

Progress in Clinical Research of Diffuse Panbronchiolitis

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Abstract: Bronchitis is a clinical disease of multiple respiratory systems, and diffuse panbronchiolitis is a new bronchial disease. Currently, there are few clinical studies on the diagnosis and treatment of this disease, and there is no specific treatment for this disease, resulting in unsatisfactory prognosis for patients with this disease. This study mainly reviewed the clinical research progress of diffuse panbronchiolitis in order to provide reference for clinical treatment of diffuse panbronchiolitis.

Keywords: Diffuse Panbronchiolitis; Pathogenic Factors; Diagnosis; Treatment; Prognosis

1. Preface

Diffuse suffused with bronchiolitis (DPB) under anoxic condition diffusepanbronchiolitis, founded in 1969 by Japanese scholars, honma, GuMu put forward in the mountains, the main diffuse exists in both lungs airway chronic inflammatory disease of respiratory bronchioles, belongs to a new type of chronic obstructive airway disease. At present, there are few clinical reports on this disease in China. In recent years, it has been confirmed that this disease is paranasal sinus bronchial syndrome, but there is no specific treatment for this disease. In clinical practice, it is generally believed that the disease is associated with genetics, harmful gases, infection and other factors. After the onset of the disease, patients will mainly have persistent cough and sputum cough symptoms, and the symptoms of shortness of breath will be significantly aggravated after the activity. If the patient's condition is more serious, it will also cause respiratory failure symptoms, increasing the pain and discomfort of patients. Due to the high similarity between diffuse panbronchiolitis and other bronchial or lung diseases, clinical diagnosis and treatment is more difficult and misdiagnosis is easy to occur. There is a high

probability of misdiagnosis of the disease as chronic obstructive airway disease, bronchiectasis and other chronic airway diseases, which will cause certain obstacles to the treatment of patients. This article will review the research progress of diffuse panbronchiolitis.

2. Overview of Diffuse Panbronchiolitis

The cases of diffuse panbronchiolitis were first reported in Japan, and then appeared successively in Europe and the United States. In 1996, it was first reported in China. Diffuse panbronchiolitis has a certain insidious onset and slow progression, and can occur in different age groups, with a high incidence of 40-50 years old. Most patients have a history of paranasal sinusitis, and the lesions mainly occur in respiratory bronchioles and gradually spread to the whole layer of bronchioles. Diffuse panbronchiolitis is a global disease with a higher incidence in Japan and South Korea than in other countries. In recent years, under the influence of environmental pollution, the number of cases of this disease has increased significantly. Clinical investigations have found that more than 80% of patients with diffuse bronchitis have a history of chronic paranasal sinusitis, and 20% have a family history of chronic paranasal sinusitis [1-2].

3. Analysis of Pathogenic Factors of Diffuse Panbronchiolitis

At present, there is no clear conclusion on the pathogenesis of diffuse panbronchiolitis in clinical practice. With the gradual deepening of domestic and foreign studies, it is found that the following factors may induce diffuse panbronchiolitis: (1) Family inheritance: Some scholars have made statistics on the family history of patients with diffuse panbronchiolitis in clinical studies and concluded that about 60% of patients have a family history of the disease, suggesting that family inheritance may increase the incidence of the disease [3]. (2) Infection:

Clinical studies have found that most diffuse panbronchiolitis has a history of chronic paranasal sinusitis, which leads to different degrees of infection in patients [4]. Meanwhile, mycoplasma infection of the lung also increases the risk of lesions.(3) External environmental stimulation: inhalation of harmful gases or severe environmental pollution will increase the incidence of the disease. Some scholars conducted a survey on patients with diffuse panbronchiolitis and found that residents living in SO₂ polluted areas had a much higher incidence of the disease than residents in other areas [5].

