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Ways to improve the diagnosis and treatment of interstitial lung disease associated with systemic sclerosis in the Siberian Federal District (materials of the advisory board of rheumatologists and pulmonologists from December 08, 2019)

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ABSTRACT

The aim of the study was to develop ways to improve the diagnosis and treatment of systemic sclerosis (SSc)-ILD. Interstitial lung disease (ILD) is a common manifestation of SSc. In the territory of the Siberian Federal District (SFD), the number of patients with the progressive phenotype of SSc-ILD is approximately 750 people. When immunosuppressive therapy is ineffective and pulmonary fibrosis progresses, lung transplantation is indicated. The emergence of new possibilities of pathogenetic therapy currently requires studying the possibilities of their applications in real clinical practice on the territory of the SFD.

Discussion. The results of a discussion of diagnostics, therapy, and routing of a rheumatology patient during the interdisciplinary observation of SSc-ILD in the SFD are presented. The reason for this discussion was the new data on the use of nintedanib in this category of patients

Conclusion. To improve the efficiency of diagnosis and treatment of patients with SSc in the SFD, it is necessary to implement the principle of a multidisciplinary approach with the obligatory involvement of a pulmonologist and a radiologist (a specialist in CT diagnostics), and, if differential diagnosis is necessary in difficult clinical situations, of a pathomorphologist. An urgent task is the introduction of an algorithm for examining patients with SSc for the timely diagnosis of ILD in the territory of the Siberian Federal District. To improve the quality of medical care in the territory of the SFD for patients with ILD-SSc it is necessary to create a reference center in the city of Novosibirsk with the possibility of initiating anti-fibrosis therapy.

Key words: systemic sclerosis, interstitial lung diseases, nintedanib, anti-fibrotic therapy.

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Пути улучшения диагностики и лечения поражения легких при системной склеродермии на территории Сибирского федерального округа (материалы совместного совета экспертов ревматологов и пульмонологов от 8.12.2019)

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РЕЗЮМЕ

Цель. Разработать пути улучшения диагностики и лечения поражений легких при системной склеродермии (ССД).

Введение. Поражение легких у больных ССД является одним из наиболее частых проявлений висцеральной патологии и рассматривается как вариант фиброзирующих диффузных интерстициальных заболеваний легких (ИЗЛ). Несмотря на продемонстрированную эффективность патогенетической иммуносупрессивной терапии, у ряда пациентов фиброзные изменения в легочной ткани имеют прогрессирующее течение, что негативно сказывается на качестве и продолжительности жизни пациента. На территории Сибирского федерального округа (СФО) количество пациентов с ССД, имеющих прогрессирующее поражение легких, составляет приблизительно 750 человек. Таким образом, проблема своевременной диагностики и лечения поражения легких при ССД оказывается весьма актуальной и для СФО. Имеющиеся в настоящее время данные об эффективности современной противофиброзной терапии ИЗЛ при ССД требуют изучения возможности ее применения в реальной клинической практике на территории СФО.

Обсуждение. Представлены результаты междисциплинарного обсуждения вопросов диагностики, терапии, маршрутизации пациентов с ССД и ИЗЛ на территории СФО. Причиной данного обсуждения явилось появление сведений об эффективности нинтеданиба у данной категории пациентов.

Заключение. Для повышения эффективности диагностики и лечения больных ССД с поражением легких необходимо реализовать принцип мультидисциплинарного подхода с обязательным привлечением пульмонолога и рентгенолога (специалиста по КТ-диагностике), а при необходимости дифференциальной диагностики в сложных клинических ситуациях – патоморфолога. Актуальной задачей оказывается внедрение на территории СФО алгоритма обследования пациентов с ССД для своевременной диагностики ИЗЛ. Для повышения качества оказания медицинской помощи на территории СФО пациентам с ИЗЛ при ССД необходимо создать референсный центр в г. Новосибирске с возможностью инициации специалистами этого центра антифибротической терапии.

Ключевые слова: системная склеродермия, интерстициальные заболевания легких, нинтеданиб, антифибротическая терапия.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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INTRODUCTION

Systemic sclerosis (SSc) is a rare autoimmune disease characterized by dysregulation of the immune system, microvascular damage, and the development of fibrosis of internal organs. One of the frequent and potentially life-threatening manifestations of visceral pathology in patients with SSc is the development of a lesion of the pulmonary parenchyma, which occurs in 80% of patients, and is currently considered as one of the variants of fibrosing diffuse interstitial lung diseases (ILD). Lung involvement in SSc is more common than in other systemic connective tissue diseases. Obvious changes in lung tissue are found in 25–65% of patients according to chest X-ray data, and in 90% of patients according to the results of high-resolution computed tomography (HRCT). At autopsy, pulmonary fibrosis with SSc is verified in 75–100% of cases [1]. Approximately one third of patients with SSc-ILD show progression of fibrosis in the lungs. Progressive lung damage in SSc is considered one of the leading causes of death and is a significant burden on the health care system [2, 3]. Data from a preliminary estimate of the prevalence of this pathology in the Siberian Federal District (SFD) indicate that the number of patients with progressive course of SSc-ILD is approximately 750 people.

