

KOUNIS SYNDROME IN MAST CELL PATIENTS

Acute coronary syndromes can occur in allergic and anaphylactic reactions. One example, called Kounis Syndrome, is possible in patients with a wide variety of mast cell activation diseases and can affect patients of any age. The main triggers of Kounis syndrome are drugs, environmental exposures, and various pre-existing conditions. When patients such as mast cell disease patients are on a protocol exposing them to many medications, the cascade leading to anaphylaxis and Kounis syndrome can be very rapid, with the heart and coronary arteries as the primary target.

Multiple mast cell mediators have direct action on coronary vessels and together result in hyperresponsiveness of mast cells, which can result in the Kounis syndrome cascade.

Please note: Coronary artery spasm induced by mast cell mediators may initiate Takotsubo Syndrome or stress induced cardiomyopathy during anaphylactic reactions.

Type 1: Normal coronary arteries, no coronary disease, no pre-disposing conditions; acute allergic attacks resulting in coronary vasospasms without elevations in cardiac enzymes OR coronary vasospasm with myocardial infarction with elevation of cardiac enzymes and troponins

Treatment of the allergic episode can terminate the type 1 variant

- corticosteroids
- H1 and H2 blockers
- Vasodilators such as calcium channel blockers and nitrates can decrease hypersensitivity induced vasospasms

Type 2: Quiescent pre-existing atheromatous disease in whom acute allergic attacks can induce either vasospastic angina or plaque erosion, or rupture manifesting acute myocardial infarction

Treatment of acute coronary event comes first, then treat allergic attack

- acute coronary event protocol
- corticosteroids
- H1 and H2 blockers

Type 3: Stent thrombosis with eosinophils and mast cells identified on pathology (Giemsa, hematoxylin-eosin stain)

Treatment of stent thrombosis with allergic attack

- corticosteroids
- H1 and H2 blockers
- Mast cell stabilizers
- Biopsy of thrombus stained for mast cells and eosinophils

CONSIDERATIONS

Nitroglycerin causes decreased blood pressure and increased heart rate. B blockers can exaggerate coronary vasospasms due to the unopposed actions of α -adrenergic receptors.

Epinephrine is the drug of choice for anaphylaxis, however epinephrine can aggravate Kounis syndrome and worsen coronary vasospasm. If the patient is on B-blockers, glucagon administration should be considered along with epinephrine. Fentanyl is the opiate with the best profile for mast cell disease patients; administer with extreme caution.

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MISSION STATEMENT

The Mastocytosis Society, Inc. is a 501(c)(3) nonprofit organization dedicated to supporting patients affected by Mastocytosis or Mast Cell Activation Disease as well as their families, caregivers, and physicians through research, education and advocacy.

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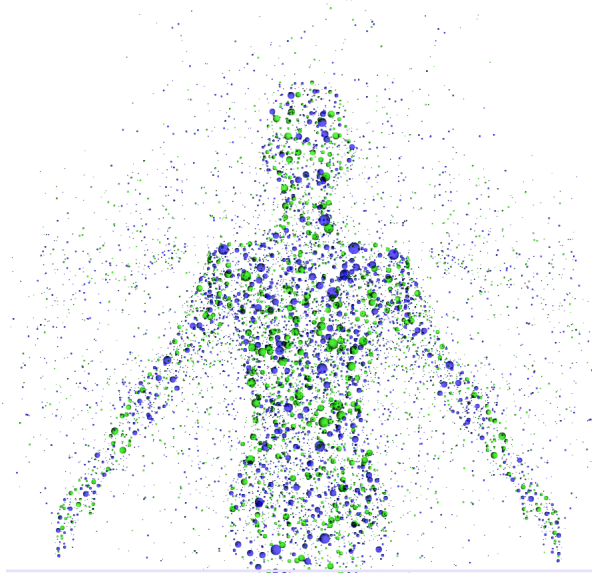
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Emergency Care For Patients with Mast Cell Diseases

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What Are Mast Cell Diseases

Mast cell diseases are characterized by abnormal mast cell proliferation/accumulation (mastocytosis), and/or activation [mastocytosis or mast cell activation syndrome (MCAS)], and affect both children and adults.

Mastocytosis can affect skin and internal organs such as the bone marrow, GI tract, liver and spleen, and most patients have either cutaneous or indolent systemic (benign) forms. Others, with more aggressive disease, may have associated hematologic disorders. Mast cell disease patients may have unpredictable symptoms that require anti-mediator therapy. Diagnosis of mastocytosis is confirmed by a bone marrow or skin biopsy. MCAS patients exhibit similar symptoms, and may or may not have increased measurable mast cell mediators for which we can currently test (serum tryptase, urinary N-methyl histamine, urinary prostaglandin D2 and 11-beta F2 alpha) during or immediately after an attack, and do respond to anti-mediator therapy.

Patients with mast cell diseases are more likely to experience life-threatening anaphylaxis than the general population. No correlation has been found between the signs and symptoms of anaphylaxis and serum tryptase levels or mast cell burden. The most common types of anaphylaxis are recurrent idiopathic anaphylaxis, hymenoptera anaphylaxis, or drug induced anaphylaxis. Anaphylaxis can also occur during anesthesia, indicating that appropriate perioperative management is critical.

