Mastocytosis

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Risk

- Rare clinical condition with an estimated incidence at 1:150,000.

Perioperative Risks

- Not an allergic disease.
- Not a risk factor of IgE-mediated drug allergy.
- Mast cell degranulation induced by various nonspecific triggers with subsequent histamine and other mediators (e.g., tryptase, leukotrienes, prostaglandins) release may result in periop clinical features involving the skin and the cardiovascular system.
- Bronchospasm usually does not occur.
- Periop course is usually uneventful when nonspecific triggers for mast cell release are avoided. Periop complications have been reported only in a few cases.

Worry About

- Main concern: Avoid nonspecific mast cell degranulation.

Overview

- Heterogeneous group of disorders characterized by an abnormal increase in tissue mast cells.
- It is classified into seven categories according to the World Health Organization consensus, which differ by the onset time of the disease (childhood or adulthood), the phenotype (cutaneous or systemic), and the clinical presentation (indolent or aggressive).
- CM, the most common phenotype, is limited to the skin. The most frequent skin presentation is consistent with *urticaria pigmentosa* in both adults (mainly monomorphic variant) and children (polymorphic variant). Other types, such as CM with bullous forms, are almost uniquely seen in children. CM is mainly reported during childhood and often resolves after puberty.
- SM infiltrates the bone marrow and other organs with or without skin involvement. Six forms of SM have been described and include indolent SM, which is the most common clinical presentation with a good prognosis, and aggressive SM with severe organ infiltration, SM with hematologic disease, mast cell leukemia, and mast cell sarcoma with a poor prognosis. SM is mainly reported during adulthood.
- Mast cell degranulation can be induced by various nonspecific triggers, such as physical pressure of skin lesions (mechanical irritation, tourniquet use), surgery itself (especially the digestive tract which is a rich source of mast cells), histamine-releasing drugs, extreme temperature (hypothermia, hyperthermia), pain, and emotional factors.
- Mast cell degranulation: Histamine, tryptases, PGD2, LTC4, and various cytokines.
- Tryptases are neutral serine proteases stored predominantly in mast cells. Pro-α tryptase reflects mast cell burden, whereas mature β-tryptase is preferentially stored in mast cell granules and released during mast cell activation.
- Total tryptase level at baseline reflects pro-α tryptase and correlates with total body mast cell burden. Tryptase level greater than 20 μg/L is associated with SM, but lower levels may be seen. Tryptase levels are less than 20 μg/L in most CM.
- Common symptoms include itching, flushing, erythema, diarrhea, abdominal pain, headache, and fatigue.
- Periop clinical features may involve the skin (erythema, rash, flushing) and cardiovascular system (hypotension, infrequently cardiovascular collapse). Life-threatening condition is extremely rare.
- CV symptoms induced by nonspecific triggers may occur in SM and CM, especially in those with excessive spreading of skin disease (diffuse CM).
- Care management is guided by the clinical presentation according to the Ring and Messmer scale. Fluid therapy should be initiated with crystalloids or colloids. Use epinephrine when required (i.e., grade III reaction according to the Ring and Messmer scale).
- In case of periop immediate hypersensitivity:
  - Measure tryptase level (will then be compared with pt's baseline level).
  - Perform skin tests (at least 4 wk later) with all drugs injected just before the occurrence of immediate hypersensitivity to prove that the clinical reaction was related to mastocytosis itself and not to drug allergy.
- Main concern: Avoid mast cell degranulation.

Etiology

- Mutation (codon D816V) in the tyrosine kinase receptor c-kit (protein involved in mast cell survival).

Usual Treatment

- H_1-receptor antagonists: Nonsedating drugs (e.g., cetirizine).
- H_2-receptor antagonists: Ranitidine, famotidine.
- Proton pump inhibitor (omeprazole) if H_2-receptor antagonist is ineffective for abdominal pain.
- Leukotriene inhibitor or disodium cromoglycate for GI symptoms.
- Psoralen combined with PUVA.
- Calcium supplementation, bisphosphonate, and estrogen replacement during postmenopause.
- Interferon.
- Targeted therapy, such as imatinib (tyrosine kinase inhibitor), in some pts.
- Splenectomy may improve survival in severe clinical forms.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Urticaria pigmentosa, mastocytoma, DCM, TMEP	Itching, erythema, flushing	Darier sign	Lesional skin biopsy
CV	Hypotension, CV collapse	Prior episodes? Potential triggers?		Serum tryptase compared to baseline tryptase level Skin tests
GI	Abdominal pain, diarrhea, PUD, malabsorption		Hepatosplenomegaly	GI biopsies
CNS	Headache, depression, moods symptoms			
MS	Osteopenia, osteoporosis, pathologic fractures, MS musculoskeletal pain			Bone densitometry, x-ray, CT
HEME	Myeloid or lymphoid leukemia			Bone marrow biopsy

Key References: Valent P, Escribano L, Broesby-Olsen S, et al.: Proposed diagnostic algorithm for patients with suspected mastocytosis: a proposal of the European Competence Network on Mastocytosis, *Allergy* 69(10):1267–1274, 2014; Dewachter P, Castells MC, Hepner DL, et al.: Perioperative management of patients with mastocytosis, *Anesthesiology* 120(3):753–759, 2014.

Perioperative Implications

Preoperative Period

- H_1- and H_2-receptor antagonists are usually recommended.
- Avoid known triggers that have precipitated prior episodes and potential triggers, such as pharmacologic, psychologic, and mechanical factors and temperature changes.
- Check for the pt's tryptase baseline before surgery (in case of periop immediate hypersensitivity, it is important to compare the tryptase level after immediate hypersensitivity to the pt's baseline level).

Monitoring

- Routine monitors

Induction/Maintenance

- Preoxygenation: Bullae may occur in any of the skin lesions with mechanical pressure from a facemask in CM. This feature is mostly limited to the first few years of life.
- Following agents can be used:
  - Benzodiazepine: Midazolam.
  - Hypnotics: Etomidate, ketamine, propofol, thiopental.
  - Halogenated gases, nitrous oxide.
  - Local anesthetics: Amide- and ester-type.
  - NMBAs: Succinylcholine, rocuronium, vecuronium, cis-atracurium, suxamethonium.
  - Analgesic: Acetaminophen (paracetamol).
  - Opioids: Alfentanil, fentanyl, remifentanil, sufentanil, and morphine (titration).
  - Plasma substitutes: Albumin, gelatin, HEA.
  - Other agents: Oxytocin, protamine, aprotinin (biologic glue), ondansetron, chlorhexidine, povidone iodine, dyes and contrast agents.
- The following histamine release agents are not recommended:
  - NMBAs: Atracurium, mivacurium.
  - Analgesic: Nefopam.
- Maintenance phase: Maintain normothermia, including warmed anesthetic gases, fluid therapy, and blood components transfusion.

Extubation

- Reversal of neuromuscular blockade, including atropine and neostigmine or sugammadex, according to the NMBA used

Other Types of Anesthetics

- There is no role to avoid regional or neuraxial anesthetics in mastocytosis.

Postoperative Period

- Continue with analgesics and usual treatment.

Anticipated Problems/Concerns

- Histamine release due to mast cell degranulation induced by histamine release drugs or surgical procedures
- Ambulatory surgery; no evidence to contraindicate ambulatory surgery in mastocytosis