



Letters

Prevention of anaphylaxis related to mast cell activation syndrome with omalizumab

The concept of mast cell activation syndrome (MCAS) has evolved during the last several decades to describe cases involving evidence of profound mast cell degranulation without an obvious trigger or evidence of aberrant mast cell proliferation.¹ In 2010 Akin et al¹ proposed a set of diagnostic criteria that included the following: (1) absence of evidence of primary or secondary causes of mast cell activation (including mastocytosis); (2) episodic symptoms consistent with mast cell mediator release that affect 2 or more organ systems; (3) evidence of an increase in a validated urinary or serum marker of mast cell activation; and (4) a decrease in severity of symptoms with antimediation therapy, including histamine₁ (H₁) and histamine₂ (H₂) receptor antagonists, leukotriene antagonists, or mast cell stabilizers. Treatment of MCAS involves the use of one or more of the aforementioned classes of medications,² whereas prednisone, cyclosporine, methotrexate, and azathioprine are alternatives when treatment with more conservative therapy fails.² Treatment of refractory cases presents a difficult dilemma for the physician. We present a case of the successful use of omalizumab (monoclonal antibody to IgE) in the treatment of a pediatric patient who met the proposed diagnostic criteria for MCAS.

Our patient is an 11-year-old boy with a history of eczema and viral-induced wheezing who presented in September 2010 for evaluation of presumed anaphylactic reactions to both cherries and blackberries. Symptoms included hives and breathing difficulty. He had an additional episode with similar symptoms for which a trigger was not identified. In the weeks preceding these events, he reported headache, flushing, abdominal pain, diarrhea, and fatigue. The results of percutaneous skin prick testing using common aeroallergen extracts and cherry were negative. A complete blood cell count revealed a white blood cell count of 12,500/ μ L with a lymphocyte predominance and normal numbers of eosinophils, basophils, and monocytes. The serum tryptase level was 15.8 μ g/dL (reference range, 0.4–10.9 μ g/dL). A monospot result was positive, which was potentially significant because the presence of heterophile antibodies can increase tryptase levels.³ The total IgE level was 26 IU/mL. The child was counseled on avoidance of cherries and blackberries, prescribed an epinephrine autoinjector, and administered oral cetirizine at 10 mg twice daily.

During the next 4 months, he continued to experience frequent abdominal pain, diarrhea, urticaria and flushing, and episodic anaphylactoid reactions that required the use of epinephrine several times per month. Tryptase levels remained elevated (17.8–19.8

μ g/dL). H₁-receptor blockade was increased to twice-daily cetirizine plus twice-daily loratadine ("4 $\times$ therapy") with continuation of twice-daily ranitidine. Symptoms improved but persisted, and a bone marrow biopsy specimen was obtained to exclude systemic mastocytosis or monoclonal MCAS. Normal marrow morphologic findings were noted, with the absence of a large population of mast cells or spindle-shaped mast cells. CD25 staining results were negative. In addition, a chronic urticaria index, which tests for the presence of autoantibodies to the high-affinity IgE (Fc ϵ RI) receptor, was within normal limits. Polymerase chain reaction for the KIT (D816V) mutation commonly found in systemic mastocytosis and monoclonal MCAS was unable to be performed because of a lack of amplifiable nucleic acid in the specimen. Upper and lower endoscopy did not reveal the presence of mast cell aggregates in the bowel wall.

The patient improved with a prolonged course of oral corticosteroids, but symptoms increased after corticosteroid therapy was discontinued, and the patient was given omalizumab as a steroid-sparing agent in April 2011. He continues to receive omalizumab, 150 mg subcutaneously every 4 weeks. He had rapid improvement in symptoms and has had one episode of urticaria with shortness of breath in the 10 months of omalizumab therapy. The patient continues to receive H₁-receptor blockade with twice-daily cetirizine and loratadine and H₂-receptor blockade with twice-daily ranitidine.

This case supports the potential efficacy of omalizumab for MCAS in children not responding to maximal antihistamine therapy. Molderings et al⁴ recently reported benefit with omalizumab therapy in 1 of 2 patients with monoclonal MCAS.⁴ There have been other reports of successful treatment of systemic mastocytosis with omalizumab.^{5,6}

The mechanisms underlying the symptomatic improvement of patients with MCAS treated with omalizumab are not fully understood. The binding and inactivation of IgE by omalizumab lead to a decreased level of IgE available for binding to mast cells, leading to downregulation of Fc ϵ RI.⁷ Others have proposed that omalizumab may interfere with mast cell mediator release.⁸ In conclusion, omalizumab may be an efficacious therapy for treatment-resistant MCAS, and additional studies are needed to ascertain what factors lead to improvement in MCAS patients receiving omalizumab.

Matthew C. Bell, MD

Daniel J. Jackson, MD

Department of Pediatrics

University of Wisconsin School of Medicine and Public Health

Madison, Wisconsin

djj@medicine.wisc.edu

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