16. Atorvastatin-Induced Autoimmune Myopathy: An Emerging Dominant Entity in Patients with Autoimmune Myopathy Presenting with a Pure Polymyositis Phenotype.

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OBJECTIVE: The classification of autoimmune myopathies (AIM) is evolving. Pure dermatomyositis and overlap myositis are dominant AIM subsets, while pure polymyositis (pPM) is uncommon and confused with myositis mimickers. Our objective was to evaluate the disease spectrum in patients presenting with a pPM phenotype and to assess clinical features, autoantibodies and membrane attack complex (MAC) in muscle biopsy, in cases of treatment-responsive, statin-exposed necrotizing AIM.

METHODOLOGY: We identified all patients from the CHUM AIM Cohort with a pPM phenotype, a documented response to immunosuppression and a follow-up of at least three years.

RESULTS: Of 17 consecutive patients with pPM, 14 patients had a necrotizing AIM, of whom 12 were previously exposed to atorvastatin (mean duration: 38.8 months). These 12 patients were therefore suspected of atorvastatin-induced AIM (atorAIM) and selected for study. None had overlap autoantibodies, anti-SRP or cancer. Anti-HMGCR autoantibodies were uniformly present.
Three clinical stages of myopathy were recognized: stage 1 (serum CK elevation, normal muscle strength, normal EMG), stage 2 (CK elevation, normal strength, abnormal EMG) and stage 3 (CK elevation, proximal weakness, abnormal EMG). At diagnosis, 10 patients (83%) had stage 3 myopathy (mean CK elevation: 7,247 U/L). However the presenting feature was stage 1 myopathy in 6 patients (50%) (mean CK elevation: 1,540 U/L), all of whom later progressed to stage 3 myopathy (mean delay: 37 months) despite atorvastatin discontinuation.
MAC deposition was observed in all tested muscle biopsies (n=13). Three patterns were seen: isolated sarcolemmal deposition on non-necrotic fibers, isolated deposition on endomysial capillaries and a mixed pattern.
Oral corticosteroids alone were unable to normalize CKs and induce remission (n=9). Ten patients (83%) received intravenous immune globulin (IVIG) as part of an induction regimen. Of 10 patients with evaluable maintenance therapy (≥ 1-year remission on stable maintenance therapy), IVIG was needed in 5 patients (50%), either with MTX monotherapy (n=3) or with combination immunosuppression (n=2). In the remaining 5 patients, MTX monotherapy (n=3) and combination therapy (n=2) maintained remission without IVIg.

CONCLUSION: atorAIM emerged as the dominant entity in patients with a pure PM phenotype and treatment-responsive myopathy. Isolated CK elevation, i.e. stage 1 myopathy, was the initial mode of presentation of atorAIM. Thus, the new onset of isolated CK elevation on atorvastatin and persistent CK elevation on statin discontinuation should raise early suspicion for atorAIM. Three patterns of MAC deposition were seen and, while non pathognomonic, were pathological clues to atorAIM. AtorAIM was uniformly corticoresistant but responsive to IVIG as induction and maintenance therapy.