Quick guide to mast cell activation syndrome (MCAS)

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What is mast cell activation syndrome?

Mast cells are immune cells that store and release many different chemicals (mediators), such as histamine, heparin, prostaglandins, growth factors, and inflammatory proteins, among others. Mastocytosis is a condition where there are too many mast cells; by contrast, mast cell activation syndrome (MCAS) is a condition where mast cells degranulate and release mediators inappropriately in response to triggers.

What are the symptoms of mast cell activation syndrome?

Symptoms do not always present as typical allergies: they can be systemic or specific; reactions may not be immediate or perfectly consistent; and they can affect any part of the body, for example:

General:
Fatigue
Flushing
Pallor
Appetite/weight changes
Chemical or physical sensitivities
Pain
Depression/anxiety disorders
Blood clotting disease or event
Erythrocytosis

Genitourinary:
Interstitial cystitis
Painful, heavy and/or irregular periods

Ears, nose, throat, & eyes:
Dry/irritated eyes
Tinnitus
Post-nasal drip

Gut:
Acid reflux/indigestion
Nausea
Diarrhoea or constipation
Bloating

Skin:
Rashes/skin conditions
Angioedema
Hair loss

Neurological:
Headaches
Sensory neuropathies
Weakness
Dysautonomia
Seizure disorders
Cognitive problems
Sleep problems

Lungs & cardiovascular:
Air hunger and/or breathlessness
Uncontrollable blood pressure
Palpitations
Allergic angina

Endocrine & metabolism:
Abnormal liver function tests
High cholesterol
Dysglycaemia
High or low ferritin

How is mast cell activation syndrome diagnosed?

For diagnosis, a patient must fulfil at least either:
Both the major criteria below; *or*
The second major criterion PLUS one minor criterion:

Major criteria:

1. Multifocal or disseminated dense infiltrates mast cells in marrow and/or extracutaneous organ(s) (e.g., gastrointestinal or genitourinary tract)
2. Constellation of clinical complaints attributable to pathologically increased mast cell activity (mast cell mediator release syndrome)

Minor criteria:

1. Abnormal spindle-shaped morphology in > 25 % of mast cells in marrow or other extracutaneous organ(s)
2. Abnormal mast cell expression of CD2 and/or CD25 (i.e. co-expression of CD117/CD25 or CD117/CD2)
3. Mast cell genetic changes (e.g. activating KIT codon 816 mutations) shown to increase mast cell activity
4. Evidence of above-normal levels of mast cell mediators (see testing options below)
5. Symptomatic response to inhibitors of mast cell activation or mast cell mediator production or action

What tests are there for mast cell mediators?

MCAS tests are limited. There are hundreds of mediators and only a handful can be tested for. This means the mediators tested for might not be the problematic mediators. Tests can also easily show false negatives if the timing of the sample is wrong (best done during or very soon after a flare up of symptoms), or from sample degradation. Depending on test availability, the following mediators may be able to be measured:

- 24-hour urine methylhistamine
- 24-hour urine prostaglandin F2α
- Urine leukotriene E4
- Serum tryptase

Results should be interpreted with the above caveats in mind, and it may be appropriate to trial treatments regardless of test results.

What treatments are there for mast cell activation syndrome?

Treating MCAS requires being systematic and consistent, trying one new treatment at a time for a few weeks (assuming no negative reaction) before increasing the dose or trying the next thing. This ensures the fewest treatments are used with maximum effect. Response to treatment should be unambiguous. The following is a guide which can be adapted according to patient needs:

Remove triggers, where possible: Triggers can be nearly anything (e.g. food, hormone changes, weather changes, fragrances)
Target histamines: H1 and/or H2 antihistamines, DAO enzymes
Target leukotrienes: Montelukast
Target prostaglandins: Aspirin (salicylates are a common trigger; caution required), ibuprofen
Target stabilising mast cells: Quercetin, high dose slow-release vitamin C, sodium cromolyn, ketotifen
Note: Patients can react to fillers; compounded medication may be required

Resources

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