

Mast Cell Activation Syndrome: Diagnosis

Mast cell activation syndrome (MCAS) work up is complex and expensive. Showing mast cells by gastrointestinal biopsies and seeing if the symptoms respond to treatment may be adequate.

Labs to look for mast cell activation syndrome include serum chromogranin A, plasma heparin, plasma histamine, and 24 hour urine collection for prostaglandin D2 and/or N-methylhistamine but these are often normal since the mast cells may live in tissues and be active locally but not secrete enough chemicals to be picked up by blood or urine tests.

Mast Cell Activation Syndrome: Treatment

Treatment for mast cells can be challenging in that patients often require multiple medicines. Patients may react to the medications used to treat the disease. A stepwise approach can be helpful. Medications, natural therapies (over the counter), and diet can be helpful. More aggressive MCAS requires aggressive therapy.

For more education, read Dr. Lawrence Afrin's book "Never Bet Against Occam: A Mast Cell Book Review and Call to Action"

MCAS step 1 therapy

Start Zantac or Pepcid (H2 blocker starting at standard dose twice a day and increasing to double dose if needed), Zyrtec, Claritin, or Allegra (non-sedating H1 blocker) 1 to 2 times per day, and Quercetin (herbal mast cell stabilizer available at GNC or elsewhere) 500 mg 4x/day. Patients who are sensitive to medicines can start them one at a time and later increase to the maximum dose as they can tolerate. 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.

Start vitamin therapy: C 500 mg twice a day, D 5000 units daily, B6 25 mg daily, and B12 500 mcg daily.

Low dose naltrexone (LDN): I generally recommend LDN to reduce inflammatory proteins that can trigger mast cell activation and by cell growth regulation. 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).

Diet therapy: one month exclusion diet - no gluten, yeast, and cow milk protein-containing foods. A low histamine diet is recommended long-term. A FODMAP-free diet can help. Looking for food triggers is important. Other natural therapies can be employed. See MCAS Natural Therapy section below.

If tolerating the above, yet symptoms continue - take Singulair 10 mg per day (if there is asthma, interstitial cystitis, or chronic prostatitis, start this early on in the treatment).

If tolerating the above, yet symptoms continue - take Cromolyn – start at 1 ampule 2 – 4 times a day and then slowly increase to 2 ampules 4 times a day.

In general avoid live vaccines and watch for drug side effects owing to dyes, filler, preservatives and certain medicines which trigger MCAS (see next)

MCAS drug triggers

Avoid drugs that can trigger mast cell release - narcotics, muscle relaxants, certain antibiotics, anti-seizure, local anesthetics, SSRI and SNRI antidepressants, IV dye, ACE inhibitors, and beta-adrenoceptor antagonists

MCAS – natural therapies

Quercetin 500 mg 4x/day (at GNC or elsewhere), Vitamin C 500 mg twice a day, Vitamin B6 25 mg daily, Vitamin B12 500 mcg, Vitamin D 5000 units, and probiotic therapy that includes *Lactobacillus rhamnosus* (Culturrelle) and *Bifidobacter* species. Over-the-counter H1 (Zyrtec or others) and H2 blockers are reasonable.

Diet therapy: one month exclusion diet - no gluten, yeast, and cow milk protein-containing foods. A low histamine diet is recommended long-term. A FODMAP-free diet can help. Looking for food triggers is important. Other natural therapies can be employed. See MCAS Natural Therapy section below.

If these fail to help, add omega-3 fatty acids (fish oil, krill oil), Alpha Lipoic Acid, N-acetylcysteine (NAC), other Methylation donors (SAME or methyl-folate), and/or DAO Enzymes with meals (UmbrelluxDAO).

MCAS second line therapy

Second line drugs: ketotifen 20 mg, one to two capsules 1-2x/day (this needs to be made at a compounding pharmacy and is not covered by insurance). Zileuton 600 mg twice a day (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. Short term use of steroids can be used for severe attacks

MCAS third line drugs

In severe cases, the following medications may be used: Xeljanz (Tofacitinib) pills (FDA-indication is for rheumatoid arthritis, 2 cases reported in 2017 showing rapid onset for this oral medicine – see below), Nucala (mepolizumab) subcutaneous injections (FDA-indication is for asthma pts), Xolair subcutaneous injections (FDA-indication is for hives and asthma – this can take a month to work), Amalizumab, Etoricoxib, hydroxyurea, tamoxifen, mercaptopurine, methotrexate, or if very severe, cyclosporine

MCAS – new therapy Tofacitinib/Xeljanz: Targeting commonly affected downstream effectors may yield clinical benefit independent of upstream mutational profile. For example, both activated KIT and numerous cytokine receptors activate the Janus kinases (JAKs). Thus, JAK-inhibiting therapies may be useful against the downstream inflammatory effects of MCAS. The oral JAK1/JAK3 inhibitor, tofacitinib, is currently approved for rheumatoid arthritis and is in clinical trials for other chronic inflammatory disorders. Herein, we report two patients with MCAS who rapidly gained substantial symptomatic response to tofacitinib (Afrin 2017).

MCAS Periodic, symptom specific therapy

Abdominal pain: butylscopolamine, proton pump inhibitor (PPI)

Anemia: iron (whether oral or parenteral) 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

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

Interstitial cystitis: pentosane (Elmiron), amphetamines

Nausea: dimenhydrinate; lorazepam; ondansetron; aprepitant;

Neuropathy: alpha lipoic acid

Osteoporosis, bone pain ⇒ bisphosphonates (Vit 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; zileuton; urgent: albuterol

Tachycardia: ivabradine

MCAS – allergic opinion – reasonable to do to help build a team of doctors

St. Louis University: 314-977-9044 - Dr. Mark Dykewicz

Washington University: 314-996-8670 - Jennifer Dy, MD, James Wedner, MD, Andrew Kao, MD

Private Practice:

314-542-0606 - Jeffrey Tillinghast, MD

314-868-6260 - Barbara Jost, MD

314-872-3104 - Hamsa Subramanian, MD