4. Diagnostic Analysis of Diffuse Panbronchiolitis

Because the clinical symptoms of diffuse panbronchiolitis are similar to those of patients with bronchial diseases and lung diseases, the diagnosis of the disease has brought certain challenges, and the diagnosis difficulty is relatively high. With the increasing development of imaging technology, the diagnosis rate of the disease has also been continuously improved. Clinical diagnostic measures for diffuse panbronchiolitis mainly include chest X-ray, CT examination, serological examination and other measures. If the patient has persistent cough, sputum, shortness of breath and other symptoms, and has a history of chronic paranasal sinusitis, the patient can be given a preliminary diagnosis. When the chest X-ray is applied for examination, if there are diffuse granular nodular shadows in both lungs and intermittent moist rales in the chest, if the titer of the serum condensing machine is above 1:64, it can be confirmed as diffuse panbronchiolitis [6]. However, it is difficult to evaluate the condition of patients with this disease when they are examined individually, which is prone to misdiagnosis and delays the best treatment opportunity for patients. In the diagnosis, it is also necessary to pay attention to whether the patient has hypercapnia, hypoxemia, and whether there is pneumococcus or acidophilus influenzae, which can be used as an important auxiliary indicator for disease diagnosis [7]. In recent years, CT has been widely used in the diagnosis of diffuse panbronchiolitis. In Lin Xia's study, the patients admitted were divided into control group and research group, and X-ray and multi-slice spiral CT were respectively examined. Table 1 showed that the diagnostic

accuracy rate of multi-slice spiral CT in diagnosing diffuse panbronchiolitis was 97.78%. It was significantly higher than 75.56% in the control group, indicating that the diagnostic effect of multi-slice spiral CT was ideal [8]. In her study, CAI Huiqing applied multi-slice spiral CT to diagnose patients with diffuse panbronchiolitis, and found that the diagnosis rate reached 98.0%, indicating that multi-slice spiral CT has high application value in the diagnosis of this disease, which can reduce the probability of missed diagnosis and misdiagnosis, and multi-slice spiral CT can be used as an imaging means to diagnose diffuse panbronchiolitis [9]. Due to the high misdiagnosis rate of this disease, it is necessary to make a comprehensive judgment in the diagnosis process, and timely screening for diseases such as bronchiolitis obliterans, bronchial asthma, bronchiectasis, etc. The symptoms of these diseases are highly similar to those of diffuse panbronchiolitis. CT and X-ray examinations need to be distinguished from interstitial lung diseases, sarcoidosis, bronchiolitis obliterans, alveolar cell carcinoma and other diseases. The imaging features of diffuse panbronchiolitis mainly show that there is a diffuse distribution of lobular central nodules in both lungs, and there is no tendency of fusion between nodules, and linear high-density shadows can be seen to be connected with the surrounding nodules. There is a certain distance between the nodules and the chest wall, and the small bronchodilation is circular or tubular. When the disease progresses, there will be significant gas retention between the nodules [10]. When diagnosing the disease from the perspective of pathological changes, as the disease has similar pathological changes to chronic bronchitis and airway central pulmonary interstitial fibrosis, etc., the diagnosis can be made according to the above criteria based on the fact that the center of pathological changes of the disease is mainly bronchioles, and most of them show inflammatory changes [11]. At present, the diagnostic criteria for diffuse panbronchiolitis in China are as follows: (1) persistent cough, thick sputum, increased shortness of breath after activity; (2) History of chronic paranasal sinusitis; (3) There were diffuse lobular central-granular nodules in both lungs. Reference items: (1) Pulmonary auscultation showed intermittent moist rales; (2) PaO₂ < 80 mmHg, FEV₁ < 70%; (3) The titer of

blood cold agglutination test showed an increasing trend. Diagnosis can be made in combination with the above items. When necessary, transbronchoscopy or thoracoscopic

lung tissue biopsy can be performed on patients, which is the gold standard for diagnosis of this disease, so as to give a definitive diagnosis in time.

