

## Psychotic disorder in the course of Systemic Lupus Erythematosus with subcortical calcifications - case report

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### Summary

Systemic Lupus Erythematosus (SLE) is autoimmune disease of connective tissue which is characterized with clinical symptoms of many systems and organs injury. There are often neuropsychiatric symptoms. Psychotic disorder is the least frequent syndrome. Neuropsychiatric symptoms are important because they deteriorate the quality of life and are poor prognostic factor.

**Aim.** The aim of the study is to present the patient with chronic, lasting for many years, skin lesions and laboratory tests results characteristic for SLE, who had psychotic disorder diagnosed as schizophrenia and in the next few years there were observed other neuropsychiatric symptoms including cognitive impairment and mood disorder.

**Conclusions.** Psychotic disorder is rare syndrome of neuropsychiatric SLE (NPSLE). It may primarily originate from SLE or be secondary either to the therapy or the complications of the disease. It is not possible to define if the psychosis is the primary schizophrenic process or secondary to the autoimmune disease in presented patient. However the clinical picture pays attention to the significance of careful diagnostic process, including neuroimaging. In head CT of presented patient there were revealed massive, bilateral, calcifications of subcortical structures which probably substantially enhanced neuropsychiatric symptoms.

**Key words:** Neuropsychiatric lupus erythematosus, schizophrenia, calcification of the basal ganglia

### Introduction

Systemic Lupus Erythematosus (SLE) is connective tissue autoimmune disease with clinical symptoms of many systems and organs injury, including Central Nervous System (CNS). In most cases neuropsychiatric symptoms occur. The most

often are cognitive impairment or even dementia which is observed in 80% of patients, and depression in about 40% of patients [1]. The anxiety disorder and rarely in 3,5-8% of cases even the psychotic symptoms may occur [2]. In 1999 research committee of American College of Rheumatology (ACR) defined 19 various syndromes of neurological and psychological symptoms because of the high prevalence of neuropsychiatric disorder, setting new special entity called Neuropsychiatric Systemic Lupus Erythematosus (NPSLE). Neuropsychiatric symptoms are important clinical problem, because they worsen the quality of patient life and they are poor prognostic factors.

The aim of this study is to present the patient with long-lasting skin lesions and the laboratory tests results specific for SLE who had psychotic disorder and was treated for schizophrenia with other neuropsychiatric symptoms such as cognitive impairment and mood disorder which occurred in later time.

### Case report

The woman at the age of 47, married, mother of one child (27 years old nowadays) was admitted to the Neurological Clinic of Medical College, Jagiellonian University in Cracow because of progressing slowness of movement and gait disorder. Since the age of 12 she has suffered from extended skin lesions on the face and head (erythematous rash). The SLE was suspected, however the proper laboratory tests were not performed. At the age of 30 the skin lesions generalized, also appeared on the trunk and legs. In the laboratory tests the titre of nonspecific antinuclear antibodies was increased (1:320), beside there was low level of C4 complement and tendency to thrombocytopenia. The SLE was diagnosed and the therapy with prednisone was performed (60 mg per day), and then continued for many years.

At the age of 39 in patient developed the persecutory delusions, delusions of reference, unveiling delusions, delusions of stealing ideas and delusions with complex and bizarre substance (e.g. the soul of mother is altered, the mother has the head of frog) accompanied by illusory and hallucinatory sensations. Under the influence of mentioned productive symptoms the patient was sometimes aggressive, with inadequate behavior. In the medical history documents there were observed formal thought disorder (perseveration, dissociation) and there was no insight into the disease. Due to the severity of the psychosis symptoms, the patient was hospitalized at the time in a psychiatric hospital. The schizophrenia was diagnosed and the therapy with antipsychotic drugs was performed, starting with haloperidol for 4 years, and then with aripiprazole and flupenthixol.