Among the functional parameters used to control the effectiveness of the therapy for ILD, the most commonly used function of external respiration (or spirometry) with the assessment of forced vital capacity (FVC). The effectiveness of therapy is indicated by a slowdown in the rate of decrease in FVC or its stabilization. The severity of respiratory dysfunction and the rate of progression of SSc-ILD vary significantly. The initial state and the rate of progression of ILD are of primary importance in the tactics of patient management.

To date, the basis of the treatment of SSc-ILD is drugs with immunosuppressive action, most often with cyclophosphamide and mycophenolate mofetil, the effectiveness of which was studied in two randomized, double-blind studies (studies of systemic sclerosis I and II (SLS-I and SLS-II)) [4, 5]. If this therapy is ineffective or intolerant, it is possible to use azathioprine or cyclosporine A. If immunosuppressive therapy is ineffective and pulmonary fibrosis progresses, lung or hematopoietic stem cell transplantation is indicated. The emergence of a new drug of pathogenetic action at present requires studying the possibility of its use in real clinical practice in the territory of the Siberian Federal District.

The aim of this study is to develop ways to improve the diagnosis and treatment of lung lesions in SSc.

To achieve this goal, the following tasks were formulated:

1. Analyze new possibilities of pathogenetic therapy of patients with SSc-ILD and assess the need for their use in the Siberian Federal District.

2. Consider the possibility of using a multidisciplinary approach to the diagnosis, differential diagnosis and treatment of SSc-ILD.

3. Develop a regulation on the routing of patients with SSc-ILD in the Siberian Federal District and the procedure for obtaining high-tech medical care, including a regional subsidy.

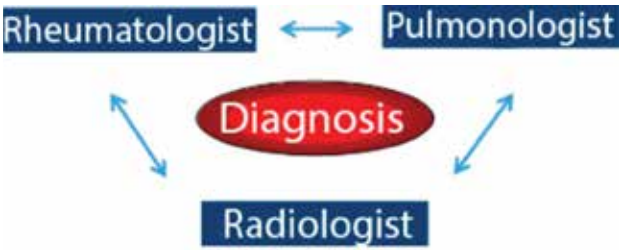
4. Assess the need to create a reference center for patients with SSc-ILD in the Siberian Federal District with the possibility of initiating antifibrotic therapy.

DISCUSSION

One of the topical issues is the routing of patients with SSc-ILD. The management of such patients should be based on the interdisciplinary interaction of various specialists: rheumatologist, pulmonologist, radiologist and pathomorphologist. By analogy with the algorithm for verifying the diagnosis in idiopathic pulmonary fibrosis, an algorithm for the diagnosis of SSc-ILD is proposed (Fig. 1).

Verification of pulmonary involvement in SSc requires a comprehensive examination of the patient, which includes an assessment of the clinical manifestations of ILD, pulmonary function tests (PFT), an examination of the diffusion lung capacity (DLC) and mandatory HRCT. It is extremely rare, especially in recent years, to resort to lung biopsy and morphological examination of the biopsy material.

PFT, DLC and HRCT should be performed when determining the diagnosis and subsequently at least once a year provided that the patient is in a stable condition. When respiratory symptoms progress, HRCT must be performed or repeated to assess the progression of ILD.



Diagnostics of SSc-ILD requires a multidisciplinary approach and experience

Fig. 1. Multidisciplinary approach to verification of the diagnosis of SSc-ILD

Most often, with SSc, the main manifestation of IDL is the so-called nonspecific interstitial pneumonia, which can be diagnosed in the presence of appropriate computed tomographic or morphological patterns.

New in-depth understanding of the mechanisms of connective tissue damage in SSc and the formation of pulmonary fibrosis in this pathology has opened a new stage in the study of the pathogenesis of SSc and the use of anti-fibrotic therapy. The data from the SENSCIS study showed that the tyrosine kinase inhibitor nintedanib was effective in patients with SSc with pulmonary involvement, as it reduced the rate of progression of pulmonary pathology. This study included 576 patients who received at least one dose of nintedanib or placebo. In the analysis of the primary endpoint, the annual rate of change in FVC was – 52.4 ml per year in the nintedanib group and – 93.3 ml per year in the placebo group (difference 41.0 ml per year; 95% confidence interval, 2.9–79.0; $p = 0.04$) [6].

The anti-fibrotic effect of nintedanib is realized by blocking the intracellular signaling pathway and inhibiting the proliferation and transformation of fibroblasts. Previously, the effectiveness of nintedanib has been proven in numerous studies involving patients with idiopathic pulmonary fibrosis, and today the drug has found wide application in the treatment of this pathology [7–9].

Currently, nintedanib has been registered and approved by the Food and Drug Administration and the Ministry of Health of the Russian Federation as the only anti-fibrotic drug for the treatment of SSc-ILD.

