Contribution of dot-blot assay to the diagnosis and management of myositis: a three-year practice at a university hospital centre

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Abstract

Objective

Idiopathic inflammatory myopathies (IIM) are heterogeneous autoimmune diseases with wide clinical spectrum that may lead to delayed diagnosis. The aim of this study was to examine the impact of IIM-specific dot-blot assay on diagnostic process of patients presenting with muscular or systemic symptoms evocating of IIM.

Methods

We collected all the prescriptions of an IIM specific dot-blot assay (8 autoantigens including Jo-1, PL-7, PL-12, SRP, Mi-2, Ku, PM/Scl and Scl-70) over a 38-month period.

Results

316 myositis dot-blot assays (MSD) were performed in 274 patients (156 women, mean age 53±10.6 years) referring for muscular and/or systemic symptoms suggesting IIM. The timing of dot prescription through the diagnostic process was highly variable: without (35%), concomitantly (16%) or after electromyographic studies (35%). Fifty-nine patients (22%) had IIM according to Bohan and Peter's criteria. Among them, 29 (49%) had positive dot (8 Jo-1, 6 PM-Scl, 5 PL-12, 5 SRP, 2 Mi-2, 2 PL-7 and 1 Ku). Various other diagnoses were performed including 35 autoimmune disease or granulomatosis (12%), 19 inflammatory rheumatic disease (7%), 16 non inflammatory muscular disorders (6%), 10 drug-induced myalgia (4%), 11 infectious myositis (4%). Except 11 borderline SRP results and one transient PM-Scl, MSD was positive only in one case of IIM. Dot allowed clinicians to correct diagnosis in 4 cases and improved the diagnosis of IIM subtypes in 4 cases.

Conclusion

This study reflects the interest of myositis dot in the rapid diagnosis process of patients with non-specific muscular symptoms leading to various diagnoses including IIM.

Key words

myositis, myalgia, myositis dot-blot assay

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Introduction

Idiopathic inflammatory myopathies (IIM) are a group of heterogeneous autoimmune diseases characterised by an inflammatory involvement of the muscle tissue leading to muscle weakness and pain (1). The wide clinical spectrum of IIM, ranging from initially isolated interstitial lung disease to phenotypes involving muscle weakness, Raynaud's phenomenon, fever, cardiac or dermatological involvement may delay diagnosis (2-4). IIM are usually subdivided into pure polymyositis (pPM), pure dermatomyositis (pDM), inclusion body myositis (IBM), myositis-overlap syndrome (MoS) and necrotising autoimmune myopathies (NAM) according to the current classifications (5-6).

Recently, new laboratory assays emerged that can provide valuable assistance in the diagnostic process of IIM. These tests have been also keys for the characterisation of more homogeneous groups of patients with a subdivision based on autoantibodies specificities. Indeed, new target autoantigens are identified allowing the subdivision of IIM autoantibodies into myositis specific autoantibodies (anti-Jo-1, -PL-7, -PL-12, -Mi-2, -SRP) and myositis-associated autoantibodies (anti-SS-A, -SS-B, -U1snRNP, PM/Scl, -Ku) according to the classification of Troyanov (6, 7). These tests in turn allowed the subdivision of myositis into anti-synthetase syndrome (Jo-1, PL-7, PL-12, OJ, EJ, KS…) and anti-SRP associated necrotising myopathies, two distinct forms of IIM with respect to features and prognosis (9-12).

Numerous dot-blot assays recently commercialised have become part of routine examinations requested for the diagnosis or monitoring of patients with suspected IIM; moreover, these assays represent a reliable alternative to more complex and time-consuming laboratory tests with cost-effective optimised and simultaneous detection of several myositis-associated autoantibodies and myositis specific autoantibodies (12-14).

Two previous studies have pointed out the interest of these dot-blot assays in the subdivision of patients with biopsy-proven IIM in homogenous subgroups leading to specific treatment and outcome (15-16); however, the interest of these dots in diagnostic procedures of patients with a suspected IIM or unspecific muscular symptoms is unknown.

