CASE REPORT

# Anesthesia in a pediatric patient with systemic mastocytosis

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## ABSTRACT

Systemic mastocytosis is a rare disorder of mast cells which carries considerable risk in the perioperative period. Unintended release of mast cell mediators has the potential to cause significant hypotension, multi-system organ dysfunction, and death. Many factors have been implicated in mast cell degranulation including heat, stress, and many medications that may be commonly used anesthetic care. We present the case of a 10 year old girl with systemic mastocytosis who required general anesthesia for reduction of a dislocated elbow. The perioperative care of such patients is reviewed and strategies for intraoperative anesthesia are discussed.

**Key Words:** Systemic mastocytosis, General anesthesia, Multi-system organ dysfunction

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## INTRODUCTION

Mastocytosis is a rare disease which originates in the bone marrow. Symptoms are secondary to infiltration of tissue with mast cells and their mediators.[1,2] Cutaneous mastocytosis (urticaria pigmentosa) exists within the spectrum of mastocytosis diseases. The incidence of the cutaneous form is thought to be between 1 in 1000 and 1 in 8000 of the general population.[3] Of those with cutaneous mastocytosis, up to 10% will have systemic involvement.[3] Patients with mastocytosis are at considerable risk during the perioperative period. Unintended mast cell degranulation can occur from a variety of inciting factors, with consequences ranging from cutaneous flushing to life threatening anaphylaxis.[4] In this case report we present the anesthetic management of a 10 year old girl with cutaneous mastocytosis who required reduction of a humorous fracture under general anesthesia. We also discuss the potential difficulties involved in the perioperative care of these patients.

## CASE REPORT

A 10 year old girl presented to the Emergency Department of our hospital after falling off a swing earlier in the day. She landed on her left upper extremity and was found to have a dislocated elbow which required reduction, potentially open, in the operating room. She had no history of prior anesthetic care. Her medical history was positive for a cutaneous mastocytoma present on her right arm. Her mother reported allergies to several topical antibiotics and alcohol, with the reaction to all being cutaneous flushing and urticaria. The mother denied any history of systemic symptoms of mastocytosis, e.g. flushing attacks, heat intolerance or palpitations. She did however; report that a previous physician had warned her of a potential for such systemic reactions. After a thorough preoperative evaluation and discussion, consent was obtained from the patient and family. Premedication included oral midazolam (0.5 mg/kg). Epinephrine was drawn up as a weight based bolus dose (10 $\mu$g/kg) in individual syringes and was made available throughout the intraoperative course.

The patient was transported to the operating room and routine monitors were placed followed by inhalation induction with increasing concentrations of sevoflurane in 100% oxygen. A peripheral intravenous line was placed and a size 3 LMA was inserted. Intravenous diphenhydramine (25 mg) was administered as prophylaxis against potential histamine release and 15 mg/kg of intravenous acetaminophen for pain control. No anesthetic agents with the potential for histamine release (propofol, morphine) were administered. No neuromuscular blockade was required for the procedure. The surgeon was able to perform closed reduction of the elbow dislocation and the LMA was removed in the operating room. Although the patient required no opioids postoperatively, fentanyl as needed was available. The patient's postoperative course was uneventful and she was discharged home later that day.

## DISCUSSION

Mastocytosis is a disease of deranged mast cell growth with abnormal accumulation in various organs, most commonly the skin.[2,5,6] It occurs more commonly in children (60-65%) than adults. Cutaneous manifestations range from a few apparently isolated lesions as noted in our patient to diffuse infiltration of the skin called urticaria pigmentosa (UP). UP is seen more commonly in the pediatric population while a rarer manifestation, telangiectasia macularis eruptiva perstans (TMEP) affects adults. Although the mast cells are localized to the skin in both UP and TMEP, degranulation and mediator release can lead to systemic symptoms. Systemic mastocytosis involves the bone marrow with isolated involvement of other organ systems.[7]

During the perioperative period, surgical stress and other factors, most importantly medications, may lead to mast cell degranulation with severe systemic involvement. The potential impact of mastocytosis on perioperative care is illustrated by a cast report of a severe systemic reaction in a 13-year-old patient with undiagnosed mastocystosis.[8] Following anesthetic induction with propofol and lidocaine, cefazolin was administered for perioperative prophylaxis. Two minutes after the administration of cefazolin, severe bronchospasm and hypotension developed which necessitated the administration of several doses of epinephrine.

