J Neurol (2017) 264:1218–1226
DOI 10.1007/s00415-017-8519-7

ORIGINAL COMMUNICATION

Clinicopathological features of multiple mononeuropathy associated with systemic lupus erythematosus: a multicenter study

Elodie Rivière[1] · Fleur Cohen Aubart[1,2,9] · Thierry Maisonobe[3] · François Maurier[4] · Christophe Richez[5] · Bruno Gombert[6] · Marie Gousseff[7] · Daniel Adoue[8] · Alexis Mathian[1] · Miguel Hié[1] · Julien Haroche[1,2] · Zahir Amoura[1,2]

Received: 1 May 2017 / Revised: 14 May 2017 / Accepted: 15 May 2017 / Published online: 23 May 2017

Abstract Multiple mononeuropathy (MM) occurs rarely during systemic lupus erythematosus (SLE) but may lead to major disability. The aim of this study was to investigate the clinic-pathological presentations of MM during SLE, as well as long-term outcomes. We conducted a multicentric retrospective study that included patients receiving a diagnosis of MM during SLE. Ten patients were included (8 women and 2 men, median age at MM diagnosis: 40.4 years). SLE was diagnosed before MM in 9/10 patients (median time 8.2 years). When MM occurred, the SLEDAI score was $\geq$6 for 6/9 patients. Presenting symptoms consisted of sensory deficits ($n = 10$), neuropathic pain ($n = 9$), and/or motor deficits ($n = 9$), sometimes symmetrical, affecting the lower limbs (10/10) and occasionally the upper limbs (5/10). All patients presented with uni- or bilateral damage of the common fibular nerve, with less frequent involvement of the tibial nerve. Serum cryoglobulinemia was positive in 5/9 patients. Electrophysiological studies confirmed the non-symmetrical involvement of multiple nerve trunks in all patients. Neuromuscular biopsy (performed in five patients) showed histological signs of vasculitis in two patients and perivascular lymphocytic inflammatory infiltrates in two others. All patients were treated with glucocorticosteroids combined with cyclophosphamide ($n = 6$), rituximab ($n = 3$), or mycophénolate-mofétil ($n = 1$). The median follow-up was 5 years. Two patients relapsed during follow-up. All patients had motor and/or sensory sequelae upon follow-up. MM associated with SLE is frequently caused by a vasculitis mechanism. Patients improve with steroids and immunosuppressive drugs. Long-term outcomes include frequent clinical sequelae and possible relapses.

Elodie Rivière and Fleur Cohen Aubart contributed equally to this work.

✉ Fleur Cohen Aubart
fleur.cohen@psl.aphp.fr

[1] AP-HP, Service de Médecine Interne 2, Institut e3 m, Hôpital de la Pitié-Salpêtrière, 75013 Paris, France

[2] UPMC Paris VI Université, Sorbonnes Universités, 75013 Paris, France

[3] AP-HP, Départements de neurophysiologie et neuropathologie, Hôpital de la Pitié-Salpêtrière, 75013 Paris, France

[4] Service de Médecine Interne, Hôpitaux Privés de Metz, 57000 Metz, France

[5] Département de rhumatologie, Hôpital Pellegrin, CHU de Bordeaux, place Amélie-Raba-Léon, 33076 Bordeaux, France

[6] Service de Médecine Interne et Rhumatologie, Centre Hospitalier de La Rochelle, 17000 La Rochelle, France

[7] Service de Médecine Interne, maladies hématologiques et maladies systémiques, Centre Hospitalier Bretagne Atlantique, 56000 Vannes, France

[8] Service de Médecine Interne et immunopathology Clinique, CHU de Toulouse, Hôpital Purpan, 31000 Toulouse, France

[9] Service de Médecine Interne 2, Institut e3m, Groupe Hospitalier Pitié-Salpêtrière, 47-83 Boulevard de l'hôpital, 75651 Paris Cedex 13, France

Keywords Systemic lupus erythematosus · Mononeuritis multiplex · Vasculitis · Rituximab

