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Perspective

Symptoms of mast cell activation
The patient perspective

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In the last decade, symptoms of mast cell activation (MCA) have been increasingly reported by patients. As diagnostic criteria for mast cell diseases (MCDs) continue to evolve with scientific advances, patient perspectives can inform physicians to provide optimal care. MCA and the release of mediators, for example, tryptase, histamine, leukotrienes, and prostaglandins, can induce symptoms in clonal and nonclonal MCDs, which include mastocytosis, mast cell activation syndrome (MCAS), and hereditary alpha tryptasemia (HαT). HαT also acts as a modifier of MCD.[1-3] In addition, signs and symptoms may result from proliferation and accumulation of abnormal mast cells (MCs) in clonal MCDs. Spontaneous and trigger-induced release of mediators affect multiple organs, producing multisystemic symptoms (Fig 1). Symptoms can be acute, episodic and recurrent, or chronic and frequent, and may present as generalized, systemic symptoms, including anaphylaxis.[1-4] To meet the proposed diagnostic criteria for MCAS, symptoms must also be severe, present concurrently in 2 or more organ systems, and respond to antimediator or mast cell–stabilizing therapy, with documented MC mediator rise.[1] Some patients with MCAS, HαT, or both MCAS and HαT, can also present with symptoms of dysautonomia and connective tissue abnormalities.[3,5]

Possible triggers of MCA are extensive, vary from patient to patient, and are not limited to immunoglobulin E–dependent allergies. They may be touched, inhaled, ingested, or experienced (Fig 1).[2,4] In some cases, patients may be unable to identify triggers.[4] Exposure to heat, cold, or changes in temperature may induce abrupt onset of symptoms. Venoms (eg, Hymenoptera, jellyfish stings; arachnid, snake, insect bites) are well-recognized potential triggers for fatal anaphylaxis in patients with MCD. Medications (eg, opioids, nonsteroidal anti-inflammatory drugs, antibiotics, some anesthetics), contrast media, and vaccines may also potentially induce MCA. Excipients as triggers in medications can make compounding necessary. Alcohol is often a trigger in topical, oral, inhaled, and injectable medications and in consumer products, such as hand sanitizers and cleaning agents. Stress—emotional, environmental, psychosocial, and physical (friction, eg, from clothing; vibration, eg, from vehicular travel)—can be particularly challenging for patients. Major and minor surgery and invasive or radiologic procedures (eg, endoscopy/colonoscopy, scans with contrast dyes, dental work) are examples of triggers that require premedication.[2] Food, beverage, and alcohol triggers can create additional barriers for socializing; in a survey of approximately 1600 respondents with an MCAS diagnosis, 71% indicated food restrictions and 41% reported being restricted to 20 foods or less.[5] Patients use strategies to mitigate trigger exposure, including avoidance, sourcing specific ingredients, brand specificity, preparation methods (cooked vs not), and freezing leftovers immediately. Patients report that even brief exposure to scents (eg, perfumes, chemicals, essential oils, food aromas) can induce MCA symptoms which can lead to anaphylaxis. To avoid MCA triggers, patients can experience psychological stress and social isolation, which further diminishes their quality of life.[4] In addition to effective therapy, recognition and avoidance of triggers are critical aspects of symptom management.

The treatment of MCD includes medications aimed at preventing MCA and controlling MC mediator actions.[1-3] Perceptions of medication effectiveness provided by those reporting an MCAS diagnosis include the following (percentage of survey respondents currently taking the medication/percentage of those currently taking the medication who report symptom improvement): H1 (93%/76%) and H2 (73%/73%) histamine receptor antagonists; MC stabilizers, such as cromolyn sodium (58%/80%); leukotriene inhibitors (39%/66%); aspirin (under supervision of a physician) (11%/63%); and corticosteroids (15%/85%).[5] Immunoglobulin E–targeted therapy was reported as effective by 61% of the 17% who were currently taking or had taken omalizumab.[5] Self-injectable epinephrine is also a critical component of treatment; 2 doses should be carried at all times. Managing multiple medications is an additional stressor. Successful medication

