

Case Report: A 12-Year History of Autoimmune Disease Systemic Lupus Erythematosus

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Abstract Systemic lupus erythematosus (SLE) is a chronic, autoimmune, connective tissue disorder with multi-organ involvement. Reported here is the case of a 33-year-old woman with a 12-year history of lupus erythematosus. The article documents the development of lupus: First phase/ preliminary phase (13-21 years of life); Second phase/acute cutaneous lupus erythematosus (22-27 years of life); Third phase/systemic lupus erythematosus (from 28 years of life). The parameters of serological test and blood test were measured regularly during the course of the disease. The MRI-investigation was carried out three times. The clinical symptoms are evaluated in relation to the laboratory parameters. All these data with the therapeutic modalities and the trigger factor(s) are disclosed.

Keywords: autoimmune disease, lupus erythematosus cutaneous, systemic lupus erythematosus, corticosteroids

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1. Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease. Autoimmune diseases resulting from a disordered immune reaction in which antibodies are produced against own proteins. Lupus is characterized by anti-nuclear antibodies (ANA), leading to inflammation. The disease starts with a preclinical phase characterised by these anti-nuclear antibodies, then it proceeds to the disease-specific clinical phase(s) [1].

The most frequent manifestations of SLE include: arthritis (64-91%), skin lesions (55-86%), blood involvement (55-89%), renal involvement (28-73%), central nervous system involvement (11- 49%), gastrointestinal symptoms (39%), pericarditis (12- 20 %) [2]. The chronic disease has variable severity and different progress with periodic courses.

The exact cause of autoimmune diseases is not fully known. People with lupus often have family members with other autoimmune diseases. There are environmental triggers like ultraviolet rays, certain medications, a virus, physical or emotional stress and trauma. Estimated incidence rates are in range from 2 to 8/100 000/year. Women are affected nine times more than men. This fact led to the assumption that the female hormone estrogen could play a role in causing SLE.

There is no curative treatment for SLE. Drugs such as corticosteroids and cyclophosphamide can be used to suppress the immune system in active SLE, but these drugs have potentially serious side effects. SLE patients receiving long-term prednisone therapy have a significant risk of morbidity due to permanent organ damage [3]. Malignancies are related to complications of longstanding disease and immunosuppressive therapy [4]. In this report

is presented the case of a 33 year-old woman with a 12-year history of lupus erythematosus. The clinical symptoms were evaluated in relation to the laboratory parameters. All these data with the therapeutic modalities and the trigger factor(s) were documented regularly during the course of the disease.

2. Case Presentation

Family history: The mother has bronchial asthma.

Personal history of the patient: In childhood (between the ages of 6-10 years) she had severe chronic traumata. It was diagnosed a post-traumatic stress disorder (PTSD). As a result the young patient developed dissociative amnesia. Repression is a natural protective function of the brain. This defence mechanism tries to eliminate the threatening facts or events from the conscious perception.

Lupus erythematosus cutaneous

In the age of 13 years she had skin rashes after exposure to sunlight. These skin exanthemas did not show the typical butterfly rashes, they were diagnosed as sun allergy. This skin problem occurred in the next years, only during the summer months and only after excessive sun exposure. The skin rashes were treated with corticosteroid (prednisone: 2x40mg; 1x30mg, 1x20mg, 2x10mg, 2x5mg). The patient had not other somatic complaints.

In 2004 (in the age of 22 years) butterfly rash occurred on the face and flat red patches on arms. The laboratory investigation (Dermatological Polyclinic, University Hospital, Basel, Switzerland) confirmed the clinical diagnosis: Lupus erythematosus cutaneous. Serological examination; (I) ANA (antinuclear antibody) = 1:1280, (reference value: <160), (II) ENA/SS-A/Ro (extractable nuclear antigens) = positive (reference value: negative).

In the following years the butterfly rash and the red patches appeared in the summer months. The immunological serum parameters (ANA, ENA) remained at high levels. The rash on the face was treated with corticosteroid ointment and prednisone (treatment schedule: see above).

Systemic lupus erythematosus

In 2010 (in the age of 28 years) the patient suffered from severe insomnia: she slept 3-4 hours per night, nevertheless she was not tired during the day. This state in

association by an acute stress situation lasted for several months.

Because of the frequently severe headaches MRI investigation was indicated. This presented several T2-high signal intensity lesions in the periventricular and subcortical white matter (**Figure 1/A**), additionally a micro-adenoma in pituitary gland. Besides headaches the patient did not have any neurological symptoms or neuropsychiatric symptoms. Cerebrospinal fluid analysis; The values of all investigated parameters were in normal range.