The aim of this study was to examine the impact of dot-blot assay on diagnostic process, prognostic and treatment of patients presenting with muscular or systemic symptoms evocating of IIM and recruited in a university hospital.

Patients and methods

The commercial assay used in our Immunology Department is the Sclero-Poly-Synthetase Profile 8 Dot (SPSdot, Alphadia Diagnostic Products, Wavre, Belgium), consisting of a membrane striped with the 8 auto-antigens Jo-1, PL-7, PL-12, SRP, Mi-2, Ku, PM/Scl and Scl-70. The assay was used according to the manufacturer's instructions. In addition to positive and negative controls made by the purchaser, for each specificity assessing high sensitivity and specificity (100%), dots were controlled in the laboratory with positive and negative sera obtained from internal recruitment in Limoges university hospital, according to the final diagnosis. They included positive control samples for SRP (2 sera), anti-PL7 (n=1), anti-PL12 (n=1), anti -Jo-1 (n=5), anti-Ku (n=2), anti-PM-Scl (n=5), anti-Scl-70 (n=5), anti-Mi-2 (n=2) and negative sera (n=10) from non-inflammatory irrelevant diseases; results were categorised as positive, negative or borderline.

Antinuclear antibodies were characterised by immunofluorescence in HEp2 cells (The Binding Site, Saint Egrève, France) and both anti-native DNA (nDNA) and anti-extractable nuclear antigen (ENA) antibodies by ELISA (Phadia, Saint-Quentin Yvelines, France). In case of an anterior anti-nuclear antibody prescription, the research of antinuclear antibodies was not repeated systematically at the time of the dot prescription.

We questioned the database of the Immunology Department in order to collect all the dot prescriptions made since the availability in the laboratory of the

myositis dot (MSD) from 01/02/2010 to 02/28/2013. The data concerning all patients with a prescription of MSD were retrospectively collected. This study was conducted in compliance with the protocol Good Clinical Practices and Declaration of Helsinki principles. In accordance with French law, formal approval from an ethics committee is not required for this kind of retrospective study.

Data regarding patients' characteristics and laboratory results were reviewed in the electronic patient record databases of the different departments concerned. The data were collected up to 01/08/2015 *via* the same process.

Statistical analyses were performed by Fisher's exact test, Student's *t*-test, Wilcoxon and Chi-square tests, as appropriate. A p-value ≤ 0.05 was considered statistically significant.

Results

Prescription of the myositis-specific dot

Over a 38-month period, 316 MSDs were performed in 274 different patients (156 women, mean age 53±10.6 years). The MSD was renewed twice or more in 23 patients.

MSD was increasingly prescribed during the study period: 46 dots (15%) were made in 2010, 86 (27%) in 2011, 155 (49%) in 2012, and 27 (9%) during January and February 2013.

The prescriptions of MSD mainly originated from the Internal Medicine Department (210 prescriptions, 77%) and the Neurology Department (32 prescriptions, 12%). Other occasional prescribers were pneumologists (n=8, 3%), rheumatologists (n=5, 2%), hepato-gastroenterologists (n=5, 2%), dermatologists (n=4, 1.5%), haematologists (n=3, 1.1%), pediatricians (n=2, 0.7%), nephrologists (n=2, 0.7%), intensive care doctors (n=2, 0.7%) and pain center specialists (n=1, 0.4 %).

Forty-eight MSD in 41 patients were positive including 16 anti-SRP (11 borderline results), 8 anti-Jo-1, 7 anti-PM/Scl, 5 anti-PL-12, 2 anti-PL-7, 2 anti-Mi-2 and 1 anti-Ku. In this MSD positive subgroup, anti-nuclear antibodies ≥ to 1/160 were detected in all cases, except for the 11 anti-SRP borderline results. Anti-SSA antibodies were positive in 12 cases {anti-Jo-1 (n=5), anti-PL12 (n=4), anti-PM/Scl (n=2), anti-SRP (n=1)}.

