

Mast Cell Activation Syndrome

Diagnosis

Mast cell activation syndrome (MCAS) is a condition where benign but highly sensitive inflammatory/allergic cells are located in a variety of areas of the body and release chemicals (mediators) which work cause many symptoms. The diagnostic work up can be complex and relatively expensive depending on insurance coverage for lab tests. One approach is to look for mast cells by gastrointestinal biopsies and see if the symptoms respond to treatment. If biopsies have been obtained in the past, we can get the “cell blocks” (not the slides) to stain the tissue for mast cells. Most allergists however believe that it is necessary to document that these mediators are documented to be elevated in the blood or urine prior to making the diagnosis. There is a good rationale to this in that there is some controversy about the number of mast cells that are needed to make the diagnosis. Experts in the field often try to detect chemical evidence of the disease to support abnormal biopsies from the gastrointestinal tract.

Laboratory test to look for evidence of mast cell activation include: serum chromogranin A, plasma heparin, plasma histamine, and 24-hour urine collections for prostaglandin D2, N-methylhistamine, 2,3 dinor 11-beta-PGF2- α , and Leukotriene E4. These tests may be normal because: 1) mast cells live in tissues and may be locally active locally and thus do not secrete enough chemicals to be picked up by blood or urine tests, 2) mast cells secrete mediators intermittently, or 3) the blood or urine is not handled properly since these chemicals are sensitive to heat. The tryptase blood level is usually normal in 85% of patients but seeing normal or low levels is helpful to exclude another cause of mast cell activation symptoms known as mastocytosis. The lab should keep your blood cold at all times (including their use of cold centrifuge). You and the lab should keep the urine cold at all times. Lab tests can be expensive and you should check with your insurance company if they will cover the costs of the tests.

Small intestinal bacterial overgrowth (SIBO), imbalanced microbiome of the colon, Helicobacter pylori infection of the stomach, mold exposure, and Lyme disease may be triggering factors for MCAS and may need to be excluded with special tests.

Treatment

Treatment for mast cells can be challenging in that patients often require multiple medicines usually given in a step-wise manner. Patients may react to the medications and/or the fillers/additives/coatings in medications. Medications, natural therapies (over the counter), and diet can be helpful. More aggressive MCAS usually requires more aggressive therapy. In general avoid live vaccines and watch for drug side effects owing to dyes, filler, preservatives and certain medicines which trigger MCAS (see section below). Gluten, dairy, and histamine-containing foods can be problems for MCAS patients. For highly sensitive patients a good compounding pharmacy can be very important.

Education

Watch Dr. Afrin on YouTube: [Afrin and MCAS](#), and read Dr. Lawrence Afrin's book “Never bet against Occam: a mast cell book review and call to action” and also listen to the following podcast, <https://drruscio.com/mast-cell-activation-syndrome-clinician-researcher-dr-lawrence-afrin/>

MCAS Dietary Approaches

This is a baseline starting point for all of the “MCAS Step Therapies” discussed below.

For one month exclude gluten, yeast, and cow milk protein-containing foods. A low histamine diet is recommended long-term. A FODMAP-free diet can help especially when SIBO or dysbiosis is present. It is important to look for food triggers.

MCAS Step 1 – Anti-histamine and Natural Therapy

Start with over-the-counter H1 blockers (Zyrtec, Claritin, or Allegra) and H2 blockers (Zantac or Pepcid) are reasonable to start early on. Quercetin 500 mg 2 - 3x/day (at GNC or elsewhere), Vitamin C 500 mg twice a day, Vitamin B6 25 mg daily, Vitamin D 1000 units, and probiotic therapy that includes *Lactobacillus rhamnosus* (Culturelle) and *Bifidobacter* species.

Note about all medicines including H2 blockers – one will be tolerated whereas another in the same drug category will not. This could be due to the chemical shape or the fillers in the pill/capsule. There are 4 over-the-counter H2 blockers and the doses for these should start low and increase gradually. Liquid versions often used for children may be good for people who are sensitive for medications. Some patients need the H2 blockers 3 times a day. Some may need double the normal dose.

If these fail to help, add DAO Enzymes with meals (UmbrelluxDAO), alpha lipoic acid 600 mg daily, omega-3 fatty acids (fish oil, krill oil), N-acetylcysteine (NAC).

Additional natural therapies that could help include:

1. Adrenal support:
 - a. DHEA - for general health
 - b. Ashwagandha herb - helps sleep –
<https://www.puritan.com/ashwagandha-1012?&scid=42614&cmp=msn-> -
[Bing NB Cat Supplements Alpha-ashwagandha](#)
2. Gut health
 - a. EndoZin from Klaire – you might need my code – F11 to order. This helps heal the leaky gut – zinc and L-glutamine – with meals 2x/day

MCAS Step 2 Therapy

- A. H2 blockers: Zantac (start at 150 mg and increase to 300 mg twice a day) or Pepcid (start at 20 mg and work up to 40 mg twice a day)
- B. H1 blockers: Zyrtec 10 mg (or either Claritin 10 mg or Allegra 60 mg) 2 times per day. Some people do better on one H1 blocker than another. Benadryl is a sedating H1 blocker and should be used at night or for severe histamine activity.
- C. Quercetin (herbal mast cell stabilizer available at GNC or elsewhere) 500 mg 2 – 4 times a day.
- D. Vitamin therapy: C 500 mg twice a day, D 1000 units daily, and B6 25 mg daily.
- E. Low dose naltrexone (LDN): I generally recommend LDN to reduce inflammatory proteins that can trigger mast cell activation. LDN cannot be used in the setting of chronic narcotic use. For LDN start at 1 mg and gradually increase dose up to 4.5 mg each morning (this needs to be made at a compounding pharmacy).

