary and metastatic neoplasms, such as sarcomas, adenocarcinomas, pleuropulmonary blastoma, etc.
2. Genetic/developmental/congenital	Birt-Hogg-Dubé syndrome Proteus syndrome, neurofibromatosis, Ehlers-Danlos syndrome Congenital pulmonary airway malformation, bronchopulmonary dysplasia, etc.
3. Associated with lymphoproliferative disorders	Lymphocytic interstitial pneumonia Follicular bronchiolitis Sjögren syndrome Amyloidosis Light-chain deposition disease
4. Infectious	*Pneumocystis jiroveci* Staphylococcal pneumonia Recurrent respiratory papillomatosis Endemic fungal diseases, especially coccidioidomycosis Paragonimiasis
5. Associated with interstitial lung diseases	Hypersensitivity pneumonitis Desquamative interstitial pneumonia
6. Smoking related	Pulmonary Langerhans cell histiocytosis Desquamative interstitial pneumonia Respiratory bronchiolitis
7. Other/miscellaneous	Post-traumatic pseudocysts Fire-eater's lung Hyper-IgE syndrome
8. DCLD mimics	Emphysema α_1-antitrypsin deficiency Bronchiectasis Honeycombing seen in late-stage scarring interstitial lung diseases

The frequency of cysts occurrence is known to increase in old age, and is usually not found in healthy individuals younger than 50 years.[1] Based on previous data, the incidence of cystic lung disease is more common in women than men.[3] The peak incidence varies between diseases, but usually occurs in the third or fourth decade of life. Patients with cystic lung disease often have the same nonspecific symptoms, such as chronic cough and shortness of breath.[1]

To diagnose cystic lung disease, the use of a multidisciplinary approach that considers the patient's clinical history, physical examination findings, and radiological examination findings is important.

Table 2. Classification of Cystic Lung Disease [2]

	LAM	PLCH	BHD	LIP/FB	Amyloid	LCDD
Personal history	Pneumothorax, angiomyolipomas, chylous effusions, and cortical tubers, seizures, skin lesions if TSC	Pneumothorax, smoking	Pneumothorax, skin lesions, renal tumors	HIV, autoimmune diseases, sicca symptoms, Raynaud's phenomenon	Sicca symptoms, autoimmune diseases	Lymphoproliferative disorders
Family history	TSC	Not relevant	Pneumothoraces, skin lesions, renal cancers	Not relevant	Not relevant	Not relevant
Extrapulmonary manifestations & other associations	Renal angiomyolipomas, chylous effusions, TSC manifestations	Diabetes insipidus, cutaneous & osteolytic bone lesions	Renal tumors, skin fibrofolliculomas	SS & other CTDs, HIV, EBV, CVID	SS & other CTDs, systemic amyloidosis	Lymphoproliferative disorders, renal failure
Laboratory testing	Serum VEGF-D	Serum & urine studies for diabetes insipidus	Genetic testing for *FLCN* mutations	Polyclonal dysproteinemia	Monoclonal dysproteinemia	Lymphoproliferative disorders, renal failure
Diagnostic yield of bronchoscopy (BAL, TBBx)	>50%	30–50%	0	Low yield	Low yield	Low yield
Consider surgical lung biopsy	Yes	Yes	No	Yes	Yes	Yes
Genetic testing	TSC mutations, but usually not clinically indicated	BRAF mutation	*FLCN* gene mutation	No	No	No
Treatment	Sirolimus	Smoking cessation, immunosuppression, cladribine	None available	Corticosteroids & other immunosuppressive agents for LIP	None available	None available

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Table 3. Radiology Imaging of Cystic Lung Disease [2]

	LAM	PLCH	BHD	LIP/FB	Amyloid/LCDD
Distribution	Diffuse, random	Upper & middle lung zones; sparing costophrenic angles	Basilar/peripheral/ subpleural and near vessels	Diffuse, random, often near vessels	Diffuse, random
Size	2 mm to 2 cm	Variable, 2 mm to >2 cm	75% <1 cm	Average size 3 mm to 1 cm	4 to 45 mm, majority larger than 1 cm
Shape	Round, uniform	Bizarre, irregular	Elliptical, lentiform	Round, variable	Round, variable
Pathological examination diagnostic	Yes	Yes	No	Yes	Yes
Pathologic findings	Infiltration by HMB-45–positive LAM cells with smooth muscle phenotype	S100- and CD1a-positive Langerhans cells with intracellular Birbeck granules by electron microscopy; stellate fibrotic scars in late stages	Intraparenchymal and subpleural cysts abutting interlobular septae and lacking abnormal cell proliferations or significant fibroinflammatory component	LIP: diffuse interstitial polyclonal lymphocytic infiltrate FB: peribronchiolar polyclonal follicular lymphoid hyperplasia with germinal centers	Amyloid: amorphous protein deposits with fibrillar ultrastructure and apple-green birefringence by Congo red stain viewed under polarized light LCDD: typically monotypic kappa light chain deposition with finely granular ultrastructure lacking apple-green birefringence by Congo red stain and polarized light
Other associated findings on HRCT	Pleural effusions	Micro and macro nodules with or without cavitation, thick-walled cysts, cavities and reticulation	Cysts frequently abut pleura and proximal vessels	Ground-glass attenuation, poorly defined centrilobular nodules, interlobular septal thickening, cysts may contain internal structure	Multiple nodules of varying attenuation and random distribution; nodules abut cyst walls

