Peripheral polineuropathy in patients with juvenile systemic lupus erythematosus

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ABSTRACT

Introduction: Peripheral polyneuropathy is one of 19 neuropsychiatric syndromes seen in systemic lupus erythematosus, according to the classification criteria proposed by the American College of Rheumatology (ACR) for neuropsychiatric syndromes. However, this manifestation has not been reported very often, especially in patients with juvenile systemic lupus erythematosus (JSLE). **Patients and methods:** From 1983 to 2007, 5,079 patients were seen at the Pediatric Rheumatology Unit of the ICr-HC-FMUSP; 228 (4.5%) patients were diagnosed with JSLE according to the criteria of the ACR. Peripheral polyneuropathy was diagnosed according to the criteria for neuropsychiatric syndromes of the ACR. **Results:** Five (2.2%) out of 228 patients with JSLE developed peripheral polyneuropathy and were described retrospectively. The diagnosis was confirmed by electroneuromyography, which showed the presence of distal peripheral polyneuropathy, sensorial and/or motor, involving all four limbs, in two patients, and the lower limbs, in three patients. Three of those patients were females, and peripheral neuropathy developed after the diagnosis of JSLE. The mean age of onset of the disease was 14 years, and the mean time between the onset of JSLE and the diagnosis of peripheral polyneuropathy was 23 months. The most common clinical presentations included muscular weakness and hyporeflexia. Antiphospholipid antibodies were present in all patients. Treatment consisted of corticosteroids in all patients, associated with intravenous cyclophosphamide in three patients. One patient evolved to functional disability and paresis of the lower limbs, requiring a wheelchair. One female patient died of severe sepsis. **Conclusions:** Peripheral polyneuropathy is a rare, severe, and occasionally incapacitating manifestation of JSLE, commonly associated with the presence of antiphospholipid antibodies.

Keywords: peripheral polyneuropathy, juvenile systemic lupus erythematosus, nervous system, neuropathy, antiphospholipid antibodies.

INTRODUCTION

Juvenile systemic lupus erythematosus (JSLE) is a rare systemic autoimmune disease of childhood and adolescence. The clinical characteristics of JSLE vary according to the organ or system involved, and includes mucocutaneous, articular, renal, hematologic, cardiac, pulmonary, and neuropsychiatric manifestations, among others.[1-3]

In 1999, the American College of Rheumatology (ACR) subcommittee proposed a nomenclature system, including 19 LES-related neuropsychiatric syndromes, standardizing the classification criteria according to the clinical manifestations, and changes in laboratorial and imaging exams. Twelve of those syndromes involved the central nervous system and seven involved the peripheral nervous system (PNS).[4] The

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neuropsychiatric involvement is associated with a high morbimortality in JSLE. Its prevalence, according to the ACR neuropsychiatric classification criteria, varies from 22 to 95% in pediatric lupus,[5-14] but involvement of the PNS is rare.[5-15]

Polyneuropathy is one of the PNS neuropsychiatric syndromes proposed by the ACR.[4] It is defined as sensorial or motor changes of the peripheral nerves, of varying duration, characterized by the symmetry of the symptoms and distal distribution, which is diagnosed by electroneuromyography (ENMG).[4] This manifestation has been rarely reported in association with JSLE, and it is usually described as case reports.[10-14]

The objective of the present study was the retrospective evaluation of the prevalence, as well as to describe the cases of peripheral polyneuropathy in children and teenagers with JSLE.

PATIENTS AND METHODS

From 1983 to 2007, 5,079 consecutive patients were seen at the Pediatric Rheumatology Unit of the Instituto da Criança (ICr) of the Hospital das Clínicas of the Medical School of the Universidade de São Paulo (FMUSP). The medical records of JSLE patients were reviewed.

The diagnosis of JSLE and peripheral polyneuropathy were determined according to the 1997 ACR classification criteria[16] and the criteria of SLE-related neuropsychiatric syndromes proposed by the ACR in 1999,[4] respectively.

The diagnosis of peripheral polyneuropathy was confirmed by ENMG of the involved members and all patients were evaluated and followed along with the Pediatric Neurology Unit of the ICr-HC-FMUSP.

Disease activity was measured by the 2000 Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K).[17] An arbitrary numeric value of eight, and above, in the SLEDAI-2K determined disease activity.

The irreversible cumulative damage caused by JSLE and/or the treatment of the disease was determined by the Systemic Lupus International Collaboration Clinics/ACR Damage Index (SLICC-ACR/DI).[18] Scores above one, evaluated after 6 months of disease activity, were considered as cumulative disease damage.