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune multi-systemic disorder principally affecting young women. It is characterized by skin and hematologic manifestations, polyarthritis, renal involvement, and seritis with a relapsing–remitting course. Peripheral (PNS) or central (CNS) nervous system involvements may also occur. In 1999, the American College of Rheumatology (ACR) subcommittee proposed a classification of neurolupus with 19 neuropsychiatric syndromes during SLE, seven of which involved the PNS [1]. Peripheral neuropathy occurs in 1.5–27.8% of SLE cases [5, 8, 11, 15, 16, 18, 19, 22, 24]. The most common type of diffuse peripheral neuropathy in patients with SLE is symmetric distal axonal sensory or sensorimotor neuropathy [15, 16, 24]. The association of multiple mononeuropathy (MM) with SLE is rare [17]. MM is a peripheral neuropathy characterized by the non-symmetrical degeneration of one or more nerve trunks [6]. The clinical presentation is painful sensorimotor deficits in the upper and/or lower extremities usually, but not always, with asymmetric distribution. Pain is common and the onset is acute or subacute. The prevalence of MM in SLE patients has been estimated to be up to 9% [8], but it may be under-diagnosed, even though it requires a specific treatment.

Because SLE-associated MM is rare, its management is based on isolated cases or small series reports. These reports have highlighted the heterogeneous presentation of SLE-associated MM and the variability of treatment efficacy. Data are lacking regarding to the long-term outcomes and prognosis of this disorder. Therefore, we conducted a retrospective multicenter study to describe the clinical, biological, electrophysiological, and histopathological features of MM during SLE, as well as treatment efficacy and long-term neurological outcomes.

Patients and methods

We performed a retrospective multicenter nationwide study in Rheumatology and Internal Medicine Departments. From September 2006 to February 2015, we identified SLE patients who received a final diagnosis of MM through the SNFMI (Société Nationale Française de Médecine Interne) and the FLEUR (French Lupus Erythematosus Network) networks. Patients were screened using local databases.

Standard Protocol Approvals, Registrations, and Patient Consents

This study was conducted in compliance with the Good Clinical Practice protocol and the Declaration of Helsinki principles.

Inclusion and exclusion criteria

Inclusion criteria were as follows:

1. A definite diagnosis of SLE according to the ACR classification criteria (≥4 criteria) updated in 1997 [14, 23].
2. A final diagnosis of MM documented by electrophysiological studies and the exclusion of other types of neuropathies (radicular neuropathies, axonal symmetrical and painless neuropathies, plexopathies, sensory or motor neuronopathies, and demyelinating neuropathies) [6].

Patients were excluded in cases of an alternative cause of MM (e.g., diabetes, nerve compression, or infection).

Data collection and outcomes

Data were collected retrospectively through medical records by the practitioners in charge of the patients and were centrally reviewed (ER and FCA). We collected clinical and biological data (blood C-reactive protein (CRP) level, complete blood cell count, antinuclear antibodies titer, anti-double-stranded deoxyribonucleic acid (dsDNA) antibodies, anti-extractable nuclear antigen (ENA) antibodies, anti-neutrophil cytoplasmic antibodies (ANCA), lupus anticoagulant (LA), anticardiolipin and antibeta2GP1 antibodies, cryoglobulinemia, rheumatoid factor (RF), C3, C4, and total complement) at the time of SLE and MM diagnoses and during follow-up. Baseline was considered to be the time of MM diagnosis. The results of the electrophysiological studies were collected at baseline and during follow-up. The results of neuromuscular biopsy were noted when available.

Electrophysiological studies

Nerve conduction studies were performed using the standard techniques of surface stimulation and recording. Motor nerve conduction studies were performed in both the lower extremities on the common fibular and tibial nerves and in the upper extremities on the median and ulnar nerves. Sensory nerve conduction studies were performed bilaterally on the fibular, sural, median, and ulnar nerves, and sometimes the radial nerves.

Follow-up

Patients were treated and followed according to the local physician's habits. Treatment dosages and durations were noted. SLE activity was retrospectively evaluated with the systemic lupus erythematosus disease activity index (SLEDAI) [9]. The modified Rankin score was used to assess neurological damage at baseline and during follow-up. The follow-up period ended in July 2016.

