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Dental management of a patient with systemic mastocytosis

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TITLE OF CASE

The Dental Management of a Patient with Systemic Mastocytosis

SUMMARY

Mastocytosis is a term encompassing a group of clinical disorders characterised by clonal proliferation of abnormal mast cells (MCs) in organ systems of the body. Mastocytosis can be systemic (with or without skin involvement) or cutaneous, and can affect organs including bone marrow, liver, spleen, lymph nodes and mucosal surfaces. Patients with systemic mastocytosis are susceptible to triggers which could cause activation of abnormal MCs, resulting in multi-organ dysfunction and life-threatening anaphylactic reactions.

Mastocytosis has a number of ramifications for the dental management of a patient with the condition. Patients are at increased risk of complications due to a number of risk factors for MC activation present within the dental context, including stress, certain prescribed drugs, oral hygiene products and dental materials. This report presents the oral management of an adult with systemic mastocytosis, discussing the implications of the condition within the context of the limited existing literature on the subject.

BACKGROUND

Mast cells (MCs) are migrant cells of connective tissue that contain numerous granules. Within these are diverse mediators including histamine, leukotrienes, prostaglandins, proteases, and heparin, as well as many other chemokines, growth factors and cytokines.^{[1][2]} Consequently, MCs play a key role in regulating normal physiological processes of many organs and tissues, including innate and adaptive immunity, vasodilation, angiogenesis, vascular and bronchial homeostasis as well as bone growth and remodelling.^[3] MCs also play a part in pathophysiological

processes of many diseases including anaphylaxis, allergy and asthma, as well as gastrointestinal and cardiovascular diseases.^[3]

Mastocytosis is a group of disorders characterised by clonal proliferation of abnormal MCs in the skin and/or other organ systems.^{[4][5]} There are three main subtypes: cutaneous mastocytosis; systemic mastocytosis (SM), where MCs infiltrate one or more extracutaneous organ (with or without skin involvement); and MC sarcoma, an extremely rare and aggressive malignant MC neoplasm.^[6] There is a lack of epidemiological evidence relating to mastocytosis, although studies estimate overall prevalence of approximately 10 per 100,000.^[7]

The symptoms and signs of mastocytosis are generally due to the release of MC mediators and/or organ infiltration by MCs. Release of MC mediators can result in constitutional symptoms (e.g. fatigue, weight loss), skin symptoms (e.g. pruritus, urticaria, dermatographism, flushing), systemic mediator-related events (e.g. anaphylaxis, syncope, tachycardia, abdominal pain, respiratory symptoms), and musculoskeletal symptoms (e.g. bone pain, osteopenia/osteoporosis, myalgia). Infiltration of MC primarily affects the bone marrow, liver, spleen, lymph nodes, and gastrointestinal tract.^[6]

Anaphylaxis is a significant risk; 49% of adults and 9% of children with mastocytosis experience anaphylaxis at some stage.^[8] Importantly there are a number of non-IgE-mediated triggers for MC activation (table-1). Dental procedures may expose the patient to many of these (e.g. anxiety and stress, pain, NSAIDs, opiates, antibiotics), and a multi-disciplinary approach to dental management is therefore essential.

Table-1. Potential triggers for MC Activation and **drugs which are typically tolerated**.^[1]

Physical Stimuli	Heat, fever, rapid temperature changes; and friction in cases where the skin is involved (urticaria pigmentosa)
Psychological Stimuli	Emotional stress and anxiety

Physiological Stimuli	Fever, strenuous exercise; and hormonal changes, alcohol	
Medicinal Stimuli	Non-steroidal anti-inflammatory drugs	Aspirin, ibuprofen, naproxen, ketorolac
	<i>Paracetamol, celecoxib, tramadol typically tolerated</i>	
	Opiate analgesics	Codeine, morphine, pethidine, buprenorphine
	<i>Fentanyl and remifentanyl are typically tolerated</i>	
	Muscle relaxants	Atracurium, mivacurium
	<i>Rocuronium, vecuronium, pancuronium, cisatracurium typically tolerated</i>	
	Antibiotics	Vancomycin, teicoplanin, quinolones
Potential dental material stimuli	Latex, zinc oxide, eugenol, cobalt, chromium, nickel, gold, palladium, methacrylate.	