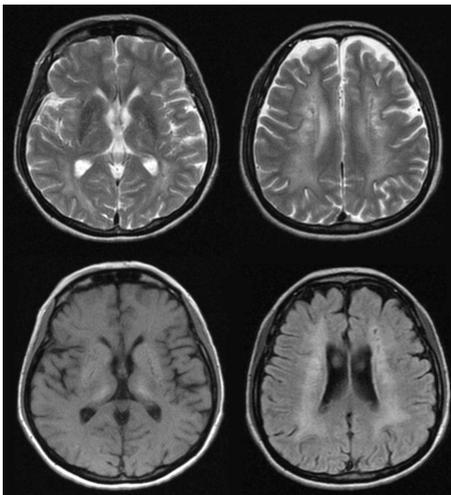
Since the age of 41 the patient was observed by her husband with progressive concentration disturbances, memory deficits and planning inability which deteriorated daily functioning at last time. Since 4 years increases moving slowness, gait disturbances and involuntary twisting movements of left extremities have occurred, in particular distally.

During the admission in neurological examination was stated: generalized slowness of movements stronger in left extremities, hypomimia, tongue dyskinesias, distal

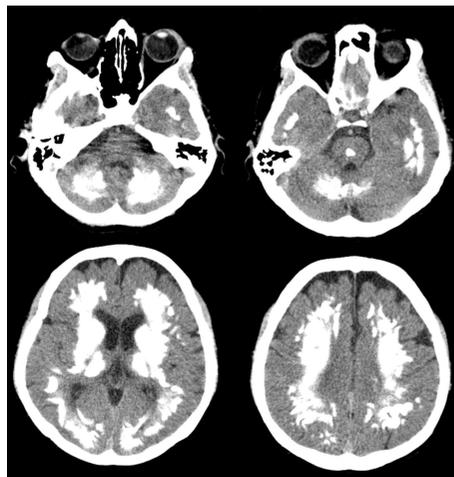
dystonic movements of left extremities, slightly increased muscle tone (rigidity) of left extremities, vivic and symmetrical deep tendon reflexes of four limbs, Oppenheim symptom in left lower limb, parkinsonian posture of anteversion, without left arm swinging, abnormal postural reflexes, MMSE- 24 points.

In psychiatric examination: the patient was properly orientated, in logical verbal contact, statements scarce, non-spontaneous. Pale affect, not adaptable, slightly depressed mood, periodical perseverations, incoherent thinking with disturbed train of thought. The patient had difficulties with transferring the attention. There was seen fatigability and psychomotor slowness. The patient was speaking about low functional activity, difficulties in performing daily life tasks, apathy, loss of interests, anhedonia, abulia, impaired concentration and attention, difficulties in initiating the activity. There were seen emptiness of thinking, purity of statements. She was talking about feeling of hopelessness, sadness, inability to think about future, resigned thoughts (actually without suicidal either thoughts or tendency). The patient was fully dependent from mother's help, retired from social life, she was avoiding interpersonal contacts, non-spontaneous. She had fully preserved criticism for past delusions and hallucinations. Actually she did not have productive symptoms. The patient acknowledged that in the past she had delusions of unveiling and sending thoughts, persecutory delusions e.g. to the hospital personnel and delusions directed to herself. Criticism for the contemporary symptoms was reduced. Working and recent memory was impaired while past memory was slightly reduced. Before the hospitalization Neurology Clinic she had suicidal thoughts however without evidence suicidal tendency.

In neuropsychological examination there were especially disturbed executive function, working memory, lower capacity of direct memory magazine for both visual



**Fig.1. The MRI of patient's head (July, 2011).**



**Fig. 2. The CT of the patient's head.**

and auditory-verbal modality. In language processes there was significantly reduced verbal fluency. There was observed bilateral, spatial dyspraxia. The disorder fulfilled the criterion for dementia by ICD-10 and DSM IV with dominant frontal and fronto-subcortical symptoms.

In the MRI of the head (Fig.1.) there were stated hiperintense areas bilaterally in T1 sequence and hypointense in T2 sequence in the region of basal ganglia. In T2 and FLAIR sequence there were also observed hiperintense areas subcortically in white matter.

Because the MRI was inconclusive the computed tomography (CT) was done (Fig.2.). The images revealed massive, bilateral calcifications in subcortical regions such as basal ganglia, pons, cerebellum and centrum semiovale.

