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To treat or not to treat with immunosuppressive therapy: psychiatric disorders in patients with systemic lupus erythematosus

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Up to 65% of patients with SLE meet the criteria for a psychiatric disorder.[1] Especially depression and anxiety are frequently present. Psychiatric disorders are important to recognise as they influence quality of life and treatment outcomes. As a myriad of causes may be responsible for psychiatric manifestations in patients with SLE, clinicians are often confronted with the question: to treat or not to treat with immunosuppressives?

In the Leiden neuropsychiatric SLE (NPSLE) clinic, patients with SLE and neuropsychiatric symptoms are evaluated by a multidisciplinary team, including a psychiatrist and a clinical neuropsychologist.[2] Neuropsychiatric symptoms are attributed to SLE in a consensus meeting based on clinical, radiological and laboratory assessment, which has been described in detail previously and is similar to the proposed classification criteria for NPSLE.[3 4] As the clinic has now existed for over 10 years, we have accumulated experience in the diagnosis and treatment of different psychiatric manifestations. Here, we provide an overview of these psychiatric manifestations and the need for immunosuppressive therapy in patients with SLE visiting our NPSLE clinic between 2007 and 2019. Psychiatric disorders were coded according to the Fifth Version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).[5] The presence of a cognitive disorder was based on extensive formal cognitive assessment.[6] Among 371 patients with SLE who visited our clinic in that time period, the mean age was 43 years (SD: 13), 87% were female and the median SLE disease duration was 4 years (IQR: 1–13). In approximately one-third of patients, neuropsychiatric symptoms were attributed to SLE (NPSLE, n=109), of whom 80 individuals had an inflammatory phenotype and 29 patients an ischaemic phenotype.

In total, 240 patients (65%) had or received a psychiatric diagnosis at the time of visit. At presentation to the clinic, cognitive disorder (without any other psychiatric comorbidity) was the most common disorder (25%), closely followed by depression (23%; see table 1). The prevalence of depression is strongly increased compared with the general population: in Dutch women, mood disorders were estimated to be present in 4.3% in 2019.[7] Psychiatric medication was frequently used: antidepressants and benzodiazepines were both used in 18% of all patients and antipsychotics in 8% of patients.

The burden of mental health disorders on psychological, social and occupational functioning was assessed by the psychiatrist during the clinic visit using the Global Assessment of Functioning (GAF) as proposed by DSM-IV, with a score from 0 to 100, with 100 indicating good mental health. This score explicitly focuses on mental health and does not take physical disabilities into account. GAF was available for 326 patients (88%) and revealed mild symptoms or impairment (score: 61–70) in 24%, moderately severe symptoms or impairment (score: 51–60) in 22%, and severe symptoms or impairment (41–50 or lower) in 21% of patients.

Our findings confirm that psychiatric disorders are highly prevalent and lead to a high disease burden in patients with SLE. Psychiatric disorders have been recognised as a manifestation of lupus for a long time, and five manifestations have been described in the 1999 American College of Rheumatology (ACR) case definitions for NPSLE: acute confusional state, cognitive dysfunction,

Table 1 Presence of psychiatric diagnoses (n=275)* in patients with SLE visiting the Leiden NPSLE clinic (N=371) with neuropsychiatric symptoms of an inflammatory or a non-inflammatory origin

	All patients (n=371)	Non-inflammatory phenotype (n=291)	Inflammatory phenotype† (n=80)
DSM-5 diagnosis at presentation, number of patients (%)			
Neurodevelopmental Disorders	5 (1)	2 (1)	3 (4) (0/3)‡
Schizophrenia Spectrum and Other Psychotic Disorders	16 (4)	11 (4)	5 (6) (5/5)
Bipolar and Related Disorders	7 (2)	5 (2)	2 (3)
Depressive Disorders	84 (23)	74 (25)	10 (13) (9/10)
Anxiety Disorders	17 (5)	16 (6)	1 (1) (0/1)
Obsessive-Compulsive and Related Disorders	1 (0)	1 (0)	0 (0)
Trauma- and Stressor-Related Disorders	16 (4)	13 (4)	3 (4) (0/3)
Dissociative Disorders	2 (1)	2 (1)	0 (0)
Somatic Symptom and Related Disorders	1 (0)	1 (0)	0 (0)
Feeding and Eating Disorders	0 (0)	0 (0)	0 (0)
Elimination Disorders	0 (0)	0 (0)	0 (0)
Sleep–Wake Disorders	2 (1)	2 (1)	0 (0)
Sexual Dysfunctions	0 (0)	0 (0)	0 (0)
Gender Dysphoria	0 (0)	0 (0)	0 (0)
Disruptive, Impulse-Control and Conduct Disorders	0 (0)	0 (0)	0 (0)
Substance-Related and Addictive Disorders	9 (2)	8 (3)	1 (1) (0/1)
Cognitive Disorders§	93 (25)	60 (21)	33 (41) (16/33)
Personality Disorders	10 (3)	9 (3)	1 (1) (0/1)
Paraphilic Disorders	0 (0)	0 (0)	0 (0)
Other Mental Disorders	12 (3)	7 (2)	5 (6) (0/5)
Medication-Induced Movement Disorders and Other Adverse Effects of Medication	0 (0)	0 (0)	0 (0)
None	131 (35)	107 (37)	24 (30)
Unknown	3 (1)	2 (1)	1 (1)

