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Inflammatory Myopathies In Lome: A Review Of Two Cases With Delayed Diagnosis

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SUMMARY

Inflammatory myopathies (IMDs) are a group of autoimmune muscle diseases that are heterogeneous in terms of their clinical presentation, their progressive profile, their possible association with extramuscular involvement and their response to treatment. We report 2 cases of IMD in Lomé with a diagnostic delay of several years. The first patient is a 37-year-old black female, who had progressive onset of peripheral neuropathy for about ten years. Clinical assessment revealed pseudo-hypertrophy of the calves and shoulders, muscular atrophy of several muscle groups, bilateral steppage gait, and tetraparesis. Creatine phospho-kinase was elevated, and the electroneuromyogram (ENMG) noted an IMD pattern. Antinuclear auto-antibodies came back positive on indirect immunofluorescence assay (IFA) with a titer of 1/320 and anti-deoxyribonucleic Acid antibodies were positive. The second patient is a 32-year-old black female with a history of myopathy who was admitted for constrictive retrosternal chest pain. Clinical assessment was remarkable for fever and pigmented macules in the upper limbs. Echocardiography was in favour of pericarditis, ENMG showed an IMD pattern, a thoracic CT showed bilateral posterior-basal septal thickening and 24-hour proteinuria was positive. Antinuclear autoantibodies (IFA) were positive at 1/1280 titer, and anti-Smith antibodies were strongly positive. Both patients were diagnosed with systemic lupus erythematosus-myositis overlap syndrome and were treated with corticosteroids and methotrexate.

Keywords: inflammatory myopathy, systemic lupus, Togo.

INTRODUCTION

Inflammatory myopathies (IMDs) are a group of rare autoimmune diseases that affect muscles. Their clinical presentation, progression, association with extramuscular damage and their response to treatment varies considerably[1]. IMDs are classified into 5 subtypes: dermatomyositis, autoimmune necrotizing myopathies (AEM),

overlap myositis including antisynthetase syndrome, polymyositis, and sporadic inclusion myositis [1], [2]. The diagnosis is not easy and is based on a range of clinical and paraclinical arguments [1]. In Lomé, studies on inflammatory myopathies are rare. In a study on chronic inflammatory rheumatism in rheumatological consultations for 9 years, the authors found 290 cases out of 20333 cases, i.e. a hospital frequency of 1.43% [3]. Polymyositis accounted for only 2% of chronic inflammatory rheumatism [3]. We believe that this proportion of inflammatory myopathy in medical consultations is underestimated in Togo, the diagnostic challenge being early diagnosis. We received 2 cases of overlapping myositis in 2023 with a diagnostic delay of 11 years for the 1st and 5 years for the second and it seemed important to us to report these cases.

CASE N° 1

The first case is that of a 37-year-old, right-handed, black female who works as a secretary. Her history is remarkable for a nodulectomy of the left breast in 2013 and a myomectomy in 2021. She had never been pregnant before. Her history was unremarkable for alcohol abuse and drug allergies. There was no family history of muscle disease and consanguinity.

Her symptoms started progressively in 2012 with physical asthenia and unexplained myalgia. In 2013, she developed a steppage gait on the left which was followed a year later by a motor deficit of the right upper limb. The motor deficit progressively extended to the left upper limb from 2013 to 2015. Between 2015 and 2017, the steppage gait aggravated. She consulted in 2017 and the clinical assessment at that time found bilateral paralysis of the external popliteal sciatic nerve, significant muscular atrophy of the thenar and right hypothenar eminence, a positive Gowers sign with pseudo-hypertrophy of the calves. Multiple mononeuropathy or distal myopathy were the differential diagnoses made. The full blood count was normal, the erythrocyte sedimentation rate (ESR) was 7 mm, serum protein electrophoresis showed polyclonal hypergammaglobulinemia, blood glucose and creatinine clearance were normal, HIV, hepatitis B, and hepatitis C serology were negative, muscle enzymes were strongly elevated (Table 1).

