

Meeting Date- 4/06/13

Speaker- **Dr. Lisa Christopher-Stine**, Rheumatologist and Co-Director of the Johns Hopkins Myositis Center

The Johns Hopkins Myositis Center

The Myositis Center was started 6 years ago, bringing together Neurology and Rheumatology. The center allows for the specialties to talk and learn from one another. There is a pulmonologist at the center as well for patients with Interstitial Lung Disease. This year, they plan to add two additional rheumatologists to the team.

Who needs to be seen at the center?

If a patient is not responding to traditional therapy or if there is a question about the type of Myositis, the center may be able to provide some answers. There is currently a cohort of over 1300 patients that are being scientifically followed. Research is done with these patients to determine new patterns, similarities, etc.

Types of Myositis

Inclusion Body Myositis (IBM)-

In a biopsy of an IBM patient, the muscle usually appears to have holes or vacuoles present. However, in many cases this is not seen until after many muscle biopsies. Sometimes these vacuoles are never seen. Doctors at the Myositis Center are not completely sure that IBM is autoimmune. With autoimmune conditions, the immune system is in overdrive. Immunosuppressants usually will help these conditions because they work to slow the immune system down. However, with IBM this is not the case. Why does the disease not respond to immunosuppressants? IBM affects men more often than women, with a ratio of 3 to 1. Patients are usually over the age of 50. In the beginning, the progression is very slow. At some point the disease seems to plateau, which is then followed by a steep decline where the patient becomes weak all over. During the plateau period, exercise can be helpful and does seem to slow this trajectory down. Isometric activities are the kind of exercise that should be done. With IBM, there is almost always finger flexion weakness present. The center is currently working with a surgeon on a study regarding tendon transfer which will hopefully allow the ability to move

again. On a pathogenic (disease causing) level, there are actually some similarities between IBM and ALS (Lou Gehrig's Disease).

Polymyositis (PM)-

The patient experiences proximal muscle weakness particularly in the hips and shoulder regions. This is not the same as muscle fatigue.

Dermatomyositis (DM)-

DM has all the symptoms of PM, plus skin involvement. There is a rash on the eyelids and/or knuckles. Patients have heliotrope rash. The rash on the knuckles is called Gottron's papules (raised) or Gottron's sign (flat). If the patient has darker skin, then it can look hyperpigmented. For example, if the person is African American then the skin can appear black. Isometric exercises are also important for DM and PM.

Juvenile Myositis (JM)-

JM begins in childhood or the teen years. The average age of onset for JDM is between six to seven years old; 25% are age 4 or less. JPM usually develops several years later. Approximately 1,000 new cases of JM are diagnosed in the United States every year.

Immune Medicated Necrotizing Myopathy- One form of this is a Statin -associated autoimmune necrotizing myopathy (or immune mediate necrotizing myopathy). Twenty percent of people who take statins will experience issues with their muscles. For the majority, when the medication is discontinued everything goes back to normal. However, a small percentage of these people continue to have issues.

Diagnosis

Increased Muscle Enzymes- CK or CPK (Creatine Kinase). However if you start to lose muscle mass, your numbers could go down while you are still feeling weak.

EMG (Electromyography)- This is an electrical test that tests if the muscles and nerves are talking to each other properly.

Biopsy- A muscle biopsy may be done to more definitively determine the diagnosis. For Dermatomyositis, a skin biopsy may also be requested. However, for some patients a biopsy is not done because the skin symptoms make the diagnosis more obvious.

Exercise

Physical therapy can be beneficial for all types of Myositis. It is important that your therapist is educated about Myositis. They need to know what your limits are. It is important to do isometric exercises. Isometric exercises are contractions of a particular muscle or group of muscles. It is a form of resistance training in which the participant uses the muscles of the body to exert a force either against an immovable object or to hold the muscle in a fixed position for a set duration of time. Isometric exercises don't effectively build strength but can help maintain muscle strength. Because isometric exercises are done in one position without movement, they'll improve strength in only one particular position. So, how much exercise should you do? You need to build up to it. If you feel like you have run a marathon then you have done too much.

Studies

For information on past and present studies relating to Myositis you can visit the following link: <http://www.clinicaltrials.gov/ct2/results?term=myositis&Search=Search>

Creatine- . Our bodies actually make creatine from the amino acids in protein. Some good food sources are herring, cod, beef, pork, salmon, and milk. Vegetarians tend to have lower stores of creatine. The jury is still out on the benefits of creatine supplements to build muscle. However, there have been small studies on its benefits in various types of Myositis. One side effect of the supplement can be decreased kidney function, so it is important to discuss creatine with your doctor before taking it. There can be some other side effects, particularly with high doses. What is the recommended dosage? 8 grams per day for one week, then 3 grams per day thereafter. If it doesn't seem like it is working, there needs to be a stopping point. It is very expensive. You can view an article about a study on creatine at the Myositis Association's website. Here is the link: <http://www.myositis.org.uk/archives4.htm>

Oxandrolone- Another study has been done on the anabolic steroid, Oxandrolone, and its effects on IBM. A double blind study was done at Harvard Medical School and the conclusions seemed positive. Here is a link to its synopsis: <http://www.ncbi.nlm.nih.gov/pubmed/11940697> Oxandrolone is not to be taken if you have or had prostate cancer or liver problems. It isn't without side effects but they are low compared to other more anabolic and androgenic agents.