Table 1 Comparison of diagnostic accuracy rates

Group	Misdiagnose	Missed Diagnosis	Make a Definite Diagnosis
Control Group (n=45)	7 (15.56)	4 (8.89)	34 (75.56)
Research Group (n=45)	1 (2.22)	0 (0.00)	44 (97.78)

5. Analysis of Treatment of Diffuse Panbronchiolitis

Erythromycin was first used to treat diffuse panbronchiolitis in clinic, and its clinical effect has been unanimously recognized by doctors and patients. In clinical studies, it was found that sputum reducing drugs, antibiotics, bronchodilators and glucocorticoids were used in the treatment of diffuse panbronchiolitis as early as 1980 [12]. However, after clinical practice, it was found that although erythromycin could alleviate the clinical symptoms of patients, it was still difficult for patients to achieve an ideal prognosis. In 1982, Dr. Kudo found that the lesions and clinical symptoms of patients with diffuse panbronchiolitis were significantly improved after drug discontinuation, mainly because the patients continued to use erythromycin for treatment. Therefore, Dr. Kudo conducted clinical trials and found that the clinical symptoms of patients with diffuse panbronchiolitis were effectively relieved after 42 months of research. And a certain effect can be achieved after 1 month of medication, so the hospital gradually applied erythromycin in the treatment. The earlier the treatment of diffuse panbronchiolitis, the better the prognosis and recovery effect. In the treatment of erythromycin, the dosage should be controlled within 600mg each time, and the adverse reactions that may occur after the application of erythromycin should be explained patiently during the treatment, and the patient should be informed that if the adverse reactions are more intense, the drug should be stopped in time. And choose clarithromycin, roxithromycin and other drugs for treatment, the application dose is within 300mg and 400mg respectively, most patients will have symptoms within 3 months of taking the drug, remember not to stop the drug in advance, need to inform patients to continue to use for 6 months or longer. Clinical studies have found that when patients with diffuse

panbronchiolitis are treated for more than 6 months, the cure rate will be significantly improved, and after the recurrence of the patient's disease, erythromycin treatment again still has a good effect [13]. In clinical studies, some scholars have used low-dose erythromycin to treat patients with diffuse panbronchiolitis, and found that low-dose erythromycin can improve the lung function of patients and avoid airway obstruction [14]. Low dose erythromycin is an effective treatment for diffuse panbronchiolitis, with an effective rate of up to 80%. At present, the therapeutic mechanism of erythromycin has not been clearly elaborated in clinical practice, and it is believed that it has a certain correlation with its anti-inflammatory effect and immune regulation. Because diffuse panbronchiolitis is still not completely cleared of bacteria after the improvement of clinical symptoms, and erythromycin concentration in serum and sputum is much lower than that of pathogenic bacteria, it can inhibit the biofilm formation of *P. aeruginosa* to a certain extent, mainly because of its anti-inflammatory effect, which can promote the host to enhance the resistance. Erythromycin can also block the chloride ion channels in the airway epithelium, resulting in a continuous decrease in the amount of water and mucus secreted, which in turn reduces the amount of sputum in patients. In addition, erythromycin can also avoid the accumulation of neutrophils on the airway mucosal surface, inhibit their unknown activity and proliferation in inflammation, and reduce the secretion of IL-6 and IL-8, thus promoting the differentiation of mononuclear macrophage system, forming an effective inhibition of inflammatory response and reducing airway mucus secretion [15]. In the application of erythromycin for treatment, it is also necessary to pay attention to the drug will produce certain adverse reactions, such as liver damage, nausea, vomiting, and some patients have allergic dermatitis, so it is necessary to pay close attention to adverse reactions in the treatment. In

