Mast Cell Activation Syndrome

A common clinical key that prevents progress.

Cogence Clinical Pearl

What the research says…

In this Cogence Clinical Pearl, we look at two papers on Mast Cell Activation Syndrome (MCAS). The first, from the *American Journal of Medical Science*, examines 413 patients and discusses comorbidities (the most common of which were gastroesophageal reflux, fatigue and dermatographism) and lab markers (the most useful of which were heparin, prostaglandin D2, histamine and chromogranin A). The second paper, from Current Allergy and Asthma Reports, discusses secondary mast cell activation, which can be a comorbidity, driven by other mechanisms that are primary, which they describe as including "chronic infections, autoimmune conditions, physical urticarias, and certain neoplasms."

Application…

Mast cell activation is not an all-or-nothing effect. It often accompanies the picture of chronic illness, with the expression being variable and dependent upon the total picture for each patient. The heterogeneity of mast cell activation presentations, combined with the challenges presented in lab assessment, make it essential to be alert for symptoms commonly associated with mast cell activation, whether it be primary or secondary. The presence of gastroesophageal reflux, fatigue and dermatographism are essential to recognize. Gastric acid production co-varies with histamine level. Because histamine doesn't always stay high, you won't always find it on a lab test, but the presence of excess gastric acid production is a good marker for it.

If mast cells are activated, either as a primary mechanism promoting chronic illness, or as a secondary mast cell activation when another disease process is primary, the substances released by the mast cells are likely to create additional problems that interfere with patient improvement and make it more likely the case will fail if you don't address the mast cell activation directly.

Mast cells release histamine, leukotrienes, platelet activating factor (PAF), Th2-promoting cytokines, and other substances. Each of these can play a problematic role that interferes with patient improvement. Histamine binds H3 receptors in the CNS, reducing the production of serotonin, norepinephrine, and acetyl choline. This can lead to depression, memory issues, and because the effects of vagus nerve motor outflow are mediated by acetyl choline, histamine elevation can interfere with vagal motor function, yielding greater GI inflammation, increased production of IL-6 by Kupfer cells in the liver, and decreased motility that leads to SIBO. PAF is a promoter of Th17 cell activation, increasing the risk of autoimmune flare activation. Th2 cytokine promotion leads to more mast cell activation, creating a loop.

In patients with mast cell activation, whether secondary or as MCAS, it's essential to inhibit Th2 cytokines (which can be done with perilla and astragalus) and essential to inhibit mast cell degranulation (which can be done with quercetin and vitamin C). And, of course, it's essential to sort

out what is driving the mast cell degranulation. You can see much more about this in Module 11, Videos 11, 11 part 2, and 11 part 3.

The Research…

Characterization of Mast Cell Activation Syndrome.

Am J Med Sci. 2017 Mar;353(3):207-215. Afrin LB, Self S, Menk J, Lazarchick J.

(Color and bold added)

Abstract

BACKGROUND: Mast cell activation syndrome (MCAS), a recently recognized nonneoplastic mast cell disease driving chronic multisystem inflammation and allergy, appears prevalent and thus important. We report the first systematic characterization of a large MCAS population.

METHOD: Demographics, comorbidities, symptoms, family histories, physical examination and laboratory findings were reviewed in **298 retrospective and 115 prospective patients with MCAS.** Blood samples from prospective subjects were examined by flow cytometry for clonal mast cell disease and tested for cytokines potentially driving the **monocytosis frequent in MCAS.**

RESULTS: Demographically, white females dominated. Median ages at symptom onset and diagnosis were 9 and 49 years, respectively (range: 0-88 and 16-92, respectively) and median time from symptom onset to diagnosis was 30 years (range: 1-85). Median numbers of comorbidities, symptoms, and family medical issues were 11, 20, and 4, respectively (range: 1-66, 2-84, and 0-33, respectively). **Gastroesophageal reflux, fatigue and dermatographism were the most common comorbidity,** symptom and examination finding. **Abnormalities in routine laboratories were common and diverse but typically modest. The most useful diagnostic markers were heparin, prostaglandin D2, histamine and chromogranin A.** Flow cytometric and cytokine assessments were unhelpful.

CONCLUSIONS: Our study highlights **MCAS's morbidity burden and challenging heterogeneity.** Recognition is important given good survival and treatment prospects.

Immunology and clinical manifestations of non-clonal mast cell activation syndrome.

Curr Allergy Asthma Rep. 2013 Feb;13(1):10-8. Cardet JC, Castells MC, Hamilton MJ.

(Color and bold added)

Abstract

There is a spectrum of disorders that clinically manifest as a result of mast cell activation. A non-clonal form has emerged in the literature where many of the clinical features of systemic mastocytosis are shared despite having a distinct mast cell biology. In this review, we summarize key features of the science behind mast cell activation relevant to what is now known as non-clonal mast cell activation syndrome (nc-MCAS). We highlight the clinical manifestations of nc-MCAS with a focus on diagnosis and treatment.

And from the same paper…

"Conditions such as **chronic infections, autoimmune conditions, physical urticarias, and certain neoplasms** may display release of mast cell mediators, which is defined as **"secondary mast cell activation."**