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Brief Report

Juvenile Parkinsonism as a Manifestation of Systemic Lupus Erythematosus: Case Report and Review of the Literature

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Abstract: Involvement of the central nervous system in systemic lupus erythematosus (SLE) has been well described. It usually includes psychiatric disturbance, seizures, and cranial nerve disorders. Movement disorders are less common, chorea being the one most frequently described. A parkinsonian syndrome may be an extremely rare manifestation of cerebral lupus. We report on a case of juvenile parkinsonism as a manifestation of SLE and review the literature. © 2002 Movement Disorder Society

Key words: parkinsonism; Parkinson's disease; systemic lupus erythematosus

Juvenile parkinsonism (JP) is a rare disorder that probably represents several different diseases. It has been arbitrarily defined that symptoms start before the age of 21 years. These patients suffer motor fluctuations and dyskinesias more commonly, earlier, and more severely than those affected by idiopathic Parkinson's disease (PD).[1] In systemic lupus erythematosus (SLE), involvement of the central nervous system (CNS) is well recognized and usually includes psychiatric disturbance, seizures, and cranial nerve disorders. Movement disorders are rarer, and the most frequently described is chorea.[2,3] A parkinsonian syndrome (PS) may be an extremely unusual manifestation of CNS lupus. We report on a case of CNS lupus and JP as manifestations of SLE and review the literature.

CASE REPORT

A 20-year-old, left-handed, Gypsy female patient developed bradykinesia and painful dystonia of the left arm at the age of 15 years. Three months later, she had resting and static tremor in this arm, bradykinesia and resting tremor in the left leg, and dystonic postures of both feet. At the age of 18, she was admitted for the first time to the hospital because of dysphagia. She also complained of asthenia, anorexia, weight loss, and thoracic and abdominal pain. Her past medical history revealed myalgia and arthralgia since age 10. Her family history was negative. General physical examination only showed livedo reticularis on her thighs and arms. Neurological examination showed a conscious but bradypsychic patient with mild memory disturbance, who appeared sad and with a tendency to cry. She had expressionless facial features, and her speech was slow and monotonous, almost unintelligible. Marked resting and static tremor, bradykinesia, and rigidity of the four extremities were noted, more prominent on the left. Generalized hyperreflexia and bilateral Babinski sign were noted. At rest, she showed dystonic postures of neck, shoulders, hands, and feet, which disappeared with action. She needed more than one attempt to rise from a chair and she walked very slowly, without swinging her arms and with short steps. Her pull test showed retropulsion but she recovered unaided.

She was diagnosed with JP and was screened for causes of secondary parkinsonism. Laboratory data were

