

CLINICAL VIGNETTE

Perioperative Management of Mastocytosis

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Introduction

Mastocytosis is a rare type of myeloproliferative neoplasm that results from the clonal proliferation of abnormal mast cells in one or more organs. Clinical symptomatology and disease aggressiveness can differ greatly depending on the organ systems and the particular subtype of mastocytosis involved. The degranulation of mast cell mediators, such as histamine, often plays prominently into presentation. The varied sequelae of mastocytosis and the potential for triggering anaphylaxis are challenges in perioperative management of these patients.

Case Report

A 27-year-old male with a history of painful right nephrolithiasis, acid reflux, and smoking was referred for pre-operative evaluation prior to an elective ureteroscopy and laser lithotripsy. The patient reported being diagnosed with mastocytosis as a young child prior to school-age. He noted gradual decrease in episodes of diffuse rashes and pruritis over the past several years. He described a single episode of anaphylaxis occurring at age 9 that was accompanied by wheezing, edema, and urticaria. He also noted erythema and swelling of his right arm shortly after receiving intravenous ketorolac in the same limb just several weeks prior during an emergency room visit for renal colic. This was treated with antihistamines and steroids prior to leaving the emergency room. He took diphenhydramine daily through childhood and adolescence but now no longer used the drug regularly and took no other medications at the time of his visit.

Physical exam demonstrated a well-nourished male with normal vital signs. He had no edema or significant cutaneous findings. There was no organomegaly on exam. Darier's sign—the urtication of skin lesions following rubbing—was not present. Laboratory evaluation revealed normal CBC and differential. Pre-operation serum tryptase was within normal limits at 3 ng/mL. Prior abdominal films showed no hepatosplenomegaly.

On the day of his procedure, the patient received diphenhydramine 50 mg IV and famotidine 20 mg IV premedication. Midazolam 2 mg IV was also given as an anxiolytic prior to entering the operating room. A neuraxial

anesthetic was considered in order to limit the drug exposure necessary during the procedure to that of only an amide local anesthetic; however, the surgeon was concerned that spontaneous breathing would lead to increased respiratory motion at the operative site compared to mechanical ventilation during a general anesthetic.

General anesthesia was induced with lidocaine and propofol. No muscle relaxant was administered during induction or throughout the case; instead, a remifentanyl bolus 1 mcg/kg followed by an infusion of 0.15 to 0.05 mcg/kg/min was used to provide analgesia and promote relaxation until the end of the ureteroscopy. Careful and frequent monitoring for urticaria and rash was maintained throughout the case. There was no change in lung auscultation or peak ventilation pressure to suggest bronchospasm and wheezing. There was a brief period of hypotension to a systolic pressure between 80 and 90 lasting 10 minutes at the case onset that resolved with 1 liter Lactated Ringer's bolus.

The patient underwent the surgical procedure and general anesthetic, including extubation, uneventfully. He recovered in the recovery room for a normal period of time prior to discharge home.

Discussion

Pediatric and adult forms of mastocytosis, despite having many similarities in molecular origin, have different prognosis and natural history. Both forms are most often associated with gain-of-function mutations in the receptor tyrosine kinase, *KIT*, that is expressed in mast cells, hematopoietic progenitor cells, germ cells, and other cell lines and interacts with the ligand stem cell factor.¹ Mastocytosis has a bimodal distribution with 55% of cases presenting prior to the age of 2 years and incidence rises again after age 15 years.² Unlike the more aggressive adult form, pediatric mastocytosis frequently has a benign course that regresses in late adolescence, similar to the history presented by this patient, and is commonly limited to cutaneous sites.¹⁻³ Adults tend to have a greater incidence of systemic mastocytosis in which mast cell hyperplasia involves and sometimes impairs extracutaneous organs such as the spleen, liver, and bone. Both forms may precipitate symptoms related to mast cell mediator release,

including histamine and tryptase, which results in varied symptoms of flushing, hives, pruritis, edema, nausea, diarrhea, bone pain, cognitive impairment, among many others. The effects of mediator release, including episodes of anaphylaxis, can be seen in both cutaneous and systemic forms of mastocytosis.

