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NEWS & VIEWS: ALGORITHMS IN ALLERGY AND CLINICAL IMMUNOLOGY

Medical algorithm: Peri-operative management of mastocytosis patients

Mastocytosis is a clonal disorder characterized by the proliferation and accumulation of mast cells (MCs) in various tissue types, preferentially skin and bone marrow (BM). Mastocytosis consists of cutaneous and systemic forms in both pediatric and adult patients. Both the excess and increased propensity of MCs to release mediators leads to a higher frequency and severity of immediate hypersensitivity reactions.[1-4]

In the peri-operative setting, systemic mastocytosis is associated with a higher risk of severe anaphylaxis.[1-7] Here, drugs such as nonsteroidal anti-inflammatory drugs, opioids and a broad range of anesthetics, temperature change, friction/pressure to the skin, and stress can cause mainly non–IgE-mediated MC (mediator) release.[1-7]

Prospective controlled studies on peri-operative hypersensitivity reactions in mastocytosis are lacking.[8] Nevertheless, expert-based advice has been given on prohibited drugs.[1] Moreover, antimediator therapy such as anti-H1, anti-H2, and corticosteroids is commonly prescribed peri-operatively.[1-7] Albeit common practice, evidence supporting the value of premedication with antihistamines and corticosteroids is lacking, nor is there evidence of the benefit of specific drug regimens. However, there is also no evidence to the contrary.

The potentially serious adverse outcomes in the peri-operative setting cause uncertainty in both doctor and patient. Position papers have discussed the available evidence in detail, resulting in recommendations for mastocytosis patients undergoing surgery under general anesthesia.[3,4] We provide an algorithm which serves as a tool for the practical management of both cutaneous and systemic, pediatric, and adult mastocytosis patients in need of procedures requiring (local or general) anesthesia in line with these recommendations (Figure 1).[3,4]

Preferably, surgery in patients with systemic mastocytosis requiring general anesthesia should take place in a mastocytosis reference center. The medical team should be aware of and able to counteract severe allergic reactions before, during, and after surgery. To limit uncertainties, an individual plan should be made for each patient considering previous events and including decisions on premedication, type of anesthesia, and intra- and postoperative analgesia. In patients that have no record of anesthesia or analgesia, or when in doubt, medication with low capacity to elicit MC mediator release is preferred.

Given uncertainties in premedication strategies, it may be useful to limit premedication to a risk group with previous anaphylaxis and/or extensive skin involvement in which excessive MC mediator release is most expected, undergoing general anesthesia.

Premedication can consist of antihistamines and corticosteroids. If premedication is chosen to be administered, antihistamines can be given orally or intravenously shortly (<30 min) before starting anesthesia. Corticosteroids may be added, especially if H1 and H2 antihistamines are not available. The choice of corticosteroids depends on the clinical setting; elective procedures allow for oral administration 12 and 2 h before surgery, while emergency procedures depend on intravenous use. The choice of corticosteroids is preferably also made upon the desired duration of effect.

Additionally, the prevention of nonspecific triggers is as much needed as any other precautions. Consider benzodiazepines for stress reduction and its probable direct beneficial regulatory effect on MCs.[8,9]

Cutaneous MC proliferation in mastocytosis patients requires extra safety measures (Figure 1). Most pediatric and many adult patients have cutaneous lesions, of which some with blistering. Friction and pressure to the skin can cause excessive MC mediator release. Therefore, applying plasters or adhesives on lesions should be avoided and the use of adhesive remover is recommended upon (slow) removal.

During surgery, anaphylaxis may consist of hypotension, often without skin involvement, or respiratory events. In case of hypotension, consider anaphylaxis as a cause.

Following surgery, MC mediator release may still occur in the next 24 h.[7] Therefore, patients should restart their regular antimediators as soon as possible and monitored carefully.

Whereas this algorithm is based on clinical guidelines, published evidence, and the authors' experience, future prospective controlled

