Dental management of a pediatric patient with mastocytosis: a case report

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Abstract

Mastocytosis is a heterogeneous group of clinical disorders characterized by an excessive number of normal mast cells in a variety of tissues (skin, bone marrow, liver, spleen and lymph nodes). It is most often seen in the skin in pediatric-onset mastocytosis presenting as urticaria pigmentosa. Children with this disorder are on a strict avoidance protocol of triggering factors to decrease the likelihood of life-threatening anaphylactic reactions. Close monitoring and the avoidance of known histamine-releasing drugs is necessary in the pediatric dental office, as is a readiness to use resuscitative measures.

A case of a 4-year, 6-month-old pediatric dental patient with mastocytosis is presented. Dental treatment was provided in an ambulatory setting utilizing nitrous oxide, oxygen analgesia and H_1 and H_2 antihistamines to prevent mast cell degranulation and to provide sedation. (*Pediatr Dent.* 2002;24:343-346)

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Mast cell disease, also called mastocytosis, is a heterogeneous group of clinical disorders that is characterized by proliferation and accumulation of mast cells in a variety of tissues, most often the skin. Determining the actual prevalence is problematic because patients without cutaneous lesions may not be diagnosed correctly. It is estimated that between 1 in 1000 and 1 in 8000 new patients visiting dermatology clinics have some form of mastocytosis.[1] Mastocytosis can present as either pediatric-onset or adult-onset. Sixty-five percent of patients with mastocytosis have their onset during the first two years of life. An additional 10% develop symptoms between the age of 2 and 15 years. In pediatric-onset mastocytosis, there is an equal gender distribution with more frequent reports among Caucasian children. While pediatric-onset mastocytosis appears to be sporadic in occurrence, reports of familial mastocytosis suggest a dominant inheritable influence.[2]

Mastocytosis is classified as indolent or aggressive based on its clinical course. Cutaneous mastocytosis constitutes 90% of the indolent cases. Urticaria pigmentosa is the most common variety, occurring in about two-thirds of patients with cutaneous mastocytosis. The tan to red-brown macules typical of urticaria pigmentosa initially emerge on the trunk and rapidly spread symmetrically and centripetally. The palms, soles, face and scalp are usually spared. The lesions may remain small and freckle-like or may evolve into papules, nodules or plaques (Fig 1). Mucous membranes may be involved.[1] Solitary mastocytomas (the occurrence of only one lesion) are common in infants and children with the cutaneous form of the disease. This cutaneous lesion is usually large (3 to 4 cm) and frequently occurs on an extremity. The lesion is pathognomic for *Darier's sign* (when the lesion is rubbed or exposed to other physical stimuli, such as heat or cold, a localized area of dermal edema and erythema or wheal occurs).

In aggressive mastocytosis, skin lesions similar to those of urticaria pigmentosa may or may not be present but are accompanied by mast cell infiltration of bone marrow, liver, spleen and lymph nodes. Many of the signs and symptoms of the aggressive disease are due to the effects of histamine, heparin, prostaglandins, leukotrienes and other chemical mediators released as a result of mast cell degranulation. While pruritis is the most common initial presenting symptom, systemic complications include formation of bullae and severe gastrointestinal bleeding or, in extreme cases, life-threatening vascular collapse.

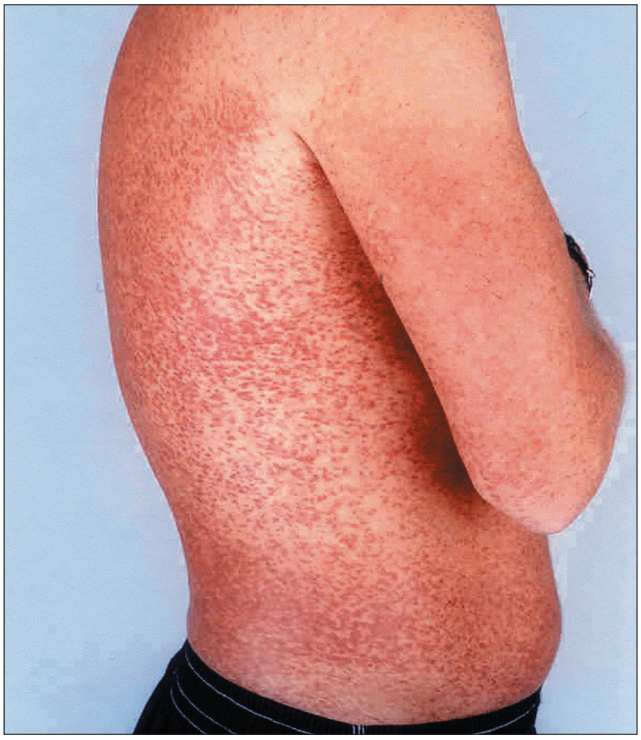

Fig 1. Skin lesions associated with mastocytosis (Courtesy of The Mastocytosis Society, www.mastocytosis.com)