Results

Patients' characteristics

Ten patients (8 females and 2 males) with a median age at SLE diagnosis of 28.5 years (range 17–53) were included in this study. Patients' characteristics are presented in Table 1. Eight patients were European and two were Afro-Caribbean. MM occurred several years after SLE diagnosis in eight cases, with a median onset time of 8.2 years from SLE diagnosis (range 3–22). In one patient, SLE diagnosis was obtained 1 month after MM onset, and in another patient, MM occurred 1 month after SLE diagnosis. Four patients had antiphospholipid syndrome, and three had Sjögren syndrome that was associated with SLE. Two patients had the previous central nervous system (CNS) involvement and five had the previous renal involvement of SLE. Renal biopsy had been performed in four patients, and the results revealed class IV ($n = 2$), class II + V ($n = 1$), or class V ($n = 1$) lupus nephritis. Anti-SS-A antibodies were positive in 7/9 patients (78%), and anti-SS-B antibody was found in 4/9 cases (44%). Antiphospholipid antibodies were detected in seven patients (70%). The nine patients, in which SLE was previously diagnosed, were being treated with hydroxychloroquine and corticosteroids at the time of MM onset. In addition, seven patients (78%) were receiving an immunosuppressive drug [azathioprine (AZA) $n = 2$, mycophenolate mofetil (MMF) $n = 2$ and methotrexate $n = 3$] when MM occurred. Four patients had previously received cyclophosphamide for renal involvement before MM onset.

Clinical, biological, electrophysiological, and histological presentation of MM

The symptoms that led to the MM diagnosis were sensory deficit ($n = 10$, 100%), neuropathic pain ($n = 9$, 90%), and/or motor deficits ($n = 9$, 90%). MM always affected the lower limbs ($n = 10$, 100%) and involved the upper limbs in five cases (50%). The sensory and motor deficits were non-symmetrical in seven cases. All patients presented uni- or bilateral damage of the fibular nerve and/or the tibial nerve. The distributions of sensory deficits are shown in Fig. 1. The median-modified Rankin score at MM diagnosis was four (range 2–4).

Three patients (#2, 7, and 9) had concomitant vascular purpura, with the histological demonstration of vasculitis via skin biopsy. One patient (#3) had necrotic skin lesions of the toes, and a skin biopsy (which was performed 2 weeks after steroids and rituximab) showed thrombosis of small vessels without vasculitis. No patients had concomitant CNS or renal involvement. At MM diagnosis, the SLEDAI score was ≥ 6 for six patients (median 9, range 2–17).

An electromyogram was performed on all patients, which confirmed the diagnosis of MM with non-symmetrical severe reduction in motor and sensory amplitudes. The median amplitudes of the compound motor action potential of the fibular (right: 0; left: 0) and tibial (right: 0.39, left: 0.85) nerves were reduced. The median sensory nerve action potentials were also significantly reduced in the fibular and tibial nerves (0 in all). The reductions in motor and sensory potential amplitudes were more heterogeneous in the upper limbs.

Neuromuscular biopsies were performed in five patients. Perivascular lymphocytic infiltration around the nerve was observed in four cases (Fig. 1), with fibrinoid necrosis of the small vessel walls in two cases. One patient had a normal nerve biopsy but perivascular lymphocytic infiltration in the muscular tissue.

Finally, eight patients demonstrated vasculitis in skin or neuromuscular biopsies. Two patients did not have any biopsy, one because of hemostasis disturbances, and the other declined the procedure.

Laboratory tests at the time of MM onset are shown in Table 1. A C4 level ≤ 0.08 g/L was observed in 8/8 patients (the measurement was not performed in 2 patients), and a C3 level ≤ 0.75 g/L was found in 5/9 patients. A rheumatoid factor was present in 5/7 patients (71%). dsDNA antibodies were present in nine patients (90%) and were detected with the Farr test in 5/6 patients (83%). Cryoglobulinemia was positive for 5/9 patients (55%) and was a type II ($n = 4$) or III ($n = 1$). C-reactive protein was ≥ 5 mg/L in 6/8 patients (75%). Two patients had positive ANCA, one without specificity (anti-proteinase 3 and myeloperoxidase antibodies were negative) and one with anti-myeloperoxidase reactivity.

Treatments and outcomes

All the patients were treated with oral corticosteroids (0.5–1 mg/kg/day in 9 cases and 10 mg/day in 1 patient), which were preceded by intravenous methylprednisolone (5000–1000 mg/pulse for 1–3 days) in six patients. In addition to steroids, an immunosuppressive drug was

Table 1 Clinical, biological, and histological characteristics of patients with mononeuritis multiplex associated with systemic lupus erythematosus