In the laboratory tests the levels of serum parathormone, ionised calcium, TSH and ceuloplasmin were within normal limits. There were detected antinuclear antibodies ANA (anti-Ro 52 kDa) with granular type of lightening in 1:640 titre and with cytoplasmatic type of lightening in 1:640 titre. The level of C3c and C4 of the complement was within normal limits. There was tendency to thrombocytopenia (129 thousand/ $\mu$ l). Moreover the genetic test for Huntington disease was negative.

### Discussion

The presented case shows complex neurological and psychopathological phenomenology in patient with the diagnosis of both SLE and schizophrenia. The important fact is that there is no possibility to resolve whether the psychotic symptoms are because of the primary schizophrenic process or they are similar to the schizophrenia syndrome and secondary to the pathophysiological process caused by SLE or the medications for autoimmune disease. First psychotic episodes occurred in relatively mature (39 years), professionally active, socially well adapted person, with stabilized family (husband, child). The psychosis was preceded by long-term SLE treatment. In the family there were no psychotic diseases. Mentioned above information argue for the conception of the organic schizophrenic syndrome origin. On the other hand psychotic episodes were recurrent and the exacerbations were independent from the SLE course and its treatment. The regression of psychosis was strictly dependent on the antipsychotic therapy and whether the patient was applying to the recommendations. Clinically acute psychotic episodes were very characteristic for paranoid schizophrenia, similarly long lasting deficit symptoms after reduction of productive symptoms.

There is multifactor etiology of actual significant social deterioration. It is caused by negative symptoms of psychosis (apathy, abulia, lack of willingness, non-spontaneity), depressive mood, cognitive impairment and motor disorder.

Nowadays there is no single test for strong diagnosis of NPSLE. The neuropsychiatric diagnosis in the course of SLE need the rheumatological examination, neuroimaging, immunoserological tests, psychiatric examination and neuropsychological tests in terms of active phase of the disease. The diagnosis needs the exclusion of other causes of symptoms, such as electrolyte imbalance, the influence of drugs including

glucocorticosteroids, renal failure (uraemia), arterial emboli and primary psychiatric disease [2]. The last condition is inconclusive in presented case.

The psychotic symptoms are present the least frequently among the syndromes of NPSLE. Usually they envelope in early phase of the disease, during the first year. Rarely they can be the only symptom of CNS disease [3]. It was evidenced that skin lesions coexists a little bit more often with psychotic disorder. In 14 years follow-up of patients with psychosis due to SLE it was observed that 60% of patients have the remission during the first year. Simultaneously the patients with fast remission are characterized with deeper psychosis. Chronic psychotic disorder, lasting for longer than 10 years occurred in 20% of cases [4]. Typically the psychotic symptoms in NPSLE are disturbed form and substance of thinking, delusions, hallucinations, limited attention, tendency to get distracted, perceive disturbances, agitation and even aggression [5].

It is important to assess properly if the symptoms are caused by the therapy or by the failure of the CNS which is more often. It is proved that severe psychotic symptoms may be complication of steroid therapy only if daily dose is more than 40 mg of prednisone [6]. But in chronic therapy the depression likewise in short therapy hypomania are more often than psychosis. Moreover the psychosis develops in first 1-2 weeks of treatment [7]. In our patient first symptoms occurred after 9 years of curing.

Until now there is only one case report of the patient with coexistence of schizophrenia and SLE. But in that patient the psychotic symptoms were first and for a long time they were isolated. They occurred 14 years before other SLE symptoms, especially skin lesions, have occurred. After excluding lupus related to the antipsychotic drugs the authors suggested the participation of antibodies in pathogenesis of schizophrenia [8]. There are several theories of the schizophrenia's etiology such as the influence of genetic, civilizational, prenatal, social and economic factors, usage of psychoactive substances, psychological, emotional and biochemical elements. However in the last few years the relation between disturbed immunological processes and schizophrenia has been raised [9].