She was lost to follow-up from 2017 to 2019. In 2019, the motor deficit on the upper limbs aggravated predominantly on the right and distal. She consulted again in January 2023 due to the onset of paresthesia (cramps) in the left lower limb. Clinical assessment was remarkable for a weight of 64 kg for a height of 160 cm giving a body mass index (BMI) of 25, pseudohypertrophy of the calves and shoulders, amyotrophy of the first interosseous, bilateral steppage gait that was pronounced on the left. She had proximal paresis on the upper limbs with a muscle strength of 2/5 at the shoulders, and 3+/5 distally. There was muscle weakness on the lower limbs which was pronounced distally (4/5 at the thighs, 2/5 distally). Deep tendon reflexes were abolished on all 4 limbs. The sensory assessment, cognitive functions and the rest of the neurological examination were unremarkable. Laboratory tests at this stage showed: creatine phosphokinase (CPK), CPK MB, myoglobinemia highly elevated, and elevated lactate dehydrogenases and aldolases (Table 2). The electrocardiogram was normal. Needle electroneuromyogram (ENMG) revealed neurogenic and myogenic tracing, concluding on an IMD pattern (Figures 1 and 2).

The workups to identify the etiology of this myopathy included, antinuclear autoantibodies by indirect immunofluorescence assay using HEp-20-10 cell, positive income at a titer of 1/320 whose appearance is speckled, native anti-Deoxyribonucleic Acid (DNA) IgG autoantibodies was positive (table 2). Based on the American College of Rheumatology (ACR) criteria, it was

concluded that systemic lupus occurred. We retained a diagnosis of systemic lupus erythematosus-overlap myositis. The patient was given a 3-day IV course of methylprednisolone at 1 g followed by a follow-up with methylprednisolone per os at 64 mg in the morning and methotrexate 7.5 mg per week was introduced and functional rehabilitation sessions were initiated. There was neither improvement nor worsening of symptoms after 6 months of these treatments.

CASE N° 2

In July 2023, a 32-year-old black, right-handed, seamstress was hospitalized in a health centre in Lomé. Her history is remarkable for myopathy of undetermined etiological diagnosis, for which she has been followed up since 2019. Her clinical presentation at the onset was characterized by polyarthralgia and myalgia with CPK elevated at five times the normal. She was on long-term treatment with prednisone, 40 mg/day. Her history was also remarkable for peptic ulcer disease, primigravida, and primiparity, with no history of alcohol use, and no known drug allergies. Her surgical history was unremarkable. There was no family history of muscle disease and no consanguinity.

The day before her admission, she suddenly developed bilateral, constrictive, retrosternal and excruciating chest pain aggravated by deep inspiration, and alleviated by the forward leaning position, associated with fever and dyspnea of rest. There was no history of infection with Mycobacterium, no night sweats, unexplained weight loss and chronic cough.

Clinical assessment found a weight of 85 kg, a height of 168 cm with a BMI of 30.11, fever with a body temperature of 38°5, a blood pressure of 120/80mmHg, and a saturation at room air of 98%. The mental status was intact, as was the general state. There was discrete oedema of the lower limbs, and fine crackles at base of the left lung. Dermatological examination revealed pigmented macules on the upper limbs (figure 3), multiple inflamed joints, post-ulceration scar tissue on the right phalanges, no malar rash, and no notion of photosensitivity. Neurological examination revealed preserved cognitive functions, no sensory or motor deficits, and no pseudo-hypertrophy of the calves. The idiomuscular contraction was difficult to assess due to the significant adipose tissue covering the muscles in this patient. Gower's sign was negative. The rest of the clinical examination, including cardiovascular and digestive examination, was unremarkable.

The ECG found a depression without the involvement of the P wave. Transthoracic cardiac ultrasound revealed circumferential minimal pericardial effusion. The troponin markers were normal. The diagnosis of pericarditis of infectious or neoplastic aetiology on a probable connective tissue disorder was made. The laboratory work-up (table 3) included a normal renal and hepatic work-up, a blood count which revealed normocytic normochromic anemia, ESR at 90 mm, and a 24-hour proteinuria was positive at 2656.80 mg/24h. The ENMG found neurogenic and myogenic tracings concluding on IMD pattern (Figure 4). Chest CT scan revealed bilateral postero-basal septal thickenings, with the absence of pulmonary fibrosis. Investigations for the subtype of this myopathy (table 3) included the assays for antinuclear autoantibodies (indirect immunofluorescence assay using HEp-20-10 cells) with a speckled appearance with a titer greater than 1/1280, negative anti-native DNA IgG autoantibodies; the results of the anti-soluble nuclear antigen auto-antibodies came back strongly positive for anti-Smith (SmD1), Soluble A 52 kD nuclear ribonucleoprotein (SSA/Ro), Uracil 1 Small nuclear ribonuclear protein (U1snRNP) and positive for anti-nucleosome. The diagnosis of overlap myositis (systemic lupus erythematosus) was finally retained.
An IV course of methylprednisolone at a dose of 500 mg was given for 5 days and methotrexate at a dose of 7.5 mg each week was introduced in addition to