Patient	Sex, age at SLE diagnosis	SLE involvement (except PNS) and associated AID	Time between SLE diagnosis and MM*	MM characteristics	Biology	Vasculitis histology	Treatment
#1	F, 27	S, A, C, H, R SS	22 years	Se–Mo Asymmetrical LL–UL	SSA+ SSB+ DNA+ APL− ANCA− RF+ Cryo−	Nerve biopsy +	CS CYC then MMF
#2	F, 28	A, C SS	4 years	Se Symmetrical LL Purpura	SSA+ DNA+ APL− ANCA− RF+ Cryo+	Skin biopsy +	CS MMF RTX then BELI
#3	F, 22	A, C, R, CNS	9 years	Se–Mo Asymmetrical LL–UL Toes necrosis	SSA− SSB− DNA+ ACL + ANCA− RF+ Cryo+	Nerve biopsy + Skin biopsy: thrombosis	CS CYC then AZA then MMF then RTX
#4	M, 32	H APS	1 month	Se–Mo Asymmetrical LL–UL	DNA+ ACL+ B2GP1+ ANCA+	–	CS CYC then AZA
#5	M, 53	A, C, H	–	Se–Mo Asymmetrical LL–UL	SSA+ SSB+ APL− ANCA−	Nerve biopsy − Muscle biopsy +	CS CYC then MMF
#6	F, 29	S, A, H, R	7 years	Se–Mo Asymmetrical LL	SSA+ SSB + DNA+ ACL+ B2GP1+ ANCA+ Cryo−	Nerve biopsy +	CS MMF
#7	F, 43	C, H, CNS APS	12 years	Se–Mo Asymmetrical LL Purpura	SSA+ DNA+ ACL+ B2GP1+ ANCA- RF+ Cryo+	Skin biopsy +	CS RTX
#8	F, 26	S, A, C, H, R, CNS APS	7 years	Se–Mo symmetrical LL	SSA− SSB− DNA+ ACL+ LA+ RF− ANCA− Cryo−	Nerve biopsy +	CS CYC then AZA
#9	F, 45	C, A, H SS	3 years	Se–Mo symmetrical LL Purpura Skin ulcers	SSA+ SSB− DNA− ACL+ B2GP1+ LA− RF+ ANCA− Cryo+	Skin biopsy + and thrombosis	CS RTX

Table 1 continued

Patient	Sex, age at SLE diagnosis	SLE involvement (except PNS) and associated AID	Time between SLE diagnosis and MM*	MM characteristics	Biology	Vasculitis histology	Treatment
#10	F, 17	C, A, H, R APS	18 years	Se–Mo Asymmetrical LL–UL	SSA+ SSB+ DNA+ ACL+ RF– ANCA– Cryo+	–	CS CYC then MMF

SLE systemic lupus erythematosus; *AID* autoimmune disease; *MM* mononeuritis multiplex; *PNS* peripheral nervous system; *CNS* central nervous system, *S* seritis, *A* arthritis, *C* cutaneous, *H* hematological, *R* renal; *APS* antiphospholipid syndrome; *SS* Sjogren syndrome; *Se* sensory, *Mo* motor; *LL* lower limbs; *UL* upper limbs; *APL* antiphospholipid (including anticardiolipid ACL, lupus anticoagulant LA and antibeta2GP1); *Cryo* cryoglobulinemia; *RF* rheumatoid factor; *ANCA* anti-neutrophil cytoplasmic antibodies; *CS* corticosteroids, *CYC* cyclophosphamide, *MMF* mycophenolate mofetil, *RTX* rituximab, *BELI* belimumab; *AZA* azathioprine

* one patient had SLE diagnosis after MM diagnosis

administered as a first-line treatment in all patients: cyclophosphamide ($n = 6$), rituximab ($n = 2$), or MMF ($n = 2$). One patient received intravenous immunoglobulins. No patient underwent plasma exchange.

Partial neurological remission was obtained after remission–induction treatment in seven cases (70%), and stabilization occurred in three patients. No patient had complete neurological remission. Treatments received by patients with partial remission, in addition to steroids, were as follows: cyclophosphamide ($n = 4$), rituximab ($n = 2$), and MMF ($n = 1$). Treatments received by patients who experienced neurological stabilization, in addition to steroids, were as follows: cyclophosphamide ($n = 2$) and rituximab ($n = 1$).

After the remission–induction period, all the patients received a maintenance therapy that was MMF ($n = 4$), AZA ($n = 3$) or rituximab ($n = 3$).