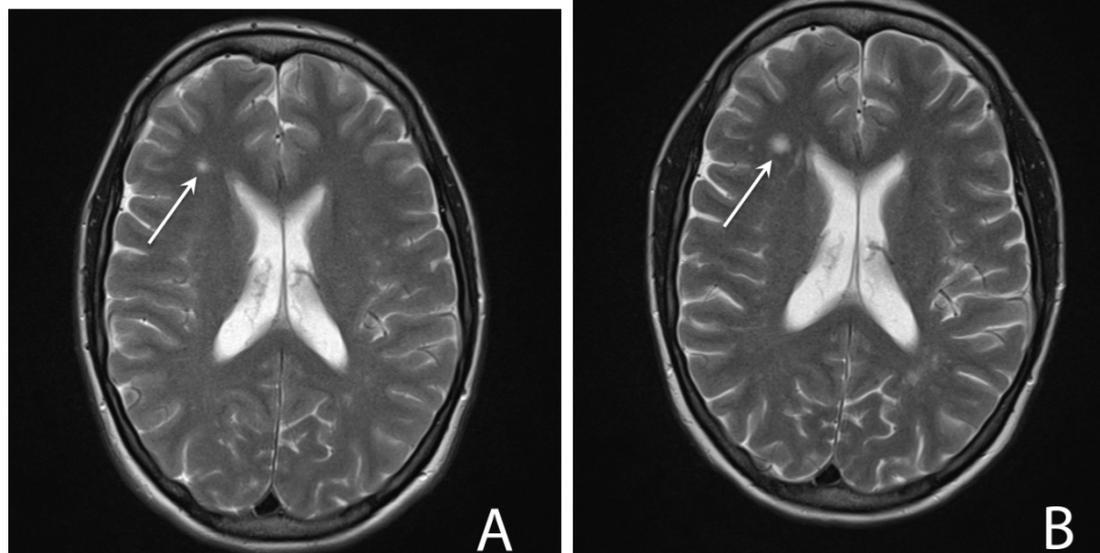


Figure 1. 33 year-young women with systemic lupus erythematosus. MRI presents the T2-high signal intensity lesions in 2010 (A) and in 2011 (B)

The arrow shows the increased size of the lesion in 2011. This was detected in 2010.

Serological examinations showed slightly/ or moderately increased values of ANA=1:320; 1: 640. The values of ENA/SS-A/Ro were positive.

Blood test; Lymphopenia: 1.0 mm³/L (normal range: 1.2-3.2).

In 2011 the health status of the young patient is very unstable. She had overwhelming fatigue, slept 12-15 hours daily.

Clinical symptoms; Fatigue, heavy myalgia and arthritis/arthralgia, additionally oral ulcers, severe headache.

Serological test; The value of ANA is very high: 1:1280, ENA/SS-A/Ro is positive, the rheumatoid factor is positive.

Blood test; Lymphopenia: 0.4 mm³/L (normal range: 1.2-3.2), Granulocytosis: 10.9 mm³/L (normal range: 1.2-6.8), Blood sedimentation is elevated: 26 mm (normal range: 6-20), CRP-value is high: 23 mg/L (normal value: <10).

The MRI investigation presented increased number and enhanced size of the T2-high signal intensity lesions detected in 2010 (**Figure 1/B**).

2011-2013; Treatment with corticosteroid for 24 months.

Dose regimen: 80-60 mg/daily during 2 months, 50-40-30-20-15 mg/daily during the next 5 weeks, then 15 mg/daily for 2 months, then 10-5 mg/daily. The treatment was carried out in the praxis of W. Hagmann, MD, rheumatologist, Switzerland/Allschwil.

(1) Effect of the corticosteroid therapy

Clinical symptoms; middle/slight myalgia and arthralgia, oral ulcers.

Serological test; ANA-value is reduced down to 1:320

Blood test; number of lymphocytes is in normal range, granulocytosis and elevated CRP-value are due to infectious diseases (see below).

(2) Side effects of the corticosteroid therapy

2012 severe allergic - infectious skin reaction and pyelonephritis both sides. The patient was hospitalised always.

Increase in body weight to 8-9 kg, slight hair loss.

In 2014-2015 (32-33 years) the disease is in a sub-chronic/chronic stage.

Clinical symptoms; fatigue, slight/middle myalgia and arthralgia, oral ulcers frequently, from time to time urinary tract infections.

Serological test; ANA-value is slightly increased (1:320), the values of ENA/SS-A/Ro are highly elevated, rheumatoid factor is positive. The increased parameter of Mi-2 IgG indicates Dermatomyositis, however the patient had never dermatological problems.

Remarks; In December 2015 the ANA-value is elevated (1:1280).

