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### Plasma Exchange in Patients with Stuporous Catatonia and Systemic Lupus Erythematosus

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Catatonia is a rare but severe psychiatric condition. The most frequent causes are psychiatric diseases (e.g. schizophrenia), but organic causes should be considered as well (e.g. Wilson's disease) [1]. The recommended treatments are symptomatic and include the use of sedative drugs and electroconvulsive therapy (ECT) [1]. Although rare cases of catatonia have been described in systemic lupus erythematosus (SLE) [2], catatonia was not included in the recent nomenclature of neuropsychiatric SLE [3]. In a recent report, we showed that plasma exchanges (PE) could be an efficient treatment option for catatonic manifestations of SLE, avoiding the use of ECT [4]. The aim of the present study was to assess the efficacy of PE for severely resistant patients with catatonia and SLE in an open trial.

The consecutive patients were recruited at Pitié-Salpêtrière Hospital from 2001 to 2004. For inclusion, the diagnosis of SLE was based on the revised criteria of the American College of Rheumatology [3]. The diagnosis of catatonia was made based on at least two catatonic motor signs, or one catatonic motor sign (catalepsy, stupor, posturing, waxy flexibility, staring, stereotypies, psychomotor excitement, automatic compulsive movements, muscular rigidity, echopraxia) combined with a nonmotor catatonic symptom indicative of severely impaired behavioral and emotional functioning (withdrawal, mutism, mannerism, echolalia, incontinence, verbigeration, refusal to eat) [5]. Clinical examinations by a psychiatrist and a physician specializing in internal medicine were repeated as needed. Psychiatric diagnoses were based on DSM-IV criteria. Additional investigations always included routine hematological tests, immunological investigations, studies of cerebrospinal fluid, electroencephalography, and neuroimaging. All patients received a symptomatic psychiatric treatment (benzodiazepine for motor symptoms, antidepressant for depression, atypical neuroleptic for psychosis and mood stabilizer for bipolarity) combined with (a) high-dose intravenous methylprednisone (1 g/day  $\times$  3) followed by oral prednisone (1 mg/kg/day), and (b) monthly pulse cyclophosphamide (0.7 g/m<sup>2</sup>) or azathioprine (2–3 mg/kg/day). In case of life-threatening conditions, severe complications of SLE or resistance to pharmacotherapy for 3 weeks, patients were asked to receive PE and written consent was obtained (from them or their families). PE (60 ml/kg) was given 2–3 times per week. Treatment efficacy was monitored using the Clinical Global Impression-Severity Scale, the Global Assessment of Functioning Scale, the modified Bush-Francis Catatonia Rating Scale (CRS) [5], the Mont-

gomery-Asberg Depression Rating Scale, the Brief Psychiatric Rating Scale and the SLE Disease Activity Index (SLEDAI) [6]. Because of their clinical specificity, the CRS and the SLEDAI were the primary variables. For the comparison of pre- and postclinical scores, we used a nonparametric test which needs a minimum of 5 patients to reach a 0.05 significance.

During the course of the study, 5 patients were admitted with SLE and catatonia. These 5 patients, all female, met the inclusion criteria. All of them (or their families on their behalf) agreed to PE. Three of the patients were teenagers who had been hospitalized for several weeks without any improvement, receiving a treatment regimen combining psychotropic medications, corticoids and immunosuppressors. Three patients exhibited life-threatening complications: 2 were severely malnourished and the third had a pulmonary infection and skin lesions due to immobility. One patient showed a severe renal involvement. The last patient was included because of resistance after 3 weeks of treatment.

Table 1 summarizes the demographic, clinical and biological characteristics, and treatments of all subjects both before and after PE. All patients had severe depression with psychotic and catatonic features. The number of catatonic signs ranged from 6 to 12, with staring, negativism and withdrawal being present in all 5 patients, and catalepsy, stupor, mutism and refusal to eat in 4. Regarding SLE, the clinical and biological manifestations varied across individuals and included asthenia (n = 5), polyarthralgia (n = 3), renal involvement (n = 3), cutaneous lesions (n = 3), weight loss (n = 2), myalgia (n = 1), generalized adenopathy (n = 1) and melena (n = 1). One patient had an abnormal neurological examination limited to moderate ataxia. All patients had biological features of SLE. Routine biological and hematological tests showed anemia (n = 3), thrombocytopenia (n = 2), lymphopenia (n = 2) and proteinuria (n = 3). The cerebrospinal fluid showed biochemical abnormalities in 3 patients but none of them had monoclonal immunoglobulin G or cell increase. MRI scans showed abnormalities in 3 patients, including cortical atrophy (n = 2) and T<sub>2</sub>-weighted hyperintensities of the frontal lobes (n = 1).

