Clinical and immunological characteristics of Polish patients with systemic lupus erythematosus

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Abstract

Background. Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with varied clinical manifestations, which creates difficulties and delays in establishing a diagnosis.

Objectives. The aim of this study was to evaluate the prevalence and nature of the clinical symptoms of SLE, both at the onset of the disease and in its further course. An attempt to assess the immunological characteristics of the patients and to analyze autoantibodies variability over time was also made.

Material and methods. This retrospective study included 71 Caucasian patients, 63 women and 8 men, meeting the criteria for diagnosis of SLE according to ACR.

Results. The ratio of women to men was approximately 7.9:1. The average age of the onset of SLE was 31.5 years. The average time from the onset of symptoms to diagnosis was 5 years. The most common first manifestation of SLE were joint and muscles symptoms – 71.8%, skin lesions – 69.0%, fever – 57.7%. The main symptoms in the further course of the disease were neurological disorders – 69.0%, joint and muscle changes – 67.7%, and general symptoms – 59.2%. There was an increase in the incidence of renal involvement and neurological symptoms throughout the disease course. The most commonly detected antibodies were anti-dsDNA – 47.9%, anti-Ro/SSA – 40.8%, anti-nucleosomal antibodies – 29.6%, and lupus anticoagulant – 22.5%. A panel of antibodies typically did not change.

Conclusions. There is no typical clinical picture of SLE, the population suffering from this disease is very various. Therefore, early and accurate diagnosis can be a big challenge for any clinician, which justifies the need for this type of study to better characterize the disease.

Key words: systemic lupus erythematosus, SLE, course of SLE, onset of SLE

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Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease. It involves many organs and systems, mainly the skin, joints, kidneys, and the central nervous system.¹ In the course of the disease, general symptoms such as fever, weight loss, and fatigue are commonly seen. The first manifestations of SLE most often occur in young adults.²

To establish the diagnosis of SLE, patients have to fulfill at least 4 classification criteria developed by the American College of Rheumatology (ACR).^{3,4} Based on the binomial coefficient, there are 330 combinations of symptoms that can be used to determine the diagnosis of SLE.

Due to this heterogeneous picture of the disease, SLE diagnosis is often delayed in relation to the appearance of the first symptoms. The occurrence of periods of exacerbation and remission is characteristic, and the course of the disease may take different forms, from mild to severe and even to life threatening.^{5,6}

The aim of this study was to assess the incidence, clinical symptoms, dominant signs which indicate SLE, and the dominant signs in the course of the disease. Particular attention was paid to the delay in establishing the diagnosis of SLE in relation to the onset of symptoms, as well as to the average age of onset.

An attempt to assess the immunological characteristics of the patients was also made. Both the incidence of various autoantibodies at the time of establishing diagnosis and their variability over time were tested. The association between the presence of specific antibodies and the involvement of various systems, as well as the severity of the disease were examined.

Material and methods

The study records of 71 Caucasian patients, including 63 women (89%) and 8 men (11%) admitted to the Department of Rheumatology and Internal Medicine of the University Hospital in Wrocław in 2009–2011, were reviewed and included in a retrospective analysis. All patients fulfilled the criteria for the classification of SLE given by the ACR. Data was obtained from the patients' records and questionnaires on the basis of clinical symptoms and laboratory results. General symptoms (fever – more than 38°C after the exclusion of infection, weight loss, fatigue), skin lesions, mucosal changes, joint and muscle ailments, sensitivity to the sunlight, hair loss, lymphadenopathy, inflammation of the serous membranes, renal involvement (proteinuria, hematuria, pyuria), neuropsychiatric disorders (e.g., headaches, mood disorders, cognitive disorders), hematological symptoms (anemia, leukopenia, thrombocytopenia), sicca syndrome, and antiphospholipid syndrome were taken into account.

The presence of antinuclear antibodies, antiphospholipid antibodies, lupus anticoagulant was recorded. Antinuclear

(ANA) and anti-double stranded DNA (anti-dsDNA) antibodies were routinely detected by indirect immunofluorescence on HEp-2 cells and *Crithidia luciliae* substrate, respectively. Antiextractable nuclear antigens (anti-Ro/SSA, anti-La/SSB, anti-Sm, and anti-RNP) antibodies were detected by qualitative enzyme-linked immunosorbent assays (ELISA), while the lupus anticoagulant (LA) was detected according to the guidelines of the International Society of Thrombosis and Hemostasis.

Specific symptoms and antibodies present in patients at the moment of diagnosis were monitored and compared at a later time in the course of the disease. The dominant frequency of symptoms and their correlation with the results of immunological studies were also considered.

The data is presented as mean values, standard deviations and percentages.

Results

In this study, the ratio of women to men was approximately 7.9:1, which correlates with the European SLE population.⁵ The average age when the first symptoms appeared was 31.5 years (SD 11.8). The percentage of people whose onset began before the age of 14 years was 6%, and those with the first symptoms over the age of 50 years was 8%. The mean age of the establishing the diagnosis of SLE was 36.5 years (SD 13.94); therefore, the delay in diagnosis was 5 years (SD 5.24).