In the case of NPSLE the neuroimaging is recommended only in special conditions such as: the age over 60, after head injury, when the cognitive impairment progresses dynamically or when new neurological symptoms occurred. However the ICD-10 criteria require the brain disease exclusion for schizophrenia diagnosis. Because in patient's head MRI the changes were inconclusive in the next step head CT was done which revealed massive calcifications of subcortical structures and cerebellum. In the literature there are only 9 case reports of patients with SLE who had massive calcifications of cerebellum and subcortical structures including striatum and globus pallidus [10-18]. In these case reports the dominant symptoms were cognitive impairment, depression and also neurological symptoms such as parkinsonism, involuntary movements, pyramidal signs, ataxia. Psychosis occurred in 2 cases. At any of two the psychotic symptoms were the only neuropsychiatric disorder. Both patients had recurrent episodes of psychosis or needed chronic psychiatric care [15, 18].

Neuropsychiatric symptoms are mainly expounded by pathogenic factors such as thrombotic incidences, vessel structure damage and hypertension vasculitis or

complications of medicines [17]. In 30% of NPSLE some small calcifications may be seen in neuroimaging. Globus pallidus is the most common structures in which the calcifications occur, however they may be also seen in striatum, cerebellum and other brain structures such as thalamus and centrum semiovale. The reason of calcifications formation is not well known. There is hypothesis that primary vessels damage due to immunological processes may induce microinfarctions and secondary dystrophic calcification, especially intensified in basal ganglia, because of strong calcium concentration in these regions [12]. In white matter the calcifications probably are induced by exuded neurotoxic factors from vein vessels and local inflammation [13]. It is possible that calcification may coexist with demyelization caused by local encephalomyelitis with immunological origin in the course of SLE [18].

Massive calcifications are rarely seen in neuroimaging and because of that it is difficult to confirm its relation to the clinical symptoms. Calcifications of basal ganglia are relatively common phenomenon which exists in 0,3-1,5% CT scans made for another reason. It is connected with aging and usually asymptomatic. Typically the calcifications are small, symmetrical and occur only in globus pallidus [20]. In the case of symptomatic subcortical calcifications the metabolic disorder should be excluded. The most common cause of calcification in globus pallidus, striatum and nucleus dentatus in cerebellum are calcium metabolism disturbances (hypoparathyroidism, pseudohypoparathyroidism) [20, 21]. However in our patient the levels of parathormone and calcium were within normal limits.

In differential diagnosis we were thinking about Fahr's syndrome. It is a genetic disease, probably with autosomal dominant inheritance. There are many neuropsychiatric symptoms occurring at the age of 30-60 years in the disease [20, 22] with existing subcortical and cerebellar calcifications [23]. Neuropsychiatric symptoms starting from mild cognitive and concentration impairment, through personality and behavior disorder, up to dementia and psychosis are the main early symptoms. Moreover at the beginning of the disease may occur: ataxia, fatigability, posture disturbances, slowness and/or slurred speech, muscle cramps and/or involuntary movements. Movement disorders such as parkinsonism (bradykinesia, rigidity, postural instability, mask face, rare blinking, dyarthria) and less likely hyperkinetic (chorea, tremor, dystonia, athetosis, oro-facial dyskinezias) are the most frequent neurological symptoms connected with the disease [24]. Fahr's disease is diagnosed in case of fulfilling specific criteria which include positive family history and excluding other causes of calcifications such as systemic diseases. Presented patient did not fulfill the mentioned criteria.

In the diagnostic process we have paid attention to the side effects of neuroleptics. Extrapyramidal symptoms such as parkinsonism with bradykinesia, rigidity, tremor or gait and posture disturbances are the main side effects of antipsychotic drugs. Moreover there may occur involuntary movements e.g. dystonic or facial, head and neck dyskinesias. Involuntary movements especially chorea may occur in SLE. They are relatively rare, however extrapyramidal signs as parkinsonism are definitely more rarely [25].

## Conclusions

Psychotic disorder are rare syndrome of NPSLE. They can primarily be caused by SLE or secondary to the steroid therapy. In presented case it is not possible to clearly define if the psychosis is primary schizophrenic process independent to SLE or it is secondary to the autoimmune disease. However presented clinical picture should pay attention to the significance of the careful diagnostic process. Patients with SLE usually are not performed neuroimaging. Meanwhile in presented patient head CT there were revealed massive, bilateral, calcifications of subcortical structures which probably substantially enhanced neuropsychiatric symptoms.

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