TREATMENTS FOR MAST CELL DISEASES

Mast Cell Activation/Mediator Release Symptoms

Controlling symptoms of mast cell activation/mediator release starts with avoiding the very triggers which we know will initiate mast cell activation in us, and the triggers can be very individual. Avoiding heat, cold, abrupt changes in temperature, sunlight, strong odors/perfumes and chemical smells can help many patients. Caution must be taken around venomous creatures such as bees, wasps, hornets, spiders, jellyfish and snakes, etc. Stress and fatigue can be major triggers for many patients, as can viruses, bacterial and fungal infections. Sometimes a simple change in routine can trigger us!

Many foods can trigger mast cells to activate and release their mediators; shellfish, peanuts, nuts, citrus, and high histamine foods are high on the list of potential triggers known to bother some people, but not others. Medications to be taken with caution include NSAIDs such as ibuprofen, toradol, aspirin (this can be confusing, because aspirin can also be used as a treatment for those with high prostaglandin levels; when used as a treatment it must be started under the supervision of a physician!), opioid narcotics, alcohol, the intravenous form of vancomycin (the oral form is usually fine), some anesthetics, some antibiotics, and topical agents, like benzocaine. However, everyone is different, and *anyone can react to anything*, *and you can even react to something that you have never reacted to before*, so always proceed with caution. Always have someone with you when taking a new medication, starting a new treatment, or traveling to a new place.

Delayed reactions may occur in mast cell activation patients when encountering a trigger or allergen to which they are allergic. Analogous to anaphylaxis, there are acute, protracted and delayed phases of reactions. The immediate phase is within minutes to hours, the protracted phase is up to 8 hours and the delayed reactions occur up to 24 hours; there is no series at 48 hours. Less than 1% of patients present only the delayed phase. In mast cell activation patients, foods and environmental triggers can induce delayed reactions up to 24-48 hours and it is a good idea to have a diary when a reaction has occurred so that it can be traced to a trigger. The reason a food can induce a delayed reaction is delayed absorption and delayed metabolism which can be induced by medications including antihistamines and generation of by-products which can be the triggers. (Mariana Castell, MD, PhD, personal communication.

Treatment of mastocytosis depends on the symptoms and the classification of disease.[1-3] Symptoms of mast cell activation/mediator release are treated with H1 and H2 antihistamines, mast cell stabilizers, leukotriene inhibitors, and possibly aspirin (under *direct supervision* of a physician). All mast cell disease patients should carry *two doses* of self-injectable epinephrine, unless otherwise contraindicated (glucagon may need to be administered for patients on beta-blockers). Patients should also be instructed on how to self-administer the epinephrine while lying down, to maximize rapid absorption of the drug. Every patient should carry a physician-signed American Academy of Allergy, Asthma and Immunology Anaphylaxis Action Plan at all times.

Treatment of MCAS is similar to that listed above for mastocytosis symptoms *related to mast cell activation and mediator release*.[4-6]

There has been growing recognition of the detrimental effects on cognition (mental clouding and other cognitive impairments) caused by long term use of antihistamines.[7] A high risk group of patients 65 years and older (defined as patients taking 50 mg per day for 3 years diphenhydramine or doxepin or 25 mg for 6 years), were found to have a significant association between diphenhydramine use and cognitive impairment.[8] Similarly, high doses of sedating antihistamines such as diphenhydramine can cause increased seizure activity, seen mostly in children. In addition, a tolerance to or a dependence upon diphenhydramine may result in a need for even higher doses.[7] Caution and restraint must be used when taking antihistamines long term in order to help preserve neurological function. While these drugs are critical to us for their antimediator effects, we must work with our physicians to titrate them to the lowest dose necessary to achieve control of mast cell activation symptoms.

Additional Symptoms of Indolent Systemic Mastocytosis

A suggested order of treatment options for adult patients with indolent systemic mastocytosis, aimed at symptom control, and including suggested therapies for osteoporosis, can be found in Table 3 of this article from the American Journal of Hematology.[9]

More on Medications to Treat Mast Cell Diseases

Advanced Disease

Therapies exist for smoldering systemic mastocytosis (SSM) and advanced systemic mastocytosis, and promising new treatments are being developed. Prominent among these newer treatments are tyrosine kinase inhibitors (TKIs) targeting the *KIT* kinase[10, 11] (e.g., midostaurin[10, 12]). Imatinib is approved therapy for adult aggressive systemic mastocytosis (ASM) patients lacking the *KIT* D816V mutation or if mutation status is unknown. Additional standard therapies for advanced variants are interferon, the chemotherapeutic agent cladribine, and tyrosine kinase inhibitors such as midostaurin.[9, 12] These chemotherapeutic agents are used in combination with antimediator therapy to control symptoms and reduce the overall mast cell burden. In patients with systemic mastocytosis with associated clonal hematologic non-mast cell lineage disease (SM-AHNMD)/systemic mastocytosis with an associated hematologic neoplasm (SM-AHN), therapy selection usually depends on the associated disease, which is commonly more aggressive than the SM part. Mast cell leukemia and sarcoma require a polychemotherapy approach. More information on therapies for advanced systemic mastocytosis variants can be found here.

More on Medications to Treat Mast Cell Diseases

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