The mean number of PE that patients received was 7.2 (range: 3–11). We found a significant improvement for all clinical variables. Mean CRS and SLEDAI scores before PE were 15 (range: 11–16) and 18.8 (range: 12–22), respectively. Both scores dramatically decreased after PE to a mean of 1.2 (range: 0–6) and 3.4 (range: 0–12), respectively (Wilcoxon paired test:  $Z = -2.032$ ,  $p = 0.042$ ). In particular, 3 patients very much improved on the Clinical Global Impression Scale after the first week of PE. The biological variables paralleled clinical improvement. At follow-up, 4 patients were still doing well; in particular, all the teenagers were able to return to school with minimal treatment for SLE. The last patient (case 4) died in her local hospital as a consequence of a septic shock 3 months after discharge.

To date, only a few case studies have reported the possible use of PE in neuropsychiatric SLE [7, 8], but catatonia was not explored. Therapeutic approaches to catatonia are mainly symptomatic. It is recommended (a) to use high doses of benzodiazepines or sedative drugs, and (b) to apply ECT in case of resistance or life-threatening conditions [1]. However, treatment of associated disorders may improve psychomotor symptoms as well. This is important when there are organic causes. Therefore, etiopathogenic investigations are mandatory when catatonia occurs [9]. In the cases studied here, benzodiazepines were inefficient, and ECT was not considered because of the associated SLE. The report that PE was an efficient treatment option for pediatric autoimmune neuropsychiatric disorders associ-

**Table 1.** Clinical characteristics and efficacy of PE in 5 patients with SLE and catatonia

Variable	Case 1		Case 2		Case 3		Case 4		Case 5	
Age, years	15		17		16		41		47	
Gender	F		F		F		F		F	
Duration of SLE, months	6		36		12		24		120	
DSM-IV diagnosis	MDE-psychotic		MDE-psychotic		MDE-psychotic		MDE-psychotic		MDE-psychotic	
Clinical variables	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE
CGI-S <sup>1</sup>	7	2	7	3	7	3	7	5	7	3
GAF <sup>1</sup>	21	72	20	65	15	59	21	40	21	90
MADRS <sup>1</sup>	46	0	40	20	39	13	47	36	50	6
CRS <sup>1</sup>	16	0	16	0	18	0	14	6	11	0
BPRS <sup>1</sup>	64	20	46	23	52	24	65	49	57	19
SLEDAI <sup>1</sup>	20	0	12	3	22	0	20	12	20	2
Biological variables										
Antinuclear antibody <sup>2</sup>	10,000	640	5,120	1,280	5,120	1,280	2,560	640	2,560	320
Anti-DNA antibody <sup>2</sup>	12	<4	5	<4	<4	<4	23	27	68	<4
C3 <sup>2</sup>	0.65	0.83	0.99	0.78	1.14	0.95	0.85	0.43	0.62	0.79
Antiribosomal P antibody <sup>2</sup>	1,290	<15	1	1	1	2	900	300	13	2
CSF	NL		NL		IgG		PROT		GLUC	
Treatment regimen										
PE	6		6		10		11		3	
Pulse cyclophosphamide	yes		yes		yes		no		no/azathioprine	
Steroids	yes		yes		yes		yes		yes	
Hydroxychloroquine	yes		no		yes		no		yes	
Psychotropic drugs	lorazepam, fluoxetine, risperidone		lorazepam, fluoxetine, valproate, olanzapine		lorazepam, mianserin		risperidone		clorazepate, paroxetine, valproate	
Variables at follow-up	2 years		1 year		1 year		3 months		4 years	
CGI-S	1		2		1		dead		2	
GAF	90		73		85				80	
SLEDAI	0		0		0				0	

MDE-psychotic = Major depressive episode with psychotic features; CGI = Clinical Global Impression Scale; MADRS = Montgomery-Asberg Depression Rating Scale; BPRS = Brief Psychiatric Rating Scale; C3 = complement fraction 3; NL = normal; PROT = / proteins; IgG = / polyclonal immunoglobulin G; GLUC = / glucose.

<sup>1</sup>  $p < 0.05$  (Wilcoxon paired test). <sup>2</sup> Post-PE values of biological variables correspond to values measured 1 month after the last PE.

ated with streptococcal infections [10] suggested that neuropsychiatric symptoms related to immune dysfunction – such as SLE – could be improved by an immunomodulatory treatment as well. In this series, the dramatic clinical improvement following PE in all patients suggests that the use of PE, combined with high-dose steroids and cyclophosphamide pulses, may be an efficient treatment option in SLE-related catatonia. However, more research is needed to definitively establish PE as an efficient treatment option in SLE-related catatonia.

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