14. An Autoimmune Myositis-Overlap Syndrome Associated with Autoantibodies to Nuclear Pore Complexes. Description and Long-Term Follow-Up of the Anti-Nup Syndrome.

[1]**Catherine Isabelle**, MSc, MD, [2]Marie-Christine Dabauvalle, PhD, [3]Marvin J. Fritzler, PhD, MD, [4]Ira N. Targoff, [1]Yves Troyanov, MD, [1]Michel Gagné, MD, [1]Jean-Pierre Raynauld, MD,[1]Jean-Luc Senécal, MD.
[1]Université de Montréal, Montréal, QC, Canada, [2]University of Würzburg, Germany [3]University of Calgary, Calgary, AB, Canada, [4]University of Oklahoma, USA.

INTRODUCTION: Autoimmune myositis encompasses various myositis-overlap syndromes, each one being identified by the presence of serum marker autoantibodies.

OBJECTIVE: To describe a novel myositis-overlap syndrome in four patients characterized by the presence of a unique immunological marker, autoantibodies to nuclear pore complexes.

METHODOLOGY: Clinical features and sera were collected from French Canadian patients followed prospectively since 1984 at the Connective Tissue Disease Clinic, Centre Hospitalier de l'Université de Montréal. Reactivity with nuclear pore complexes was identified by indirect immunofluorescence on HEp-2 cells displaying a positive ANA with a distinct punctate peripheral (rim) fluorescent pattern of the nuclear envelope, and confirmed by immunoelectron microscopy.

RESULTS: In a cohort of 100 French Canadian patients with autoimmune myositis, sera from 4 (4%) patients displayed a high titer ANA with a fluorescent pattern characteristic of nuclear pore complexes. Clinically, these four patients shared a clinical phenotype characterized by prominent myositis in association with erosive, anti-CCP positive and rheumatoid factor positive arthritis, trigeminal neuropathy, mild interstitial lung disease, Raynaud phenomenon and weight loss. The myositis was typically chronic, relapsing and refractory to corticosteroids alone, but remitted with the addition of a second immunomodulating drug. There was no clinical or laboratory evidence of liver disease. The prognosis was good with 100% long-term survival. The nuclear pore complex fluorescent ANA pattern was not observed in sera from 393 adult patients with systemic sclerosis (n=112), mixed connective tissue disease (n=35), systemic lupus (n=94), rheumatoid arthritis (n=45), or other rheumatic diseases (n=107) nor was it observed in 62 normal adults.

Autoantibodies to nuclear pore complexes were predominantly of IgG isotype. No other IgG autoantibody markers for defined connective tissue diseases or overlap syndromes were present, indicating a selective and highly focused immune response. In three patients, anti-nuclear pore complex autoantibody titers varied in parallel with myositis activity, suggesting a pathogenic link to pathophysiology. The nuclear pore complex proteins, i.e. nucleoporins (nup), recognized by these sera were heterogeneous and included Nup358/RanBP2 (n=2 patients), Nup90 (n=1), Nup62 (n=1) and gp210 (n=1). Taken altogether the data suggested that nup autoantigens themselves drive the anti-nup autoimmune response.

CONCLUSION: We report a novel subset of autoimmune myositis in our population of French Canadian patients with connective tissue diseases. This syndrome is recognized by the presence of a unique immunologic marker, autoantibodies to nuclear pore complexes that react with nups, consistent with an ""anti-nup syndrome".