At the end of the follow-up period (median 5.5 years; range 1–17), the modified Rankin score was improved (median 2; range 0–3). Two patients (#3 and 9) relapsed during follow-up. Patient #3 experienced a flare of MM with new localizations (Fig. 1). This patient had been initially treated with cyclophosphamide, then azathioprine. The patient stopped all the treatments after 8 years. Four months later, a severe sensory-motor flare occurred and rituximab was used leading to partial remission at 6 months. Patient #9 had an increase in neuropathic pain and worsening of electrophysiological study results after she spontaneously stopped the corticosteroids treatment. The symptoms improved after the steroids treatment was resumed and after maintenance rituximab infusion was performed.

The electromyogram showed sensory-motor sequelae for nine patients and sensory sequelae for one patient.

Discussion

Here, we have described ten cases of MM associated with SLE, most of which occurred several years after the diagnosis of SLE.

SLE causes various neurological manifestations that may affect any part of the nervous system [10]. Involvement of the PNS is less frequently observed than CNS involvement, occurring in less than 10% of patients with SLE, although systematic electrophysiological studies may be abnormal in up to 23% of cases [8, 16, 18, 19, 22, 24]. MM is rare and has, therefore, been described in few studies; some of these studies that contain sufficient data are detailed in the Table 2 [4, 8, 12, 13, 17, 20].

The causes of peripheral neuropathy during SLE include toxic effects of drugs (e.g., thalidomide), infections, compression, and the direct effect of SLE. In the latter case, the

