Inflammatory or necrotizing myopathies, myositides and other acquired myopathies, new insight in 2011

Olivier Benveniste¹,², Jean-Marc Léger²

¹. Université Pierre-et-Marie-Curie, Assistance publique–Hôpitaux de Paris, hôpital Pitié-Salpêtrière, service de médecine interne 1, 75013 Paris, France
². Institut de myologie, centre de référence des pathologies neuromusculaires Paris Est, GHU Pitié-Salpêtrière, 75013 Paris, France

Correspondence:
Olivier Benveniste, Groupe hospitalier Pitié-Salpêtrière, service de médecine interne 1, 47–83, boulevard de l’Hôpital, 75651 Paris cedex 13, France.
olivier.benveniste@psl.aphp.fr

As reminded by D. Hilton-Jones in this issue’s review [1], the classification of myositides is currently changing. Since 1975, when Peter and Bohan [2] defined the diagnostic criteria for polymyositis (PM) and dermatomyositis (DM), the development of new pathological tools [3,4] permitted to refine the diagnosis criteria, but also, together with fundamental research in immunology [5] and neurosciences [4] to approach the various physiopathological events leading to the different acquired inflammatory and/or autoimmune myopathies. Beside the now “classical and well recognized” PM and DM, new insights have been done for the recognition of inclusion body myositis (IBM) [4] that must be distinguished from PM, but also, for the recognition of immune-mediated necrotizing myopathies (IMNM) [5] that clearly differ from inherited myopathies or dystrophies [6]. Among IMNM, some are related to the presence of particular specific auto-antibodies (anti-SRP), others are associated with neoplasia and the remaining are also recognized [7] for their property to be treatable by immunosuppressants. The recent discovery of a new auto-antibody specifically associated to IMNM (neither paraneoplastic, nor anti-SRP positive) [8] highlights the potential toxic trigger role of statins in the genesis of IMNM/myositis, since the presence of this antibody was frequently associated with statin exposure [8]. A few weeks later, the same team also discovered and published the target of this antibody, which is the 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) [9], the key enzyme in the cholesterol biosynthetic pathway specifically inhibited by statins. They also showed that statins up-regulate the expression of HMGCR on regenerative muscle fibers (HMGCR being the major target of autoantibodies in statin-associated IMNM). Undoubtedly, commercial kits for the routine dosage of this auto-antibody will soon be available, facilitating the diagnosis of this condition. We will then see if all the myopathies due to the statins are due to the presence of this antibody.

In the same vein, during the past few years, the burden of the dosages of the different myositis-specific (or associated) auto-antibodies has increased, an important step forward, since it may...
facilitate, at a modest cost, the diagnosis of these diseases. Within a very short time, we have now a routine access to the dosage of different antisyntetasen antibodies anti-J0-1 (histidyl-tRNA synthetase), PL-7 (threonyl-tRNA synthetase), PL-12 (alanine-tRNA synthetase), OJ (isoleucyl-tRNA synthetase), Ej (glycyl-tRNA synthetase), but also of anti-SRP, Mi-2, Ku, PM-Scl, RNP antibodies. Furthermore, each year brings the discovery of new antibodies, not only new anti-synthetases [KS (asparaginyl-tRNA synthetase), ZO (phenylalanyl-tRNA synthetase), thyrosyl-tRNA synthetase], but also other antibodies, notably in DM, which have remarkable particularities for the clinician, such as to be frequently associated with cancer [10,11] or with rapidly progressive interstitial lung disease [12]. Here again, the target antigens have been recently precised (respectively TIF1-γ and MDAS) [13], ELISA have been developed, leading to think that routine test will soon be available.

All these efforts for the development of immunological or pathological tools and finally for a better classification of the myositides are aimed to define homogeneous groups of patients, receiving appropriate treatments. It is now accepted that conventional immunosuppressants (corticosteroids, methotrexate, azathioprine, intravenous immunoglobulins…) have no (or transient and modest) effects on muscle strength during IBM. It is then extremely important to distinguish this condition from PM, to avoid useless (and potentially dangerous) treatments. Nevertheless, the debate is still open concerning the primum movens of IBM: is it an immunological [5] or a degenerative [4] phenomenon? The development of future therapeutic strategies (and trials) will thus depend of the investigator’s convictions: unconventional immunosuppressant and/or modulator (such as certain biotherapies) in one hand or anti-amyloid (such as in Alzheimer disease) on the other. Nonetheless, for the other more easily treatable myositides, one may be surprised, in 2011, by the weakness of evidence-based medicine [14] and the lack of recommendations. It is also surprising that in most of the studies, PM, DM, overlap syndrome with muscle inflammation or IMNM are indistinguishably treated in the same manner [14], despite their different physiopathogenesis. This is presumably due to the rarity of these diseases, and the lack of worldwide, concerted effort to date.

However, things are undisputedly changing, as preclinical models are now mature [3], that will help for the choice of the molecules to be tested. Efforts are made to set up and standardize diagnostic criteria and to define outcomes for the future clinical trials, not only in PM/DM/IMNM[7] but also in IBM [15,16] and other international workshops are planned. Furthermore, big pharmaceutical companies are developing biotherapies potentially targeted for myositis and their interest for these diseases seems to progress. We can thus be quite enthusiastic: no doubt that all these efforts will allow, in the near future, to start multicentric, prospective, randomised trials for the benefit of the patients.

Conflict of interest: none

References