The following antiphospholipid antibodies were evaluated in all patients with peripheral polyneuropathy: IgM and IgG anticardiolipin antibodies (determined by ELISA) and lupus anticoagulant (determined according to the recommendations of the Subcommittee on Lupus Anticoagulant/Antiphospholipid Antibody of the Scientific and Standardization Committee).[2,3,19] Antiphospholipid antibody syndrome (APAS) was defined, according to the new international classification consensus, by the presence of vascular thrombosis (arterial, venous, or small blood vessel thrombosis in any tissue or organ) or by the presence of gestational morbidity associated with the positivity of one or more antiphospholipid antibodies in at least two occasions with a minimal interval of 12 weeks.[20]

RESULTS

Of the patients followed by the Rheumatology Unit of the ICr-HC-FMUSP in the 24-year period described, the diagnosis of JSLE was made in 228 cases (4.5%). Five (2.2%) of those patients developed peripheral polyneuropathy; they underwent a retrospective evaluation, and were described. Table 1 shows the demographic data, clinical and laboratorial manifestations, treatment, and clinical evolution of peripheral polyneuropathy in JSLE.

CASE 1

Female patient born in Goiânia/GO/Brazil who was diagnosed with JSLE[16] at age 7, characterized by malar erythema, arthritis, positive antinuclear factor (ANA), and proteinuria (1.5 g/day) with diffuse proliferative glomerulonephritis.[16] In 2005, at age 19, the disease reactivated with edema of the lower limbs and macroscopic hematuria. At that time, laboratorial exams revealed: hemoglobin (Hb) 14 g/dL, hematocrit (Ht) 40%, leukocytes 24,000/mm^3 (67% neutrophils, 5.2% lymphocytes, 5% monocytes, 4% eosinophils), platelets 260,000/mm^3, erythrocyte sedimentation rate (ESR) 30 mm in the first hour (normal < 20 mm in the first hour), C-reactive protein (CRP) 4.21 mg/dL (normal < 5 mg/dL), ANA 1/1280, anti-RNP positive, anti-double stranded DNA 419 IU (normal up to 50 IU), anticardiolipin (IgM 15 MPL and IgG 30 GPL), positive lupus anticoagulant and anti-P, C3 < 0.155 g/L (normal 0.5 to 1.8 g/L), C4 0.05 g/L (normal 0.1 to 0.4 g/L), proteinuria 2.16 g/day (normal < 0.5 g/day), urinalysis (pH 5.5, specific gravity 1.024, leukocytes 100,000/mL, erythrocytes 12,000/mL), and urine culture positive for *Escherichia coli*. One month later, the physical exam revealed muscle weakness [grade III (Medical Research Council – MRC®)],[21] hyporeflexia, and hyperesthesia in all four limbs. Electroneuromyography was compatible with chronic demyelinating peripheral polyneuropathy in all four limbs. Pulse therapy with methylprednisolone, intravenous cyclophosphamide, and azathioprine was instituted. She presented SLEDAI-2K of 18 and SLICC/ACR-DI of 1. The patient developed acute amaurosis secondary to bilateral retinal necrotizing vasculitis associated with infection with

Table 1
Demographic data, clinical and laboratorial manifestations, physical activity and cumulative damage, treatment, and clinical evolution of five patients with juvenile systemic lupus erythematosus (JSLE) and peripheral polyneuropathy

Case	1	2	3	4	5
Age of onset of JSLE (years)	7	14	7	14	16
Δt (months) between the diagnosis of JSLE and polyneuropathy	144	23	88	2	1
Gender	F	F	F	M	M
Peripheral neurological manifestations	Muscular weakness, hyporeflexia, and hyperesthesia in all four limbs	Muscular weakness, hyporeflexia, and paresthesia in both feet	Muscular weakness, hyporeflexia, and hyperesthesia in the lower limbs	Muscular weakness and areflexia in the lower limbs	Muscular weakness and hyporeflexia in all four limbs
SLEDAI-2K / SLICC-ACR/DI	18 / 1	10 / 1	16 / 0	10 / 0	10 / 0
Laboratorial exams	ANA, ACL, LA, Anti-P	ANA, ACL, Anti-DNA, Anti-Ro, Anti- RNP	ANA, ACL, LA, Anti- RNP	ANA, ACL, Anti-SM, Anti-P	ANA, ACL, LA, Anti-DNA
Treatment of the polyneuropathy	Pd, AZA, CFM	Pd	Pd, AZA, CFM, CLQ,MPT	Pd, PM, AZA, CFM, MPT	Pd, MPT
Evolution	Death due to sepsis	Remission	Remission	Functional incapacity	Remission