Clinical reasons for dot prescription

Thirty-eight MSD (12%) were prescribed during the follow-up of 38 patients with a previously diagnosed muscular disease including 27 probable or definite IIM according to Peter and Bohan's criteria (1).

Other reasons for prescribing a MSD were myalgia (n=165, 52%), muscle weakness (n=75, 24%), interstitial pulmonary involvement (n=33, 10%), cutaneous lesions (n=41, 13%), Raynaud's phenomenon (n=56, 18%) and increased muscle enzymes (n=168, 53%). Presence of muscle weakness, Raynaud's phenomenon, interstitial pulmonary involvement or increased muscle enzymes was significantly associated with MSD positivity (Table I). Additionally, muscle weakness, cutaneous lesions evocative of dermatomyositis and increased muscle enzymes were significantly associated with a diagnosis of biopsy-proven IIM (Table I).

Dot prescription in cases of previously known muscular disorders

Thirty-eight MSD were prescribed during the follow-up period of previously diagnosed muscular diseases: 27 IIM {polymyositis (n=13), myositis-overlap syndrome (n=6), dermatomyositis (n=5), anti-Jo-1 positive anti-synthetase syndrome (n=3)}, 3 aspecific myositis, 1 muscular dystrophy, 1 interstitial myositis, 1 macrophagic myofasciitis, 1 camptocormia, 1 inclusion myositis, 1 mitochondrial disorder, 1 dystonia, 1 myasthenia gravis. The results of muscular biopsy supported diagnosis in all patients but 6 (2 dermatomyositis, 3 myositis-overlap syndrome, 1 myasthenia gravis).

Interestingly, MSD results allowed clinicians to correct diagnosis in 4 cases: *(i)* 3 patients priorly diagnosed with polymyositis (n=2) or muscular dystrophy, all of whom had some degree of muscle necrosis on biopsy, were reclassified in 3 anti-SRP necrotising myopathies and *(ii)* a patient previously diagnosed with myositis overlap syndrome received a new diagnosis of an anti-PL12 anti-synthetase syndrome.

The specific diagnosis of IIM subtypes was improved by dot realisation in 4 other cases: *(i)* one anti-Mi2 positive dermatomyositis, *(ii)* one ENA negative, dot-positive anti-Jo-1 positive anti-synthetase syndrome previously labeled pPM and *(iii)* 2 PM/Scl positive myositis-overlap syndrome with a previous diagnosis of pPM. The follow-up of these 2 patients confirmed myositis-overlap syndrome with the onset of clinical signs of systemic sclerosis such as sclerodactylies and calcinosis.

Sequence of dot prescription in patients with a suspected muscular disease

In order to investigate if a MSD result may influence the diagnosis procedure of IIM, we analysed the chronological sequence of dot prescription, electromyographic studies (EMS) and muscular biopsy.

Dot prescription without EMS

In 95 cases (35%), diagnosis process did not include electromyographic studies (EMS), with the realisation of biological tests including MSD at first. MSD were positive in 5 patients (SRP borderline results n=3, PM/Scl n=1, PL-12 n=1). Seven patients presenting with increased muscle enzymes had muscular biopsy, which was abnormal in 4 (one dot-negative dermatomyositis, one dot-negative polymyositis, one acute necrotising myositis complicating a DRESS syndrome and one MacArdle disease). For the other 88 patients, the diagnosis process was not pursued beyond the MSD. In fact, none of these patients but 2 (one interstitial pneumonia related to anti-PL-12 positive anti-synthetase syndrome and one PM-Scl overlap syndrome) had a muscular disorder. Four patients had transient dot positivity (one PM-Scl positivity related to a viral infection and 3 borderline positivity of anti-SRP).

EMS and dot performed concurrently

EMS and MSD were performed concurrently in 44 patients (16%).

Dot-blots were positive in 12 patients (4 anti-SRP including 2 borderline results, 2 anti-PL-7, 3 anti-Jo-1, 2 anti-

Table I. Positivity of the myositis dot-blot assay according to the main reasons for prescribing it.