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as follows: anaemia (red blood cell count, 3.8×10^6/mm^3; haemoglobin, 11.8 g/dl; hematocrit 33.7%), lymphopenia (840/mm^3), and erythrocyte sedimentation rate of 41 mm per hour. Coagulation study showed a prothrombin time of 15.7 seconds (normal, 11.0–13.0 seconds) and an activated partial thromboplastin time of 40 seconds (normal, 25.0–38.0 seconds). A combined deficiency of all coagulation factors of the intrinsic pathway, especially of factors VIII (46%) and XII (28%), was noted. No acanthocytes were detected. General biochemistry, lipid profile, hepatitis markers, rheumatological tests, parathyroid and thyroid hormones, proteins, tumoral markers, levels of vitamin B12 and folic acid were normal. Arsenic, lead, mercury, and copper levels were negative in blood and urine. Ceruloplasmin level was normal. Immunological study showed a decrease of CD4/CD8 ratio (0.44%), immunoglobulin (Ig) G and IgM hypergammaglobulinemia (2,035 and 442 mg/dl, respectively), C4 hypocomplementemia (11 mg/dl), and the presence of circulating immune complexes (34.2 μg/dl). The antinuclear antibody (ANA) test was positive on three occasions with a speckled pattern at the titer of 1:320. Anti-ds DNA antibody was also positive (23.8 U/ml; normal < 6 U/ml). Extractable nuclear antigens (i.e., anti-Ro/SS-A, anti-La/SS-B, anti-Sm, and anti-RNP) were negative. Neither LE phenomenon nor circulating lupus anticoagulants were detected. Cold autoagglutinins were positive. Serological test for syphilis showed a false-positive VDRL (negative FTA-abs) and IgG and IgM anticardiolipin antibodies were positive at low titers (18 and 22 GPL/ml, respectively; normal < 15). *Borrelia burgodorferi*, human immunodeficiency vires, cytomegalovirus, Epstein-Barr virus, and influenza A and B viruses serology were negative. Urinalysis showed proteinuria (730 mg/day) with a global hyperaminoaciduria. Oligopolysaccharides, mucopolysaccharides, and glycosphingolipid levels in serum and urine were normal. A cerebrospinal fluid (CSF) study was refused by the patient. Findings on electrocardiogram, chest X-rays, carotid and vertebral arterial Doppler ultrasonography, electroencephalogram, cervical computed tomography (CT) scan, and cranial CT and magnetic resonance imaging (MRI) scans were normal. Cerebral angiography and single photon emission computed tomography (SPECT) were refused by the patient. Ophthalmological examination excluded the presence of Kayser-Fleischer ring. Bone marrow and skin biopsy were normal, and hepatic biopsy was refused. A diagnosis of SLE was established on American Rheumatism Association criteria.[4] Steroid pulse therapy (1 g daily of methylprednisolone for 3 days) was given followed by 30 mg daily of oral prednisolone. The PS improved dramatically, and the patient was discharged. Six months later, she was readmitted to our department because of a new impairment by the parkinsonian symptoms. Another methylprednisolone pulse was given followed by 60 mg a day of oral prednisolone with little improvement. Treatment with levodopa (L-dopa; 300 mg/day) and bromocriptine (15 mg/day) resulted in a good benefit but with residual functional disability. After 6 months, she experienced *on–off* motor fluctuations and severe bilateral peak-dose chorea and *off*-period painful dystonia. These motor complications were never controlled with conventional therapy with L-dopa (1,000 mg/day) and bromocriptine (40 mg/day), despite increasing the number of intakes and decreasing their intervals (total dose of L-dopa and bromocriptine divided into nine dosages every 2 hours), nor with a levodopa/carbidopa/ascorbic acid solution orally at hourly intervals (1,000 mg/L water/day of L-dopa divided in 17 intakes, i.e., 58.8 mg of L-dopa/hour). At the age of 20, we programmed the bilateral implantation of VIM thalamic stimulators, after which dyskinesia were less disabling and affected just her right side. Before her discharge, another methylprednisolone pulse was administered and further improvement was achieved. She was discharged with L-dopa solution orally at hourly intervals (52.9 mg of L-dopa/hour for 17 intakes) and 30 mg/day of oral prednisone. Six months later, the initial improvement was sustained.

LITERATURE REVIEW

It is possible that the first cases of parkinsonism associated with SLE were described by Seminario and Pesano in 1930, who reported 4 patients with SLE who developed "cigarette rolling" tremor with rigidity "resembling paralysis agitans."[5] Thirty years later Poch, in his book *Enfermedades del Colágeno: Manifestaciones neurológicas, musculares y psiquiátricas,* described 4 other SLE patients with cogwheel rigidity without tremor that he called "cogwheel rigidity pseudosign" because he could not prove its extrapyramidal nature.[6] Willoughby and colleagues described a 30-year-old male SLE patient with cogwheel rigidity of the arms and right Babinski sign who died from meningitis and endocarditis and who was diagnosed with "parkinsonism secondary to vasculitis or brain abscess in the left hemisphere." Their autopsy revealed multiple areas of encephalomalacia in the basal ganglia.[7] In 1981, Yancey and associates reported on a series of 37 children with SLE 2 cases with parkinsonism: cogwheel rigidity in 1 child and parkinsonian-like symptoms with paraparesis in a 16-year-old girl who gradually lapsed into a coma lasting for 2 months, but subsequently, made a nearly complete functional recovery within 3 months. Although the authors did not de-