Diagnosis of the disease can be difficult. The three criteria for establishing the diagnosis of mastocytosis are (1) histopathology of a skin lesion, (2) histologic evidence of systemic involvement with or without an underlying hematologic disorder and (3) biochemical markers of mast cell activity. The presence of all three of these criteria in each patient is not required.[1] Treatment of pediatric mastocytosis is largely symptomatic.

Specific precautions to prevent life-threatening anaphylactic reactions are recommended. These include avoidance of clinically relevant triggering factors (mast cell degranulators), such as:

- Physical stimuli—exercise, skin friction, hot baths, cold exposure (especially swimming), ingestion of hot beverages, spicy foods and ethanol;
- Drugs—aspirin, alcohol, narcotics (morphine, codeine), polymyxin B, Amphotericin B, thiamine, D-turbocurarine, radiographic dyes (containing iodine), scopolamine, procaine, opiates, nonsteroidal anti-inflammatory agents, gallamine and decamethonium;
- Others—intravenous high molecular weight polymers (dextran), emotional stress, bacterial toxins, snake venoms, biologic polypeptides released by ascaris, jellyfish, crayfish and lobsters.[4]

The need for special medication for these patients in preparation for general anesthesia is controversial. Close monitoring, the avoidance of known histamine-releasing drugs and readiness to use a full range of therapeutic and resuscitative drugs may be sufficient management for patients with cutaneous mastocytosis undergoing general anesthesia.[5,6] The emergency treatment of shock in association with massive mast cell mediator release is the same as that of anaphylaxis. Fluids, epinephrine, antihistamines, and pressor agents are often required. Patients with mastocytosis are advised to wear medical alert bracelets and carry epinephrine-filled syringes.

Prognosis of the disease is related to severity. Hence, children with indolent skin involvement tend to have resolution of the disease by adulthood. For children with aggressive forms of mastocytosis, the prognosis is generally limited to that of any associated hematologic malignancy and treatment is limited to that malignancy. Many patients die of bleeding caused by severe thrombocytopenia.

Case report

A 4-year, 6-month-old Caucasian male presented to the dental clinic at Children's Hospital, Boston, with a chief complaint (as reported by his parents) of "cavities in some bottom back baby teeth." His past medical history was significant for the diagnosis of mastocytosis limited to multiple skin lesions on his trunk. He was not taking any medications, but had a positive history of allergies to aspirin, alcohol, morphine, codeine, scopolamine and amoxicillin. He had been referred to Children's Hospital by a local pediatric dentist because of the complexity of his medical/dental management. There was no history of pain or swelling.

The patient was very timid and agitated during his dental examination. He had a complete primary dentition with clinical dental caries on the occlusal surface of his mandibular right first and second primary molars and the mandibular left second primary molar. He had a mesial step molar and Class I canine occlusion with a 20% overbite and 2 mm overjet. Primate spacing was present. His oral hygiene was good and no oral habits were noted. His extraoral examination was within normal limits, except for positive palpable bilateral submandibular nodes, which were not found on subsequent visits.

Two bitewing and two mandibular posterior periapical radiographs were taken by the referring dentist and a prophylaxis and fluoride treatment had been accomplished at that visit, as well. The radiographs confirmed the clinical findings and showed the close proximity of the caries to the pulp on the mandibular primary molars (Fig 2). The operative treatment plan consisted of indirect pulp cap and occlusal amalgam vs pulpotomy and stainless steel crown on the mandibular primary second molars and occlusal amalgam on the primary first molar.

In light of the diagnosis of mastocytosis, there was concern about the potential triggers for mast cell degranulation during the dental procedures. The parents were very clear that they did not wish to have their child treated under general anesthesia because of the numerous known anaphylactic triggers. After a consultation with pediatric dermatologists and pediatric anesthesiologists, it was decided to treat this child's dental needs utilizing conscious sedation with H_1 and H_2 antihistamines and nitrous oxide/oxygen, but no local anesthesia in the ambulatory dental clinic. As the patient

weighed 18 kg, he was premedicated with 1 mg/kg diphenhyramine (Benadryl), an H_1 antihistamine which has sedative properties, and 3 mg/kg ranitidine (Zantac), an H_2 antihistamine which also has sedative properties. These two medications were administered orally one hour prior to the dental procedure.

