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Professional paper

RESPIRATORY COMPLICATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract

Systemic Lupus Erythematosus (SLE) is a chronic systemic autoimmune disease of the connective tissue with but still unknown etiology, Besides appearing on the skin, SLE also affects other organs such as kidneys, lungs, heart, etc. As a result of the action of LES, among others, we also have pulmonary complications,which consist of pleurisy ,pleurisy, pneumonia,interstitial lung dise-ase, pulmonary hypertension,alveolar hemorrhage, pulmonary embolism,vasculitis, frequent respire-tory infections, etc. Recent studies have documented from 50-70% of patients with SLE, of which 4-6% of them (most often in men) during the course of the disease show symptoms of respiratory tract diseases[1].Clinical symptoms are mani-fested by:pain or feeling of pressure in the chest, fever,shortness of breath, tachypnea, tachy-cardia, palpitations,cyanosis, malar rash on the face in the form of a butterfly and other skin rashes, polyarthralgia,renal involvement and pleuro-pulmonary.The aim of the work: the aim of the work was the impact of SLE on the respiratory tract as well as the influence of risk factors on the appearance of respiratory manifestations in patients with SLE.

Keywords: respiratory diseases, systemic lupus erythematosus

1 Introduction

Pulmonary involvement is widespread and is seen in 50-70% of patients with SLE and may even be the presenting feature in 4-5% of patients. SLE is a chronic, systemic autoimmune disease with a relapsing-remitting course and characterized by the production of a wide range of autoantibodies. Although people of any age and gender can be affected, women of childbearing age are most affected, with a female to male ratio of about 9:1[2-[2-5].Recently, a new set of classification criteria was proposed by the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR-ACR/EULAR), designed to increase sensitivity and specificity of classification for inclusion in LES studies and trials[6]. Pulmonary complications are common and include pleural disease, interstitial lung disease, pulmonary embolism, vasculitis, pulmonary hypertension,large airways disease, obstructive lung syndrome contraction and infection.The clinical picture can be changed from asymptomatic to life-threatening diseases (diffuse alveolar hemorrhage, acute lupus pneumonitis, etc.) Although pulmonary involvement in SLE is common, the heterogeneity of SLE and the individual symptomatology and complications make clinical examinations by which is also based on the management and treatment of respiratory diseases with various immunosuppressive agents (such as azathioprine, methotrexate and cyclophosphamide, etc. LES, as usual from the respiratory system, most often affects the pleura-lupus pleuritis (unilateral or bilateral) which is manifested by symptoms of pain , dyspnea, pleural effusion, temperature (>38oC), fever, shortness of breath, etc[7].LES is characterized by an impairment of the cleaning of apoptotic cells by phagocytes, autoreactivity of B and T cells that leads to an abnormal production of autoantibodies and in the formation of immunocomplexes with nuclear and cytosolic antigens, which helps the appearance of inflammation and damage to the lungs, kidneys, skin and other organs.During the course of the disease, 50% of patients with SLE at least once have manifestations of symptoms of respiratory tract. Of the pulmonary infections caused by lupus, bacterial infection is the most frequent cause. In lupus pleurisy, pleural effusions are usually

small and are bilateral in 50% of patients. Biochemical analysis of the fluid reveals that they are exudative in nature. Pleurisy management in mild cases should begin with broad-spectrum antibiotics, non-steroidal anti-inflammatory drugs while in the most severe cases, treatment with corticosteroids should also be applied and, if necessary, immunosuppressive therapy(Methothrexate, Mycopheno-late,Cyclophosphamide,Cyclosporine, Aza-thioprine, etc.).Interstitial lung disease in patients with SLE occurs in 1-15% of patients[8,9,10].In recent years, the association European League Against Rheumatism EULAR explicitly and the latest recommendations based on the latest facts and studies for the management of LES and manifestations in organs and systems of the organism[11,12].The pathogenesis of SLE is multifactorial and not fully understood, and involves an interaction between genetic predisposition, hormonal and environmental factors, ultimately leading to a change in innate and acquired immunity. In particular, the pathogenesis of SLE is characterized by an impairment of the clearance of apoptotic cells by phagocytes, the autoreactivity of B cells and T-cells leading to an abnormal production of autoantibodies and the formation of immune complexes with nuclear and cytosolic antigens. Immune complexes, on the other hand, can activate the classical pathway of the complement system contributing to inflammation and damage in target organs. Although the exact prevalence is unknown, respiratory tract involvement may be present in 50- 70% of patients with SLE, being the presenting symptom of the disease in 4-5% of cases and more frequent in men [13,14].Any part of the respiratory tract can be involved: upper and lower respiratory tract, vessels, pleura, lung parenchyma and respiratory muscles. Respiratory manifestations can be acute or chronic, primary (directly caused by the disease) or secondary (due to associated complications such as infections). Interestingly, acute manifestations may be associated with generalized lupus disease activity, while chronic complications may progress independently of generalized disease activity[15].