If tolerating the above, yet symptoms are not substantially improved then the next 3 options are substitutes for Quercetin and include:

Singulair (montelukast) 10 mg per day (if there is asthma, interstitial cystitis, chronic prostatitis, pain, or brain fog, I will start this early on in the treatment).

Cromolyn - start at 1 ampule 2-4 times a day and then slowly increase to 2 ampules 4 times a day.

Ketotifen 2 mg one to two capsules 1-2x/day (start at night since it may be sedating) - this needs to be made at a compounding pharmacy and is not covered by insurance.

MCAS Step 3 Therapy

Ziluten 600 mg twice a day (this is especially good when there is asthma and/or interstitial cystitis). Accolate is another option. Low doses of aspirin can be tried but this should be closely monitored since allergic responses may occur (start at 81 mg and increase to 650 mg twice a day). Short term use of steroids can be used for severe attacks of pain or hives. Benzodiazepines can be helpful.

MCAS Step 4 Therapy

In severe cases, the following medications may be used: Xolair subcutaneous injections (FDA-indication is for hives, angioedema and asthma; risk of anaphylaxis is 1/1000 and is riskier for those who have many allergies and drug reactions), Imatinib (Gleevec; FDA approved for CML; clinical experience with MCAS), immune globulin injections (FDA-indication for IVIg included hives and angioedema), Tofacitinib pills (Xeljanz; FDA-indication is for rheumatoid arthritis; case reports for MCAS), and hydroxyurea (FDA-indication, leukemia, sickle cell – helpful for MCAS with deep muscle and bone pain – case reports for MCAS).

MCAS – dietary supplementation

Options to improve nutrition include: Physicians' Elemental Diet by Integrative Therapeutics (tolerable oral nutrition). In severe cases feeding tube placement into the small intestine with an elemental diet is required: Neocate Jr. or Elecare Jr. can be used in place of Vivonex which is standard.

MCAS Drug Triggers

Avoid drugs that can trigger mast cell release - narcotics, muscle relaxants, certain antibiotics, anti-seizure, local anesthetics, IV dye, ACE inhibitors, and beta-adrenoceptor antagonists. When Xolair is considered, beta-blockers should be stopped.

MCAS periodic, symptom specific therapy

Abdominal pain: butylscopolamine, proton pump inhibitor (PPI), steroids, Ativan, Xanax

Anemia: iron (in particular IV) must be given cautiously due to risk for potentially intense mast cell activation; alternatively, red blood cell transfusion should be considered

Angioedema: tranexamic acid; icatibant

Arthralgias: celecoxib

Brain fog: nasal cromalyn

Conjunctivitis (after exclusion of a secondary disease) preservative-free eye drops with H₁-antihistamine, cromolyn, ketotifen, or glucocorticoid (brief courses)

Chest pain: extra H₂ blocker, PPI

Colitis: budesonide; prednisone

Diarrhea: cholestyramine; nystatin; montelukast; ondansetron; aspirin (50–350 mg/day w extreme caution (in steps test each drug for 5 days until improvement of diarrhea)

Hypercholesterolemia: atorvastatin

Itching: palmitoylethanolamine (PEA), cromolyn-containing ointment

Insomnia: triazolam, doxepin

Interstitial cystitis: pentosane (Elmiron), amphetamines

Nausea: dimenhydrinate; lorazepam; ondansetron; aprepitant (Emend);

Neuropathy: alpha lipoic acid

Osteoporosis, bone pain ⇒ bisphosphonates (Vitamin D plus calcium is second-line Rx d/t limited reported success and an increased risk for stones); calcitonin; teriparatide (with caution; cases of cholestatic liver failure reported); denosumab (dental clearance required prior to Rx with bisphosphonates and anti-RANKL therapies)

Respiratory mucus and obstruction: montelukast; Ziluten; urgent: albuterol

Tachycardia: ivabradine

Healthcare Team

It is important to build a team of doctors to help take care of your total health. In addition to your primary care doctor, specialists can be helpful. This is especially the case when there is the addition of two common syndromes associated with MCAS: postural orthostatic tachycardia syndrome (POTS) and hypermobile Ehlers-Danlos syndrome (EDS).

MCAS – for this condition allergists can be helpful

Private Practice:

Jeffrey Tillinghast, MD - 314-542-0606

Barbara Jost, - MD314-868-6260

University care:

W.U.: 314-996-8670 - Jennifer Dy, MD, Jennifer Monroy, MD

For those with POTS – an autonomic nervous system syndrome, a cardiologist and neurologist can be helpful

Cardiology Private Practice:

Craig Reiss, MD

Cardiology University care:

W.U.: Mitchell Faddis, MD

Neurology Private Practice:

Laurence Kinsella, MD

EDS – for this connective tissue syndrome, a physical therapist, pain management doctor, and orthopedic doctor can be helpful

Leonard Weinstock, MD – edited 3/29/18; adapted from Dr. Molderings and Dr. Afrin's articles