scribe how they treated each particular case, apparently all children with neurolupus received oral prednisone in high doses (2 mg/kg/day). Some of them derived benefit from pulse steroids (30 mg/kg methylprednisolone) and cytotoxic agents (cyclophosphamide or azathioprine).[8] Nagakoa and coworkers described a 35-year-old woman with SLE associated with akinesia, muscle rigidity, and neurogenic bladder whose parkinsonian symptoms were controlled by 40 mg daily of methylprednisolone and antiparkinsonian drugs.[9] Kunas and colleagues reported the presence of antibodies against dopaminergic cells (anti-DA) in a 34-year-old woman with SLE and a complex autoimmune disorder associated with a rapidly progressing PD and with a normal cranial MRI.[10] Miyoshi and associates reported a 39-year-old woman diagnosed with SLE who, 3 years later, was admitted to hospital for disorientation, sleep disturbance, and anxiety. Her neurological examination showed hypomimia, slow and monotonous speech, cogwheel rigidity, short-stepped gait, pill-rolling tremor, akinesia, hyperreflexia, and bilateral Babinski sign. Cranial MRI showed no focal findings of ischemia or demyelination in the striatonigral region. After high-dose corticosteroid and pulse therapy, her parkinsonian symptoms dramatically improved and antiparkinsonian drugs were not necessary.[11] Osawa and coworkers described a 31-year-old woman who, 10 years after her SLE diagnosis, developed transverse myelitis that resolved after pulse methylprednisolone but who, after reduction of steroid, developed a PS with rigidity, akinesia, hypomimia, and hypophonia, which improved with L-dopa therapy.[12] Shahar and colleagues reported on 3 girls, 15, 16, and 12 years old, respectively, with florid PS complicating SLE. The first one presented with rigidity, akinesia, swallowing difficulties, irritability, and mutism; the second girl presented bradykinesia and apathy. Both of them had normal findings on cranial MRI scans, and ^{99m}Tc-HmPAO SPECT cerebral scanning detected decreased regional cerebral blood flow at the basal ganglia. Both patients improved after antiparkinsonian treatment. The third patient was referred after completion of the manuscript; therefore, the study was not completed. She showed an overt parkinsonism represented by hypomimia, marked bradykinesia, swallowing difficulties, and cogwheel rigidity, along with brisk deep tendon reflexes and extensor plantar responses.[13] Lim and associates reported on a young male patient who presented with steroid-responsive parkinsonism, posthemiplegic dystonia, thrombopenia, and systemic illness who was diagnosed with SLE and in whose MRI scan thalamic lesions were demonstrated.[14] We described a 16-year-old adolescent with JP and serological SLE data without other clinical manifestations of SLE and normal findings on brain MRI scan.[15] Kwong and associates reported on 2 girls with SLE who developed extrapyramidal parkinsonian features after an initial stormy course. One patient presented with generalized tonic clonic seizure and was then noted to have akinetic mutism and masked face. EEG showed generalized slowing of background. Brain MRI scan showed symmetrical low signal intensity on T1-weighted images and high signal intensity on T2-weighted images in caudate nucleus, putamen, and external capsule. The second patient was found unconscious and then developed bradykinesia, mutism, and shuffling gait. A suppressed and slow EEG background was observed. Brain MRI showed hyperintense signals in right lentiform nucleus and external capsule on T2-weighted images. In both patients, cerebral SPECT demonstrated hypoperfusion in basal ganglia, but the authors did not mention the radioisotope used. Both of the patients improved after intravenous immunoglobulin therapy.[16] Recently, Tan and coworkers described a patient with SLE and parkinsonism with enhancing subcortical lesions on MRI scan who improved after treatment with prednisolone and cyclophosphamide. A brain CT scan showed basal ganglia calcifications. Another MRI, 3 months after treatment, demonstrated resolution of the abnormal subcortical white matter enhancement.[17]

RESULTS

After an extensive review of the literature, we have found 14 reports with 25 cases of probable parkinsonism associated with SLE.[5–17] The general and neurological clinical manifestations of SLE in these cases are summarized in Tables 1, 2, and 3. There were 18 women (85%) and 3 men (15%). Their mean age was 22.4 years (range, 9–57 years). The most frequent general manifestations were arthralgia (56%) and cutaneous lesions (56%), followed by constitutional syndrome (43%) and fever (43%). Four patients had Raynaud's phenomenon. Among extrapyramidal signs, rigidity was the most frequent manifestation, followed by akinesia (91% and 52%, respectively). Tremor was present only in 10 patients (43%). The main syndrome associated was a pyramidal syndrome with hyperreflexia and Babinski sign, often bilateral, present in at least 7 patients (30%). One patient presented with transverse myelitis and another with hemiplegia; 2 other patients had paraparesis with areflexia. No case of oculogyric crises, cranial nerve palsy, or cerebellar dysfunction was found. Neither respiratory disturbance nor sleep-cycle alterations were reported. Three patients had signs compatible with peripheral neuropathy. Four patients had seizures. Some striking associations included altered consciousness and