	Dot +	Dot -	Total	*p*	IIM +	IIM -	Total	*p*
Rhabdomyolysis +	32	136	168	***0.01***	35	89	124	***0.01***
Rhabdomyolysis -	6	78	84		23	122	145	
Myalgia +	22	143	165	*0.45*	37	128	165	*0.56*
Myalgia -	18	90	108		21	87	108	
Muscle weakness +	18	57	75	***0.01***	27	48	75	***0.0002***
Muscle weakness -	22	176	198		31	167	198	
Raynaud +	13	43	56	***0.04***	16	40	56	*0.13*
Raynaud -	27	190	217		42	175	217	
Cutaneous lesions +	10	31	41	*0.06*	19	22	41	***<0.0001***
Cutaneous lesions -	30	202	232		39	193	232	
IPD +	10	23	33	***0.01***	12	21	33	***0.02***
IPD -	30	207	237		45	192	237	

IPD: interstitial pulmonary disease; IIM: idiopathic inflammatory myopathies).

PL-12 and 1 anti-PM/Scl). Among these 12 patients, 8 had a myopathic pattern on EMS and underwent muscular biopsies, which revealed a dot-positive IIM in 4. The results of 4 muscular biopsies were normal.

Nineteen patients were characterised by a negative dot with a myopathic pattern on EMS. Of these patients, 16 underwent muscular biopsy, which yielded muscular diseases in 9 (2 dot-negative polymyositis, 2 dot-negative dermatomyositis, one periarteritis nodosa with muscular involvement, one myositis complicating the course of systemic sclerosis and one enzymopathy).

Thirteen patients had negative MSD and normal EMS; based on clinical symptoms and elevated muscle enzymes, 5 of them had a muscular biopsy which revealed inclusion body myositis in one, and were normal in the other 4.

Finally, 4 positive dot were interpreted based on clinical, laboratory and pathological features as false positive results. One patient with anti-PL7 positivity had biopsy-proven inclusion body myositis, whereas 3 patients with anti-SRP positivity had various diseases clearly distinct from IIM (transient unexplained rhabdomyolysis, HLA-B27 positive spondylopathy, primary Sjögren's syndrome with muscular pain).

EMS performed before dot

In 96 patients (35%), MSD was ordered with the results of a prior EMS that revealed a myogenic disorder in 46 patients. MSD were positive in 22% of the patients with positive EMS (n=10): 2 anti-Jo-1, 2 anti-SRP, 2 anti-PL-12, 2 anti-PM/Scl, 2 anti-Mi2. Among these 10 patients, 9 underwent muscular biopsy, which confirmed IIM. No biopsy was performed in the last patient, with a typical picture of anti-PM-Scl myositis-overlap syndrome. Of the 36 cases of patients with positive EMS and a negative MSD, 34 underwent a muscular biopsy, 8 of which revealed IIM (5 polymyositis and 3 dermatomyositis).

Of the 50 patients with both negative EMS and MSD, 9 underwent a muscular biopsy revealing one polymyositis, one drug-induced myositis and one lipidosis.

Final diagnosis

After clinical, biological investigations including MSD and paraclinical tests (*i.e.* EMS, muscular biopsies…), and a 2-year follow-up, various diagnosis were made in our cohort of patients (Table II):