prednisone at 40 mg in the morning. The outcome was favourable with the regression of fever, chest pain and dyspnea allowing her to be discharged home on day 10 of hospitalization. The evolution at 6 months notes clinical stability with a rarity of relapses

Table 1: Main biological analyses in 2017

BLOOD TESTS	RESULTS	STANDARDS
ALT	**521.9 IU/L**	N [0-30 IU/l]
AST	**239.3 IU/l**	N [0-40 IU/l]
ALP	**264 IU/l**	N [0-240 IU/l]
GGT	**645 IU/l**	N [5-42 UIL/l]
CPK-MB	**27.24 mg/ml**	N [0-3 mg/ml]
Blood count	Hb 12.7 g/dl	N [12-16 g/dl]
	MCV =72.8 fl	N [80-100 fl]
	MCHC=24.8 pg	N [27-34 pg]
	Leukocytes 5070 µ/l	N [4000-10,000 µ/l]
	Platelets 250 0000 µ/l	N [150,000-300,000 µ/l]
ESR	7 mm 1st hour	N<20mm
CRP	5 mg/l	N <5 mg/l
Urea	0.16 g/l	N [0.15-0.45 g/l]
Creatinine	06 mg/l	N [07-14 mg/l]
Glycemia	0.75 g/l	N [0.70-1.10 g/l]
Creatinine clearance (CPK-EPI)	143.76 ml/min	N> 90 ml/min
Serum protein electrophoresis	**Polyclonal hypergammaglobulinemia**	
HIV, hepatitis B and hepatitis C serology	Negative	

Legend: AST: aspartate aminotransferase, ALT: alanine aminotransferase, GGT: gamma-glutamyltransferase, ALP: alkaline phosphatase, LDH: lactate dehydrogenase, CPK: creatine phospho-kinase, Hb: hemoglobin level, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin content, ESR: sedimentation rate, CRP: C-reactive protein, HIV: human immunodeficiency virus.

Table 2: Main biological analyses in 2023

BLOOD TESTS	RESULTS	STANDARDS
CPK	**1072 IU/l**	N [24-190 IU/l]
CPK-MB	**24.76 IU/l**	N [0-5 IU/l]
LDH	**476 IU/l**	N [225-450 IU/l]
Aldolase	**9.1 IU/L**	N ≤7.6 IU/l
Myoglobine	**500 ng/ml**	N [0-70 ng/ml]
Antinuclear antibodies (IFA)	**Title at 1/320 Speckled appearance**	N <1/160
Anti-native DNA antibodies	**21 IU/ml**	N <10 IU/ml
SSA/Ro (60 kDa, 52 kDa)	2 IU/ml	N <7 IU/ml
SSB/LA	2 IU/ml	N <7 IU/ml
SmD1	2 IU/ml	N <5 IU/ml
U1snRNP	3 IU/ml	N <7 IU/ml
Jo1	2 IU/ml	N <7 IU/ml
SCL70	2 IU/ml	N <7 IU/ml
Centromere	3 IU/ml	N <7 IU/ml

Legend: CPK: creatine phospho-kinase, LDH: lactate dehydrogenase, IFA: indirect immunofluorescence assay using HEp-20-10 cells, DNA: Deoxyribonucleic acid, SSA/Ro: Soluble A

nuclear ribonucleoprotein, SSB/La: Sjögren syndrome B, SmD1: Smith, U1snRNP: Uracil 1 Small nuclear ribonuclear protein, Jo1: anti-aminoacyl-t-RNA-synthetases, Scl 70: anti-topoisomerase I.