TABLE 1. *Parkinsonism and systemic lupus erythematosus*

Author (ref.)	Sex/age (yr)	General clinical features of SLE
Seminario and Pessano[5]	M/17	Constitutional syndrome, fever, arthralgias, cutaneous lesions, hepatosplenomegaly, aortectasia, pneumonia
Seminario and Pessano[5]	F/19	Constitutional syndrome, fever, arthralgias, myalgias, cutaneous lesions, lymphadenopathy, aortectasia,
Seminario and Pessano[5]	F/30	Constitutional syndrome, fever, arthralgias, cutaneous lesions, hepatomegaly, lymphadenopathy, pneumonia
Seminario and Pessano[5]	F/23	Constitutional syndrome, fever, arthralgias, cutaneous lesions, pneumonia
Poch[6]	F/21	Constitutional syndrome, arthralgias, myalgias, cutaneous lesions, Raynaud's phenomenon
Poch[6]	F/43	Livedo reticularis
Poch[6]	F/27	Fever
Poch[6]	F/28	Constitutional syndrome, fever, arthralgias, myalgias, cutaneous lesions
Willoughby et al.[7]	M/30	Constitutional syndrome, fever, arthralgias, myalgias, cutaneous lesions, hepatosplenomegaly, lymphadenopathy, pneumonia, myocardial ischemia, nephropathy
Yancey et al.[8]	N	N
Yancey et al.[8]	F/16	N
Nagaoka et al.[9]	F/35	Arthralgias, cutaneous lesions, Raynaud's phenomenon
Kunas et al.[10]	F/34	Fever, arthralgias, cutaneous lesions, Raynaud's phenomenon, thyroiditis, vitiligo
Miyoshi et al.[11]	F/42	Arthralgias, cutaneous lesions, Raynaud's phenomenon
Osawa et al.[12]	F/31	Arthralgias, cutaneous lesions
Shahar et al.[13]	F/15	N
Shahar et al.[13]	F/16	Constitutional syndrome, arthralgias, alopecia
Shahar et al.[13]	F/12	N
Lim et al.[14]	M/24	Constitutional syndrome, fever, arthralgias
Chacón et al.[15]	F/16	N
Kwong et al.[16]	F/9	Fever, cutaneous lesions, lymphadenopathy
Kwong et al.[16]	F/12	Cutaneous lesions, lymphadenopathy
Tan et al.[17]	F/57	N
This report	F/15	Constitutional syndrome, arthralgias, myalgias, livedo reticularis, precordial pain, abdominal pain

N, not done or not testable.

TABLE 2. *Parkinsonism and systemic lupus erythematosus: Neurological clinical findings, treatment, and outcome*

Author (ref)	Sex/ age (yr)	Tremor	Rigidity	Akinesia	Abnormal speech*	Masked facies	Short-stepped gait	Increased DTR	Babinski
Seminario and Pessano[5]	M/17	+	+	N	N	N	N	N	N
Seminario and Pessano[5]	F/19	+	+	N	N	N	N	N	N
Seminario and Pessano[5]	F/30	+	+	N	N	N	N	N	N
Seminario and Pessano[5]	F/23	+	+	N	N	N	N	N	N
Poch[6]	F/21	N	+	N	N	N	N	N	N
Poch[6]	F/43	N	+	N	N	N	N	N	N
Poch[6]	F/27	N	+	N	N	N	N	N	N
Poch[6]	F/28	N	+	N	N	N	N	N	N
Willoughby et al.[7]	M/30	N	+	N	N	N	N	+	+
Yancey et al.[8]	N	N	+	N	N	N	N	N	N
Yancey et al.[8]	F/16	N	N	N	N	N	N	N	N
Nagaoka et al.[9]	F/35	N	+	+	N	N	N	N	N
Kunas et al.[10]	F/34	+	+	+	N	N	N	N	N
Miyoshi et al.[11]	F/42	+	+	+	+	+	+	+	+
Osawa et al.[12]	F/31	N	+	+	+	+	N	N	+
Shahar et al.[13]	F/15	+	+	+	+	+	N	+	+
Shahar et al.[13]	F/16	N	+	+	N	+	+	+	+
Shahar et al.[13]	F/12	N	+	+	N	+	N	+	+
Lim et al.[14]	M/24	−	+	+	+	+	+	N	+
Chacón et al.[15]	F/16	+	+	+	N	N	+	N	N
Kwong et al.[16]	F/9	+	N	+	N	+	N	N	N
Kwong et al.[16]	F/12	N	+	+	+	+	+	+	+
Tan et al.[17]	F/57	−	+	+	+	+	+	N	N
This report	F/15	+	+	+	+	+	+	+	+