In the study group, joint and muscle symptoms dominated at diagnosis. They were present in 51 of 71 patients, which constituted 71.8%. The second most common signs were skin lesions – 69.0%. General symptoms were present in 57.7% of patients, including the dominant fever. Photosensitivity was observed in 52.1% of patients.

The average time between the appearance of the first symptoms and the conducted study examination was about 9 years, which allowed us to assess the subsequent course of the disease, in which neurological and psychiatric symptoms were dominant (occurring in 69.0%). The most frequent were headaches, mood disorders (depression), cognitive disorders, and cerebrovascular disease. Changes in joints and muscles were also important, as reported by 67.7% of the study group. General symptoms were present in 59.2% of patients, and the most commonly observed symptom was fatigue.

The prevalence of all symptoms evaluated in this study, both at the beginning and in the later stages of the disease, are included in Table 1 and Fig. 1 (A, B).

General symptoms

At least 1 of the general symptoms occurred in 62.0% of people in the early stage of disease and in 59.2% in the later course of SLE. Initially, the dominant general symptom was fever, which was observed in 47.9%

of patients. Fatigue (36.6%) and weight loss (26.8%) occurred less often. In the later stages of the disease, fever occurred less frequently (38.0%), and the most common symptom was fatigue (47.9%) and weight loss (19.7%).

Musculocutaneous symptoms

In our sample, the incidence of skin lesions at the disease onset was 69.0%, decreasing thereafter to 47.9%. Hypersensitivity to sunlight was observed in 52.1% of patients at the onset of the disease, and in 28.2% in its later course.

Table 1. Prevalence of all symptoms evaluated in this study, both at the beginning and in the later stages of SLE

The incidence of selected symptoms				
symptom	the initial period of the disease		the later period of the disease	
	number of patients	% (N = 71)	number of patients	% (N = 71)
Joint and muscle changes	51	71.8	48	67.6
Skin changes	49	69.0	34	47.9
Neuropsychiatric symptoms	42	59.2	51	71.8
Sunlight sensitivity	37	52.1	20	28.2
Fever	34	47.9	27	38.0
Fatigue	26	36.6	34	47.9
Anemia	24	33.8	30	42.3
Leucopenia	23	32.4	24	33.8
Alopecia	21	29.6	20	28.2
Weight loss	19	26.8	14	19.7
Headache	17	23.9	22	31.0
Proteinuria	16	22.5	32	45.1
Serositis	16	22.5	15	21.1
Sicca syndrome	14	19.7	15	21.1
Thrombocytopenia	13	18.3	9	12.7
Lymphadenopathy	11	15.5	6	8.5
Antiphospholipid syndrome	9	12.7	7	9.9
Hematuria	7	9.9	18	25.4

The presence of alopecia during the study was also pointed out, which was reported in 29.6% of patients at the time of diagnosis, dropping slightly to 28.2% as the disease progressed.

Erosions in the mouth were mainly manifested from the mucosal changes. Such changes were reported in 22.5% of patients at the time of appearance of the first symptoms, and in 19.7% at the later stages of the disease.

Symptoms of joints and muscles

The high prevalence of these symptoms was observed. About 71.8% of patients reported non-characteristic arthritis at the beginning of the disease, and 67.7% at a later stage, which makes it the most common first symptom and the second common ailment at the course of the disease.

Renal involvement

Proteinuria, hematuria and pyuria were the clinical symptoms evaluated in the study. In the initial stage of disease, at least 1 of these symptoms occurred in 23.9% of patients. Proteinuria occurred in nearly all patients (in 22.5% of patients and in 94.1% of patients with symptoms of renal involvement), whereas hematuria and pyuria occurred less often (in 9.9% and 5.6% of all patients, respectively). In the later period, symptoms of kidney disease were reported in 52.1% of patients. The incidence of proteinuria (45.1%) and hematuria (25.4%) was doubled. The incidence of pyuria (15.5%) was tripled.

Neurological and psychiatric symptoms

In the initial stage of the disease, neurological symptoms were found in 40.8% of patients. At a later course of the disease, 69.0% of the patients

Fig. 1. The most frequent symptoms, both at the beginning and in the later stages of the disease

complained of at least 1 of the disorders of the nervous system. The most commonly reported disorders were headache (23.9% at the beginning and 31.0% in the advanced stage), and affective disorders (9.9% at diagnosis and 28.2% in the later course of the disease). Cognitive impairment in an advanced stage of SLE was manifested in 16.9% of patients. Symptoms of cerebrovascular disease, including stroke, were experienced by 9.9% of patients.

Hematological changes

In more than half of the patients (53.5%), hematological changes (anemia, leucopenia, thrombocytopenia) were observed at the beginning of the disease. The percentage of patients who suffer from these symptoms remained the same in the later course of SLE, but with an increased number of patients who experienced at least 2 of these 3 symptoms. Leucopenia (32.4%) and anemia (33.8%) occurred initially with similar frequency, while in the course of the disease anemia (42.3%) was significantly more frequently demonstrated than leucopenia (33.8%). Thrombocytopenia was initially diagnosed in 18.3% of patients, and in the further course of SLE incidence fell about 30% and amounted to 12.7%.