Table 3: Key Biology Casework Analysis Results

BLOOD TESTS	RESULTS	STANDARDS
Troponin I	0.01 ng/ml	N< 0.1 ng/ml
D-Dimer	320 ng/ml	N<500 ng/ml
ALT	15 IU/l	N [0-30 IU/l]
AST	17 IU/l	N [0-40 IU/l]
ALP	54 IU/l	N [35-104 IU/l]
GGT	25 IU/l	N [5-42 UIL/l]
TP	86,5%	N [70-100%]
Blood count	**Hb 10.7 g/dl**	N [12-16 g/dl]
	MCV=72.8 fl	N [80-100 fl]
	MCHC=24.8 pg	N [27-34 pg]
	Leukocytes 13090 µ/l	N [4000-10,000 µ/l]
	Platelets 357,000 µ/l	N [150,000-400,000 µ/l]
ESR	90 mm	N<20mm
CRP	200.41 mg/l	N <6 mg/l
Urea	0.15 g/l	N [0.15-0.45]
Creatinine	05 mg/l	N [07-14 mg/l]
Glycemia	0.90 g/l	N [0.7-1.1 g/l]
Creatinine clearance	143 ml/min	N> 90 ml/min
TSH	0.68 µIU/mL	N [0.39-6.16 µIU/ml]
HIV, hepatitis B, hepatitis C and SARS-CoV-2 serology	Negative	
Serum protein electrophoresis	**Polyclonal hypergammaglobulinemia**	
Rheumatoid factor	5 IU/l	N [0-14 IU/l]
CPK	36 IU/L	N [24-170 IU/l]
Myoglobin	17.81 ng/ml	N [0-70 ng/ml]
24-hour proteinuria	**2656.80 mg/24h**	N<150 mg/24h
Blood ionogram	Normal	
Antinuclear antibodies (IFI)	**Title > to 1/1280**	N <1/160
	Speckled appearance	
Anti-native DNA antibodies	05 IU/ml	N <10 IU/ml
SSA/Ro 60 kD	0,2	N <7 IU/ml
SSA/Ro 52 kD	**100 IU/ml**	N <7 IU/ml
SSB/LA	0.05 IU/ml	N <7 IU/ml
SmD1	**75 IU/ml**	N <5 IU/ml
U1snRNP	**30 IU/ml**	N <7 IU/ml
Jo1	2.10 IU/ml	N <7 IU/ml
SCL70	0.1 IU/mL	N <7 IU/ml
Centromere	0.57 IU/mL	N <7 IU/ml
Nucleosome	**10 IU/ml**	N <7 IU/ml
Ribosomal anti protein P	1.39 IU/ml	N <7 IU/ml
Histone	9.69 IU/mL	N <7 IU/ml

Legend: ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma-glutamyltransferase, ALP: alkaline phosphatase, TP: prothrombin level, ESR: sedimentation rate, CRP: C reactive protein, LDH: lactate dehydrogenase, CPK: creatine phospho-kinase, TSH: thyroid-stimulating hormone Hb: Hemoglobin level, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin content, , CRP: C-reactive protein, HIV: human immunodeficiency virus, IFI: Indirect immunofluorescence on Hep 20-10 slides, DNA: Deoxyribonucleic acid, SSA/Ro: Soluble nuclear ribonucleoprotein A SSB/La: Sjögren syndrome B, SmD1: Smith, U1snRNP: Uracil 1 Small nuclear ribonuclear protein, Jo1: anti-aminoacyl-t-RNA-synthetases, Scl 70: anti-topoisomerase I.