*Speech low, sparse, monotonous.
DTR, deep tendon reflexes; +, present or abnormal; −, normal or absent; N, not done or not testable.

TABLE 3. *Parkinsonism and systemic lupus erythematosus: Neurological clinical findings, treatment, and outcome (continuation)*

Author (ref.)	Sex/ age (yr)	Incontinence	Altered consciousness	Psychiatric	Others features	Treatment	Outcome
Seminario and Pessano[5]	M/17	N	N	N	Insomnia, neuritic pain	N	Death
Seminario and Pessano[5]	F/19	N	N	+, depression	Dizziness	N	Death
Seminario and Pessano[5]	F/30	N	N	N	Insomnia, migraine	N	Death
Seminario and Pessano[5]	F/23	N	N	N	Photophobia	N	Death
Poch[6]	F/21	N	N	N	Headache, hyporeflexia	N	N
Poch[6]	F/43	N	N	N	Paraparesis, areflexia, sensory level L_3-L_4, Romberg	N	N
Poch[6]	F/27	N	N	N	Headache, areflexia, "glove and stocking" hypoesthesia	C	Improvement
Poch[6]	F/28	N	N	N	Hyporreflexia, sock hypoesthesia, seizures	N	N
Willoughby et al.[7]	M/30	N	+	N	Meningitis, seizures	C	Death
Yancey et al.[8]	N	N	N	N	N	N	N
Yancey et al.[8]	F/16	+	+	+	Paraparesis, areflexia	N	Improvement
Nagaoka et al.[9]	F/35	+	N	+	Neurogenic bladder	C + APD	Improvement
Kunas et al.[10]	F/34	N	N	+	Concentration difficulty, memory disturbance	APD	Improvement
Miyoshi et al.[11]	F/42	N	N	+	Disorientation, sleep disturbance, akathisia	C	Improvement
Osawa et al.[12]	F/31	N	+, coma	+, psychosis	Spastic paraplegia, sensory disturbance	C + PP + APD + Cy	Improvement
Shahar et al.[13]	F/15	N	+	+, psychosis	Disorientation, mutism, akathisia	APD	Recovery
Shahar et al.[13]	F/16	N	N	+, depression	Memory disturbance	APD	Improvement
Shahar et al.[13]	F/12	N	N	+, depression	Frontal phenomena	APD	N
Lim et al.[14]	M/24	N	N	N	Headache, hemiplegia	C + Cy	Improvement
Chacón et al.[15]	F/16	N	N	N	N	APD	Improvement
Kwong et al.[16]	F/9	N	+	N	Mutism, seizures, hemiplegia	C + Cy + IgG	Recovery
Kwong et al.[16]	F/12	N	+	N	Mutism, seizures	C + Cy + IgG	Recovery
Tan et al.[17]	F/57	–	–	+, depression	N	C + Cy	Improvement
This report	F/15	–	–	+, depression	Bradyphrenia, memory disturbance, *on-off* fluctuation	APD + C + surgery	Improvement

N, not done or not testable; +, present or abnormal; C, corticoids; APD, antiparkinsonian drugs; PP, plasmapheresis; Cy, cyclophosphamide; IgG, immunoglobulin G; –, normal or absent.