Calcinosis Laser Treatment – Currently, the departments of Dermatology and Rheumatology at the George Washington University Medical Faculty Associates are conducting a 24 week study involving laser and a topical medication called sodium thiosulfate. This will be used for treating superficial calcinosis in patients with adult or juvenile dermatomyositis who have not responded to other treatments. Participants must be between the ages of 18-65 years, have stable disease which is mildly active or in remission, and have failed at least one therapy for superficial calcinosis. The study consists of 8-10 treatments of laser and topical medication during the

course of the study. Assessments, questionnaires, blood testing, imaging, and an optional skin biopsy will be performed. Participants will receive \$25.00 per visit. There is no charge for the treatment and diagnostic tests. If you are interested in enrolling call 1-202-741-2230.

MYORISK- Doctors at the NIH are conducting a study regarding environmental factors and Myositis. The study is led by Dr. Fred Miller. They are collecting dust samples from people's home and seeing if there is any correlation. Participants must have been diagnosed within the last twelve months. They are still recruiting patients and more information can be found at the following address:

<http://www.niehs.nih.gov/research/clinical/join/bethesda/participants/studies/erftas/>

STAMP- Dr. Christopher is working with an organization called STAMP (Standardizing Treatment Approaches for Myositis Patients) which is trying to work towards standardizing treatment. All medicines do not work for all people. There is no standardized treatment plan for Myositis. It is impossible to do large studies because Myositis is so rare. Only 1 in 50,000 to 100,000 people have the disease.

Gene Therapy- A clinical trial is being done in Ohio by Dr. Jerry Mendell on the effects of gene therapy in IBM. Patients will receive an injection of a modified virus carrying the gene for the muscle growth-stimulating protein, follistatin, into their quadriceps muscles. Preliminary studies in mice with muscular dystrophy demonstrated that follistatin delivered in this manner can cause significant increases in the size of injected muscles. If successful, this can potentially increase the size of the thigh muscle and potentially prolong a patient's ability to walk. More information can be found at the following site: <http://www.clinicaltrials.gov/ct2/show/NCT01519349>

Possible Causes of Myositis

Viral- Dr. Christopher feels that sometimes the cause is a combination of genetics with a viral trigger. Whenever you have a virus, your body releases a protein called interferon in response. Interferon increases with PM and DM and an AINM interferon is elevated to fight a virus, she believes that for some reason this does not shut off. This could be the trigger combined with the genetic factor.

Stress is also a potential trigger. Sun is a potent trigger for DM. If you look at a map, the density of DM is centered near the equator.

The NIH is doing a study called Myorisk. They are studying people who are within one year of diagnosis by analyzing the dust in their homes to see if there are any links.

Statins- Dr. Christopher has seen over 80 patients who are believed to have statin induced Myositis. Twenty percent of people who take statins will experience issues with their muscles. When they discontinue the medication, everything goes back to normal. However, a small percentage of these people continue to have issues. Researchers have determined if you have the

following genetic background- HLADRB1101 and you see this toxin, then Myositis is a very high risk.

PM can possibly turn into IBM, but can DM turn into IBM? It is very rare, but it is possible. It is not possible to have both DM and PM. The muscle biopsy is very different. It is possible to have a DM biopsy with no rash. DM is not just PM without the rash. They look very different under the microscope.

Cancer and Myositis

DM has a higher cancer risk- 20% of patients get cancer in the first 3-5 years after diagnosis. After this time not much screening is done. In PM, 8-9% of patients are affected with cancer. Cancer is not known to be linked with IBM.

Interstitial Lung Disease (ILD) and Antibodies

MSA- Myositis specific antibody. Autoantibodies protein directed towards.

Antibodies that you make have particular clinical features that go along with these antibodies.

Lungs are involved in 30% of Myositis patients. With Interstitial Lung Disease (ILD), there is a problem with gas exchange. They can't inflate properly. You are more likely to develop ILD if you certain antibodies. These are as follows:

Jo 1 synthetase- DM

PL-12- DM and PM

PL- 7- DM and PM

PM-Scl

MDA5

????- None of these but still has lung involvement. If you have one of these, a Pulmonary Function Test (PFT w/ DLCO) should be done. This shows how air sacs exchange. If lungs become stiffer and stiffer then this could create Pulmonary Hypertension which affects the heart.

Walk Proceeds

The proceeds from the walk go towards clinical studies. They have hired a clinical fellow to look at the heart and a connection to Myositis. Many people with Myositis have abnormalities in their EKG. They have also hired a technician who is looking carefully at muscle tissue to see

how the immune system is activated in different myopathies. Perhaps, this will translate into understanding how and why people respond differently to different medication.