In addition to anaphylaxis, advanced forms of mastocytosis can complicate the oral presentation and dental management of patients with the condition. These patients can have thrombocytopenia, anaemia, or bone lesions; and localised heparin release from mast cells in any involved mucosa can produce bleeding, although not severe. The treatments of these advanced forms of mastocytosis include tyrosine kinase inhibitors, more conventional chemotherapeutic agents, interferon alfa, and occasionally allogeneic haematopoietic stem-cell transplant; some of which can impair wound healing and increase risk of infection.

Osteopenia and osteoporosis are also common in SM, and the use of bisphosphonates or other antiresorptive agents (e.g. denosumab) may affect the patient's dental care, due to increased risk of medication related osteonecrosis of the jaw.^[9]

Despite being a rare disease, there is presumably extensive cumulative experience of the dental management of patients with mastocytosis, but published evidence is surprisingly sparse, being limited to review papers and a small number of case reports, mostly focussing on dental considerations for children with cutaneous mastocytosis.^{[10][11]} The aim of this report is to describe the dental management of an adult patient with systemic mastocytosis.

CASE PRESENTATION

A 48-year-old female was referred to the oral surgery team, Plymouth Community Dental Service, requesting extraction of the lower left first permanent molar which had a history of failed treatment including root-canal therapy.

She had presented to the Immunology and Allergy Service in 2020 with a 10-year history of urticaria pigmentosa predominantly on her thighs and chest. She developed flares of rashes on exposure to heat, cold, exercise, excessive alcohol consumption, and psychological stress. She described intermittent flushing, abdominal cramping and diarrhoea, and occasionally presyncope. She was a non-smoker and consumed an average of five units of alcohol weekly.

Investigations revealed a baseline serum MC tryptase of 18.8ng/mL (local reference interval <11.6ng/mL). A bone marrow biopsy was performed, which demonstrated several small aggregates of mast cells, the majority of which had spindle-shaped morphology. These were immunophenotypically abnormal, expressing CD117+, CD33+ CD9+ CD2+, and CD25+ markers. The D816V C-KIT gene mutation was also detected in peripheral blood and bone marrow. These results fulfil a diagnosis of indolent SM according to the WHO diagnostic criteria.^[6]

Her medications included the non-sedating antihistamines; fexofenadine and cetirizine; and sodium cromoglicate, a MC stabiliser. Omalizumab was started 2 months prior to the dental procedure to ameliorate the spontaneous urticaria she was experiencing in response to non-allergic triggers. A secondary potential benefit of omalizumab may be a reduced risk of anaphylaxis.^[12]

At her dental assessment the patient presented with rash and pruritis of the chest and lower limbs. Following clinical and radiographic assessment, a diagnosis of symptomatic periapical periodontitis of the root-treated and crowned lower left first molar was made (figure-1). The agreed treatment plan involved extraction. She had significant dental anxiety, particularly following attempted extraction of this tooth two years previously, where anaesthesia was reported not to have been achieved. Since then, she had not received interventional dental care.

Given the complexity of mastocytosis and the fact that at dental visits, patients are subject to various possible triggers for MC activation, a management protocol was agreed in liaison with the immunology team. This included continuation of all anti-mediator medications related to mastocytosis, including omalizumab. An additional dose of fexofenadine 180mg and cetirizine 10mg was administered one-hour preoperatively.

The patient's emotional stress and dental anxiety were considered to be potential triggers for a severe reaction including an anaphylactic event. With the view of achieving anxiolysis and having assessed the patient for her suitability for conscious sedation, the procedure was conducted under nitrous oxide sedation. Conscious sedation is a safe and viable alternative to general anaesthesia, especially given that a number of drugs associated with general anaesthesia are potential triggers for MC degranulation. Neither midazolam nor nitrous oxide are considered risks for MC degranulation.