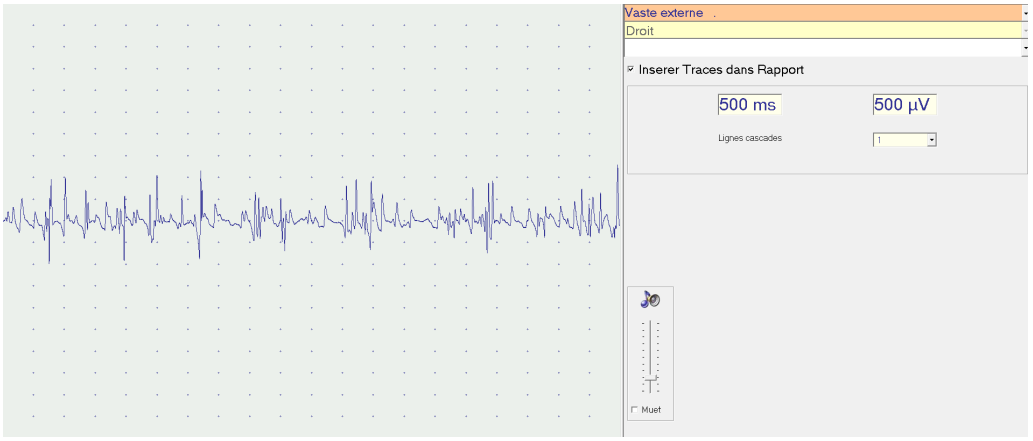

Figure 1: Neurogenic tracing at the right vastus lateralis muscle

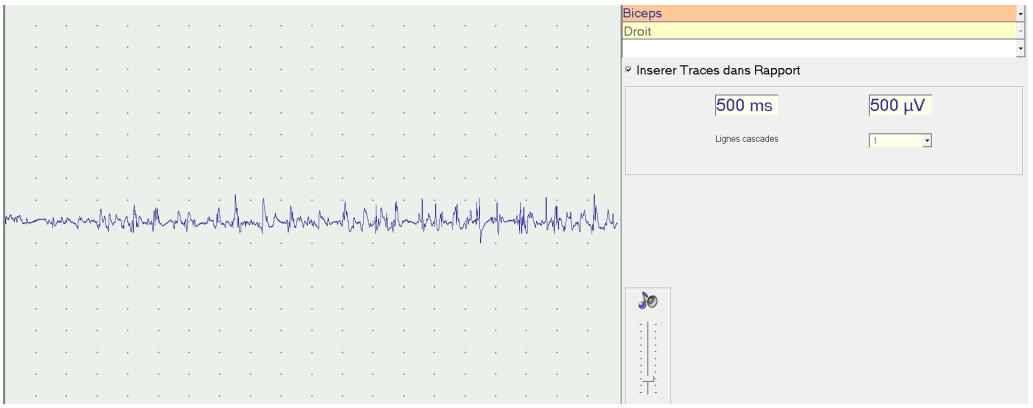

Figure 2: Myogenic and neurogenic tracing at the right biceps

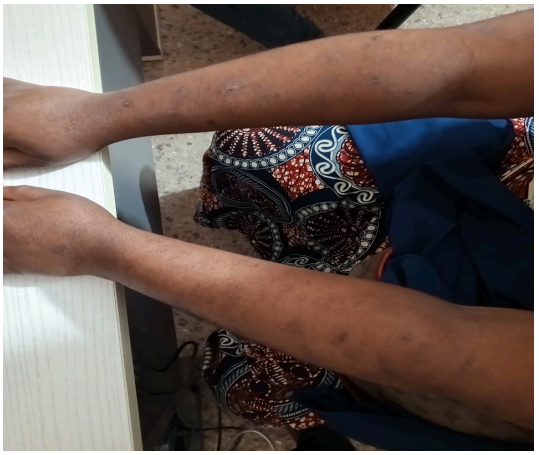

Figure 3: Pigmented macules sequellary to the upper limbs

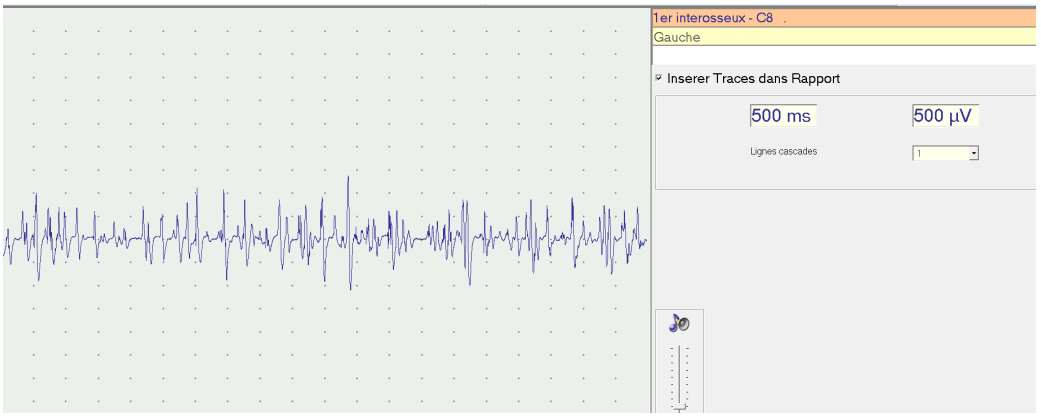

Figure 4: Neurogenic tracing at the 1st left interosseous

DISCUSSION

Inflammatory myopathies are described as a complication of systemic lupus erythematosus in 4–16% of cases [4], [5], [6], [7]. In the association of lupus and inflammatory myopathy, there is a clear female predominance (100% according to several series) [4], [5], [6], [8]. Our 2 reported cases are women. Black patients [5], [7] and those with childhood lupus [6] have a higher risk of developing inflammatory myopathy.