addition to erythromycin, patients with diffuse panbronchiolitis can also be treated with glucocorticoids, which has good immunosuppressant and anti-inflammatory effects. Prednisone can be selected, and the dose is controlled at 1mg·kg in the initial application, and the dose can be gradually reduced after the symptoms are improved. The treatment is usually combined with macrolides. Can promote the treatment effect to be improved. Zhai Yishu found in his study that low-dose macrolide antibiotics combined with methylprednisolone could effectively reduce the levels of serum TIMP-1 and MMP-9 and alleviate inflammation [16]. Patients with diffuse panbronchiolitis usually have influenza-acidophilic infection at the early stage of the disease, and with the progression of the disease, the main development is pseudomonas aeruginosa infection. However, the application of macrolides can antagonize the pseudomonas aeruginosa and reduce the infection of patients. After taking the drug for 6 months, the symptoms of patients can be improved in time. Long-term medication is also needed to curb the progression of the disease. Patients with diffuse panbronchiolitis can also choose antibacterial treatment, which requires a clear identification of the type of pathogenic bacteria and the selection of targeted antibacterial drugs. Xu Huijuan et al. gave patients azithromycin treatment in the study, which effectively improved the pulmonary function indicators of patients with fewer adverse reactions. The main reason is that azithromycin can inhibit the production of reactive oxygen species by neutrophils, reduce the damage to vascular endothelial cells, reduce the expression level of neutrophilic chemokines such as leukotriene B4 and IL-8, and enhance the phagocytosis rate of alveolar macrophages on neutrophils and bronchial epithelial cells with latent apoptosis, thus reducing the inflammatory response [17]. Klebsiella pneumoniae, Haemophilus influenzae and pseudomonas aeruginosa are common pathogenic bacteria of diffuse panbronchiolitis. However, it should be noted that long-term use of antibiotics is easy to cause drug resistance in patients, and thus hinder the improvement of treatment effect. At the same time, patients can be given oxygen therapy for auxiliary treatment, but also can integrate the patient's condition, the implementation of paranasal sinusitis treatment, bronchitis

dilatation treatment, etc., in order to achieve a good therapeutic effect. In addition to the above western medicine treatment, traditional Chinese medicine can also be used for auxiliary treatment. Cong Xiaodong et al used the methods of tonifying spleen and clearing lung and eliminating phlegm and pus in the study to treat patients with diffuse panbronchiolitis, which gradually stabilized the patients' condition and reduced the number of attacks of the patients, which played an important role in the prognosis of the patients [18]. In the study, Li Qing et al. used Astragalus mulberry and Danshen Decoction combined with erythromycin to treat patients, including Astragalus, mulberry, white art, poria, cinnamon, orange peel, salvia miltiorrhiza, Angelica, dilong, Qingpi, Fructus aurantii, Bupleurum and scutellaria, which had the effect of promoting blood circulation and removing blood stasis, effectively controlling the infection of patients and improving the pulmonary microcirculation of patients [19]. Due to the high incidence rate of diffuse panbronchiolitis and the difficulty of prolonged treatment, the quality of life of patients continues to decline, so it is necessary to take effective treatment measures in accordance with the condition of patients in order to achieve the ideal prognosis.

6. Prognosis of Patients with Diffuse Panbronchiolitis

In the past, it was considered that diffuse panbronchiolitis was a disease with poor prognosis. Without erythromycin treatment, the 5-year survival rate of patients with this disease was even less than 50%, and if there was pseudomonas aeruginosa infection, the 5-year survival rate would even drop to less than 10%. With the gradual application of macrolides and erythromycin in clinic, the therapeutic effect of patients with diffuse panbronchiolitis has also been improved to a certain extent. Clinical studies have found that after 5 years of treatment with erythromycin in patients with diffuse panbronchiolitis, the survival rate of patients can reach more than 90%, thus reducing the mortality rate of patients. Provide guarantee for the life safety of patients [20]. Therefore, patients with diffuse panbronchiolitis need to be given early treatment in time to improve the effectiveness of treatment.

7. Summary

The incidence of diffuse panbronchiolitis is high, which brings serious life troubles to patients. Due to the lack of research reports on the disease, there are certain deficiencies in the clinical diagnosis and treatment of the disease, which often leads to the occurrence of late treatment and delays the intervention of patients. Therefore, it is necessary to continue to conduct in-depth research on the disease in the future to form scientific diagnosis and treatment standards. Clinicians also need to strengthen the knowledge of diffuse panbronchiolitis, in order to lay a scientific basis for diagnosis and treatment, and to solve the disease for more patients.

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