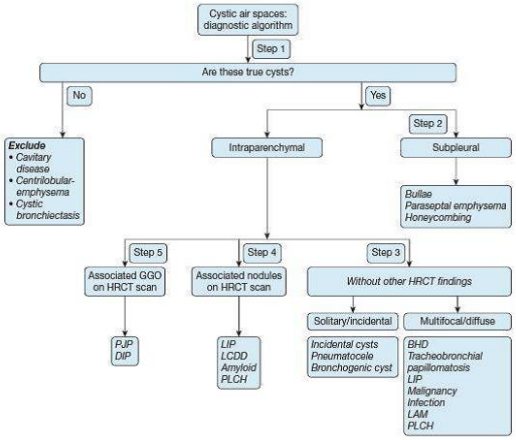

Figure 1. Diagnostic Algorithm of cystic lung disease [4]

In the evaluation of cystic lung disease, it is important to ensure that the lesions on HRCT are indeed cysts. What needs to be considered is the appearance or formation that resembles a cyst, including cavities, centrilobular emphysema and cystic bronchiectasis should be excluded first according to the definition descripted in the Table 4. 4.

Table 4. Radiology definition of Lesions [4]

Lesion	Definition
Cyst	Thin-walled (<2 mm), spherical parenchymal lucency interfaced with normal lung.
Cavity	Gas-filled space within pulmonary consolidation, mass, or nodule, typically thick walled (>2 mm) and more irregularly shaped than cysts.
Bulla	Spherical focal lucency, ⩾1 cm in diameter, bounded by a thin wall (usually <1 mm). It is usually accompanied by emphysematous changes in the adjacent lung.
Bleb	Cystic air space bounded by a thin wall adjacent to the visceral pleura, typically <1 cm in size.
Pneumatocele	Approximately round, thin-walled, air-filled space in the lung. Most frequently caused by infections, trauma, or aspiration of hydrocarbon fluid and is usually transient.

HRCT is the imaging modality of choice for detecting and differentiating various causes of cystic lung disease. HRCT findings that should be regarded when evaluating patients with cystic lung disease include: lung volume; size, wall thickness, shape and distribution of pulmonary cysts; and associated findings, such as pulmonary nodules, thickening of the septum, pleural effusions, lymphadenopathy and extra-thoracic abnormalities.[4] Recognition of a pulmonary parenchymal cystic is often followed by histological confirmation through adequate tissue samples, such as bronchoscopy biopsy, transbronchial lung biopsy, video-assisted thoracoscopic surgery biopsy, or even open lung biopsy, depending on the patient's condition and diagnostic benefits.[3] Certain immunohistochemical stains could be done to establish the type of cystic lung disease. Some examples of the test are red kongo, CD1a, S100, HMB-45.[5]

The clinical course of cystic lung disease varies widely. The disease severity could also be assessed by HRCT. HRCT findings correlates with lung function tests, gas exchange, and exercise performance. HRCT computer analysis could measure the percentage of lung volume affected by the cyst and evaluate the texture of the area not involved with the cyst.[6] Estimated survival varies widely, and is more likely to increase in general over the last few decades, perhaps because of the wider use of CT scanning.

One of the long-term complications that could occur in patients with cystic lung disease is cardiovascular disorders. Long-term complications in the cardiovascular system include pulmonary hypertension and cor pulmonale.[7]

2. Case Report

The 15-year-old female patient complained of shortness of breath for 2 months, occurred especially when the patient coughed and improved when sputum could be removed. Complaints of shortness of breath getting worse in 1 month, shortness of breath is affected by activity and if walking long and fast. DOE (+), PND (-).