Δt = time interval; ACL = anticardiolipin; ANA = Antinuclear factor; AZA = Azathioprine; CFM = Pulse Cyclophosphamide; CLQ = chloroquine; LA = lupus anticoagulant; MPT = Motor physical therapy; Pd = prednisone; PM = Pulse methylprednisolone; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000;[17]
SLICC-ACR/DI = Systemic Lupus International Collaborating Clinics-ACR/Damage Index.[18]

the varicella-zoster virus. On the third day of treatment with intravenous acyclovir, she received two doses of intravitreal gancyclovir and intravenous gamma globulin (2 g/kg/dose), with partial recovery of visual acuity. However, after one month, she developed with septic shock and died.

CASE 2

Female patient born in São Paulo. In 2002, when she was 12 years old, she developed malar erythema, livedo reticularis, and painful erythematous nodes in the lower limbs. A working diagnosis of vasculitis was made and biopsies of a subcutaneous node and muscle were requested, which revealed a perivascular and periadnexal lympho-histiocytary inflammatory infiltrate in the medium upper dermis, with positive direct immunofluorescence for IgM, IgG, and C3, compatible with JSLE. However, the patient developed spontaneous remission of the cutaneous lesions without specific treatment. In 2004, at the age of 14 years, she developed malar erythema, photosensitivity, and alopecia, and laboratorial exams showed: Hb 11.8 g/dL, Ht 37.9%, leukocytes 3,400/mm^3 (44% neutrophils, 47% lymphocytes, 3% eosinophils), platelets 219,000/mm^3, ESR 35 mm in the first hour, CRP negative, ANA 1/80, anticardiolipin IgG 24.5 GPL, and the presence of anti-double stranded DNA, anti-Ro and anti-RNP. The diagnosis of JSLE[16] was made at this point and treatment with prednisone (0.5 mg/kg/day) and hydroxychloroquine sulfate (5 mg/kg/day) was instituted. In 2006, at the age of 16 years, the patient developed distal muscular weakness MRC grade IV[21] with decreased deep tendon reflexes and paresthesia in the lower limbs. Laboratory exams showed: Hb 12.9 g/dL, Ht 37.5%, leukocytes 4,400/mm^3 (61% neutrophils, 33% lymphocytes, 2% eosinophils), platelets 161,000/mm^3, ESR 26 mm in the first hour, CRP 0.15 mg/dL, C3 0.97 g/L, C4 0.11 g/L, AST 20 U/L (normal 5 to 26 U/L), ALT 29 U/L (normal 19 to 44 U/L)m, BUN 25 mg/dL (normal 15 to 45 mg/dL), and creatinine 0.15 mg/dL (normal 0.6 to 0.9 mg/dL). Electroneuromyography was compatible with chronic demyelinating peripheral polyneuropathy, predominantly distal, in both lower limbs. The patient presented SLEDAI-2K of 10 and SLICC/ACR-DI of 1. She was treated with prednisone (0.5 mg/kg/day) and showed clinical improvement without sequelae. She is, currently, 18 years old, and she is taking prednisone (5 mg/day) and hydroxychloroquine sulfate (5 mg/kg/day) with a SLEDAI-2K of 0.

CASE 3

Female patient born in São Paulo. In 2000, when she was 7 years old, she was diagnosed with JSLE,[16] since she presented

