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Case Report
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A Remarkable Case of Neuropsychiatric Systemic Lupus Erythematosus

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Abstract

Systemic Lupus Erythematosus (SLE) may manifest with neuropsychiatric symptoms, even in older, male patients. Excluding other diseases is crucial. The Systemic Lupus International Collaborating Clinics (SLICC) criteria may support the diagnosis.

Introduction

Systemic Lupus Erythematosus (SLE) is a complex auto-immune disease [1]. Patients may experience a broad range of symptoms, which makes it challenging to diagnose SLE. The typical presentation is a young female with cutaneous symptoms and arthritis. Cerebral and renal involvement is common, but more or less every organ can be involved [2]. Neuropsychiatric SLE means that the central or peripheral nervous system is damaged [3]. We present a remarkable case of neuropsychiatric SLE, and provide advice on steps in the diagnostic process of this disease.

Case Presentation

A 59-year old male patient of Moroccan origin was admitted because of loss of appetite and body weight, and dehydration. His medical history included arthritis of a knee (1.5 years ago), type 2 diabetes, hypertension and a depression. He did not smoke. Laboratory analyses yielded an elevated erythrocyte sedimentation rate, microcytic anemia, leucopenia and mild elevation of liver enzymes. He did not use medication toxic for the liver. Blood cultures were negative, as were serology and polymerase chain reaction for viral hepatitis, infectious mononucleosis, and HIV. An interferon gamma release assay for tuberculosis (Elispot®) was negative. Chest and abdominal CT-can showed no malignancy or lymphadenopathy. No abnormalities were found at gastroduodenoscopy with biopsy.

We considered an auto-immune disease with liver involvement as one of the differential diagnoses, and found a positive anti-ds DNA test (147 iU/mL), which pointed towards Systemic Lupus Erythematosus (SLE). Additional laboratory tests were performed (Table 1). On patient's request, further management was done as an outpatient. One month later, four months after the start of his illness, he presented with an acute state of confusion, hallucinations and muscle weakness. Physical examination revealed apathy, hypertonia and a tremor in the face and right arm. The anti-dsDNA titre was higher than before (169 iU/mL). A brain CT and MRI showed a specific white matter hyperintensities. The Cerebrospinal Fluid (CSF) contained an elevated protein concentration (1.26 g/L, normal value <0.80 g/L) without leucocytosis (4/μL). Infectious encephalitis was ruled out by negative PCR testing on CSF for several neurotropic viruses, and negative cultures. *Borrelia* serology was negative. An Electro-Encephalogram (EEG) showed signs of diffuse encephalopathy. Serum paraneoplastic antibodies were absent. A chest CT scan, performed because of persistent tachypnea, showed hilar node enlargement and a consolidation in the left lower lobe with pleural effusion. The pleural fluid was an exudate with negative cultures. SLE was diagnosed based on the clinical symptoms (Table 1) and exclusion of other diagnoses. He was treated with methylprednisolone 1000 mg/day intravenously for 3 days, followed by oral prednisone 60 mg/day and cyclophosphamide as induction treatment. His mental and physical state improved substantially over the first 3 days. Currently, he is treated with low dose prednisone and hydroxychloroquine and his illness is in remission.

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Table 1: Systemic Lupus International Collaborating Clinics (SLICC) classification criteria [10].

	Clinical criteria	This case	Reference values
1	**Acute cutaneous lupus**		
	Lupus malarrash		
	Bullous lupus rash		
	Toxicoepidermal necrolysis		
	Maculopapular lupus rash		
	Fotosensitive lupus rash		
2	**Chronic cutaneous lupus**		
	Classic discoid rash		
	Hypertrophic lupus		
	Lupus panniculitis		
	Mucosal lupus		
	Lupus erythematosus tumidus		
	Chillblains lupus		
3	**Oral or nasal ulcers**		
4	**Alopecia**		
5	**Synovitis** of ≥ 2 joints, or pain in ≥ 2 joints with ≥ 30 min morning stiffness		
6	**Serositis**		
	Pleuritis		
	Pericarditis		
7	**Renal disorder**		
	≥ 500 mg urine protein/24 h		
	Red bloodcell casts		
8	**Neurologic**		
	Seizures		
	Psychosis		
	Mononeuritis multiplex		
	Myelitis		
	Peripheral or cranial neuropathy		
	Acute confusional state		
9	**Hemolytic anemia**		
10	**Leukopenia <4.0 10^9/L**	1.1 × 10^9/L	3.0-10.0 × 10^9/L
	Lymphopenia <1.0 10^9/L	0.1 × 10^9/L	0.8-3.7 × 10^9/L
11	**Thrombocytopenia <100 10^9/L**		
	Immunologic criteria		
1	**Anti-nuclear antibodies**	Positive	Negative
2	**Anti-ds DNA antibodies**	169	≤ 15 iU/mL
3	**Anti-Sm antibodies**		
4	**Antiphospholipid antibodies**		
	Positive lupus anticoagulant	Negative	Negative
	False positive test for syphilis	Negative	Negative
	Anticardiolipin antibodies (IgA, IgM of IgG)	IgG: 24	<10 GPL-U/mL
		IgM: 28	<10 MPL-U/mL
	Anti-bèta 2 glycoprotein I (IgA, IgM of IgG)	IgG: 6,7	<7 U/mL
		IgM: 13	<7 U/mL
5.	**Low complement**		
	Low C3	0.77	0.90-2.05 g/L
	Low C4	0.06	0.15-0.45 g/L
	Low CH50		
6.	**Direct Coombs test without hemolysis**		