2 The aim of the work

The aim of the work was the impact of SLE on the respiratory tract as well as the influence of risk factors on the appearance of respiratory manifestations in patients with SLE.

3 Materials and methods

The study included 30 patients with SLE and various manifestations of the respiratory system (of which 20 were female with an average age of 22.80±6.40 years while 10 were male with an age average of 24.50±5.70 years old) treated with therapy for over three years(table number 1).. The following laboratory analyzes were determined in all patients: pulmonary echography, X-ray pulmonary et cor, computerized tomography of the lungs, erythrocyte sediment, hmogram (Er, Hb, Htc, platelets-Th, Le), differential blood count (lymphocytes, granulocytes, monocytes), C Reactive Protein (CRP),C3 and C4 and antinuclear antibodies (ANA).

Table 1: Presentation of patients with SLE according to gender and average age

Total number of patients with =30	**Females-20 (66%)**	**Males-10 (34%)**
Mean age±SD	**22.80±6.40**	**57.00±8.50 years**

4 Statistical processing of the results

The results obtained from the patients examined with IRK, IRKT and the control group were statistically processed with arithmetic mean value, standard deviation X ± SD, with the student's "t" test, Wilcoxon test. The results were processed with the SPSS V26 program.

5 Results

Out of the total number of female patients (no-20), five patients from themmanifested clinical symptoms of acute pneumonia and 8 acute pleurisy, while 7 women manifested symptoms of chronic obstructive bronchitis. In the male gender (out of the total number of 10 patients), 3 patients had acute pneumonia,4 with acute pleurisy, while 3 men had symptoms of chronic bronchitis Obstructive. Smoking patients were eliminated from the study. Laboratory examination of all patients revealed: low oxygen saturation (Spo): 75-78% (normal SpO: 96-99%), increased C Reactive Protein (PCR) increased erythrocyte sedimentation, increased leukocytes, while pulmonary X-ray and lung CT consisted of signs of pneumonia, acute pleurisy in both pulmonary lobes (mainly in the basal parts of the lungs) with which examinations the diagnosis of respiratory and clinical manifestations was also verified in patients with SLE.Table number 2: distribution of patients with LES and according to diseases and respiratory manifestations.

Table number 2:distribution of patients with SLE and according to diseases and respiratory manifestations

Respiratory manifestations	**Females=20**	**Males=10**
Pleuritis ac	**8**	**3**
Acut Pneumoni	**5**	**4**
Bronchitis chr.obstructiva	**7**	**3**

The results obtained at the beginning of the study (for all patients with SLE and respiratory disease: women and men) and after treatment are presented in tables number 3 and 4

Table number 3: Results obtained from the examined parameters of patients with SLE and respiratory manifestations at the beginning of the study

Examined parameters	**Females with SLE and respirat.manifest.No=20**	**Males with with SLE and respirat. manifest.No=10**
Sedimen.(SE) mm/30 min(r.v.=4-10)	**58.00±5.00**	**65.00±6.80**
C-Reactive Protein(CRP mg/l, RV=0-50)	**65.00±6.40**	**68.40±4.80**
C3 (RV=80-128 mg/dl)	**C3<38**	**C3<37**
C4 (RV=12-42 mg/dl)	**C4<8**	**C4<10**
ANAs(Antinuclear antibodies RV=≤1:60)	**>180 (positive)**	**>190 (positive)**

Table 4: the results obtained after the treatment

Examined parameters	Females with SLE and respirat.manifest.No=20	Males with with SLE and respirat. manifest.No=10
SE mm/30 min(RV=4-10)	**35.40±6.20**	**45.00±5.60**
CRP mg/l (RV=0-50	**38.00±1.60**	**40.00±4.60**
C3 (RV=80-128 mg/dl	**C3<60**	**C3<70**
C4 (RV=12-42 mg/dl)	**20**	**22**
ANA(Antinuclear antibodies-ANAs (RV=≤1:60)	**>100**	**>110**

Table number 4 shows that after drug treatment (broad-spectrum antibiotics, nonsteroidal anti-inflam-matory drugs,doses of Aspirin (80-160 mg/day, antimalarial-hydroxy-chloroquine(Plaquenil, Chloro-quine,Quinacrine) S. 200 mg 1-2×/day) ,Corticosteroid (Methylprednisone in doses of 40-60 mg 1×day (the dose was according to the clinical picture)) the condition of the pulmonary manifestations apparently improved.