- Fifty-nine patients (22%) had IIM according to Peter and Bohan's criteria, including 50 definite or probable and 9 possible IIM (1). Among these patients, 29 (49%) had positive MSD with the following specificities: Jo-1 (n=8), PM/Scl (n=6), PL-12 (n=5), SRP (n=5), Mi-2 (n=2), PL-7 (n=2) and Ku (n=1). According with the new propositions of classification, we divided the IIM into the following subgroups: 14 anti-synthetase syndromes, 13 myositis overlap syndromes excluding anti-synthetase syndrome, 11 pure polymyositis, 8 dermatomyositis, 6 para-neoplastic myositis, 5 necrotising autoimmune myopathies with anti-SRP antibodies and 2 inclusion body myositis (5, 6, 17). Among the 30 patients with negative MSD, 7 patients presented with positive anti-SSA antibodies detected by the anti-ENA test.
- Sixteen patients (6%) had non inflammatory muscular disorders including muscular dystrophy (n=3), mitochondrial myopathy (n=2), lipidosis (n=1), myasthenia gravis (n=2), macrophagic myofasciitis (n=2), Hereditary angiopathy with nephropathy, aneurysms and muscle cramps (HANAC) syndrome (n=1), acyl-CoA deshydrogenase deficiency (n=1), alpha-dystroglycan deficiency (n=1), limb-girdle muscular dystrophy-2L (LGMD2L) (n=1), Becker congenital myotony (n=1) and primary camptocormia (n=1). The dot was always negative in this subgroup.
- Ten patients (4%) had drug-induced myalgia, one half related to statins. Neither of these patients had positive MSD or a positive search for anti-HMGCoA reductase antibodies (18).
- Eleven patients (4%) had infectious myositis (9 viral, 1 bacterial and 1 parasitic). Of these, only one had a transient positivity of the dot (PM-Scl specificity) concomitantly with a viral myositis.
- A final diagnosis of inflammatory rheumatic disease was made for 19 patients (7%): polymyalgia rheumatica (n=9), unclassificated inflammatory rheumatic diseases (n=5), spondylarthropathies (n=3) and rheumatoid arthritis (n=2).
- Thirty five patients (12%) were diagnosed with autoimmune disease or granulomatosis: systemic sclerosis (n=9), Sjögren's syndrome (n=8), systemic lupus erythematous (n=7), mixed connective tissue disease (n=5), undifferential connective tissue disease (n=2), Hashimoto's thyroiditis (n=1), sarcoidosis (n=1), autoimmune hepatitis (n=1) and autoimmune haemolytic anaemia (n=1).
- Twelve patients (6%) had fibromyalgia.

Table II. Results and specificity of the dot according to the diagnosis (IIM: idiopathic inflammatory myopathies).

	Dot +	Dot -
IIM	29	30
Inflammatory rheumatic disease	1 (SRP borderline)	18
Other auto-immune disease	3 (SRP borderline)	32
Fibromyalgia	0	12
Neurological disorder	0	13
Muscular disorder	0	16
Drug-induced myalgia	0	10
Infectious myositis	1 (Pm-Scl)	10
Pulmonary disease	0	8
Vasculitis	0	4
Other and undetermined diagnosis	7 (SRP borderline)	78

- Thirteen patients (5%) had neurological disorders: polyradiculoneuropathy (n=4), restless leg syndrome (n=4), cerebrovascular stroke (n=3), multiple sclerosis (n=1) and amyotrophic lateral sclerosis (n=1).
- Eight patients (3%) had pulmonary disease: idiopathic pulmonary fibrosis (n=6), and drug-induced immune-allergic pneumonitis (n=2).
- Four patients (2%) had vasculitis: ANCA-associated vasculitis (n=2), 1 polyarteritis nodosa (n=1) and 1 giant-cell arteritis (n=1).
- Eight patients (3%) had psychiatric disorders with somatisation.
- Twenty-eight patients (10%) had other diagnoses.
- Eighteen patients (6%) were lost to follow-up after initial muscular investigations.
- Finally 33 patients (17%) had no diagnosis as of August 2015. Among them, there was a spontaneous disappearance of muscular symptoms in 9 cases.

Except 9 borderline SRP results, one transient PM-Scl, MSD was only positive in case of IIM.

Clinical interest of repetitive MSD

Thirty-one patients had more than one MSD performed; 5 borderline SRP results became negative at the second MSD (none of these patients have necrotising autoimmune myopathies). All initial negative MSD (n=16) remained negative. Conversely, all initial specificities were confirmed by subsequent dots (n=15). Repeated MSD in the same patient evidenced an interest in one case only; in this patient, a recurrence of MSD positivity heralded by several weeks the clinical relapse of a necrotising autoimmune myopathy, allowing adaptation of rituximab maintenance treatment.