Sjögren's syndrome and inflammation of the serous membranes

In the study, these symptoms were present in 22.5% of patients at the time of diagnosis. A similar incidence of occurrence (21.1%) was noted in the further course of the disease. Sicca syndrome accompanying SLE was reported in 19.7% of patients initially and in a similar number of patients (22.5%) in the further course of the disease.

Immunological profile of patients

ANA positive result was observed in the initial period in 87% of patients, and later in 94% of them. The full panel of antibodies was not determined for each patient in the initial stage of the disease. However, the available data shows that the most common antibodies in SLE patients in this period were anti-double stranded DNA (anti-dsDNA) and anti-Sjögren's-syndrome-related antigen A (anti-SSA autoantibodies). Similarly, in the later stages of the disease, anti-dsDNA (47.9% of patients) and anti-SSA (40.8%) were most common, followed by anti-nucleosomal antibodies (29.6%), and lupus anticoagulant (22.5%). Anti-ribosomal P protein was checked in 39 patients. All patients with a positive test result (6/39, 15.4%) had neurological symptoms. However, 21.2% of patients with negative test result also had neurological symptoms.

In 40 patients, data was available from both the onset of the disease as well as during its duration; an antibody panel in these patients mostly did not change.

Discussion

Numerous studies showing the incidence of SLE in the world has been previously established. Petri et al. and Alarcon et al. studied the American population, Wang et al. investigated the Asian population, and Cervera et al. covered European population in a large cohort study Euro-lupus.^{5,7–9} Clinical manifestation of SLE varies considerably depending on the geographical region and, therefore, it was decided that this study should be performed based on the Polish population. Data was collected in 1 region of Poland, the Lower Silesia.

The presented results are similar to those shown in the study of the Euro-Lupus. Despite the significant difference in the number of patients in groups, similar basic symptoms of SLE were observed in both cases. These include changes in joints and muscles, as well as skin.

However, a considerably lower number of documented changes in kidney disease symptoms, such as proteinuria, hematuria and pyuria were found at the beginning of the disease. Nevertheless, analyzing the incidence of nephropathy in the further course of SLE, its presence was observed in 50% of patients (Euro-Lupus 27.9%). Similar results were included in the research on the US population (55.6%). In the Asian population, nephropathy was present in 74% of patients. This shows that the variability in the incidence of particular symptoms differs significantly depending on the geographical region and needs to be studied in particular groups to determine the natural history of SLE.

Clinical manifestation of symptoms also varies with the duration of illness. Initial dominance of presentation of skin symptoms is later replaced by symptoms of the nervous system, such as headaches, mood disorders, cognitive disorders, and vascular changes. The incidence of depression drastically increased. This indicates the need for more frequent neurological, psychological and mental health consultations throughout the course of the disease.

SLE is a disease appearing mainly in young adults. In the present study, the vast majority (86%) of the first symptoms of SLE appeared at the age of 15–49 years, but 6% were observed at a younger age, and 8% in the elderly. In the group of 50+ years of age, female dominance is not as strongly pronounced (only 67%), while in the youngest group it is equal to 100% (in the whole study population 89%). In neither the younger nor the older age group was there a significant difference in the incidence of individual symptoms of SLE in comparison to the general population, as suggested by other studies.^{5,10–13}

The observed time from the appearance of the first symptoms of the disease to the time when 4 of the ACR criteria were met was 5 years, and it is significantly longer compared to a European study (2 years).⁵ This difference may be due to the milder initial course of the disease in the Polish population, or to other methods of collecting information (Euro-Lupus is a prospective study; the current study collected data retrospectively).

Although headaches are the most frequently reported neuropsychiatric symptoms, they have a low specificity for SLE and are classified as minor syndromes. Studies also demonstrated that headaches are not more common in people suffering from lupus compared to the population of healthy people, and characteristic features of the pain were not observed.^{14,15}

Depression may also result from causes not directly related to the SLE disease process. It can be due to steroid therapy, among others, and likely depends on the predisposition of the individual. The appearance of seizures and vascular lesions in the brain (stroke, transient ischemic attack – TIA) are related largely to the presence of antiphospholipid antibodies, which are responsible for the occurrence of prothrombotic state.^{16,17}

In the study population, the most common symptoms at presentation were changes in muscle and joint system, skin, general symptoms, and sensitivity to UV light. As the disease progresses, the percentage incidence of neurological symptoms and renal involvement are increased, while syndromes from joint and muscle system and the skin continue to be an important concern. The average time from onset of symptoms to diagnosis was 5 years. Profile of autoantibodies did not change during the course of the disease with anti-dsDNA and anti-SSA as the most common autoantibodies.

SLE as a systemic disease is characterized by the presence of many symptoms associated with the activity of various organs. Most of them are non-specific, and even those characteristics of lupus are present only in some patients. There is no typical clinical picture of SLE; therefore, the patient population suffering from this disease is very various. Differences in the course of the disease are also evident due to the geographic area. Therefore, early diagnosis can be a big challenge for any clinician, which justifies the need for this type of study to better characterize the disease.

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