6. Discussion

SLE is a chronic autoimmune disease characterized by a large number of clinical and immunological disorders . LES in its course can affect a number of organs and systems starting from the skin, renal, cardiac and respiratory system. Complications related to LES can affect all anatomical parts of the lungs and are manifested by: pleurisy, pneumonia, interstitial disease of lungs, thromboembolic events, pulmonary hypertension, alveolar hemorrhage, etc[16-18]. Clinical evaluations of patients with SLE should include t; all laboratory, immunological, microbiological and imaging examinations related to respiratory diseases[19,20]. Even some patients with SLE and respiratory diseases may be asymptomatic during random lung imaging examinations or lung function tests, but the increase of double-stranded DNA (dsDNA) antibody titers, again require further examination to assess whether the persistence of new respiratory symptoms is caused by LES[21,22] In recent years, it has been reported that about 50-70% of patients with SLE develop lung involvement. Older age and anti-RNP antibodies are predictors of progression to early irreversible lung damage. Pulmonary manifestations of SLE-related mortality vary depending on the type and level of lung involvement observed. Chronic kidney disease associated with SLE can have a negative impact on patients' well-being, physical performance, and quality of life[23,24,25]. Respiratory manifestations can be acute (consisting of generalized lupus activity), or chronic (these may progress independently of the overall lupus activity), primary (directly caused by the disease), or secondary(due to of associated complications from infections). Respiratory manifestations of SLE are associated with a variable degree of mortality, depending on the type of involvement, its extent and the presence of concomitant diseases.Therefore, the evaluation and treatment of lung involvement in patients with SLE should to be performed immediately. The preferred examination methods are: hemogram, erythrocyte sediment, C-reactive protein,RTg pulm et cor, computerized tomography, immunological tests (ANA, C3, C4), etc. Our study aimed to evaluate the degree of pulmonary involvement in patients with SLE and to identify the factors associated with the occurrence and severity of such involvement, because the identification of factors is very essential for the provision of comprehensive care for patients with SLE, as it may help to identify those at

higher risk and potentially guide interventions to mitigate severe complications. Although our study was limited with a small number of patients, we found that the involvement of pulmonary complications in our patients was 26-32%, although with different symptoms between cases. The clinical picture of the most significant number of patients was dominated by symptoms such as: cough, dyspnea, fever, chest pain, tachypnea, palpitations, etc. From the anatomical parts of the lungs, the LES as the most frequent region is the pleura and varies from an asymptomatic manifestation to pleuritic pain present in about half of the patients. Multiple studies have verified that higher levels of type 1 interferon (IFN), circulating immune complexes, and neutrophils are closely associated with Les, and that they play a critical role in promoting lung inflammation, fibrosis, and tissue destruction. tissues[26].In our study we observed that there is a significant association between SLE involvement and the incidence of pulmonary complications, and that pulmonary injuries were significantly higher within the first five years after SLE diagnosis.The study also emphasizes the importance of identifying factors of the risk of lung involvement in patients with SLE. In our patients, they discovered low levels of complement, high levels of PCR, erythrocyte sedimentation, neutrophils, Anti-dsDNA, etc. Patients with SLE and lung involvement should always be evaluated for infection, especially due to bacteria or viruses. As many patients with SLE are immuno-compromised due to underlying disease or ongoing medications, opportunistic infections (eg, mycobacteria or fungi) should also be considered. Summary of clinical manifestations of SLE in adults and children and a summary of pulmonary disease in children with SLE. Other airway involvement includes upper airway angioedema, necrotic tracheitis, and bronchial stenosis. Small airway obstruction with bronchiolitis is found in 13% to 21% and bronchiectasis as a result of direct involvement of SLE or as a consequence of bronchopulmonary infections[26,27,28].Treatment should be started imme-diately with broad-spectrum antibiotics, oxygen therapy, high doses of corticosteroids are the basis of treatment. In severe cases, daily doses of methylprednisolone can be used from 1-2 mg/kg per day for three to four days) with a subsequent decrease according to the clinical response, in severe cases it is preferable to give immunoglobulins, immunosuppressants such as cyclophosphamide (CYC) and azathioprine, biological drugs (monoclonal antibodies) such as Rituxan, Rituximab or plasma exchange can be used in severe refractory cases. Management of treatment, progress and prognosis may vary significantly depending on the clinical picture.

7 Conclusion

In conclusion, we can prefer that the early identification and diagnosis of the above-mentioned pulmonary symptoms in patients with Les, effective treatment (with broad-spectrum antibiotics, bronchodilator, and corticosteroids, etc.) and immediate can significantly affect the improvement of worsening of the disease and slowing down the progress of the disease. Pulmonary complications in patients with LES are frequent and can affect any segment of the respiratory system, but their severity can range from insignificant to life-threatening symptomatology and to end with exitus lethalis.

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