A detailed history of the clinical course of symptoms, the topography of the muscles involved, and the extramuscular manifestations are indispensable for the determination of the IMD subtype. In addition, measurements of muscle enzymes, the results of ENMG and muscle imaging, muscle biopsy and, in some conditions, the presence of autoantibodies are equally important [1]. This makes diagnosis difficult in countries with limited resources, such as those in Sub-Saharan Africa.

There was a significant delay in diagnosis in both cases. The delay in diagnosis in the first case is essentially the result of the patient being lost to follow-up. With positive antinuclear antibodies, we used the American Rheumatology Association (ACR) criteria [9] to make the diagnosis of systemic lupus. In the second patient, the diagnosis of IMD was finally made after the fever and extramuscular involvement that turned out to be pericarditis. The subtype has long been discussed between dermatomyositis and overlap myositis. Again, given the high positivity of antinuclear antibodies, the ACR criteria [9] were used to establish the diagnosis of systemic lupus.

Etiological investigations in our two patients resulted in overlap myositis which is defined as an inflammatory muscle disorder occurring as a result of systemic diseases [1], [2]. This subtype of IMD is not only found in systemic lupus but also sarcoidosis, systemic scleroderma, Sjogren's syndrome, and antisynthetase syndrome [1], [2]. While in Sub-Saharan Africa, studies on IMD are rare [10], those with the Overlap Myositis (OM) subtype are rare. In Senegal, in a study of 15 cases of DM and 6 cases of polymyositis, scleroderma accounted for 50% of OMs [11]. In a South African study in Durban with 104 cases of IMD, OMs accounted for 39.4% of cases [10]. The subtypes of OM represented were scleroderma in 63.4% of cases, systemic lupus (22%), rheumatoid arthritis (12.2%), and mixed connective tissue disease (2.4%).

Due to the involvement of multiple organs, patients with IMD can be found in a variety of medical specialities. In our second patient, it was the multidisciplinary collaboration that made it possible to establish a diagnosis. It is therefore essential to encourage this multidisciplinary approach, which is essential for the diagnosis and management of IMD.

The delay in diagnosis led to a delay in treatment. The treatment of IMD is mainly based on corticosteroids and immunosuppressants [2]. The most commonly prescribed corticosteroid is prednisone, initiated at a dose of 0.5 to 1 mg/kg/day up to a maximum of 80 to 100 mg/day. Other immunosuppressive therapies may be offered as an adjuvant to corticosteroid therapy or initiated immediately in combination with it: methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, cyclosporine, tacrolimus, intravenous immunoglobulins, rituximab, etc.

Immunosuppressive therapy in the first patient was initiated 10 years after the onset of symptoms, and the second patient was already receiving long-term treatment with corticosteroid therapy. It was combined in both cases with methotrexate. In the Maazoun series in Tunisia, 6 patients were treated with prednisone 1 mg/kg/day and then the dose was tapered to 10 mg/day, 3 patients received 1 g of methylprednisolone for 3 days, one patient was treated with monthly intravenous courses of cyclophosphamide in combination with corticosteroid treatment [8]. In South Africa, methotrexate (43.8%) and azathioprine (41.5%) were the most frequently used immunosuppressants [9].

Studies on the prognosis of systemic lupus-associated myopathies are conflicting [4], [6], [8]. Some authors report a benign course while others find no difference in terms of morbidity and response to treatment [4], [8]. Others report a poor prognosis with early death [6]. The presence of RNP auto-antibodies is thought to be a predictive factor for poor prognosis [6]. In our second patient in whom these antibodies were found, we do not have enough hindsight to judge the evolution.

CONCLUSION

IMDs are rarely reported in Togo due to their heterogeneity, clinical polymorphism and limited technical platform. Their care is multidisciplinary. The clinician should think about IMDs in a case of myalgia in a young woman.

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