TMA: Twenty Years Later – Progress inMUnderstanding Myositis

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Major Advances in Myositis

- Better recognition of myositis and new diagnostic and assessment tools
- More understanding of the different types of myositis
- Identification of genes and possible environmental triggers
- New insights into how inflammation and damage develop
- New and improved treatments
- National and international networks working together to gain knowledge and improve treatment
- The Myositis Association's critical role in patient, caregiver and physician education, patient support and advancing research in all areas above

Better Recognition of Myositis and New Diagnostic and Assessment Tools

 New autoantibody tests – over a dozen diagnostic autoantibodies discovered for PM/DM and recently for IBM (anti-cytoplasmic 5'nucleotidase)





- Better appreciation of muscle biopsy features/stains rimmed vacuoles, MHC class I staining, others
- New imaging methods particularly magnetic resonance imaging (MRI)
- New diagnostic genetic testing for non-myositis cases
- New validated and standardized clinical assessment tools for determining disease activity and damage and to define when patients improve

Different MRIs Show Disease Damage (T1) and Disease Activity (STIR)



STIR - MRI



Active DM

Active PM

Active IBM

Genetic Tests to Diagnose Mimics of Myositis



The Broad Spectrum of Myositis

By Diagnosis

Polymyositis (PM)

Dermatomyositis (DM)

IBM

Necrotizing myopathy

Amyopathic DM

Myositis in overlap

Cancer and myositis

Focal myositis

Other

Courtesy Dr. Jiří Vencovský

By Autoantibody Negative Jo-1 SRP Mi-2 p155/140 **CADM-140** MJ Cyto. 5'nucleotidase U1-RNP Other

By Organ Involvement Skin Lung Esophagus Intestines Calcinosis Joints Heart **Blood vessels** Other

Different Types of Myositis Have Different Problems and Treatment Responses

Moderate to severe weakness, Lung and heart disease, Moderately difficult to treat

PM

Mild to moderate weakness, calcium deposits, Ulcerations, fat loss in skin, Better treatment responses

DM/JDM

More DM and men, Severe weakness and rashes, Older age, Lower CK, Need to focus treatment on cancer

Cancer Myositis

More older males, shoulder, wrist, hand and leg weakness, Asymmetry, atrophy, swallowing problems

IBM

Different Antibody Types Have Different Problems and Treatment Responses

Anti-Jo-1

Anti-SRP

Anti-Mi-2



Lung disease, arthritis, fevers, persistent disease needing longer treatments Acute, severe weakness, swallowing problems, muscle pain, more difficult to treat Classic dermatomyositis, V-sign & shawl rashes, good response to treatment

Different Juvenile DM Antibody Types Have Different Problems and Responses

Anti-MJ

Anti-p155/140







Severe skin rash, moderate to severe weakness, difficult to treat and chronic disease Muscle cramps, calcium deposits, GI ulcers, easier to treat and single course of disease Joint pains, fever, lower CK, easier to treat and single course of disease

Genes Differ in Different Myositis Types

- Immune genes that normally protect us from environmental agents are the most important genes in myositis (called HLA genes)
- PM, DM, and IBM all share some HLA genes, but also each has unique risk or *protective* HLA genes
- Different autoantibody groups also have different genes
- New approaches to evaluate genes across the entire human genome are finding additional genes for myositis that may help in diagnosis and treatment in the future

Possible Environmental Triggers of Myositis

Infections

- Viruses: Echovirus, HIV, Coxsackievirus, Hepatitis, others
- Bacteria: Group A Streptococcus, Lyme, others
- Parasites: Toxoplasma, others
- Non-Infectious agents
 - Drugs: D-penicillamine, growth hormone, cytokines, cimetidine, estrogens, statins, others
 - Foods: L-tryptophan, dietary supplements, ciguatera toxin, others
 - Occupational exposure: Silica, super glues, others
 - Other environmental exposures: Collagen implants, smoking, overexertion, stress, sunlight, others

Sunlight Levels Predict the Proportion of Dermatomyositis World-wide and in the U.S.



Possible Ways that Inflammation and Damage Develop in Myositis



New Treatment Options and Understanding the Need for More Aggressive Therapy



New Treatment Options and Understanding the Need for More Aggressive Therapy



More International Networks/Collaborations

- International Myositis Assessment and Clinical Studies Group (IMACS)
- The International Myositis Collaborative Study Group
- International Myositis Genetics Consortium (MYOGEN)
- EuroMyositis
- Paediatric Rheumatology International Trials Organisation (PRINTO)
- International Myositis Classification Criteria Project (IMCCP)
- Childhood Arthritis and Rheumatology Research Alliance (CARRA)

MA's Major Impact on Myositis

- Education and support
 - Thousands of patients, caregivers and family members have a better understanding of their disease and know that others are there to help them
 - Hosted many patient meetings
 - Established September 21st as National Myositis Awareness Day
 - Published books and other information
- Fostered Research
 - Hosted many scientific meetings to enhanced understanding, and advanced research into the causes and treatments of all forms of myositis
 - 34 research grants approved for a total of \$4.2 million
 - At least 50 publications in the medical literature supported by TMA
 - Currently playing an active direct role in research MYOVISION





MYOVISION

- A registry of ~2000 patients diagnosed with adult and juvenile DM, PM, IBM and other rarer forms of myositis
- Data collected through paper and online surveys
- Only patients residing in the United States or Canada at the time of onset were eligible
- Joint collaboration between NIEHS Environmental Autoimmunity Group, The Myositis Association and the Cincinnati Children's Hospital Medical Center

MYOVISION GOALS

• Establish a myositis patient registry to investigate:

- Demographics
- Manifestations of illness
- Treatments
- Medications received
- Types of physicians involved in care
- Investigate potential environmental exposures related to onset of disease
- Evaluate impact of disease on quality of life
- Examine additional exploratory research questions related to environmental risk factors
- Create a population resource that can be re-contacted for future studies

Summary - Major Advances in Myositis

- Over the last twenty years there have been many advances in diagnosis, disease assessment, understanding the types of myositis, how they come about and how to best treat them
- The Myositis Association has played a critical role in patient, caregiver and physician education, patient support and advancing research in all of the above areas
- Much more needs to be done to understand the causes and best treatments for each type of myositis, to find cures, and to eventually prevent the development of myositis in the future