Anti-fibrotic therapy for patients with SSc with pulmonary involvement requires an assessment of the initial severity of the disease, as well as the risk of its progression. According to modern ideas about the mechanisms of the pathogenesis of the disease and the data of clinical trials, nintedanib therapy should be initiated in the following cases:

1. Patients with verified ILD according to HRCT with clinical manifestations of lung lesions (dyspnea, cough) and FVC ≤ 70% and (or) DLC ≤ 60% at the time of diagnosis.

2. When signs of SSc-ILD progression are detected, which is determined based on the presence of one or more criteria:

– decrease in FVC by 10% or more from the previous examination;

– decrease in FVC by 5–10% from the previous examination with worsening respiratory symptoms;

– decrease in FVC by 5–10% from the previous examination with the presence of negative dynamics according to HRCT associated with the underlying disease;

– progression of respiratory symptoms and an increase in the spread of pulmonary fibrosis according to HRCT data.

These criteria are relevant only in cases of exclusion of pulmonary infection and other causes of respiratory symptoms, as well as changes according to HRCT data characteristic of other interstitial lung lesions, pulmonary lesions caused by cardiac pathology (acute left ventricular heart failure, pulmonary embolism). The algorithm for prescribing anti-fibrotic therapy was determined based on the initial severity of ILD and in the presence of an obvious risk of disease progression (Fig. 2).

The appointment of anti-fibrotic therapy should be carried out by the decision of the medical commission, taking into account the existence of vital indications in patients of this group. It should also be borne in mind that nintedanib is currently the only drug with an appropriate approved indication for this. Based on the results of the examination, the patient should be sent for a medical and social examination at the place of residence to establish a disability group. Based on the status of a disabled person, the patient will be entitled to free drug provision for outpatient treatment on a regular basis at the expense of the regional or federal budget. Before obtaining the status of a disabled person, drug provision is carried out at the expense of monthly individual purchases based on the decision of the medical commission.

CONCLUSION

Thus, based on the above, the members of the Advisory Board consider it necessary to:

– actualize the problem of diagnostics and therapy of SSc-ILD on the territory of the Siberian Federal District;

– introduce an algorithm for examining patients with SSc-ILD;

– be guided by a multidisciplinary approach to the diagnosis and treatment of SSc-ILD with the obligatory involvement of a pulmonologist and a radiologist (a specialist in CT diagnostics), and a pathomorphologist if differential diagnosis is necessary in difficult clinical situations;

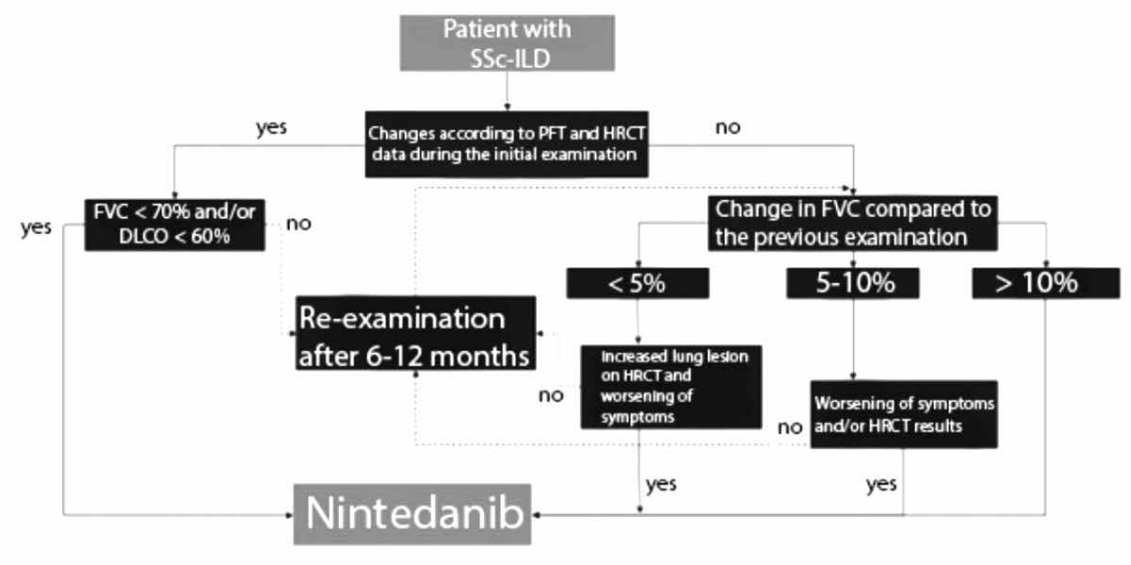


Fig. 2. Algorithm for prescribing anti-fibrotic therapy for patients with SSc-ILD

– develop a regulation on the routing of patients with SSc-ILD and the procedure for receiving high-tech medical care, including receiving anti-fibrotic drug therapy as a regional subsidy, in each region of the Siberian Federal District;

– create a reference center in the city of Novosibirsk with the possibility of initiating anti-fibrotic therapy to improve the quality of medical care in the territory of the Siberian Federal District for patients with SSc-ILD;

– initiate work with public organizations.

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