Neuropsychiatric Challenges in Undiagnosed Mast Cell Activation Syndrome: A Case Study

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CASE

A 47-year-old Caucasian female with a past medical history of eating disorder, OCD, MDD, GERD, gastroparesis, IBS constipation type, chronic hypokalemia requiring infusion every 3 days and chronic kidney disease, was referred to psychiatry for management of depression and anxiety by her primary care provider.

The patient's psychiatric presentation was most notable for demoralization in the context of multiple ongoing, poorly controlled GI symptoms attributed to a functional GI disorder. These symptoms included nausea, vomiting, severe constipation, GERD, and cramping. On review of systems, The patient also noted a recurrent pruritic hive-like rash, chronic sinus headaches, and hot flashes. Physical examination findings included dermatographia and erythema nodosum.

Upon taking a careful history, the patient reported a worsening of her mood and all the above symptoms after she stopped taking cetirizine. Given her episodic inflammatory symptoms involving more than two organ systems and resolution of symptoms with the treatment of an anti-mast cell mediator, she met criteria for Mast cell activation syndrome (MCAS) .[1,2] She was then started on treatment for MCAS (*cetirizine 10 mg QAM, famotidine 20 mg BID, and montelukast 10 mg BID*), resulting in significant improvement in both her mood and physical symptoms. Oral Cromolyn sodium was prescribed, but not covered by her insurance, this was challenged and is now being used.

BACKGROUND

Mast cell activation syndrome (MCAS) is a systemic inflammatory process that leads to overactivation and release of mast cell allergic and pro-inflammatory mediators, such as histamine and leukotrienes. Clinically, this can present on a spectrum with symptoms such as anaphylactoid reactions, syncope, abdominal pain, nausea, cramping, urticaria, headache, and fatigue.[3] It is also associated with neuropsychiatric symptoms, such as anxiety, depression, and cognitive dysfunction.[4] With a broad presentation that overlaps with many other conditions, variation in severity of symptoms, and sometimes unremarkable allergy workup, it often goes undiagnosed or incorrectly diagnosed as a functional disorder, somatic symptom disorder, or panic disorder.[2,5]

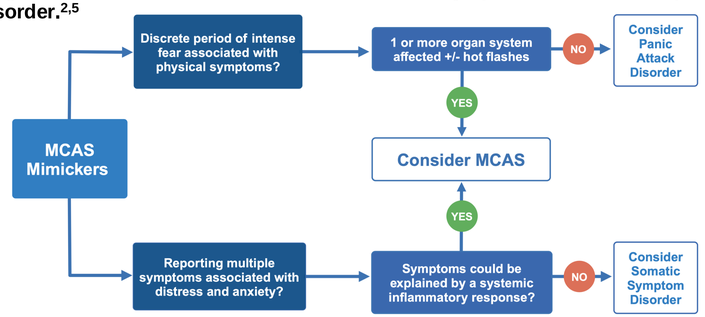

Figure 1: Example of common neuropsychiatric mimickers of MCAS [7,9]

IDIOPATHIC MCAS DIAGNOSTIC CRITERIA

Valent Criteria [3] Must meet all 3 criteria	Molderings Criteria [1] Must meet major criteria and 1 or more minor criteria
CRITERIA 1: Episodic symptoms involving at least two organ systems that are consistent with mast cell mediator release. (see figure 1)	MAJOR CRITERIA: Episodic symptoms involving at least two organ systems that are consistent with mast cell mediator release. (see figure 1)

CRITERIA 2:
• One or more positive laboratory result
• Serum tryptase: An increase of 20% + 2 ng/mL above baseline (especially within 4 hours of symptoms).
• Urinary markers: Increased levels of 24-hour urinary N-methylhistamine, prostaglandin D2, or 11-β prostaglandin F2α.
• Other tests: Chromogranin A, plasma histamine.
	MINOR CRITERIA:
	• Elevation in serum or urine markers indicative of MC activation;
	  • serum tryptase or chromogranin A
	  • plasma heparin or histamine
	  • urine N-methylhistamine, prostaglandin D2, leukotriene e4
	• Greater than 20 MCs per HPF in extracutaneous tissue (GI tract or bladder)
	• Positive clinical response to mast-cell-directed therapy

CRITERIA 3: Positive clinical response to mast-cell-directed therapy	

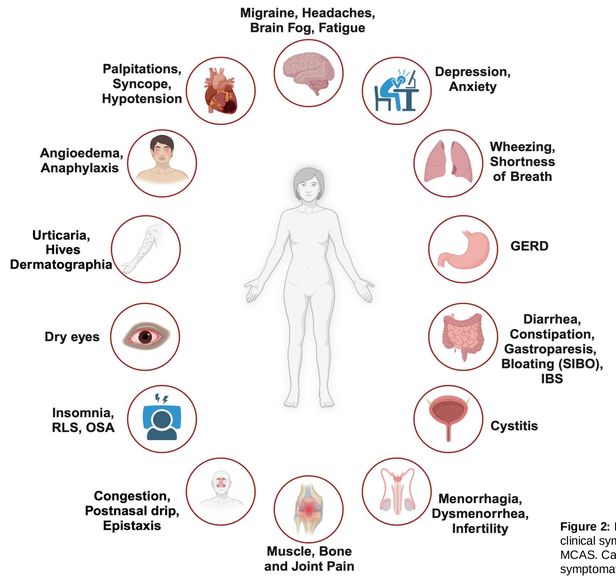

Figure 2: Description of various clinical symptoms associated with MCAS. Cases can vary in symptomatology and severity.[2,4,9]

MANAGEMENT AND TREATMENT

The overarching goal of treatment is to reduce mast cell degranulation and mitigate effects of histamine release. Nonpharmacologic treatment is focused on identifying and avoiding potential environmental triggers. This includes low histamine and gluten/dairy-free diets, such as FODMAP.[6] First-line pharmacologic treatment is described in the table below. Patients should also be referred to an Allergy/Immunology physician for further care and follow up, particularly if patients are prone to anaphylactic type reactions. An at home Epi-pen may be indicated for these patients.[2,3]

First Line Pharmacologic Treatment	
Histamine 1 (H1) Blocker -Cetirizine, loratadine	Control allergy-like symptoms
Histamine 2 (H2) Blocker - Famotidine	Control gastrointestinal symptoms
Leukotriene Receptor Antagonist -Montelukast	Management of respiratory symptoms Help with urticaria and GI symptoms
Mast Cell Stabilizer - Cromolyn Sodium	Prevent mast cell degranulation Help with GI symptoms Reduce overall symptom flare-ups

DISCUSSION

This case highlights the importance of considering immunologic etiology for patients who are presenting purported functional disorders in multiple organ systems. MCAS has been poorly understood until relatively recently and the estimated prevalence is 17%.[2] Many of these patients have seen multiple providers and trialed various medications and therapies without relief of their symptoms. Thus, leading to the misdiagnosis of functional disorder, somatic symptoms disorder, or malingering. Weinstock, et. al. have suggested that MCAS may be particularly unrecognized in patients with functional GI disorders. Misdiagnosing these patients can perpetuate sigma and lead to exacerbating negative medical outcomes. Treatment is typically low risk for MCAS, which involves H1 blocker, H2 blocker, and montelukast.[2,4]

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