Discussion

MSD is a key-examination in the management of patients suspected of IIM, in addition to electromyographic studies and muscular biopsy (7, 13). We analysed dot prescription practices in a French University Hospital. MSD is usually prescribed in Internal Medicine department and in the Neurology Departments, the 2 principal units investigating muscular symptoms in our hospital. The interest of our study is slightly limited by the dot used, which did not include EJ, MDA-5 and Tif1gamma specificities, only performed in our center in 2014 (19, 20). However, no IIM associated with these 3 specificities was diagnosed in our cohort during the follow-up period (August 2015).

Interestingly, the timing of dot prescription through the diagnostic process was highly variable, the dot being ordered either before, concomitantly or after the EMS. A dot negativity does not appear to have compelled clinicians to avoid muscular biopsy, which was performed in 37% of the cases in the setting of an obvious muscular problem. By contrast, the finding of a negative MSD certainly helped limiting further invasive investigations in patients with symptoms of fibromyalgia or somatisation, who were referred for IIM suspicion. The combination of MSD and muscular biopsy remain however essential as a number of IIM have no autoantibody or sub-specificity detectable on the routine laboratory tests and the biopsy may occasionally reveal muscular dystrophy (21). It is worth noting that one patient with a previous diagnosis of dystrophy actually had anti-SRP positive necrotising autoimmune myopathy, allowing an appropriate immunosuppressive treatment to be started (22). In fact, it is worth remembering that the diagnosis of muscle disorders is based on a detailed history, thorough clinical examination and various laboratory investigations among which testing for muscle enzyme elevation, immunological tests including MSD, EMS and muscle biopsy play key roles.

By contrast, the EMS would become unnecessary in patients with clinical features strongly suggesting anti-synthetase syndrome and a positive MSD. However, our study suggested that the MSD appears to be not well-known by some specialists involved in initial care of patients with IIM. This may especially be true when interstitial pneumonia is the leading feature of IIM at its onset (23-26). Better diffusion of the MSD indication to pneumologists is mandatory since anti-synthetase syndrome lung disease may precede other feature by months. Anti-synthetase lung disease is generally refractory to conventional treatments of idiopathic interstitial pneumonia and is associated to a poorer prognosis (23-26). The French Pulmonary Society only recommends the search for antinuclear antibodies by immunofluorescence in isolated interstitial pneumonia (27). As previously shown, anti-synthetase syndrome in patients with idiopathic interstitial pneumonia was detected in 10% to 38% of the cases (12, 28-30). Such prevalence suggested that MSD needs to be performed in patients diagnosed with idiopathic ILD who express other mild clinical characteristics evocating anti-synthetase syndrome (12, 28-30). In our study, the dot was negative in all 6 patients with an exclusive pulmonary presentation. Moreover, patients with a pulmonary involvement related to IIM always had other symptoms evocating of an anti-synthetase syndrome. Altogether, this suggested that mild symptoms

of anti-synthetase syndrome are often in the background of the clinical picture dominated by interstitial pneumonia and must be systematically sought. In keeping with the French Pulmonary Society recommendations for the screening of autoimmunity in idiopathic ILD, the antinuclear antibodies search using HEp2 cells makes it possible to detect, in 70% of the cases, a cytoplasmic fluorescence pattern, suggesting anti-synthetase antibodies (27). Once evidenced, such a fluorescence pattern should be systematically characterised by a MSD, to avoid an exceedingly delayed diagnosis of ASS (21-32).

In our study, MSD diagnostic performance was poor in patients presenting exclusively with pulmonary (0/6) or rheumatic symptoms (0/12). In fact, of 18 such patients, none had a positive dot or received a diagnosis of IIM. Our results regarding the MSD performance in "isolated" interstitial lung disease or unclassified polyarthritis sharply contrast with previous studies (12, 28-31). However, in these studies, patients characterised with prominent single pulmonary or joint involvement presented also mild symptoms associated with IIM (12, 28-31); the results of MSD remains a significant help to highlight these symptoms and to move from a misdiagnosis to a clearer picture of anti-synthetase syndrome or other IIM.

