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INFORMATION ON MAST CELL ACTIVATION SYNDROME (MCAS)

Mast cell activation disorders are among the great “mimickers” of many conditions in medicine. It often takes many years to reach the diagnosis simply because these disorders resemble other conditions so closely.

Mast cell are frequently referred to as types of “allergy” cells but play an important role in many functions including various immune functions. The mast cells release a variety of chemicals when activated. A variety of medical conditions are known to exist whereby mast cells become activated at time when they should not normal become activated. Patients with mast cell diseases frequently have an array of symptoms that at first glance seem all unrelated to each other. Theses seem to affect many different part of the body. With further understanding that these symptoms in a person with mast cell activation syndrome (MCAS) are all due to mast cell becoming activated the underlying cause of the array of different symptoms begin to make sense.

Common examples of symptoms that a patient with MCAS might experience are fatigue, nausea, diarrhea, cramps, IBS like symptoms, heartburn, depression, headaches, skin hives, asthma or shortness of breath, runny nose, and dizziness or light headedness. It would seem like the person in this example has a gastrointestinal problem, lung problem, allergy problem and psychiatric issue. In some ways, that is true – but all these issues come from one underlying issue – activated mast cells releasing their chemicals into the tissue and blood stream.

The proper and thorough evaluation of possible mast cell disorder is complex and best left to an allergist/immunologist. The allergist/immunologist will often work together with other specialties to complete the proper work up (depending on which symptoms the patient is finding problematic. Example of these specialties may include Gastroenterology, Hematology, Neurology, Psychiatry, Rheumatology and Dermatology.

While waiting for referral, a baseline serum tryptase may be considered (provided a patient is not using antihistamines). Many patients are then given a blood test requisition form and advised to go back to the lab right away if symptoms flare to get another repeat tryptase. The other approach is for the person to consider using antihistamines (and not go for the tryptase blood tests until advised to do so by the allergist). Information about benefits of antihistamines will be helpful information for the allergist when the time for the allergy appointment finally arrives.

Other blood tests can be considered while waiting. These include the following

1. CBC
2. LDH
3. AST, ALT, Bilirubin
4. Creatinine
5. Sodium, potassium
6. PT/PTT, ANA, RF, TSH, anti TPO antibodies and anti-thyroglobulin antibodies

Other blood tests will also be ordered after full review by the allergist and referral to other specialists may even be considered.

Besides the blood test for the mast cell mediator “tryptase”, other specialty tests are generally ordered by the allergist/immunologist and include

- Chromogranin A
- Chilled plasma histamine
- Chilled heparin
- Chilled PGD2
- Chilled urine PGD2
- Chilled urine 11 beta PGF2
- Rarely chilled urine LTB4, LTC4, LTD4

Classification of Mast Cell Activation Disorders

Primary	<ul style="list-style-type: none">• Associated with clonal mast cell disorder• Monoclonal mast cell activation syndrome (MCAS) <i>MCAS with no underlying cause is termed idiopathic MCAS</i>
Secondary	<ul style="list-style-type: none">• Allergic Diseases• Mast Cell Activation associated with chronic inflammation, neoplastic disease, chronic autoimmune urticaria

Work up

1. Referral to Allergy/Immunology
2. Baseline tryptase levels (3.8 to 11.4 ug/L) is needed. This is usually normal in MCAS
3. Serum tryptase levels within 4 hours of any flare.
 - An increase in tryptase levels to above [baseline x 1.20 + 2 ng/mL] is important in the diagnosis of MCAS
4. CBC
5. LDH
6. AST, ALT, (liver enzymes often elevated in MCAS)
7. PT/PTT, ANA, RF, TSH, thyroid antibodies
8. Specialty Tests ordered by the allergist/immunologist
 - a. Chromogranin A
 - b. Chilled plasma histamine
 - c. Chilled heparin
 - d. Chilled PGD2
 - e. Chilled urine PGD2
 - f. Chilled urine 11 beta PGF2
 - g. Rarely chilled urine LTB4, LTC4, LTD4