Recurrent Cough in the last 2 months producing white-colored phlegm and no blood. Fever is absent, night sweats (-), The patient has been sweating for most of the day since the onset of cough. Weight loss (+) 7 kg in 2 months, no decrease in appetite. There are no abnormalities in urinary or gastrointestinal system.

At 3 months before hospitalization, the patient complained of coughing and went to a primary health facility, given medicine in the form of tablets and syrup. Complaints of coughing ameliorated. 2 months before hospitalization, the patient complained of coughing again and went to

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a primary health facility, but even after the medicine ran out, the complaints did not decrease. Laboratory tests and chest X-Ray were carried out and the patient was referred to the lung policlinic in Lavalete Hospital.

The patient came to the ER of RSSA on December 11th, 2017 with a stable hemodynamic condition, blood pressure of 107/79 mmHg, heart rate of 108x/minute, respiratory rate of 20x/minute, and axillary temperature of 36.9°C. Lung examination showed a symmetrical respiratory movement, normal stem fremitus, normal percussion, and bronchovesicular breath sounds accompanied by rhonchi in all areas of the left hemithorax and lower areas of the right hemithorax.

Radiologi Examination (Figure1) showed:

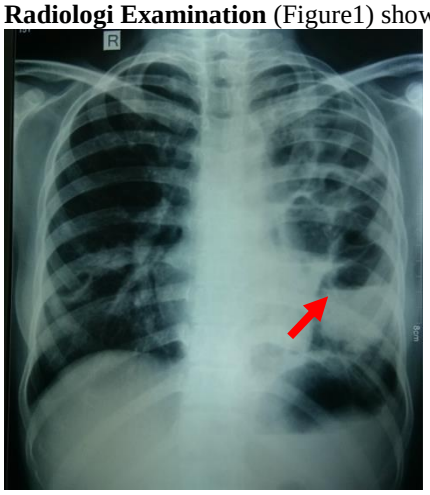

Figure 2. Chest Xray PA November 11th, 2017 showed multiple cystic with air fluid level, conclussion: Policystic lung with secondary infection

Laboratory examination had indicated leukocytosis (leukocyte = 14.990/µL), neutrophilia (neutrophil = 86,1%), lymphocytopenia (lymphocyte = 5,9%), monocytosis (monocyte = 7,6%). AFB examination had showed +3/+3/+3. TCM examination had indicated MTB detected high, rifampicin resistance not detected. From sputum examination was obtained the colony of Streptococcus salivarus ssp sensitive to cefotaxime, ceftriaxone, levofloxacin, linezolid, vancomycin. BGA examination had indicated uncompensated metabolic acidosis (pH = 7,33, pCO2 = 35,3mmHg, pO2 = 99,4mmHg, HCO3 = 18,6 mmol/L, BE -7,6 mmol/L, O2 saturation = 97,5%). ECG examination had indicated sinus tachycardia 111x/minute.

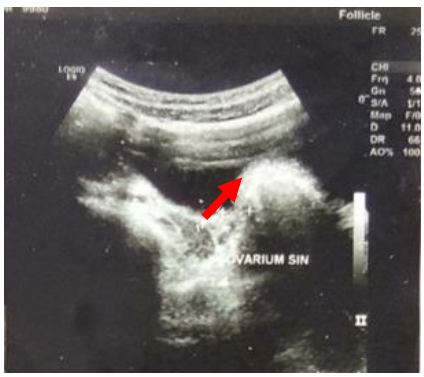

Figure 3. Abdominal USG on Desember 11th, 2017 showed simple cystic lesion in left ovarium

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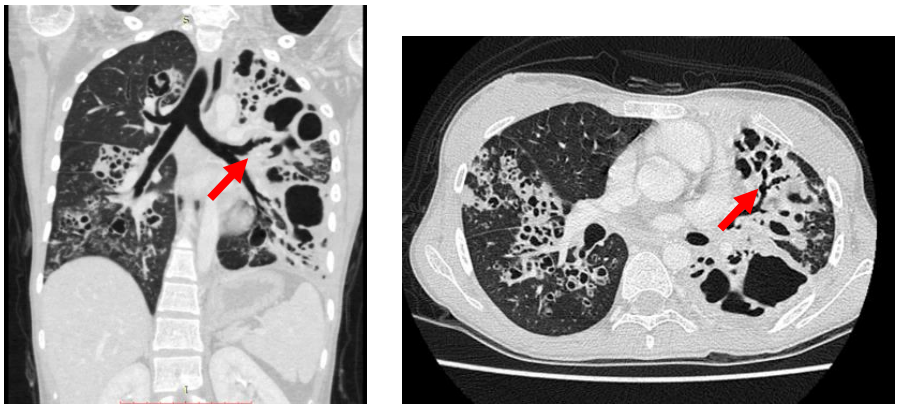

Figure 4. CT Scan Thorax on December 12th, 2017 showed multiple cystic with traction bronchiectasis.

