CASE REPORT

Medical Journal of Western Black Sea
Batı Karadeniz Tıp Dergisi

Med J West Black Sea 2024;8(3): 363-367
DOI: 10.29058/mjwbs.1446791

Drug Allergy Testing in a Pediatric Patient with Diffuse Cutaneous Mastocytosis

Yaygın Kutanöz Mastositozlu Çocuk Hastada İlaç Alerjisi Testi

Öner ÖZDEMİR[1], Talha DURSUNOĞLU[2], Fahri YILMAZ[3]

[1]Sakarya University Faculty of Medicine, Research and Training Hospital of Sakarya, Department of Pediatrics, Division of Allergy and Immunology, Sakarya, Türkiye

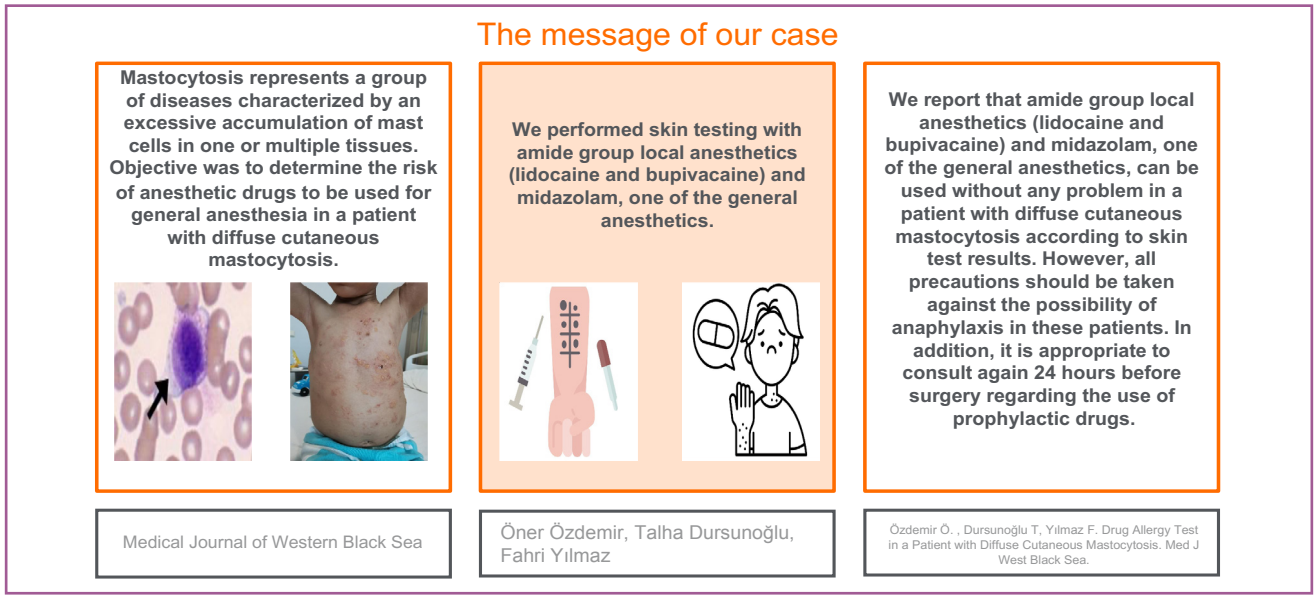
[2]Sakarya University Faculty of Medicine, Adapazarı, Sakarya, Türkiye

[3]Sakarya University Faculty of Medicine, Research and Training Hospital of Sakarya, Department of Pathology, Sakarya, Türkiye

ORCID ID: *Öner Özdemir 0000-0002-5338-9561, Talha Dursunoğlu 0009-0009-3533-2850, Fahri Yılmaz 0000-0001-7965-6229*

Cite this article as: *Özdemir Ö et al. Drug allergy testing in a pediatric patient with diffuse cutaneous mastocytosis. Med J West Black Sea. 2024;8(3):363-367.*