neuropsychiatric manifestations (memory disturbances, mutism, disorientation, depression, and psychosis). Table 4 summarizes published diagnostic investigations carried out in patients. The data are partial in most of the reports, and they do not allow one to draw solid conclusions. However, is notable that the finding of anaemia was inconsistent, thrombocytopenia only was present in three of the cases, lymphopenia was found in only 4 cases but proteinuria was a constant finding. ANAs were positive, but mostly at not very high titers except for the cases of Miyoshi and colleagues and Tan and associates.[11,17] CSF studies were infrequently reported, and no conclusion can be drawn. However, it is notable to state the presence of a mild pleocytosis in the Miyoshi and Osawa's cases (28 and 11 cells/ml, respectively), an abnormal IgG index, which was 0.79 (normal, below 0.6), indicating intrathecal IgG production in the Kuna's case and an elevated protein level of 62 mg/dl in the first patient of the Kwong' series.[10–12,16] We believe that the pleocytosis (8,000 cells/ml) and the high protein level (155 mg/dl) in the case of Willoughby cannot be taken into account because the patient was diagnosed of meningitis.[7] An abnormal EEG, characterized by generalized diffuse slowing, was documented in 9 of 12 patients (75%). Cranial CT scan obtained in 6 patients was normal in all of them. Brain MRI showed basal ganglia abnormalities in 4 of the 11 cases in whom it was performed. Brain SPECT showed functional abnormalities in all the patients examined by this method but, unfortunately, the radioisotope used was mentioned only in the report by Shahar and coworkers.[13] The only case autopsied had multiple areas of encephalomalacia in the basal ganglia.[7] All of the patients improved after treatment, with the exception of the cases described by Seminario and Pessano in the 1930s, before the steroid era, and the dramatic case, reported by Willoughby and colleagues,

TABLE 4. *Parkinsonism and systemic lupus erythematosus: Laboratory, electroencephalographic, and imaging findings*

Author (ref.)	Sex/ age (yr)	ESR	Anemia	Lymphopenia	Thrombopenia	Proteinuria	ANA	Anti-DNA	Anti-SM	EEG	MRI	SPECT
Seminario and Pessano[5]	M/17	N	+	N	N	N	N	N	N	N	N	N
Seminario and Pessano[5]	F/19	N	N	N	N	+	N	N	N	N	N	N
Seminario and Pessano[5]	F/30	N	N	N	N	N	N	N	N	N	N	N
Seminario and Pessano[5]	F/23	N	N	N	N	+	N	N	N	N	N	N
Poch[6]	F/21	113	–	–	–	–	N	N	N	N	N	N
Poch[6]	F/43	N	N	N	N	N	N	N	N	N	N	N
Poch[6]	F/27	86	–	–	–	+	N	N	N	N	N	N
Poch[6]	F/28	98	–	–	–	N	N	N	N	N	N	N
Willoughby et al.[7a]	M/30	N	+	–	–	+	N	N	N	+	N	N
Yancey et al.[8]	N	N	N	N	N	N	N	N	N	+	N	N
Yancey et al.[8]	F/16	N	N	N	N	N	N	N	N	+	N	N
Nagaoka et al.[9]	F/35	46	+	–	N	+	1:320	56	160	N	N	N
Kunas et al.[10]	F/34	20	N	N	N	N	1:320	–	N	N	–	+
Miyoshi et al.[11]	F/42	70	+	–	–	+	1:1280	43	71	–	–	N
Osawa et al.[12]	F/31	12	–	–	–	N	1:40	5	N	+	–	N
Shahar et al.[13]	F/15	N	N	N	N	N	N	N	N	+	–	+
Shahar et al.[13]	F/16	N	N	N	N	N	+	+	N	+	–	+
Shahar et al.[13]	F/12	N	N	N	N	N	N	N	N	+	N	N
Lim et al.[14]	M/24	N	+	N	+	N	1:256	–	N	N	+	N
Chacón et al.[15]	F/16	–	–	+	–	–	1:320	–	–	–	–	N
Kwong et al.[16]	F/9	N	N	+	+	N	+	+	N	+	+	+
Kwong et al.[16]	F/12	+	N	+	+	N	+	–	N	+	+	+
Tan et al.[17b]	F/57	57	N	N	N	N	1:800	95	N	N	+	N
This report	F/15	41	+	+	–	+	1:320	24	–	–	–	N