Potential Signs of Mast Cell Activation

BODY SYSTEM	SYMPTOM TO REVIEW	YES	NO
Constitutional	<p>Does the patient experience</p> <p>..... fevers?</p> <p>..... chills?</p> <p>..... fatigue?</p> <p>..... sweating?</p> <p>..... weight changes?</p>		
Gastrointestinal	<p>Does the patient (or has the patient) experience:</p> <p>..... nausea?</p> <p>..... vomiting?</p> <p>..... diarrhea?</p> <p>..... cramps?</p> <p>..... IBS?</p> <p>.....GERD/reflux?</p> <p>.....heartburn?</p> <p>.....increased liver enzymes?</p> <p>..... malabsorption?</p> <p>.....GERD/reflux?</p> <p>.....splenomegaly?</p> <p>.....hepatomegaly?</p> <p>.....ascites?</p>		
NEUROLOGIC	<p>Does the patient (or has the patient) experience:</p> <p>..... confusion?</p> <p>.....brain fog?</p> <p>..... headaches?</p> <p>..... anxiety?</p> <p>..... depression?</p> <p>..... vertigo?</p> <p>.....syncope?</p> <p>.....tremor?</p> <p>.....weakness?</p> <p>.....dysautonomia?</p>		
SKIN	<p>Does the patient (or has the patient) experience:</p> <p>..... rashes?</p> <p>..... hives?</p> <p>..... flushing?</p> <p>..... angioedema?</p> <p>..... skin itching?</p>		

PULMONARY	<p>Does the patient (or has the patient) experience:</p> <p>..... wheezing?</p> <p>.....asthma?</p> <p>..... cough?</p> <p>..... shortness of breath (dyspnea)?</p> <p>..... skin itching?</p>		
ENT	<p>Does the patient (or has the patient) experience:</p> <p>..... rhinitis?</p> <p>.....rhinorrhea?</p> <p>..... post nasal drip?</p> <p>..... congestion?</p> <p>..... laryngeal edema?</p> <p>..... Irritation in the ears?</p> <p>..... hearing problems?</p> <p>..... tinnitus?</p> <p>..... eye irritation?</p> <p>..... decreased focus/vision?</p> <p>..... mouth sores?</p> <p>..... throat itching?</p> <p>..... poor dentition?</p> <p>..... dysphagia?</p>		
HEART	<p>Does the patient (or has the patient) experience:</p> <p>..... tachycardia?</p> <p>.....hypotension?</p> <p>..... light headedness?</p> <p>.....palpitations?</p> <p>.....dizziness?</p>		
MSK	<p>Does the patient (or has the patient) experience:</p> <p>..... osteoporosis?</p> <p>.....bone pain?</p> <p>..... soft tissue pain?</p>		

MAST CELL “TRIGGERS” TO ENQUIRE ABOUT

TRIGGERS	YES	NO
Has the patient experienced flares from any of the following:		
..... opioids ?		
.....ASA ?		
..... NSAIDS ?		
..... local anesthetics ?		
..... muscle relaxants ?		
..... heat ?		
..... cold ?		
..... pressure ?		
..... exercise ?		
..... estrogen ?		
..... progesterone ?		
..... menstrual cycle changes (women) ?		
..... Antibiotics (vancomycin) ?		
..... Antibiotics (ciprofloxacin) ?		
..... radiology contrast dyes ?		
..... specific drugs ?		
..... infections ?		
..		
..... stress ?		
..... alcohol ?		
..... venom stings ?		
..... contrast dyes ?		
..... pets ?		
.....		
..... food (dairy) ?		
..... food (egg whites) ?		
..... food (fermented or leftovers) ?		
..... food (gluten) ?		
..... food (nuts) ?		
..... food (soy) ?		
..... food (shellfish) ?		
..... food (strawberries) ?		
..... food (tomatoes) ?		

Proposed Criteria for Mast Cell Activation Syndrome

1. Episodes of typical mast cell related symptoms in two or more organ systems

a) see chart above

2. Quantitative Evidence the mast cells are activated

a) increase in tryptase to a level above $[\text{baseline} \times 1.20 + 2 \text{ ng/mL}]$

b) evidence of mast cell markers in the serum (tryptase, heparin, chromogranin A, histamine)

c) evidence of mast cell markers in the urine (ie PGD₂, 11 beta PGF₂)

3. Evidence of a Clear Benefit from Medications that Suppress Mast Cells

a) H1 antihistamines (Benadryl, Claritin, Allegra, Zyrtec)

b) H2 antihistamines (ranitidine, cimetidine, famotidine)

c) Leukotriene antagonists (Montelukast, etc)

d) Cromolyn Sodium

e) Ketotifen