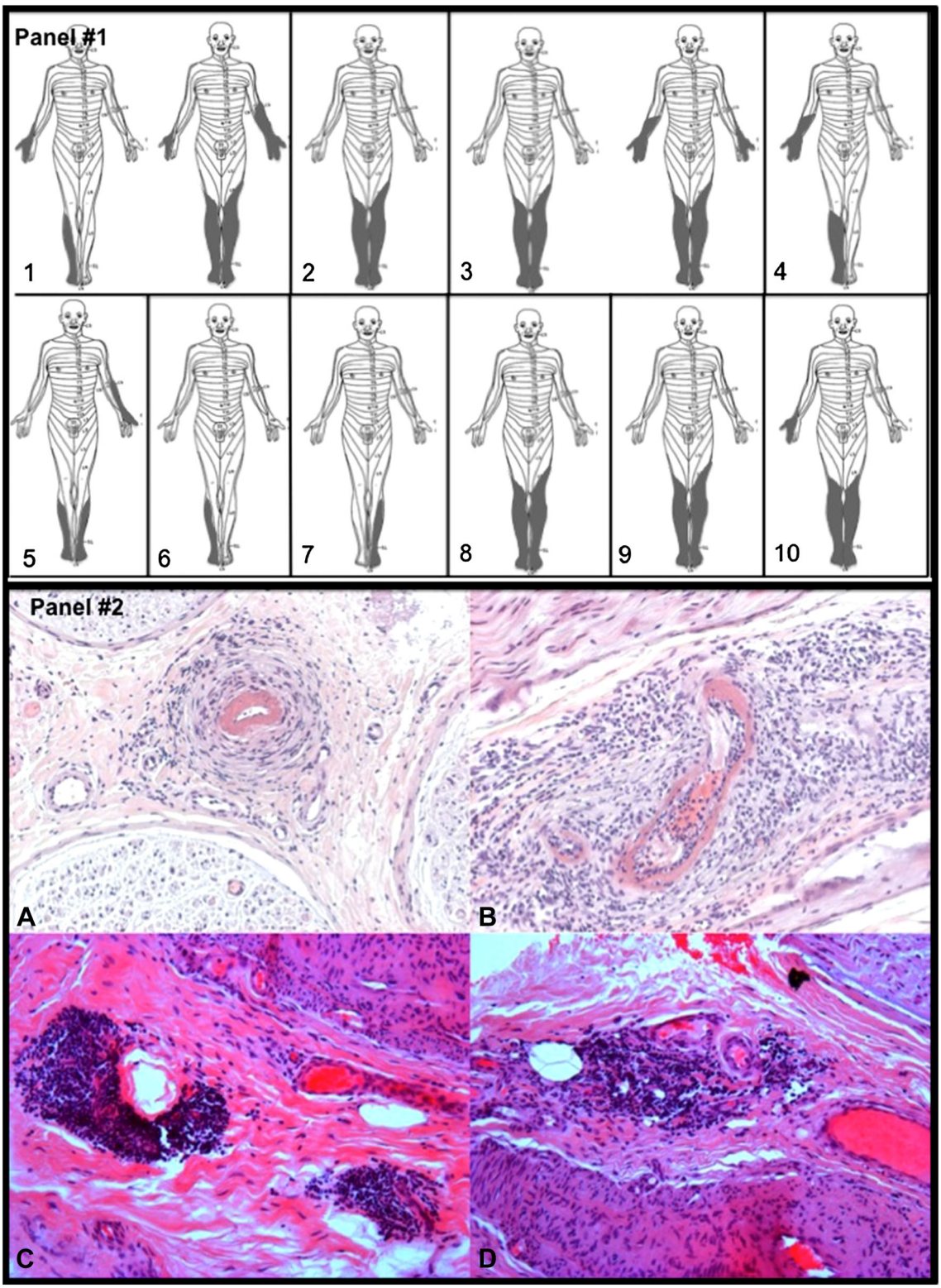

Fig. 1 Clinico-pathological presentations of MM associated with SLE. **Panel #1** Distribution of sensory deficits in the ten patients. **Panel #2** Histological patterns of the peripheral nerve biopsy of two patients. **a** and **b** Fibrinoid necrosis affecting small vessels. Nerve biopsy of patient # 1, HES × 20—**c** and **d**. Lymphocytic infiltration of small vessels. Nerve biopsy of patient # 8, HES × 20

Table 2 Previously reported cases of mononeuropathy multiplex associated with systemic lupus erythematosus

Case	Sex age	SLE: involved sites	Biology	Delay between SLE and MM	Clinical signs	Histology	Treatments	Outcomes
Astudillo et al. [25]	W 57	Arthritis	LA + ACL + C3–C4 normal Cryoglobulinemia: NA	3 years	SM	NA	Corticosteroids	Progressive improvement
Martinez-Taboada et al. [17] #2	W 23	Skin, arthritis	C4 normal Low C3 Cryoglobulinemia: NA	3 days	SM	Necrotizing vasculitis	Corticosteroids and CYC	Very good improvement No maintenance therapy
Martinez-Taboada et al. [17] #1	W 51	Skin, arthritis	Low C3 and C4 Cryoglobulinemia: NA	6 years	SM	Necrotizing vasculitis	Corticosteroids	Partial recovery Maintenance therapy with MTX
Harel et al. [12] #1	W 20	Thrombocytopenia, arthritis, skin, nephritis	aCL+	5 years	SM	NA	Steroids (intravenous then oral), gabapentin	Recovered after an 8-month treatment
Harel et al. [12] #2	W 17	Skin, oral ulcers, nephritis	aCL+	4 years	SM	NA	Prednisone, carbamazepine	Responded dramatically within 2–3 weeks
Harel et al. [12] #4	M 9	Leukopenia, arthritis, purpura, nephritis	aCL+	1 year	SM	NA	Prednisone, intravenous immunoglobulins	Partial response
Ryan et al. [20] #1	W16	Arthritis, nephritis, cerebritis	NA	4 years	SM	Necrotizing small vessels vasculitis with fibrinoid necrosis	High dose intravenous steroids	Full recovery, free of neurological symptoms
Ryan et al. [20] #2	M 17	Hematological, cerebritis, meningitis	Low C4, SS-A and SS-B− dsDNA− ANA+	5 months	SM, cranial nerves	NA	High dose steroids and rituximab	Persistent left radial nerve palsy
Ryan et al. [20] #3	W 13	None	ANA−	0	SM, multiple flares	Lymphocytic infiltrates	None	Sustained spontaneous remission
Bhowmik and Banerjee[4]	W 11	Articular	Cryoglobulinemia: NA	10 days	SM	No vasculitis	Corticosteroids	Stabilization

NA not available; *SM* sensory and motor deficits; *ANA* antinuclear antibodies; *MTX* methotrexate; *W* woman; *LA* lupus anticoagulant; *ACL* anticardiolipid antibodies; *SLE* systemic lupus erythematosus; *MM* mononeuritis multiplex; *CYC* cyclophosphamide

physiopathology is poorly understood. In our study, MM was found to be mainly due to vasculitis, although thrombosis or other lymphocytic inflammations have also been observed as a cause of MM. In particular, we highlighted the role of cryoglobulinemia in several cases, which was not always associated with Sjögren syndrome. The histological demonstration of vasculitis in the case of SLE-associated MM has also been reported in the previous cases (Table 2) [17, 20] and was highlighted in a study reporting on a series of patients with vasculitis during SLE. In this study, 19 cases of MM were observed among 194 patients presenting with SLE and vasculitis [7], and MM was the most frequent sign of the visceral involvement of vasculitis (excluding the skin). Thus, we suggest that MM is frequently an overlapping manifestation of SLE with cryoglobulinemic vasculitis.