malar erythema and photosensitivity, and laboratorial exams showed autoimmune hemolytic anemia (Hb 5.7 g/dL, Ht 15%, reticulocytes 9.7%, and positive direct Coombs), leukocytes 6,200/mm^3 (76% neutrophils, 21% lymphocytes, 3% monocytes), platelets 250,000/mm^3, ESR 8 mm in the first hour, CRP < 0.17 mg/L, ANA 1/640, anti-double stranded DNA 52 IU, positive anti-RNP, C3 78 mg/dL, and C4 1 mg/dL. In 2004, the patient stopped the follow-up appointments and treatment when she was taking prednisone, 20 mg/day, and chloroquine diphosphate, 250 mg/day. Twenty days after she stopped taking her medication, the patient was admitted to an intensive care unit for septic shock requiring antibiotics, mechanical ventilation, and vasoactive drugs. During hospitalization, she developed psychotic behavior, seizures, and thrombosis of the right lower limb, secondary to an intravenous catheter, but antiphospholipid antibodies were not present. She was treated with pulse methylprednisolone for three days, followed by pulse therapy with intravenous cyclophosphamide (2004-2005), with good response. In November 2007, the patient was hospitalized for a non-healing ulcer on the external malleolus of the left lower limb and associated muscular weakness. In February 2008, the leg ulcer was biopsied and showed the presence of fibrin and vascular proliferation extending to the subcutaneous tissue on the border of the lesion, and a muscular biopsy showed a perivascular lymphomononuclear infiltrate and disturbed intermyofibrillar cytoarchitecture, compatible with polymyositis. The patient was treated with weekly pulse methylprednisolone for four months, until healing the ulcer. In April 2008, at age 14, the patient developed pain and paresthesia in her feet. Physical exam revealed distal muscular weakness, MRC grade IV[21], with decreased deep tendon reflexes, and hyperesthesia in the lower limbs. At this point, laboratory evaluation showed: Hb 10.6 g/dL, Ht 30%, leukocytes 16,500/mm^3 (12% bands, 77% neutrophils, 8% lymphocytes, 0% eosinophils), platelets 210,000/mm^3, anti-double stranded DNA > 1,000 IU/mL, ANA 1/1280, C3 0.58 g/L, C4 0.13 g/L, CRP 171 mg/L, BUN 18 mg/dL, creatinine 0.49 mg/dL, prothrombin time (PT) 75%, INR 1.11, activated partial thromboplastin time (aPTT) 50.5 sec, UA (pH 6.5, specific gravity 1.030, protein ++, leukocytes 75,000/mL, erythrocytes 6,000/mL, hyaline casts +++), D-dimer 300 ng/mL (normal < 200 ng/dL); echo-Doppler of the lower limbs showed sequelae of prior thrombosis of the right common femoral vein (2004). Electroneuromyography revealed moderate chronic, mixed (axonal and demyelinating), sensitive-motor peripheral neuropathy of the lower limbs. At this time the patient presented SLEDAI-2K of 16 and SLICC-ACR-DI of 0. She was treated with monthly pulse intravenous cyclophosphamide (750 mg/m^2/month) and weekly motor physical therapy. In April 2008, antiphospholipid antibody syndrome (APAS) was diagnosed according to the criteria of Myakis *et al.* (2006), due to the presence of anticardiolipin autoantibodies (isotype IgM 41 MPL) and positive lupus anticoagulant in two occasions. In august 2008, the patient was in complete remission of her symptoms without neurological sequelae, taking oral prednisone, 60 mg/day, pulse intravenous cyclophosphamide (750 mg/m^2/month), azathioprine 100 mg/day, hydroxychloroquine sulfate 250 mg/day, low molecular weight heparin 40 mg/day, gabapentin 400 mg/day, amitriptyline 50 mg/day, and carbamazepine 250 mg/day.

CASE 4

Male patient, born and living in São Paulo. In June 2007, at age 14, he was diagnosed with JSLE.[16] At that time, he developed malar erythema, pleuritis, oral ulcers, arthritis, and laboratorial exams showed: autoimmune hemolytic anemia (Hb 10 g/dL, Ht 30.6%, and positive direct Coombs), leukocytes 4,800/mm^3 (64% neutrophils, 32% lymphocytes, 5% monocytes), platelets 285,000/mm^3, CRP 10.3 mg/L, ESR 47 mm in the first hour, UA (specific gravity 1.010, pH 6.0, leukocytes 7,000/mL, erythrocytes 157,000/mL, hyaline casts ++), negative proteinuria in 24 hours, normal myelogram, ANA 1/200, C3 0.35 g/L, and C4 0.02 g/L. The autoantibodies investigated included: anticardiolipin (IgG 20 GPL and negative IgM), anti-RNP 1/600, anti-SM 1/400, and positive anti-ribosomal P protein. In August 2007, two months after the diagnosis, the patient was hospitalized for left cervical adenopathy with septic shock secondary to *Streptococcus pneumonia*; he evolved with hemodynamic instability requiring the use of vasoactive drugs, mechanical ventilation, and admission to the intensive care unit. During hospitalization, he developed muscular weakness MRC grade II[21] with decreased deep tendon reflexes, without sensorial changes, either tactile or painful, and a sacral pressure sore. Laboratorial exams showed: Hb 9.7 g/dL, Ht 28.3%, leukocytes 15,700/mm^3 (7% bands, 87% neutrophils, 5% lymphocytes), platelets 174,000/mm^3, negative anti-double stranded DNA, C3 0.61 g/L, C4 0.05 g/L, PT 85%, aPTT 38.9 sec, INR 1.08, BUN 148 mg/dL, creatinine 3.28 mg/dL, phosphorus 6,2 mg/dL (normal 3.1 to 5.3 mg/dL), calcium 7.5 mg/dL (normal 8.9 to 10.7 mg/dL), potassium 5.7 mEq/L (normal 3.6 to 4.8 mEq/L), sodium 141 mEq/L (normal 135 to 147 mEq/L), CRP 302 mg/L, ALT 80 U/L, and AST 205 U/L. Echo-Doppler showed mild dilation of the left cardiac chambers, mild mitral insufficiency, and mild tricuspid insufficiency and pulmonary hypertension; SLEDAI-2K of 10 and SLICC-ACR-DI of 0. Electroneuromyography