ANAPHYLAXIS

Anaphylaxis is an acute, life-threatening, systemic reaction that results from the **sudden, rapid**, systemic release of mediators from mast cells and basophils.

Anaphylaxis symptoms present as new or worsening symptoms including:

- > **Mouth:** itching, swelling of lips and/or tongue
- > **Throat:** itching, tightness, closure, hoarseness
- > **Skin:** itching, hives, redness, swelling, flushing
- > **Gut:** nausea, vomiting, diarrhea, cramps
- > **Lung:** shortness of breath, cough, wheeze
- > **Heart:** weak pulse, dizziness, passing out

Only a few of these symptoms may be present. Although the diagnosis usually depends on the involvement of 2 organ systems, even if anaphylaxis presents with 1 organ system, epinephrine administration may be indicated. Anaphylaxis may present as an acute cardiac or respiratory event or with hypotension as the only manifestation of anaphylaxis.

Symptoms can be life-threatening! ACT FAST!

COMMON TRIGGERS OF MAST CELL REACTIONS AND ANAPHYLAXIS

Triggers are unique to each patient. If a patient tells you that a certain drug, substance or environmental factor is a mast cell trigger for them, believe the patient even if it does not seem plausible.

Triggers can include, but are not limited to:

- > Unknown trigger- Idiopathic anaphylaxis
- > Hymenoptera venom and other venoms such as ant, snake, jellyfish and insect
- > Medications including, but not limited to morphine and derivatives, IV Vancomycin, aspirin, NSAIDS; can be tolerated in some patients. Proceed with caution.
- > Anesthesia drugs (succinylcholine, D-tubocurarine, gallamine, decamethonium) and radiocontrast dyes
- > Food or beverage, including alcohol
- > Emotional stress, anxiety and fatigue
- > Physical stress, e.g., heat, cold, change in temperature
- > Friction of skin lesions or vibration
- > Exercise
- > Latex, odors/perfumes

ANAPHYLAXIS GRADES

- > **Grade I:** hives/rash, itching or swelling of mouth/throat
- > **Grade II:** any of the above, plus- hypotension, tachycardia, dyspnea, presyncope, GI distress, including, but not limited to: pain, nausea, vomiting, diarrhea
- > **Grade III:** any of the above, plus- profound hypotension, bradycardia or tachycardia, confusion, cardiovascular collapse, bronchospasm, hypoxia [SaO₂<92%]
- > **Grade IV:** cardiac arrest

ANAPHYLAXIS TREATMENT IN A PRE-HOSPITAL SETTING: FOR PATIENTS

It is important to work with your primary mast cell physician to set up a signed home and emergency room protocol for anaphylactic/mast cell degranulation episodes. This protocol should include:

- > When to take rescue medications, and what medications to take
- > When to use IM epinephrine
- > When to call 911 and go to the emergency room
- > Assemble an emergency protocol packet, together with the names of doctors, care-givers, phone numbers, medications you take, diagnoses, allergies and mast cell protocol signed by your physician. Have multiple copies of these documents available for emergency personnel.
- > Request copies of all records including labs, x-rays, and treatments for your files. Remember to take these with you any time you go to the emergency room.
- > If ER visit is required, go by ambulance if possible, and give the EMT all of your paperwork.
- > If someone is driving you, recline as far back as you can or lie down in the back seat, have them pull up to the ER door, and alert emergency personnel that you are having anaphylaxis.

ANAPHYLAXIS TREATMENT IN A HOSPITAL SETTING: FOR PHYSICIANS

- > Epinephrine should be administered as soon as the diagnosis of anaphylaxis is suspected. Although the diagnosis usually depends on the involvement of 2 organ systems, even if anaphylaxis presents with 1 organ system, such as the skin, epinephrine administration may be indicated.
- > Anaphylaxis may present as an acute cardiac or respiratory event, with hypotension as the only manifestation.
- > **Epinephrine given IM** (Vastus Lateralis muscle) is the drug of choice for treatment of anaphylaxis- concentration is 1:1000 (1mg/1ml) solution- 0.2mg-0.5mg for adults and 0.01ml/mg/kg for children- may repeat in 5-15 minutes, if needed.
- > When giving epinephrine to a patient with a mast cell disease who is experiencing anaphylaxis, care must be given to be sure the patient is not allergic to any of the ingredients in the epinephrine. Preservative free epinephrine may be preferable.
- > "Because of the risk of potentially lethal arrhythmias, epinephrine should be administered IV **only** in profoundly hypotensive patients or patients in cardio/respiratory arrest who have failed to respond to IV volume replacement and several injected doses of epinephrine."¹³
- > Administer Oxygen
- > Start large bore IV access
- > Administer IV fluids if hypotensive.
- > Consider inhaled bronchodilators if wheezing is present
- > H1 and H2 Blockers as supportive therapy, preferably IV administration, including diphenhydramine as an H1 blocker, given 25mg-50mg, adults, and 1mg/kg, up to max 50mg dose in children; given **very slow** IV diluted in normal saline over 2-5 minutes. Hydroxyzine is an alternative H1 blocker in this situation. H2 antagonist, such as Famotidine, IV, should also be given. All IV meds should be alcohol free.
- > Corticosteroids may prevent prolonged anaphylaxis, although they may not have efficacy in the initial treatment of anaphylaxis.
- > All mast cell disease patients must be monitored for biphasic reactions.