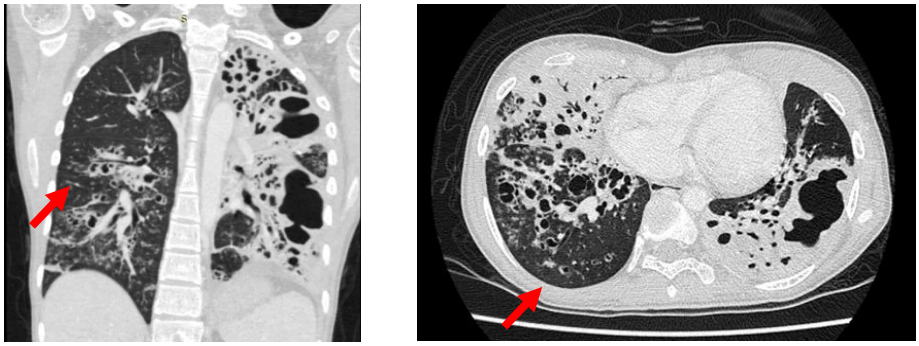

Figure 5. CT Scan Thorax on December 12th, 2017 showed multiple cystic lession with three bud appearance

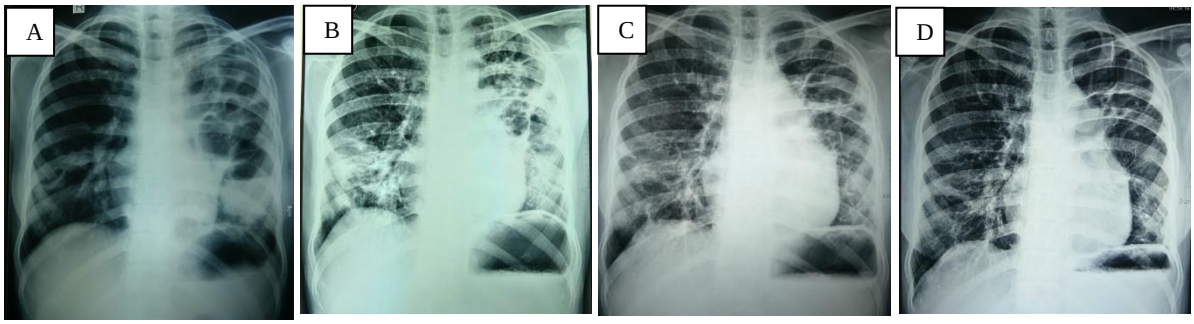

Figure 6. CXR evaluation and comparison. (A) Before therapy on November 11st 2017 (B) 4 month after therapy on April 12nd 2018. (C) 6 months after therapy on July 2nd 2018 and (D) 8 months after therapy on September 20th 2018 show Multiple cystic lesion with reduced infiltrate components

3. Discussion

In this case, a 15-year-old woman was reported with Polycystic Lung Disease accompanied with secondary infection in the form of pulmonary TB, MTB detected high, rifampicin resistance not detected. The diagnosis is made through an anamnesis, physical examination and supporting examinations—CXR and CT scan.

From anamnesis, the patient's demographic obtained was a female, aged 15 years old, in which, based on several literatures, the incidence of cystic lung disease varies greatly depending on the type or classification of cystic lung disease itself. The available demographic data allows the prevalence of cystic lung disease to be the same between male and female, and can be found in a wide age range—between 2-70 years. However, for the gender, several types of cystic lung disease were still dominantly found in female patients.[3]

In this case the patient complained of coughing for 2 months accompanied with shortness of breath. Based on previous studies, the symptoms of cystic lung disease are very diverse, it can be asymptomatic until acute, life-threatening symptoms—such as pneumothorax—occur. The symptoms of cough can be found in several types of *cystic lung disease*.[2]

The symptom of chronic cough was in accordance with the secondary infection found in this case. Symptoms of chronic cough and weight loss is very commonly found pulmonary tuberculosis infection, in addition to the confirmation of molecular rapid test which resulted in the detection of tuberculosis bacteria in the sputum sample sent.