The patient became well sedated (Level 3, non-interactive/arousable with moderate stimulus) and was then administered nitrous oxide/oxygen analgesia at a rate of 30% nitrous oxide and 70% oxygen for 30 minutes and then 100% oxygen for 5 minutes at the termination of the procedure. The standard American Academy of Pediatric Dentistry (AAPD) monitors for an oral sedation were used (a precordial/pretracheal stethoscope, pulse oximeter, pediatric sphygmomanometer and capnography). The patient's mother was present in the operatory and understood that the treatment would be aborted if the patient became symptomatic or exhibited behavior consistent with discomfort.

Cotton roll isolation was employed in this patient as rubber dam isolation could be a potential skin friction trigger. Both mandibular primary second molars received indirect pulp caps and amalgam restorations. The mandibular right primary first molar received an occlusal amalgam.

The patient remained with his parents for two hours postoperatively until the patient met AAPD postsedation criteria for discharge.[6] He was then discharged to the care of his parents alert and well aware, with vital signs at presedation levels. As a result of the treatment experience, his family became very motivated to assist the patient with an oral hygiene regimen that included parental-assisted brushing, flossing and proper diet. The patient will be seen on recall every three months and have fluoride varnish applied to his teeth after the prophylaxis. After the first three-month recall, assuming all teeth are asymptotic and there is no new caries activity, the patient will be put on a six-month recall. Recalls will consist of exam, charting, prophylaxis and fluoride varnish application.

Discussion

Although amide local anesthetics have not been implicated as a trigger for mast cell degranulation, procaine is a known trigger. It has been reported that antihistamines, such as diphenhydramine, could be used as a very potent local anesthetic for dental procedures, although a burning sensation has been reported with a mandibular block.[7,8] There was concern by attending pediatric anesthesiologists that the potential for emotional stress during the administration of the intraoral local anesthesia may be sufficient to trigger an anaphylactic response. It was finally decided that the combination of oral H_1 and H_2 antihistamines would provide enough sedation to remove caries when used in combination with nitrous oxide/oxygen analgesia and no local anesthesia. Additionally, both H_1 and H_2 blockers can be used in combination to prevent and treat anaphylaxis (although epinephrine is the treatment of choice).

H_1 antihistamines inhibit the effects of histamine on capillary permeability. They also inhibit the effects of histamine on vascular, bronchial and many other types of smooth muscle. H_1 antihistamines also possess local anesthetic activity. The side effect with the highest incidence, and the one common to all H_1 antihistamines, is sedation. Although diphenhydramine was used in this patient, hydoxyzine is another H_1 antihistamine that could have been used as it also has sedative properties as a side effect.

The addition of an H_2 antihistamine is indicated for amelioration of gastrointestinal symptoms (diarrhea, abdominal pain, nausea and vomiting). Both sedating antihistamines were also utilized in this child, as not all mast cells have H_1 receptors, and H_2 blockers may also decrease cutaneous symptoms by inhibition of smooth muscle contraction.

It was further decided that, since both local anesthesia and general anesthesia were risky for dental treatment in this child's case, caries removal would proceed under the proposed sedation. If it was found intraoperatively that the caries on the primary second molars necessitated treatment by