Blood test; Leukopenia and Lymphopenia.

The MRI investigation presents an unaltered situation regarding T2-high signal intensity lesions in brain in comparison with the findings from 2011.

3. Discussion

Lupus erythematosus is a chronic autoimmune disease in which the immune system produces antibodies to cells causing inflammation and tissue damage. There are two

main forms: (1) Cutaneous lupus erythematosus (CLE) and (2) Systemic lupus erythematosus (SLE). Flat red patches on the face called as butterfly rash are the most common form of ACLE (acute cutaneous lupus erythematosus) and show sensitivity to the sun (photosensitivity). Systemic lupus erythematosus is autoimmune disease of the multiple organ systems. It belongs to the connective tissue disorders.

This case report presents the three-phase-course of lupus erythematosus in a young women. The criteria of ACR (American College of Rheumatology) for the diagnosis of lupus erythematosus are fulfilled (seven from eleven criteria are positive) (requirements: ≥ 4 criteria).

Table 1 present the course of lupus erythematosus in relation to the clinical and laboratory parameters in the period between 2004- 2015.

Table 1. Time course of lupus erythematosus in relation to the clinical and laboratory parameters

	2004-2006	2010	2011	2012	2013	2014	2015
Lupus erythematosus cutaneous	+++	+	+	+	+	+	+
Malar (butterfly) rash							
Immunological disorder	+++	see below					
Systemic lupus erythematosus	++	+	+	+	+	+	++
Photosensitivity							
Oral ulcers / Infections	∅	∅	+	+	+	+	+
Arthritis / Arthralgia	∅	∅	+++	+	+	∅	++
Myositis / Myalgia	∅	∅	+++	++	+	+	++
Neurologic disorder	∅	+	++	ND	ND	ND	++
Renal disorder	∅	∅	∅	+++	+	+	+
Hematologic disorder	∅	+	+++	+++	+++	++	∅
Immunological disorder	+++	++	+++	ND	+	+	+++

ND = not determined; ∅ = no pathological findings; Score = + slight, ++ middle, +++ high.

First phase/ Preliminary Phase: The patient had sun allergy from the 13th year of life. Sun allergy is often used to conditions in which red rash occurs on skin with exposition to sunlight. The successful therapy with corticosteroid supported the hypothesis that these skin rashes were the preliminary stage of the cutaneous lupus erythematosus. The measurements of immunologic parameters regarding autoimmune diagnostics were not carried out at this time.

Second phase/Acute cutaneous lupus erythematosus (ACLE): It appeared for first time in the age of 22 years. The clinical diagnosis was confirmed by immunologic parameters. The characteristic malar (butterfly) rash remained intensively until 2010, thereafter it was attenuated.

Third phase/Systemic lupus erythematosus: Cutaneous disease is associated with higher early systemic lupus disease activity [5]. In our patient ACLE developed into systemic lupus erythematosus 6 years after onset of the cutaneous lupus.

Clinical symptoms and pathological findings in the patient

- Fatigue and vitamin D deficiency: Systemic lupus erythematosus is often characterized by fatigue, with significant effects on physical functioning and wellbeing. Fatigue is probably multifactorial and has been related to not only disease activity or complications but also to pain, poor sleep, vitamin D deficiency/insufficiency [6].

- Musculoskeletal complaints: Arthralgia, myalgia on the hands, arms and knees. Musculoskeletal alterations are frequently found in 90% of patients having SLE, and may be related to the disease activity. The degree of involvement may range from a transitory arthralgia to a severe presentation of deforming arthropathy. In 5% to 10% of lupus patients inflammatory myopathy is also observed [7].

- In the patient was diagnosed a micro-adenoma in pituitary gland. She did not have and does not have any

hormonal disturbances. The size of the micro-adenoma did not alter. It was reported a non functioning pituitary macro-adenoma in a patient having systemic lupus erythematosus [8]. It can be assumed that such adenomas are incidental findings and have not an association with lupus.

- It is reported that 70% patients with SLE have multiple white matter lesions in brain. These appear as T2 high signal intensity, correlated to small vessels involvement. These are small focal cortical microinfarcts [9]. The lesions can due to impairment of the microcirculation associated with vascular endothelial cell injury [10]. Our patient had these lesions already 2010, with a significant increase in 2011 (Radiology, St. Clara Hospital, Basel, Switzerland). The lesions stained stable in the next years and did not lead to neurological or neuropsychiatric symptoms (Neuroradiology, University Hospital, Basel, Switzerland).