This patient's history of primarily cutaneous involvement with a rash consistent with urticaria pigmentosa and episodes of anaphylactic symptoms portended a better prognosis than aggressive systemic mastocytosis and an onset in adulthood. His low preoperative serum tryptase reflects a low mast cell burden. Tryptase levels may also correlate with a greater degree of symptom severity and be used to diagnose events caused by mast cell degranulation.^{2,4}

Despite the patient's relatively benign presentation, the safe conduct of his urologic procedure focused upon testing for associated organ impairment, avoiding potential triggers of mast cell release, minimizing the symptoms of mast cell mediator release, and preparing for the treatment of an anaphylactic episode. Intraoperative histamine release during a general anesthetic is especially dangerous due to the patient's unconscious state and surgical draping, which leaves the late signs of cardiovascular instability and bronchospasm more likely to be the first noted abnormalities as opposed to more subtle cutaneous findings. Prior to the conduct of the procedure, the patient received H1 and H2 receptor blockers prophylactically.

Consideration was also given to avoid as many medication and environmental triggers for histamine release as possible. There are no medications truly contraindicated, although it is reasonable to minimize exposure to drugs with a higher likelihood of histamine release. Substances such as muscle relaxants (e.g., succinylcholine or rocuronium), latex, antibiotics (β -lactams), hypnotics, contrast agents, nonsteroidal anti-inflammatory drugs, and opioids are commonly implicated in perioperative reactions.^{5,6} As the most common cause of anaphylaxis during anesthesia, muscle relaxants for intubation and intraoperative maintenance were avoided entirely, and instead, the potent opioid remifentanyl was used to minimize patient movement. Unlike morphine, meperidine, codeine, and several other opioids, remifentanyl does not cause histamine release when tested *in vivo*.⁷

A report of 29 anesthetics performed on 22 patients with various forms of pediatric mastocytosis at a single institution found no significant perioperative complications, though several case reports have described serious life-threatening reactions.^{4,8,9} In general, awareness of potential difficulties and careful planning and preparation are the most important ingredients for safe conduct of anesthetics. No particular aspect of routine anesthesia is contraindicated as long as there is thoughtful consideration of the risks and benefits.

REFERENCES

1. **Pardanani A.** Systemic mastocytosis in adults: 2015 update on diagnosis, risk stratification, and management. *Am J Hematol.* 2015 Mar;90(3):250-62.

- doi:10.1002/ajh.23931. Review. PubMed PMID: 25688753.
2. **Frieri M, Quershi M.** Pediatric Mastocytosis: A Review of the Literature. *Pediatr Allergy Immunol Pulmonol.* 2013 Dec 1;26(4):175-180. Review. PubMed PMID:24380017; PubMed Central PMCID: PMC3869446.
3. **Lim KH, Tefferi A, Lasho TL, Finke C, Patnaik M, Butterfield JH, McClure RF, Li CY, Pardanani A.** Systemic mastocytosis in 342 consecutive adults: survival studies and prognostic factors. *Blood.* 2009 Jun 4;113(23):5727-36. doi:10.1182/blood-2009-02-205237. Epub 2009 Apr 10. PubMed PMID: 19363219.
4. **Carter MC, Uzzaman A, Scott LM, Metcalfe DD, Quezado Z.** Pediatric mastocytosis: routine anesthetic management for a complex disease. *Anesth Analg.* 2008 Aug;107(2):422-7. doi: 10.1213/ane.0b013e31817e6d7c. Review. PubMed PMID:18633019; PubMed Central PMCID: PMC2736554.
5. **Moss J, Rosow CE.** Histamine release by narcotics and muscle relaxants in humans. *Anesthesiology.* 1983 Oct;59(4):330-9. Review. PubMed PMID: 6193743.
6. **Hepner DL, Castells MC.** Anaphylaxis during the perioperative period. *Anesth Analg.* 2003 Nov;97(5):1381-95. Review. PubMed PMID: 14570656.
7. **Sebel PS, Hoke JF, Westmoreland C, Hug CC Jr, Muir KT, Szlam F.** Histamine concentrations and hemodynamic responses after remifentanyl. *Anesth Analg.* 1995 May;80(5):990-3. PubMed PMID: 7726445.
8. **Desborough JP, Taylor I, Hattersley A, Garden A, Wolff A, Bloom SR, Morgan M.** Massive histamine release in a patient with systemic mastocytosis. *Br J Anaesth.* 1990 Dec;65(6):833-6. PubMed PMID: 2265056.
9. **Vaughan ST, Jones GN.** Systemic mastocytosis presenting as profound cardiovascular collapse during anaesthesia. *Anaesthesia.* 1998 Aug;53(8):804-7. PubMed PMID: 9797525.

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