It was previously suggested that peripheral neuropathy during SLE was associated with older age [16], active forms of lupus [24], high levels of serum immunoglobulins [24], and antiphospholipid [5, 21] and anti-SS-A antibodies [5, 22]. In our series, we did not have a control group, and we thus could not make conclusions about such associations. However, the most prominent feature of the patients in the present study was a high SLEDAI score at the time of MM occurrence. This difference is explained by the fact that MM is distinct from other forms of peripheral neuropathy.

The definitive diagnosis of neuropathy in patients with SLE is important, because it prompts appropriate treatments. Features such as acute or subacute onset, pain, asymmetrical pattern, motor involvement, and the rapid involvement of the upper limbs may act as "red flags" and lead to biological screening for elevated CRP, cryoglobulinemia, and finally neuromuscular biopsy if necessary. As demonstrated in our study, the clinical presentation of MM is frequently non-symmetrical. However, in severe confluent MM, the presentation may be pseudo-symmetrical. Electrophysiological studies may help in determining a non-symmetrical pattern.

MM usually presents with sensory-motor deficits, although pure sensory neuropathy is possible. Urgent treatment is required for MM and leads to variable outcomes. In our series, cyclophosphamide was the most frequently used immunosuppressive drug as it has been demonstrated to be effective in severe forms of neuropsychiatric SLE [2, 3, 10]. Rituximab also seemed to be effective.

In conclusion, although the occurrence of MM is rare during SLE, the early recognition and aggressive therapy of systemic necrotizing vasculitis is essential for the successful management of these patients. Electrophysiological studies are essential for the diagnosis of MM. Cryoglobulinemia should be tested in the case of an MM pattern, since cryoglobulinemia vasculitis frequently overlaps with SLE in this case.

Compliance with ethical standards

Conflicts of interest The authors declare no conflicts of interest.

Ethical standards The study was conducted in compliance with the Good Clinical Practice protocol and the Declaration of Helsinki Principles. According to the current French Legislation (Loi Jardé 2002 and its subsequent amendments https://www.legifrance.gouv.fr/affichTexte.do;jsessionid=D8DE76AD02196EE756E078C9212A0C6E.tpdila13v_3?cidTexte=JORFTEXT000032719520&categorieLien=id), an observational and retrospective study that does not change the routine management of patients does not need to be declared to the local ethics board.

Financial support None.

References

1. Liang MH, Corzillius M, Bae SC, Lew RA, Fortin PR, Gordon C, Isenberg D, Alarcón GS, Straaton KV, Denburg J, Denburg S (1999) The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum 42:599–608
2. Barile-Fabris L, Ariza-Andraca R, Olguin-Ortega L, Jara LJ, Fraga-Mouret A, Miranda-Limon JM, Fuentes de la Mata J, Clark P, Vargas F, Alocer-Varela J (2005) Controlled clinical trial of IV cyclophosphamide versus IV methylprednisolone in severe neurological manifestations in systemic lupus erythematosus. Ann Rheum Dis 64:620–625
3. Bertsias GK, Ioannidis JP, Aringer M, Bollen E, Bombardieri S, Bruce IN, Cervera R, Dalakas M, Doria A, Hanly JG, Huizinga TW, Isenberg D, Kallenberg C, Piette JC, Schneider M, Scolding N, Smolen J, Stara A, Tassiulas I, Tektonidou M, Tincani A, van Buchem MA, van Vollenhoven R, Ward M, Gordon C, Boumpas DT (2010) EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs. Ann Rheum Dis 69:2074–2082
4. Bhowmik A, Banerjee P (2012) Mononeuritis multiplex complicating systemic lupus erythematosus. Indian Pediatr 49:581–582
5. Borowoy AM, Pope JE, Silverman E, Fortin PR, Pineau C, Smith CD, Arbillaga H, Gladman D, Urowitz M, Zummer M, Hudson M, Tucker L, Peschken C (2012) Neuropsychiatric lupus: the prevalence and autoantibody associations depend on the definition: results from the 1000 faces of lupus cohort. Semin Arthritis Rheum 42:179–185
6. Callaghan BC, Price RS, Chen KS, Feldman EL (2015) The Importance of Rare Subtypes in Diagnosis and Treatment of Peripheral Neuropathy: a Review. JAMA neurology 72:1510–1518
7. Drenkard C, Villa AR, Reyes E, Abello M, Alarcon-Segovia D (1997) Vasculitis in systemic lupus erythematosus. Lupus 6:235–242
8. Florica B, Aghdassi E, Su J, Gladman DD, Urowitz MB, Fortin PR (2011) Peripheral neuropathy in patients with systemic lupus erythematosus. Semin Arthritis Rheum 41:203–211
9. Gladman D, Ginzler E, Goldsmith C, Fortin P, Liang M, Urowitz M, Bacon P, Bombardieri S, Hanly J, Hay E, Isenberg D, Jones J, Kalunian K, Maddison P, Nived O, Petri M, Richter M, Sanchez-