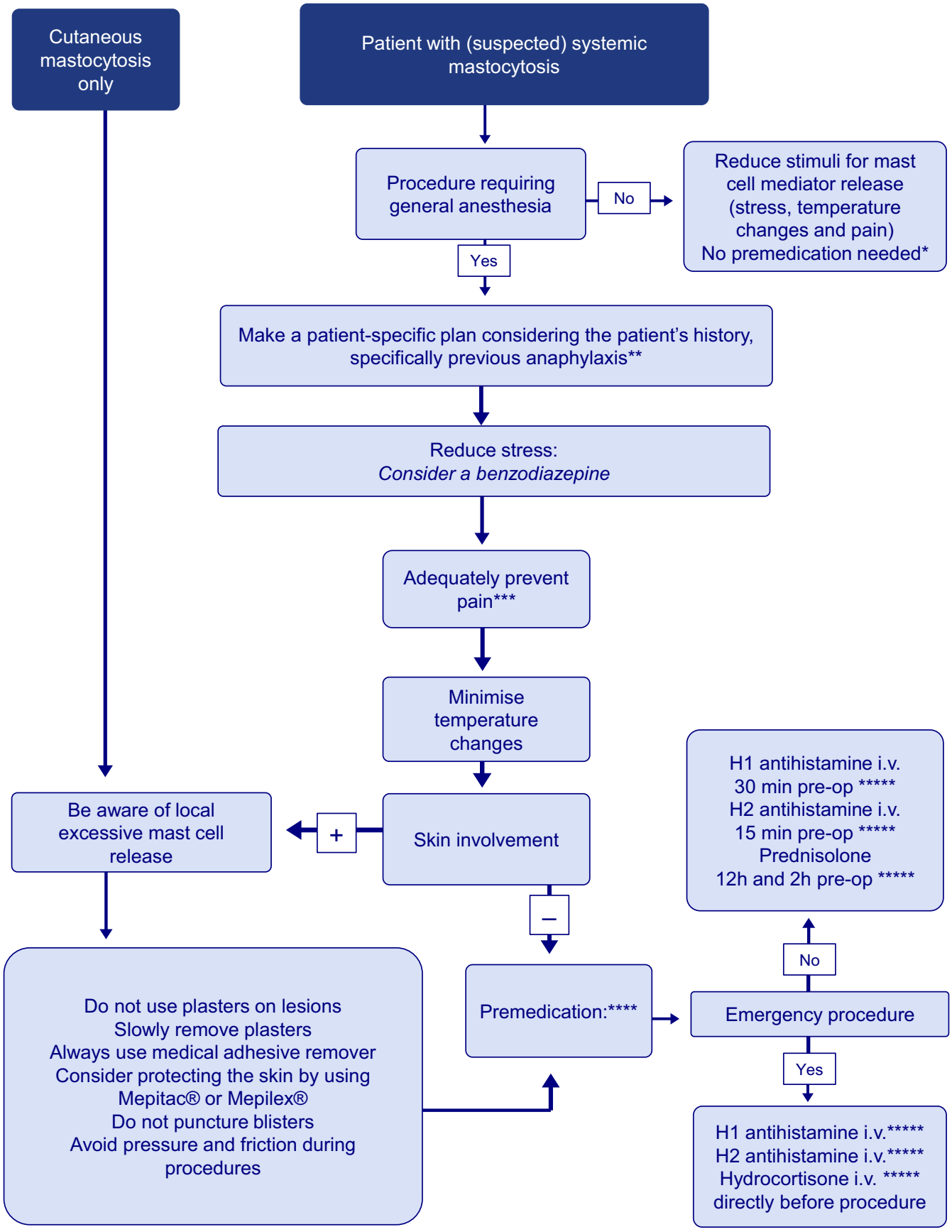
Cutaneous mastocytosis only
Patient with (suspected) systemic mastocytosis
Procedure requiring general anesthesia
No
Reduce stimuli for mast cell mediator release (stress, temperature changes and pain)
No premedication needed*
Yes
Make a patient-specific plan considering the patient's history, specifically previous anaphylaxis**
Reduce stress:
Consider a benzodiazepine
Adequately prevent pain***
Minimise temperature changes
Skin involvement
+
Be aware of local excessive mast cell release
–
Premedication:****
H1 antihistamine i.v.
30 min pre-op *****
H2 antihistamine i.v.
15 min pre-op *****
Prednisolone
12h and 2h pre-op *****
No
Emergency procedure
Yes
H1 antihistamine i.v.*****
H2 antihistamine i.v.*****
Hydrocortisone i.v. *****
directly before procedure
Do not use plasters on lesions
Slowly remove plasters
Always use medical adhesive remover
Consider protecting the skin by using Mepitac® or Mepilex®
Do not puncture blisters
Avoid pressure and friction during procedures

FIGURE 1 Algorithm for peri-operative management of mastocytosis patients. Patients with a suspicion for underlying mastocytosis may undergo diagnostic testing needed for diagnosing mastocytosis (eg, bone marrow biopsy), requiring general anesthesia. This especially applies to pediatric patients. In this case, systemic mastocytosis is suspected, but not yet officially confirmed. It is, however, useful to create awareness of this probable underlying condition and prevent massive mediator release. This algorithm does not apply for adult patients with elevated tryptase and confirmed hereditary alpha tryptasemia. *No severe reactions are seen using local anesthetics, however, be aware of mast cell mediator release by friction, pressure, and (removing) plasters. ** In case of previous anaphylaxis: always use premedication (both antihistamines and corticosteroids). *** Analgesics: Recommended: Sufentanil, Remifentanil, Oxytocin, Alfentanil, Acetaminophen, Fentanyl.° Unclear: Morphine°°, NSAIDs°°° Discouraged: Codeine, Nefopam. ° One case of severe anaphylaxis to fentanyl in our center (pediatric patient with systemic mastocytosis). °° Titrate slowly if morphine is used. °°° Do not use NSAIDs if they were not used previously.[1] ****Only in systemic mastocytosis. The use of both antihistamines and a benzodiazepine is recommended. When antihistamines are not available, use corticosteroids. In cutaneous mastocytosis, no premedication is required. *****For children: use dosage according to body weight

studies on peri-operative hypersensitivity reactions are needed to further improve peri-operative management of mastocytosis patients.

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