The patient had and has recurrent headaches, supporting the diagnosis of micro- infarcts resp. disturbance in the microcirculation. In view of the author of this report and of the physician (W. Haggmann, MD, rheumatologist) it is proposed to treat the patient with aspirin 100 mg/daily in case of the recurrent and/or chronic daily headaches to prevent stroke.

- The young patient has oral ulcers and urinary tract infections from time to time. Oral ulcers are frequent symptoms in SLE. The damaged epithelial tissue can be infected from bacterial flora in the mouth leading to the extension of the ulcerative process. The ulceration and the urinary tract infections with complications are due to hematological deficiencies: Lymphopenia and/or leukopenia.

- In the last 20 months the typing of lymphocytes-subpopulation was carried out more times. The percentage of CD4 cells (T helper cells) is increased slightly, the percentage of CD8 cells (T cytotoxic cells) is in normal

range. As consequence the CD4/CD8 ratio is above the normal value. These findings are in contrast to the disclosure that the numbers of CD4 cells are decreased in SLE and there is an inverse relation between CD4 cells counts and disease activity [11,12].

Systemic lupus erythematosus (SLE) is characterized by increased pathologic autoantibody production. Antinuclear antibodies (ANAs) bind to contents of the cell nucleus. Over 90 per cent of patients with SLE-test are positive for different antibodies, which are important in the diagnosis, in the monitoring of the disease activity and in the treatment [13,14].

- In our patient the ANA-values were during the observation period of 12 years in a pathological range. The elevated values of anti-SSA/Ro and anti-SSB/La antibodies present an association with photosensitivity [13].

Trigger factor(s) in the disease

The autoimmune diseases have both genetic and environmental causes. SLE is caused by environmental trigger(s), acting on persons with genetic susceptibility and with defects in the immune system. The environmental triggers are: ultraviolet rays, certain medications, a virus, physical or emotional stress, and trauma.

It can be assumed, that these triggers are individual, which means that the patients react differently to these factors.

The disease is incurable and the course of SLE is unpredictable, with periods of flare-ups. These exacerbations lead to organ-damages. For this reason it is very important to recognize the triggers to avoid new episode and the progression in the disease.

- Our patient had during the observation time of 12 years three times highly elevated ANA values (1:1280); (a) 2004 in association with the manifestation of lupus erythematosus cutaneous, (b) 2011 when lupus erythematosus cutaneous developed into systemic lupus erythematosus, (c) 2015 in association with a high level of cortisol. At each time the patient had severe stress situations.

Physical and psychological stress are implicated in the development of autoimmune disease. Retrospective studies found that up to 80%) of patients reported uncommon emotional stress before disease onset [15]. Stress is a trigger for flares in systemic lupus erythematosus [16].

The stress-triggered neuroendocrine hormones lead to immune dysregulation. Inflammation is accompanied by raised levels of cytokines like interleukin- 6 or tumour necrosis factor -alpha that can activate the hypothalamic-pituitary-adrenal (HPA) axis [17].

Our patient had infections in association with stress situations. The musculoskeletal complaints: arthralgia, myalgia also exacerbate in association with stress situations. The photosensitivity tends to be more serious in cases of stress. Other trigger factors (certain medications, a virus, physical stress) are excluded.

These facts given evidence for psychological stress as trigger factor in SLE-flares of the patient presented in this case report.

Acute stress leads to increased levels of cortisol. In chronic stress cortisol is secreted again and again. If this

state persists over a long period, then the cortisol production exhausted in the adrenal cortex.

We will follow at regular intervals the course of the disease: To measure the serum levels of cortisol, blood parameters, serological- parameters in relation to clinical condition/symptoms and psychosocial stressors.

Disease management

The disease management program includes – without major organ involvement and without flare-ups – the following steps: (1) The patient has in every third month a telephonic consultation with the clinician, (2) In every half year (6 months) the patients is examined by the clinician, (3) Laboratory parameters (serological test, blood test) will be measured six-monthly, (4) MRI -investigation will be carried out in every second/third year. The clinician closely cooperates with the author of this paper: She is an immunologist. Special investigations will be carried out in the University Hospital of Basel, Switzerland. This hospital brings together 50 clinics, units and institutes.

4. Conclusion

Systemic lupus erythematosus (SLE) is an incurable chronic autoimmune disorder. Young women in the reproductive age suffer from this disease. The disease occurs in phases and presents individual course. For this reason it is important and necessary to document regularly the clinical symptoms in relation to the laboratory parameters. This is fundamental in the management of this disorder. The tabular presentation is given a good overview and may be useful for the prognosis. Prevention is to avoid worsening of the disease and related illnesses. For this reason it is essential to know the individual trigger(s) of this disease.

5. Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editorial Office of this journal.

Conflict of Interest

The author has no competing interests.

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