Guerrero J, Snaith M, Sturfelt G, Symmons D, Zoma A (1996) The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 39:363–369
10. Hanly JG (2014) Diagnosis and management of neuropsychiatric SLE. Nat Rev Rheumatol 10:338–347
11. Harboe E, Tjensvoll AB, Maroni S, Goransson LG, Greve OJ, Beyer MK, Herigstad A, Kvaloy JT, Omdal R (2009) Neuropsychiatric syndromes in patients with systemic lupus erythematosus and primary Sjogren syndrome: a comparative population-based study. Ann Rheum Dis 68:1541–1546
12. Harel L, Mukamel M, Brik R, Blau H, Straussberg R (2002) Peripheral neuropathy in pediatric systemic lupus erythematosus. Pediatr Neurol 27:53–56
13. Hirabayashi Y, Saito S, Takeshita MW, Kodera T, Munakata Y, Ishii T, Fujii H, Shimura M, Sasaki T (2003) Mononeuritis multiplex, protein-losing gastroenteropathy, and choroidopathy seen together in a case of systemic lupus erythematosus. Mod Rheumatol 13:265–269
14. Hochberg MC (1997) Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 40:1725
15. Huynh C, Ho SL, Fong KY, Cheung RT, Mok CC, Lau CS (1999) Peripheral neuropathy in systemic lupus erythematosus. J Clin Neurophysiol 16:164–168
16. Jasmin R, Sockalingam S, Ramanaidu LP, Goh KJ (2015) Clinical and electrophysiological characteristics of symmetric polyneuropathy in a cohort of systemic lupus erythematosus patients. Lupus 24:248–255
17. Martinez-Taboada VM, Alonso RB, Armona J, Fernandez-Sueiro JL, Gonzalez Vela C, Rodriguez-Valverde V (1996) Mononeuritis multiplex in systemic lupus erythematosus: response to pulse intravenous cyclophosphamide. Lupus 5:74–76
18. Mok CC, To CH, Mak A (2006) Neuropsychiatric damage in Southern Chinese patients with systemic lupus erythematosus. Medicine 85:221–228
19. Oomatia A, Fang H, Petri M, Birnbaum J (2014) Peripheral neuropathies in systemic lupus erythematosus: clinical features, disease associations, and immunologic characteristics evaluated over a twenty-five-year study period. Arthritis Rheumatol 66:1000–1009
20. Ryan MM, Tilton A, De Girolami U, Darras BT, Jones HR Jr (2003) Paediatric mononeuritis multiplex: a report of three cases and review of the literature. Neuromuscul Disord 13:751–756
21. Santos MS, de Carvalho JF, Brotto M, Bonfa E, Rocha FA (2010) Peripheral neuropathy in patients with primary antiphospholipid (Hughes') syndrome. Lupus 19:583–590
22. Su YJ, Huang CR, Chang WN, Tsai NW, Kung CT, Lin WC, Huang CC, Su CM, Cheng BC, Chang YT, Lu CH (2014) The association between autoantibodies and peripheral neuropathy in lupus nephritis. Biomed Res Int 2014:524940
23. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, Schaller JG, Talal N, Winchester RJ (1982) The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 25:1271–1277
24. Xianbin W, Mingyu W, Dong X, Huiying L, Yan X, Fengchun Z, Xiaofeng Z (2015) Peripheral neuropathies due to systemic lupus erythematosus in China. Medicine 94:e625
25. Astudillo L, Sailler L, Godel A, Cousin F, Couret B, Arlet-Suau E (2003) Une multinévrite révélant un lupus érythémateuxsystémique. La revue de médecine interne 24(Supplément 1): 1–131