[a]Autopsy done only in Willoughby's case.
[b]Cranial CT abnormal only in Tan's case.
ESR, erythrocyte sedimentation rate; ANA, antinuclear antibodies; Sm, extractable nuclear antigen; EEG, electroencephalogram; MRI, magnetic resonance imaging; SPECT, single photon emission computed tomography; +, present or abnormal; –, normal or absent; N, not done or not testable.

who died.[5,7] No difference was found between the cases treated with corticoids alone, antiparkinsonian drugs alone, or both combined. It is worth mentioning that the 2 cases reported by Kwong and associates showed complete recovery after corticoids, cyclophosphamide, and intravenous IgG treatment.[16]

DISCUSSION

Movement disorders are a rare manifestation of neurolupus, the most frequently described being chorea.[2,3] Torticollis, blepharospasm, and hemiballismus have also been reported.[18–21] However, a parkinsonian syndrome may be an extremely unusual manifestation of CNS lupus. The pathogenesis of neurological dysfunction of SLE remains unknown. Unfortunately, the incompleteness of the data provided by the published cases does not allow one to establish solid correlations between them. However, it is notable that there was a high frequency of association of a pyramidal syndrome to the parkinsonian syndrome and that the latter was predominantly rigid–akinetic. The additional neurological and psychiatric features, including asthenia, anorexia, and mutism, suggest more widespread CNS involvement and the cases discussed in the literature are reminiscent of encephalitis lethargica. But the absence of a history of encephalitis, oculogyric crises, or sleep-cycle alterations rejected this diagnosis. The lack of lesions on an MRI scan (7 of 11 cases) together with a positive SPECT scan (5 of 5 cases) and abnormal EEG (9 of 12 cases) were the most constant findings. This finding suggests that EEG could be a helpful functional monitor and that SPECT could be considered as a sensitive tool in evaluation of SLE-related CNS complications. On the other hand, although 80% of cases of CNS lupus have abnormal findings on MRI (brain atrophy, focal lesions in white matter beneath the corticomedullary junction, and less frequently in periventricular regions), basal ganglia involvement is extremely uncommon.[16] A thorough review by Moore and Lisack discussing the immunopathogenesis of neurolupus refers to a combination of direct immune-mediated effects, including immune complexes, autoantibodies, cytokines, and activated lymphocytes; and indirect effects, including vasculopathy, coagulopathy, emboli from cardiac disease, and bleeding disturbances. Given that the thalamostriate arteries supplying the basal ganglia are end arteries not supplied by collateral circulation, we could speculate that vasculopathy of such vulnerable vessels may be a major contributing factor in the evolution of parkinsonism. A few mechanisms leading to vas-

culopathy may be suggested, such as circulating immune-complex deposition in the vessel wall, as well as direct injury to the wall caused by autoantibodies.[22] CSF antineural antibodies are found in 90% of patients with cerebral lupus and autoimmune pathogenesis could promote the development of PS in some cases.[23] So, anti-asialo GM1 antibody, anti-ribosomal P protein antibody, and anti-neural cell antibody against neural cells have been detected in both sera and CSF from SLE patients.[23–25] More specifically, Kunas and colleagues demonstrated antibodies against dopaminergic cells in serum from a patient with SLE showing PS. According to Kunas and associates, anti-DA antibodies could be specific to neurolupus with parkinsonian symptoms and not a general epiphenomenon of SLE, because they did not detect them in 10 serum or in 2 CSF samples from a control population with serologically and clinically active SLE, 5 of whom had cerebral involvement but no parkinsonism.[10] Thus, a pathogenic role of the immune system may explain the decrease of the striatal dopaminergic activity, as shown by SPECT and PET in some works. Therefore, it is conceivable that autoimmune mechanisms start destroying the dopaminergic cells, but also that toxic or degenerative events lead to an exposure of cryptic antigens, which subsequently elicit an humoral immune response and thereby promote the loss of dopaminergic neurons. On the other hand, as substantial loss of dopaminergic neurons precedes the clinical debut of parkinsonian symptoms, it is possible that the parkinsonism in SLE may reflect a late stage of the immunoinflammatory disease. Early detection anti-neural antibodies and their neutralization potential would have a prophylactic role in the later development of parkinsonian picture. In summary, we consider that SLE should be taken into account in the differential diagnosis of JP. Further studies are required to determine the role of autoimmune mechanisms in the pathogenesis of PS associated with SLE.

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