The present study highlights the MSD interest not only in the characterisation of a suspected IIM, as previously demonstrated (15,16) but also, for the first time, in the diagnostic procedure of 274 patients presenting with muscular symptoms or other clinical characteristics evocating anti-IIM.

Among 274 patients assessed with the MSD, only 59 (22%) had unquestionably an IIM. Only 48 of the 316 tested sera were positive. This 15% rate of positivity reflects the prevalence of inflammatory myositis in an unselected cohort of patients suspected of a muscular disease or referring for dermatological and/or pulmonary symptoms. This result highlights also the complexity of the diagnosis procedure of such patients. In a recent study, the prevalence of IIM in an unselected cohort of patients referring for myositis suspicion was also low, below 7% (33). The place of the dot, characterised with a high specificity and a low sensitivity, appeared also not clearly identified in the diagnosis process of IIM at our institution. Indeed, MSD was performed without (35%), either before (14%), concomitantly (16%) or after (35%) more invasive diagnostic procedure. A final diagnosis was obtained in most of the patients (85%). Altogether, these results suggest that the MSD should not be used as a surrogate for clinical approach, targeted prescriptions of EMS and muscle biopsy in patients suspected of IIM or presenting with extra-muscular symptoms suggesting an anti-synthetase syndrome. The extreme variety of final diagnosis and the wide range of prognosis found in our sample of patients highlight the complexity of diagnostic procedures to apply to patients referred for muscle complaints or other system disorders potentially related to IIM in a tertiary care hospital.

Interestingly, 6% of patients referred for a suspected IIM had non-inflammatory muscular disorders. Indeed, patients with other acquired myopathies or genetic muscle diseases may have remarkably similar presentations. The possibility of an inherited muscular disease must be kept in mind throughout the diagnostic procedure. A negative MSD should raise the possibility of an alternative diagnosis and not delay confirmatory investigations including muscular biopsy (34).

Our results pointed out that anti-SRP specificity helped to avoid the confusion between dystrophy and a progressive form of necrotising immune-mediated myopathy as previously described (23); the high specificity of anti-SRP antibody for necrotising immune-mediated myopathy has been demonstrated (35). Surprisingly, our study highlighted the possibility of false positive anti-SRP results in patients with other autoimmune diseases (primary Sjögren's syndrome) or inflammatory rheumatic disease (rheumatoid arthritis or spondylopathy). The follow-up of these patients excluded the possibility of an associated necrotising immune mediated myopathy. False positive results of SRP antibodies have not been previously described in a study characterised with, at least, a two years follow-up. In another study, a search for anti-SRP antibodies was made in the sera of 3500 patients and were positive in 23 patients with necrotising immune mediated myopathies and in 4 patients with rheumatoid arthritis, and in two with no features of myositis (36).

The interest of the MSD is also predictive. As demonstrated in our study for the SRP specificity, many studies have shown that the reappearance of autoantibodies preceded clinical relapse particularly for anti-SRP (10), anti-HMG-CoA reductase (37) and possibly for anti-Jo-1 antibodies allowing refining the monitoring of biotherapies or other immunosuppressive treatments (38).

Conclusion

The contribution of MSD to the diagnostic procedure of patients with non-specific muscular or systemic symptoms suggesting the possibility of an IIM is evidenced in this study. Its interest was demonstrated whatever its chronological prescription. Indeed, the precise identification of autoantibodies specificities is essential for the diagnosis and the management of IIM. The new generation of this test that allows the research of anti-TIF-1γ, MDA-5 and HMG-CoA reductase antibodies will become the key of IIM diagnostic procedure.

MSD is part of the key of both rapid identification of IIM and differential diagnosis in patients referred with muscular symptoms, pulmonary or joint involvement suggesting IIM, non-inflammatory muscular disorders or autoimmune disease.

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