The provision of effective local anaesthesia is an essential factor in the completion of dental treatment and management of peri-operative stress.^[13] Lidocaine and articaine were therefore utilised during the procedure. True allergy to these amide anaesthetics is extremely rare and local anaesthetics are not considered risk factors for MC activation.^[14]

Continuous monitoring of the patient's physiological and psychological status is vital and was achieved by observation and electromechanical monitoring of heart rate, pulse oximetry and blood pressure. Monitoring in relation to blood pressure was of importance; anaphylaxis in mastocytosis often presents predominantly with

hypotension, often with flushing but without the urticaria and angioedema classically associated with an anaphylactic event.. The clinic was equipped with appropriate medications to manage anaphylaxis were it to have occurred, according to the Resuscitation Council UK anaphylaxis guidelines.^[15]

The extensive coronal restoration and existing root canal treatment left the structure of the lower left first molar weak and prone to fracture. Following an initial conventional approach to tooth removal, a surgical extraction became necessary. This surgical extraction was successfully completed following induction of nitrous oxide, titrated to a maximum of 65%, and administration of effective local anaesthesia. Post-operative recovery included routine oxygen flush, and a prolonged period of observational and electro-mechanical monitoring.

Simple interrupted resorbable sutures were placed with the view of aiding haemostasis. However, the patient presented to the surgery 24-hours later with post-surgical haemorrhage. A large jelly-like 'liver clot'; forming as a result of slow venous haemorrhage and incomplete fibrin clotting, was present, covering a significant portion of the lower left quadrant (figure-2).

This clot was carefully dislodged using a curette and the socket base visualised following irrigation using 0.2% sodium chloride. Bleeding was from the base of the socket rather than the soft tissues, so the sutures were left in situ, and the socket packed with surgicel. After 15 minutes of sustained pressure, haemostasis was observed and having determined that discharge was safe, the patient was placed on 5-day review. This event demonstrates the need to consider bleeding risk in a patient with mastocytosis; MC granules contain heparin, which activates antithrombin III and thus inhibits Factor Xa and Thrombin, both of which play key roles in the final stages of the coagulation cascade.

Paracetamol was used for analgesia following the procedure in order to avoid NSAIDs and opioids as potential trigger drugs for MC degranulation.

DISCUSSION

On the basis of the patient's medical condition, it was considered that further interventional dentistry would be provided under a specialist-lead team within the Community Dental Service.

This case highlights the complexity of planning dental interventions in patients with mastocytosis. A multidisciplinary approach to treatment is vital, so that procedures can be planned according to the risk of a degranulation event and other complications including bleeding and/or infection.^[10] In this case, effective pain management, anxiolysis, close monitoring, avoidance of histamine releasing drugs and the readiness of resus drugs was sufficient for the management of the patient in an ambulatory setting. However, a different patient or procedure may be more appropriately managed in an acute care environment.^[11]

LEARNING POINTS

- Mastocytosis is a rare condition which should be carefully considered when planning interventional dental treatment
- A multidisciplinary approach involving the patient's immunology, haematology, and/or dermatology consultants is required to ensure that the potential complications are considered and planned for.
- It is important to be aware of potential triggers for mast cell degranulation within the dental setting, including stress, prescribed drugs and dental materials
- A mast cell degranulation event resulting in anaphylaxis should be managed conventionally
- Ensure the use of local haemostatic measures to minimise risk of an adverse bleeding event and monitor closely post-operatively for infection.

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FIGURE/VIDEO CAPTIONS

Figure-1 Periapical radiograph demonstrating suboptimal length and condensation of root treatment lower left first molar, with associated peri-apical radiolucencies.

Figure-2 Liver-clots removed following post-operative haemorrhage

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