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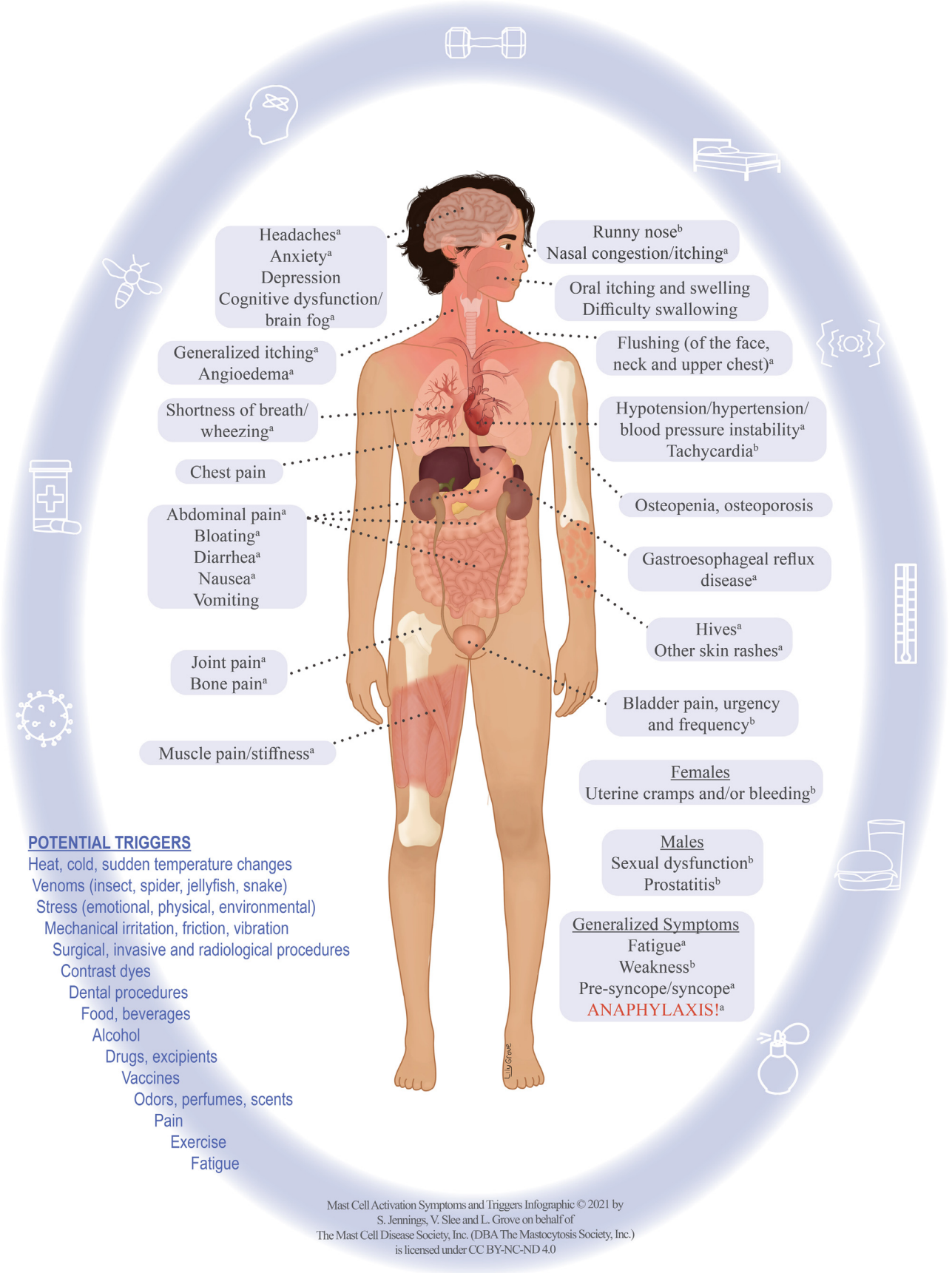

Figure 1. The most common presenting symptoms and potential triggers of mast cell activation.[1,2,4] Symptoms and triggers are unique to the individual. Specific criteria, as noted in the article text, must be met to fulfill a diagnosis of MCAS. Not all patients react to each of the listed triggers or experience each of the listed symptoms. Mast Cell Activation Symptoms and Triggers Infographic 2021 printed with permission from The Mast Cell Disease Society, Inc (DBA The Mastocytosis Society, Inc). The superscript letter "a" indicates symptoms reported by more than 45% of TMS MCAS survey respondents as affecting them either moderately or severely in the course of their illness with MCAS.[5] The superscript letter "b" indicates symptoms not queried in the TMS MCAS survey. DBA, doing business as; MCAS, mast cell activation syndrome; TMS, The Mast Cell Disease Society, Inc.

management is highly dependent on access to and collaboration with a physician well informed on MCDs who can make appropriate medication adjustments.

Despite the available therapeutics for targeting the effects of MCA, patients experience considerable disruption of daily life owing to the presentation of MCA symptoms.[4,5] For 85% of patients reporting an MCAS diagnosis, daily life is interrupted moderately or extremely by the "unpredictability of the sudden onset of symptoms," affecting school, work, social and family activities.[5] Unpredictable and severely disabling symptoms may include abdominal pain and bloating, diarrhea, headache or migraine, lightheadedness or syncope, blood pressure changes, shortness of breath, tachycardia, fatigue, flushing, itching, brain fog or other neurocognitive difficulties, muscle pain, joint pain, and anaphylaxis. Blood pressure instability presents more frequently as hypotension, but also as hypertension. Itching is described as internal and external. Fatigue, moderately or severely affecting more than 80% of patients reporting an MCAS diagnosis,[5] is very disabling. Bone, joint, and muscle pain are reported by many patients as a daily symptom that significantly interrupts their quality of life.

Nearly 30% of patients diagnosed as having MCAS report experiencing anaphylaxis requiring injectable epinephrine 3 or more times per year, whereas 6% report experiencing this 1 to 2 times per week or more.[5] The presentation of anaphylaxis may be unique, with patients experiencing a combination of flushing and tachycardia, swelling of the mouth, tongue, and/or throat, severe gastrointestinal symptoms (abdominal pain, diarrhea, nausea), and lightheadedness progressing to syncope. MCD specialists advise the use of a signed emergency protocol or anaphylaxis action plan for patients, available on tmsforacure.org.

Patients with an MCD who experience disabling MCA symptoms face challenges affecting their social, emotional, and physical well-being, including the lack of understanding and acknowledgment by others of the serious risk that triggers present. Quality of life is so reduced by MCAS symptoms that activities of daily living were limited by poor physical or mental health, an average of nearly 15 of 30 days, and physical health was reported as "not good," an average of 18 of 30 days.[5] In patients reporting an MCAS diagnosis, symptoms interrupted daily life "extremely" or "moderately" for 88% and "very frequently" or "often" for 89%.[5]

A multispecialty approach to disease management, focused on quality of life, is essential for the care of patients who experience debilitating MCA symptoms. Patient support and advocacy groups, such as The Mast Cell Disease Society, Inc, in the United States (tmsforacure.org), or in other countries (mastocytosis-mcas.org), play a critical role in helping patients and families cope with the complex challenges of having an MCD.

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