(58.4, 75.5 cmH2O seropositive and 65.3, 87.1 cmH2O seronegative) trend lower in seropositive patients but were not clinically significant. The PROMIS dyspnea results showed no significant difference between the two groups. These findings amongst a large cohort of IBM patients, support previous studies showing seropositive IBM patients may have more severe respiratory involvement.

http://dx.doi.org/10.1016/j.nmd.2024.07.141

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INSPIRE-IBM: an NIH-funded, two-year, multicenter, observational study in inclusion body myositis (IBM)-an update

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A huge unmet need in sporadic inclusion body myositis (IBM) research is the lack of long-term prospective longitudinal data on disease behavior and progression and the influence of the various blood biomarkers (NT5c1A antibodies and highly differentiated T lymphocytes) on disease behavior and progression. A 13-center observational prospective study is ongoing involving 150 patients with IBM. The study is funded by NIAMS/NIH. Primary eligibility criteria are a diagnosis of IBM, fulfilling the ENMC 2011 criteria for clinicopathologically defined, clinically defined, or probable IBM, within 10 years of onset. Each subject will be seen every 6 months (5 times points) over a 2-year period, and will have serial collection of disease related data, including physical exams, outcome measures (IBMFRS, sIFA, IBM-HI, PROMIS, quantitative muscle strength and grip strength testing, timed get up and go, pulmonary function tests, fall diary, and mobility device assessment). Collection for serum and PBMCs will be done to assess for NT5c1A antibodies, select cytokines, and detailed immunophenotyping for blood-based lymphocytes. RNA and DNA has been collected for future analyses. A subset of 40 patients will undergo fresh open muscle biopsy, along with concurrent blood collection, to assess muscle pathology and correlate blood markers with markers in muscle tissue. The study has completed enrolment of 150 patients as of January 2024. Seventy-two (49.7%) were seropositive for the NT5c1A antibody and 73 (50.3%) were seronegative (5 results pending). Five subjects changed antibody status from the Baseline to the Month 12 visit. Demographics: 30.6% female, 69.4% male; 90% White, 4% Asian, 4% Black, 1.3% more than one race, 8.7% Hispanic or Latino. The study will provide the largest dataset to date on the natural history of IBM including a repository of PBMC, DNA, RNA and muscle tissue from highly characterized and phenotyped IBM patients.

http://dx.doi.org/10.1016/j.nmd.2024.07.142

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Riboflavin-responsive MADD, a modern day problem?

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Multiple acyl-CoA dehydrogenase deficiency (MADD) is a disorder of fatty acid oxidation which is known to cause a lipid myopathy that can be associated with peripheral neuropathy. Patients may present at any age from the neonatal period to adulthood. It is diagnosed by identifying elevated levels of multiple acylcarnitine species in blood and increased excretion of organic acids in urine. It is caused by biallelic pathogenic variants in the ETFA, ETFB or ETFDH. It is potentially treatable with riboflavin supplementation. Over the last few years, there appears to be a growing number of patients with the typical clinical, serological and urinary, and histopathological findings of MADD without pathogenic variants being identified in the known disease associated genes. Here, we report two gene-negative cases of riboflavin responsive MADD (RR-MADD). Both patients were women and presented with a relatively rapid onset limb-girdle weakness and distal sensory impairment. Investigations showed a lipid storage myopathy on the muscle biopsy in one case and electromyographic and MRI findings consistent with a myopathy in the other case. Serological tests showed increased creatine kinase levels, and acylcarnitines. Urinalysis revealed increased excretion of organic acids. Further history elucidated that both women had a high calorie but nutritionally poor diet, and both were being treated with sertraline. Riboflavin supplementation led to clinical improvement in both cases. The increased incidence of RR-MADD in the recent years appears to be related to diet and/or iatrogenic. A detailed dietary and drug history is necessary in the assessment of patients presenting with the clinical features of a myopathy and/or neuropathy, especially since this condition is potentially treatable.

http://dx.doi.org/10.1016/j.nmd.2024.07.143

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A single center Indian cohort of inclusion body myositis

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Sporadic inclusion body myositis (sIBM) is rarer in Indians compared to Caucasian population. Only a handful of cases have been described from this country. We aimed to study the clinicopathological profile of IBM in a single tertiary care Centre from South India. We retrospectively screened the electronic medical records over 8 years from March 2017 till March 2024 to identify patients with IBM who attended the Neurology Clinics of our Centre. The patients who met the European Neuromuscular Centre (ENMC) 2011 diagnostic criteria for sIBM were included in the study. Their clinical and histopathological details were collected, and descriptive analysis was performed to classify them into clinicopathologically defined, clinically defined and probable IBM. 9 patients met the ENMC criteria for clinically defined IBM and one patient met the criteria for probable IBM. Mean age at symptom onset was 54 years, four had onsets below the age of 50 years. Men and women were equally affected with a ratio of 1:1. The presenting symptom was quadriceps weakness in 7 patients and finger flexion weakness in 2 patients. Dysphagia preceded limb weakness by 2 years in one patient. Two patients had shoulder abductor weakness also at onset and two had severe myalgia at the onset. The mean duration of symptoms from onset to diagnosis was 2.7 (±1.6 SD) years and follow up duration was 3 (± 2.1SD) years. None of the patients had respiratory or cardiac involvement at last follow up. The serum creatine kinase level ranged from 150 to 1803 IU/L. Myositis antigen profile showed Ku and PM Scl 100 positivity in one patient and another had comorbid rheumatoid arthritis with rheumatoid factor and anti CCP antibody positivity. Anti-cN1A test was not done for any of the patient as this was not accessible in India. Muscle biopsy showed presence of rimmed vacuoles and endomysial inflammatory infiltrates. Electron microscopy was not available. Except one patient, all others received a trial of immunotherapy including steroids and Mycophenolate mofetil with no significant response. The one with coexisting rheumatoid arthritis received steroids along with Methotrexate and Rituximab and remained in the bed-bound state as at the onset. This single Centre Indian cohort identified 9 patients with clinically defined IBM and 1 patient with probable IBM. Clinico-pathological profile was largely similar to global reports. A few atypical features noted were dysphagia onset and proximal muscle weakness.

http://dx.doi.org/10.1016/j.nmd.2024.07.144

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Capillary abnormalities in immune-mediated necrotizing myopathy: more than collateral damage?

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Immune-mediated necrotizing myopathy (IMNM) is a form of idiopathic inflammatory myopathy (IIM) characterized by severe, rapidly progressing muscle weakness, creatine kinase elevation and muscle fibre necrosis. IMNMs are divided into three subgroups depending on the presence of muscle specific autoantibodies: anti-SRP-positive, anti-HMGCR-positive and seronegative IMNM. Vascular abnormalities, particularly alterations in capillaries, have been mentioned in IMNM. However, the link between autoimmune muscle damage and abnormal capillary morphology has remained unclear. The type of capillary pathology is a relevant feature, since vascular damage is key e.g. in dermatomyositis and systemic sclerosis as highlighted recently. In this project, we aimed to characterize vascular/capillary abnormalities in muscle biopsies derived from HMGCR-Ab, SRP-Ab, and seronegative IMNM patients. Light and electron microscopy were used to assess structural changes in capillaries, while quantitative real-time PCR was used to study the expression of genes related to vascular function. Additionally, we analyzed the proteomic signature of IMNM in relation to vascularization. Distinct patterns of capillary abnormalities were identified in all IMNM subgroups. Capillaries showed a spectrum of alterations, including a broad range of basement membrane duplications, activation of endothelial subcellular organelles featuring