From the radiological imaging, it can be seen that there were multiple cysts in the right and left lungs. From the CT scan of the chest, it was found that there were multiple cavities in the entire lung field with consolidation around it, a larger cavity and a pan-lobular emphysema. Based on several literatures, the CT scan findings can be classified as diffuse spread of the cyst. There may be other features such as nodules, cavities, effusions, pneumothorax and ground glass opacities. Diagnosing or classifying cystic lung disease requires steps to determine the type of cystic lung disease with certainty.[1]

UGS examination of the abdomen had found right ovary with the size of 1.68 x 1.13 cm and the left ovary of 1.9 x 1.17 cm, with simple cystic lesions resembling follicles. This suggested that the presence of cysts in organs other than the lungs indicated that cystic lung disease is related to genetics. From literatures, cystic lung disease can be classified into various types. Cystic lung disease can be broadly

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classified according to the underlying etiology, such as those caused by neoplasms, genetics, polyclonal or monoclonal lymphoproliferative disorders, infections, interstitial lung disease, smoking, and congenital or developmental disabilities. Several types of CLD associated with genetic etiology are LAM and BHD.[2]

In this case, non-radiological examination results cannot support in diagnosing a type of cystic lung disease. Apart from the use of radiological imaging, there are several other tests that can provide support in making the diagnosis. Some cases can be helped by histopathological results obtained using biopsy. Based on literatures, in several types of cystic lung disease—apart from HRCT—histopathological examination is also needed to make a diagnosis. In addition, immunohistochemistry can also be done on the biopsy sample. Certain immunohistochemical stains can establish the type of cystic lung disease. Some of the examples are: red kongo, CD1a, S100, HMB-45.[5]

In this case, the patient was given no intervention. Based on literatures, intervention measures such as FOB and tissue biopsy have a role that can help in making the diagnosis of cystic lung disease.[2]

Based on the evaluation results after care and treatment, the patient showed a decrease in quality of life. Currently the patient is a grade 7 student at a public high school in Malang. Daily activities at school are difficult to follow due to the shortness of breath and the patient's condition to get tired and congested—especially if you walk fast and carry heavy luggage. This also causes the patient to frequently absent from school. Based on literatures, decreased quality of life is associated with prognosis and complications of the patient's disease. Patients with multiple cysts tend to have lower FEV1 and DLCO, lower peak oxygen uptake (V.O2 max), and more hypoxemia induced by exercise or strenuous activity. HRCT findings correlates with lung function test result, gas exchange, and exercise performance.[6]

Estimation of survival in this patient depend on lung function and radiologic features. Data from baseline, large case series show that 38% to 78% of patients were alive 8.5 years after the onset of the disease. Other data reported a 91% chance of survival at 8.5 years, 79% at 10 years, and 71% at 15 years.[6]

The patient in this case was given anti-tuberculosis drugs as the treatment, in accordance with the results of the infection found, which indicated tuberculosis. After undergoing therapy, symptoms—such as coughing—have reduced but other

symptoms—such as shortness of breath, especially walking fast and carrying heavy loads—still present. Definitive therapy still cannot be given, because the type of cystic lung disease is not known. Based on some articles and literatures, the therapy for cystic lung disease is based on the etiology of cystic lung disease itself. Therapy can include smoking cessation, immunosuppressants, corticosteroids and other types of therapy. [8]

4. Conclusion

A 15-year-old woman was reported with clinical symptoms of cough, shortness of breath and weight loss. Microbiological examination of the sputum TCM had found that MTB was detected high, rifampicin resistant was not detected. The chest X-ray showed multiple cysts with air fluid levels inside, and the CT scan showed an image of multi cystic lung disease with bronchiolitis, suggestive of active TB ddx Jirovicii pneumonia infection. Thus, the patient was diagnosed with Policystic Lung disease accompanied by secondary infection in the form of pulmonary TB. On abdominal ultrasound examination, the right ovary was found to be 1.68 x 1.13 cm in size, the left ovary was 1.9 x 1.17 cm, and there were simple cystic lesions resembling follicles.

The diagnosis of cystic lung disease was still not established in this patient. Other tests are needed to make a diagnosis or confirm the type of cystic lung disease. A biopsy followed by an immunohistochemical examination can confirm the type of cystic lung disease.

Currently the patient is given anti-tuberculosis drugs—4FDC—treatment with a dose of 1x2 tablets, and routine control at the pulmonary polyclinic Lavalete Hospital every 1 month is needed. After treatment, the patient had experienced improvement in symptoms—such as the cough had alleviated and the body weight had started to increase. Other symptoms—such as shortness of breath—are still felt by the patient, especially after walking fast and carrying heavy loads. This affects the patient's quality of life. The patient rarely attend school due to the persistent symptoms.

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