Triggering agents that have been implicated in the release of mast cell mediators include stress, temperature, morphine, antibiotics, contrast media, and the tetrahydroisoquinoline class of neuromuscular blocking agents, e.g. atracurium, mivacurium etc.[7] There is, however, no consensus in the literature as to which medications are truly contraindicated[9] ; it seems reasonable to avoid those medications which have been shown to have a high likelihood of histamine release. *In vivo* studies have shown that succinylcholine and cis-atracurium have the lowest degree of mast cell activation among the commonly used neuromuscular blocking agents. Thus, they are theoretically the safest to use in the setting of mastocytosis. Aminosteroidal neuromuscular blocking agents (rocuronium and vecuronium) were shown to have an intermediate degree of mast cell activation while atracurium and mivacurium were the most potent activators.[9]

Propofol is the most commonly used agent for the intravenous induction of anesthesia in many countries of the world. However, an *in vitro* study has shown a wide variety of mast cell reactions to propofol which vary among patients as well as mast cell type.[11] This may explain the wide variety of anaphylactoid reactions seen in response to propofol and warrants caution with its use in the setting of mastocytosis. Histamine release has also been demonstrated with the barbiturates. Given these concerns, we chose to proceed with an inhalation induction with our patient and avoid propofol or thiopentone. Histamine release does not occur with the use of volatile anesthetic agents.[12] In the event of the need for an intravenous induction agent, we would suggest that ketamine be considered.[11] There is considerable variation among opioids in this regard. Codeine and morphine have both been shown to cause histamine release.[13] This release is not related to their effects on the $\mu$ opioid receptor and as such, the synthetic opioids can be used safely in this patient population. More specifically, codeine is known to be a strong promoter of cutaneous mast cell degranulation in patients with mastocytosis.[14] Similar studies have found no histamine release with fentanyl, sufentanil, remifentanil, and naloxone.[13]

There is minimal literature on regional anesthesia in the setting of mastocytosis. While regional anesthesia may reduce the use of potential histamine releasing medications including intravenous induction agents and opioids, reactions to local anesthetic agent must still be considered. Case reports have associated lidocaine with hypotensive episodes in patients with mastocytosis[15], although the use of preservative free preparations is generally considered safe.[16] Various case reports have demonstrated the safe use of lignocaine for neuraxial blockade including epidural anesthesia while one report describes a severe urticarial reaction after Bier block.[15-18]

The chronic treatment of mastocytosis is aimed specifically at blocking mast cell mediators, with antihistamines playing the most prominent role. Histamine receptors, both $H_1$ and $H_2$, mediate the vasodilatory response to histamine, thus pharmacologic blockade of both receptors is often initiated in these patients.[19,20] The failure of some patients to respond to blockade of the histamine receptors demonstrates that other humoral factors including the prostaglandins may be responsible for the systemic manifestations. Although cyclooxygenase inhibition with aspirin has been shown to be beneficial in these patients[21], non-steroidal anti-inflammatory agents may mediate mast cell degranulation and lead to systemic symptoms. With respect to perioperative premedication with histamine receptor antagonists, there is no consensus in the literature as to which is appropriate or whether any is needed at all. Given our patient's low risk procedure which required a limited number of medications, we chose an $H_1$-receptor antagonist (diphenhydramine). Some patients may also present with chronic medications to prevent mast cell degranulation (cromolyn sodium, nifedipine, ketotifen), which need to be continued perioperatively.

In the setting of acute systemic symptoms, resuscitation should follow standard guidelines with support of airway, breathing and the circulation. During acute crises, antihistamines and corticosteroids will have limited utility.[22] For anaphylaxis, the drug of choice remains epinephrine.[22] Epinephrine not supports hemodynamic function and relieves bronchospasm, but also prevents mast cell degranulation by acting directly on cell surface receptors.[23]

## CONCLUSION

In summary, there are limited data on the perioperative care of these patients and the conflicting reports in the literature with the safe use of specific medications in some and severe reactions in others, emphasize the need for careful perioperative preparation of these patients. In general, medications that result in histamine release should be avoided. References 24 and 25 present a nice review of various anesthetic regimens that have been used in patients with mastocytosis.[24,25] Epinephrine 1:10,000 should be prepared for ready use in the operating room, as no anesthetic technique or medication can be assured to be completely safe in this unique patient population.

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## My Most Memorable Patient

One of my patients had a workplace accident and broke several of her bones. One year latershe discovered that she also had severe nerve damage. Her doctors tried various pain medications and physical therapy interventions on her for more than one year. She kept trying to return to her job as a carpenter, but had to stop working due to unbearable pain. She was finally put on total disability and told that she would have to learn to live with her pain. No one explained to her how she could live with pain and still have a functional and satisfactory quality of life.

She was finally referred to a pain clinic that I was consulting with. I worked with her and her doctors to find out why nothing had so far succeeded in relieving her pain. On my first assessment I noticed that seven of twenty of her identified pain symptoms were neuropathic in nature. I also discovered that she never had had an MRI for her back. When she was finally referred for an MRI, the results showed significant nerve impingements and damage.

Understanding what was really going on with her was the start of her transition from hopelessness to a renewed hope for her future. Within six months, she had adequate pain relief and was undergoing vocational rehabilitation in computer programming, so excited about her future. Without this healthy transition, she would have been at high risk for moving into demoralization.

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