GRAPHICAL ABSTRACT



ABSTRACT

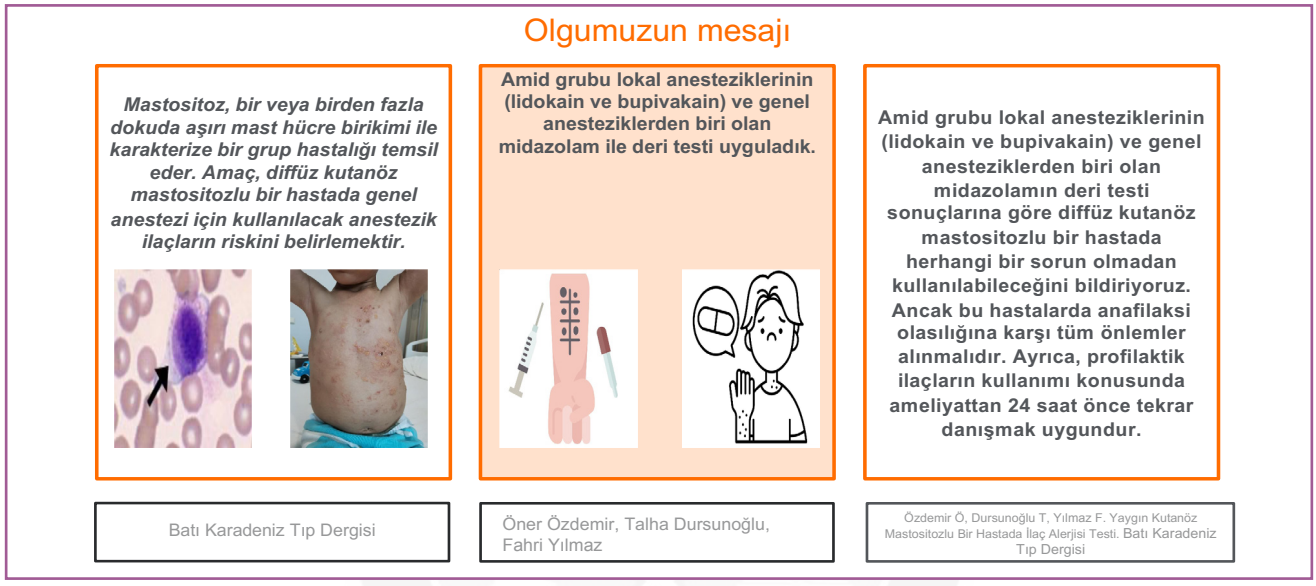
Mastocytosis represents a group of diseases characterized by excessive accumulation of mast cells in one or more tissues. It can affect only the skin or have systemic involvement. It has a low prevalence and the prognosis in children is benign. Patients with pediatric mastocytosis often require sedation or anesthesia for diagnostic and therapeutic procedures. Here, we report our experience with anesthesia in a pediatric patient with diffuse cutaneous mastocytosis undergoing surgical intervention for circumcision. The aim was to determine the risk of anesthetic drugs to be used for general anesthesia in a patient with diffuse cutaneous mastocytosis. A 5-year-old male patient who was consulted with anesthesia for circumcision operation and diagnosed with diffuse cutaneous mastocytosis by skin biopsy was not operated because of the risk of drug allergy and referred to the pediatric allergy and immunology department. Routine hemogram and biochemistry

Corresponding Author: Öner Özdemir ✉ ozdemir_oner@hotmail.com **Received:** 05.03.2024 **Revision:** 07.08.2024 **Accepted:** 07.09.2024

laboratory results were within normal limits. Occasional elevation of serum tryptase level was observed. Skin prick test with lidocaine did not show any significant change compared to the negative control due to dermatographism. However, intradermal tests with lidocaine 1:1 and 1:10 dilutions were negative. For drug allergy provocation test, increasing doses of lidocaine were administered subcutaneously and no reaction developed. Intradermal tests with midazolam and bupivacaine were also negative. There was no early or late reaction to any of these. In conclusion, it has been presented in the literature which drugs can be used without any problem according to intradermal test results as in our case. However, all precautions should be taken against the possibility of anaphylaxis in these patients. Re-consultation 24 hours before surgery regarding the use of prophylactic drugs is appropriate.