*240 of 371 patients received a psychiatric diagnosis, of whom 208 received one diagnosis and 32 patients received two or more diagnoses.
†An inflammatory phenotype indicates that neuropsychiatric symptoms were attributed to lupus activity in the multidisciplinary assessment based on clinical, radiological and laboratory assessment. One patient with an inflammatory phenotype had transverse myelitis and a depressive disorder triggered by the somatic disorder.
‡(n/total n) indicates the number of patients with an inflammatory phenotype who received immunosuppressive therapy solely for this specific psychiatric manifestation.
§Cognitive disorder after exclusion of patients with other psychiatric disorders. Acute confusional state is considered a (neuro)cognitive disorder.
DSM-5, Diagnostic and Statistical Manual of Mental Disorders; NPSLE, neuropsychiatric SLE.

mood disorder, psychosis and anxiety disorder.[8] In clinical practice, physicians are often confronted with the question whether these psychiatric manifestations are due to lupus activity and whether immunosuppressive treatment is required. In our experience, immunosuppression is only indicated for psychiatric syndromes in the minority

of cases. After multidisciplinary assessment, 31 patients (13% of all patients with a psychiatric disorder) received immunosuppressive therapy solely for the psychiatric presentation. In decreasing prevalence, these manifestations were cognitive disorders (acute confusional state, n=9; severe cognitive dysfunction, n=7), mood disorder with or without cognitive dysfunction (n=9), and psychosis (n=5). Interestingly, anxiety disorder was infrequently diagnosed in general (5%) and not considered present due to SLE activity in any patient. Cognitive disorders were common (n=154), and after excluding patients with other psychiatric morbidity were present in 93 patients. Of these patients, only 16 received immunosuppressive treatment for their cognitive disorder (10% or 17%, including or excluding other psychiatric morbidities). Although mood disorder was common (84 patients), only in nine cases (11%) immunosuppressive treatment was required. These cases were usually refractory to conventional antidepressant therapy, combined with (severe) cognitive dysfunction and present in combination with systemic inflammation. Psychosis, on the other hand, was a rare manifestation, but more frequently required immunosuppressive treatment (5 of 16, 31%).

Our study is the first to look at a diverse range of psychiatric manifestations in patients with SLE and to evaluate the frequency of psychiatric symptoms as reason for initiating immunosuppressive therapy.

Several limitations have to be acknowledged. During the psychiatric evaluation, more attention is given to specific major diagnoses such as psychosis than, for example, sexual dysfunction, which might have led to an underdiagnosis of some psychiatric disorders. In addition, as it is a single assessment that lasts 1 hour, it is possible that the topics that patients consider harder to address or irrelevant to their current main symptoms (such as traumas) are also underestimated. Furthermore, as data were collected retrospectively from patient files, there was some interphysician variation in the extent of reporting psychiatric findings. However, all psychiatrists reported their main conclusion regarding the current diagnoses in a standardised way; therefore, we expect that this has only influenced the information based on patient history. Lastly, as these are results from a tertiary referral centre, it is expected that the prevalence of psychiatric morbidity is lower in the general lupus population. Nevertheless, our findings regarding the prevalence of depression are similar to those in previous reports on patients with lupus.[1]

In conclusion, these data demonstrate that psychiatric disorders in SLE are common, especially cognitive disorder and depression, and lead to a high disease burden in patients referred for assessment of possible neuropsychiatric lupus. However, even in a tertiary referral centre, only around 10% of the most common psychiatric disorders are primarily caused by lupus activity and require immunosuppressive treatment.

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