revealed motor and sensitive polyneuropathy (axonal) of the lower limbs. The patient was treated with monthly pulse methylprednisolone for three consecutive days and monthly pulse intravenous cyclophosphamide from October 2007 to March 2008. In August 2008 he was taking 25 mg/day of prednisone, 250 mg/day of chloroquine diphosphate, and 150 mg/day of azathioprine, and attended weekly sessions of motor physical therapy. At that time, he also experienced pain and muscle weakness MRC grade III[21] in the lower limbs, decreased deep tendon reflexes, and required the use of a wheelchair.

CASE 5

Male patient born in São Paulo. In July 2000, at the age of 15 years, the patient developed deep venous thrombosis (DVT) in the left lower limb, being treated with heparin sodium for two months. In November 2000, the patient had a new episode of DVT in the same limb; he was treated with heparin sodium for one month, followed by warfarin. At that time, the etiology of the thrombosis was unknown. In March 2001, at the age of 16 years, the diagnosis of JSLE[16] associated with APAS[20] was made due to the presence of arthritis, proteinuria of 1.0 g/day, ANA 1/1280, and the presence of the following antibodies: lupus anticoagulant, anticardiolipin (IgM, 15 MPL, and IgG, 32 GPL) and anti-double stranded DNA. He was treated with 60 mg/day of prednisone, which was later reduced to 20 mg/day, and maintained on warfarin. In April 2001, a renal biopsy showed membranous glomerulonephritis. At that point, the patient experienced paresthesia on both feet, muscular weakness MRC grade IV[21] and hyporeflexia, without sensorial changes in the upper and lower limbs. Laboratorial exams were as follows: Hb 13 mg/dL, Ht 40%, leukocytes 11,200/mm^3 (neutrophils 75%, and lymphocytes 17%), platelets 340,000/mm^3, ESR 4 mm in the first hour, CRP 0.76 mg/dL, ANA 1/1280, anti-double stranded DNA, C3 65 mg/dL, C4 11 mg/dL, AST 17 U/L, ALT 69 U/L, BUN 28 mg/dL, creatinine 0.5 mg/dL, and proteinuria of 0.05 g/dia. Electroneuromyography showed motor and sensitive (axonal) polyneuropathy in all four limbs; SLEDAI-2K of 10, and SLICC/ACR-DI of 0. The dose of prednisone was increased to 60 mg/day and motor physical therapy was added to the treatment, the patient showed an excellent response, without developmental sequelae.

DISCUSSION

The present study showed a low prevalence (2.2%) of peripheral neuropathy associated with lupus in a tertiary Pediatric Rheumatology Unit in Brazil during a 25-year period. Besides, it showed that severe neuropsychiatric manifestation were more prevalent in patients with positive antiphospholipid antibodies and/or APAS[20] secondary to JSLE.[16]

Peripheral polyneuropathy is one of those neuropsychiatric syndromes that affect the peripheral nervous system, according to the criteria of the ACR.[4] According to the literature, the incidence of this manifestation in adult patients with lupus varies from 5 to 27%.[15] In 2001, Costallat *et al.*[22] observed an incidence of 4% of peripheral polyneuropathy, as defined by the ACR nomenclature of psychiatric manifestations, in a population of 527 adult patients with lupus being treated in the city of Campinas, SP, Brazil.