Table 2: Neuropsychiatric SLE symptoms according to the American College of Rheumatology [3].

Central nervous system
Aseptic meningitis
Cerebrovascular disease
Demyelinisation syndrome
Headache (including migraine en benigne intracranial hypertension)
Movement disorder (chorea)
Myelopathy
Epileptic insults
Acute consfusional state
Anxiety disorder
Cognitive dysfunction
Mood disorder
Psychosis
Peripheral nervous system
Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome)
Autonomic dysfunction
Mononeuropathy/multiple mononeuropathy
Myasthenia gravis
Cranial nerve dysfunction
Plexopathy
Polyneuropathy

Discussion

The typical SLE patient is a 15 to 50 year's old female with cutaneous manifestations. Atypical neurologic symptoms like a headache and mood disorder are prevalent among SLE patients, but severe neurologic symptoms are rare with an incidence of 8 per 100 person years [4]. Table 2 presents all possible cerebral SLE manifestations. Cerebral involvement early in the disease process is uncommon, especially for a male patient aged 59 years. In the work-up of a clinical presentation with cerebral symptoms, one should therefore exclude an electrolyte/metabolic disturbance, acidosis, uremia, and infection; including a lumbare puncture to exclude punctureto exclude encephalitis or meningitis. An intoxication or psychiatric illness should also be considered. If these examinations do not lead to a diagnosis, an EEG and cerebral MRI are indicated to exclude demyelination, thromboembolic process, or ischemic event. Neuropsychiatric SLE should be considered at this stage. The Systemic Lupus International Collaborating Clinics (SLICC) classification criteria are not diagnostic, but may guide further examinations. There is not a single test, or combination of tests, which proves or rejects the diagnosis neuropsychiatric SLE with sufficient certainty. For example, a recent Chinese study found that 34% of patients with neuropsychiatric SLE did not have any abnormalities on an MRI of the brain [5]. The presence of specific antibodies in the liquor makes the diagnosis neuropsychiatric SLE more likely. Besides antiphospholipid antibodies, previous studies found anti-ribosomal P, anti-neuronal and anti-N-Methyl-D-Aspartate (NMDA) receptor antibodies to be present in patients with neuropsychiatric SLE [6]. However, the cornerstone in the diagnostic process remains anamnesis and physical examination. Excluding differential diagnoses is crucial. In our patient, anticardiolipin antibodies were present. Antiphospholipid antibodies are detected in 20% to 30% of patients with SLE, especially those with neuropsychiatric involvement. Their presence gives an absolute yearly risk of thrombosis of about 5% [7]. The Antiphospholipid Syndrome (APS) is defined as repeatedly detected antiphospholipid antibodies, and thrombotic manifestations. In the absence of thrombosis, the diagnosis APS was not made in our patient. SLE patients have a 3 times higher risk of premature death compared to the general population [2]. Most important causes of death are end-stage renal failure and infections, potentially partly due to nephrotoxic medication and immunosuppressants. Lupus cerebritis, which was present in our patient, is a rare cause of death [8]. Major neuropsychiatric SLE manifestations, like cerebral ischemia, seizures and psychosis, are associated with an even worse prognosis than generalized SLE activity without neuropsychiatric manifestations [9]. Combining glucocorticoids and immunosuppressive therapy results in 60-80% of these patients in quick improvement with disappearance of symptoms within 2 to 4 weeks. However, relapses occur in up to 50% of patients [10].

Conclusion

This case shows that neuropsychiatric SLE should be considered if a patient presents with inexplicable neurologic symptoms, even if the patient does not fit the typical SLE profile (i.e. young female with cutaneous manifestations).

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