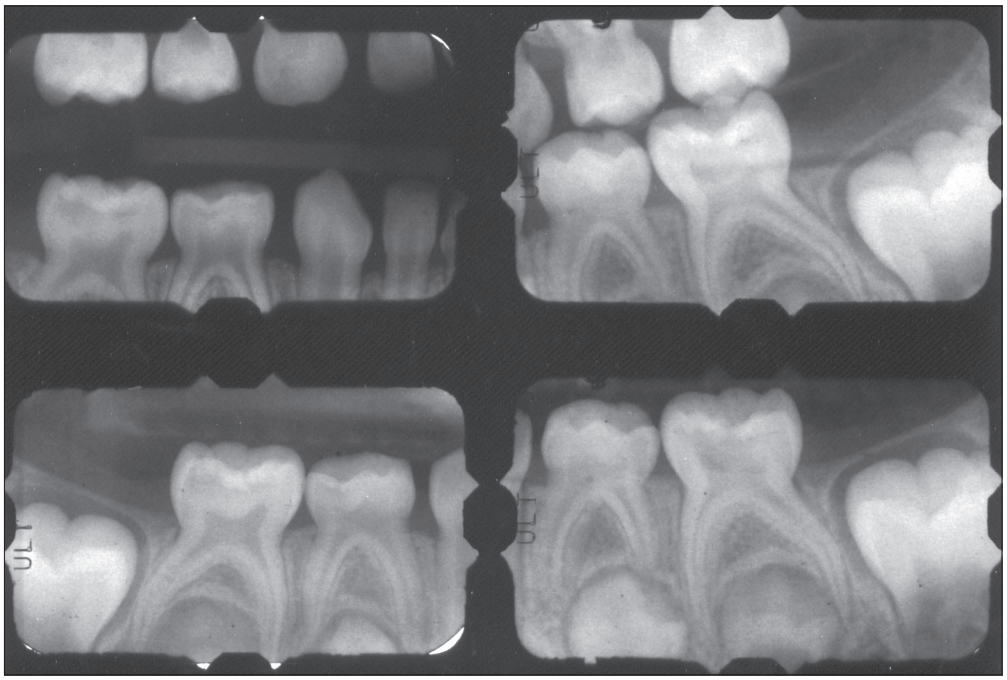

Fig 2. Intraoral radiographs

pulpectomy or extraction, the exposure would be pulp-capped and the child would be treated under general anesthesia as soon as possible as the only remaining alternative. If a pulpotomy had been necessary, the authors could have used formocresol or ferric sulfate as they both do not contain any known triggers for mastocytosis and have high rates of success .

As H_1 antihistamines also have weak anticholinergic effects, salivary flow was decreased enough to perform an indirect pulp cap procedure with cotton roll isolation. A rubber dam was not employed for these procedures, as this isolation technique could be a potential skin friction trigger. It was felt that, although the cotton roll isolation was sufficient for an indirect pulp, the cotton roll isolation did not afford a dry enough field for a composite or other esthetic restoration. The teeth that required indirect pulp capping did not have enough tooth structure removed to necessitate a stainless steel crown, and amalgam restoration was deemed sufficient.

If these teeth had required stainless steel crowns, the authors would have placed the crowns, as stainless steel had not been a prior trigger in a review of the medical history. Had this child required a more extensive treatment plan, such as extractions, dental treatment under sedation would not have been suggested to the parents and treatment under general anesthesia would have been the only viable option. If the indirect pulp caps should fail at future recall and this child had evidence of pulpal infection, he would have extractions performed in the operating room under general anesthesia.

This was discussed in detail with the parents preoperatively. In the presence of frank swelling, the child would have been treated with clindamycin, in light of his amoxicillin allergy, prior to the extractions. Pulpectomies would not have been contraindicated for this patient, although the rate of success would have to have been considered.

Additionally, had this child exhibited the signs and symptoms of anaphylaxis due to mast cell degranulation, a "code" would have been called, as the crash team was alerted to the treatment and location within the hospital preoperatively. Epinephrine 1:1000 would have been injected immediately intralingually 0.125 ml (0.01 mg/kg up to a maximum dose of 0.025 mg/kg), the nitrous oxide/oxygen analgesia would have been discontinued and the child would have been masked with 100% oxygen using a positive pressure pediatric mask.

This child is considered a high-risk caries patient and will be placed in a three-month recall cycle until he becomes a lower-risk caries patient based on his caries activity. Fluoride varnish will be applied to all teeth after prophylaxis. The use of over-the-counter fluoride rinses before bedtime was recommended. Diet and oral hygiene were reviewed with both parents and the child. The parents understood the challenge of treating their child's dental caries and became quite motivated towards preventive modalities.

Conclusions

The Mastocytosis Society, an international patient support organization, recommends that a team approach that includes the family and health care providers be utilized when treating patients with mastocytosis.

It is challenging to treat a patient with mastocytosis because it is difficult to predict the course of the disease and a patient's symptoms and responses to medications. There is no cure for preventing mastocytosis patients from producing too many mast cells. H_1 and H_2 antihistamines help stabilize and block mast cell degranulation. It is important for the pediatric dentist to have knowledge of the chemical and environmental triggers that induce mast cell release.

Children with systemic diseases, such as mastocytosis, involving such a high potential for life-threatening emergencies during dental treatment are best suited for treatment in a hospital setting where immediate high-level emergency procedures can be instituted. Pediatric dentists must be flexible in the dental management of these children and be prepared to alter their treatment modalities based upon the risk/benefit of the treatment in light of an anaphylactic response.

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