On the other hand, this syndrome is rarely reported in children and adolescents with JSLE, and it is usually described as case reports, and the rare studies on the prevalence of this disorder were done with small- or moderate-size populations. Harel *et al.*[13] described 5/35 (14%) cases of peripheral neuropathy associated with JSLE in Israel. Benseler & Silverman, of the Hospital for Sick Children in Toronto (Canada), observed a prevalence of 2/91 (2.2%) of peripheral neuropathy in pediatric patients with lupus.[11] Yu *et al.*,[12] in Taiwan, observed an incidence of 3/185 (1.6%) of peripheral polyneuropathy in patients with JSLE.

As for gender, the literature indicates a predominance of females in both adult[15] and pediatric[13] populations, similar to that observed in the present study. However, two cases of polyneuropathy were observed in boys, and it is possible that the incidence of this syndrome is proportionally higher in the male population. It was also observed the evolutionary onset of the clinical manifestations of peripheral neuropathy, mainly in the first two years of JSLE, similar to the reports in the literature. In fact, neuropsychiatric and renal involvements are considered prognostic factors in pediatric lupus and are more common in the beginning of the disease.[1]

The predominant clinical manifestations of peripheral polyneuropathy include: paresthesia, pain in the limbs, distal muscle weakness, hyporeflexia, and sensorial changes, usually symmetrical, affecting especially the lower limbs. This syndrome is usually associated with systemic disease activity,[13] which can be seen in all cases presented here. Besides, another interesting aspect is that at the time of the diagnosis of peripheral polyneuropathy, this manifestation of the PNS was isolated and not associated with the other neuropsychiatric syndromes, which was also observed by other authors.[13,14]

The pathogenesis of peripheral neuropathy involves several possible unknown mechanisms. Inflammation and damage of the nerves can be due to autoantibodies, deposit of immune complexes, or direct damage with vasculitis of the "*vasa*

nervorum".[23] McCombe *et al.*[23] found axonal degeneration and vasculitis in sural nerve biopsies, with higher expression of class II antigens along the fascicular sheath. Besides, in 2002, Galeazzi *et al.*[24] investigated a population of European adults with SLE and observed the association among the different neuropsychiatric manifestations and anti-ganglioside antibodies. The IgG fraction was associated with peripheral neuropathy, suggesting that this class of antibodies could be involved in the pathogenesis of this disorder. In 2004, Erten *et al.*[25] described a case of ischemic peripheral neuropathy with axonal degeneration, demonstrated by biopsy of the sural nerve, in a female patient with catastrophic APS. The pathogenic mechanism could be related with microthrombosis of the "*vasa nervorum*".

Neuropsychiatric manifestations, especially headache, seizures, stroke, chorea, and spinal cord and peripheral neurophathies, have been associated with antiphospholipid antibodies.[2,3,9,12,22] All patients with peripheral neuropathies in the present study had antiphospholipid antibodies and two had APS, similar to that observed in other reports of pediatric lupus with this PNS manifestation.[13,14]

As for the other antibodies, two patients were positive for anti-ribosomal P protein, which is considered specific for lupus. This autoantibody is associated with the neuropsychiatric manifestations of SLE, especially psychosis and depression; however, those were not observed in the patients in the present study.[26]

As for the ENMG, axonal degeneration is the most common pathological change seen in nerve fibers.[13,23] In the present study, this test was done in all patients to confirm the diagnosis, whose predominant pattern was represented by peripheral sensorial-motor neuropathy predominantly axonal.

The treatment of peripheral polyneuropathy includes corticosteroids and immunosupressors drugs, especially azathioprine and/or cyclophosphamide,[13,14] which were used to treat the patients of the present study. Physical therapy should be instituted early to avoid sequelae, such as muscular atrophy and difference in the size of affected limbs. Only one patient showed important limitations. This patient developed this syndrome after a pneumococcal septic shock. Prolonged immobilization due to the hospitalization and infection could have contributed for the severity of this case.

Peripheral polyneuropathy can be prevalent in pediatric lupus, severe, and rarely diagnosed since those patients can have subclinical manifestations or even non-specific pain that can be mistaken by growing pains and juvenile fibromyalgia. Further studies evaluating systematically this manifestation in JSLE are necessary.

At the Pediatric Rheumatology Unit of the ICr-HC-FMUSP, peripheral polyneuropathy has been systematically investigated, with ENMG, in patients with JSLE with pain in the limbs, distal muscular weakness, hyporeflexia, and sensorial changes.

To conclude, in the present study, peripheral polyneuropathy was a rare, severe, and occasionally incapacitating manifestation in JSLE, associated with the presence of antiphospholipid antibodies.

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