Keywords: Mastocytosis, anesthesia, drug, allergy

GRAFİKSEL ÖZET



ÖZ

Mastositoz, bir veya birden fazla dokuda aşırı mastosit birikimi ile karakterize bir grup hastalığı temsil eder. Sadece deriyi etkileyebileceği gibi sistemik tutulumu da olabilir. Düşük bir prevalansa sahiptir ve çocuklarda prognoz iyi huyludur. Pediatrik mastositozlu hastalar sıklıkla tanısal ve terapötik prosedürler için sedasyon veya anestezi gerektirir. Burada, sünnet için cerrahi girişim uygulanacak diffüz kutanöz mastositozlu bir pediatrik hastadaki anestezi deneyimimizi sunmaktayız. Amaç, diffüz kutanöz mastositozlu bir hastada genel anestezi için kullanılacak anestezik ilaçların riskini belirlemekti. Sünnet operasyonu için anestezi ile konsülte edilen, cilt biyopsisi ile diffüz kutanöz mastositoz tanısı konulan 5 yaşındaki erkek hasta, ilaç alerjisi riski nedeniyle operasyona alınmayarak çocuk alerji ve immünoloji bölümüne yönlendirilmişti. Rutin hemogram ve biyokimya laboratuvar sonuçları normal sınırlarda bulundu. Hastada zaman zaman serum triptaz düzeyinin yükseldiği görüldü. Lidokain ile yapılan deri prick testi, dermatografizm oluşması nedeniyle negatif kontrole göre anlamlı bir değişiklik göstermedi. Ancak lidokain 1:1 ve 1:10 dilüsyonları ile intradermal testler negatif bulundu. İlaç alerjisi provokasyon testi için artan dozda lidokain subkutan uygulandı ve hastada herhangi bir reaksiyon gelişmedi. Midazolam ve bupivakain ile yapılan intradermal testler de negatifti. Bunlardan hiçbirine erken veya geç reaksiyon oluşmadı. Sonuç olarak, olgumuzdaki gibi intradermal test sonuçlarına göre hangi ilaçların sorunsuz kullanılabileceği literatürde sunulmuştur. Ancak bu hastalarda anafilaksi gelişme ihtimaline karşı tüm önlemler alınmalıdır. Ayrıca profilaktik ilaçların kullanımı ile ilgili olarak ameliyattan 24 saat önce tekrar konsültasyon yapılması uygundur.

Anahtar Sözcükler: Mastositoz, anestezi, ilaç, alerji

INTRODUCTION

Mastocytosis is a rare disease characterized by abnormal accumulation of neoplastic mast cells (MC) in places such as skin, bone marrow, spleen, liver, gastrointestinal tract and lymph nodes (1).

In 2016, the World Health Organization (WHO) divided the disease into three main clinical variants: cutaneous mastocytosis (CM), systemic mastocytosis and locally aggressive disease known as MC sarcoma (2).

Diffuse cutaneous mastocytosis (DCM) is a rare form of cutaneous mastocytosis (CM) usually seen in children and

less frequently in adults. It is characterized by small lichenified papules with an orange peel appearance due to diffuse mast cell infiltration over the entire skin. Darier's sign and dermatographism are often positive. Pruritus is the most common symptom (3-5).

Patients with CM often require sedation or general anesthesia for diagnostic and therapeutic procedures. Mast cells, implicated in anaphylaxis, are high in number in mastocytosis patients, raising concerns about adverse reactions to drugs that can degranulate mast cells during anesthesia. The literature data suggests that opioids, muscle relaxants, analgesics, and volatile anesthetics may stimulate mast cells. Despite these concerns, the dread of anaphylaxis should not hinder the utilization of beneficial opioids or muscle relaxants during the perioperative phase, emphasizing the need for raised awareness of possible mast-cell mediator release consequences (4,5).

Here, we aimed to present our clinical experience in a pediatric patient with DCM undergoing surgical intervention for circumcision before administration of general anesthesia drugs.

CASE PRESENTATION

A 5-year-old male patient diagnosed with DCM with skin biopsy in 2019, who was consulted with anesthesia for circumcision operation last week, was not taken into the operation due to the risk of drug allergy and referred to the pediatric allergy and immunology department.

The patient was diagnosed with CM four months after birth and has no other disease. However, the family thought that he was allergic to many things since the diagnosis. He has been followed up by us since that month. Again, there is no family history.

Physical examination revealed that the general condition and vital signs of the patient was good. On skin examination, the patient had scars and pigmentations on the trunk, which were left behind after the bullae had been wounded and then healed (Figure 1). Respiratory, cardiovascular and other system examinations were normal.

Blood cell analyses (Hb: 11,6g/dl, leukocyte: 8.600/mm3, thrombocyte: 213.00/mm^3) and biochemistry laboratory results (urea: 24mg/dl, creatinin: 0.3mg/dl, Na+: 135mEq/L, K+: 4 mg/dl, AST: 10 U/L, ALT: 29 U/L) were found to be within normal ranges.

During the active phase of his disease, he has widespread bullous eruptions (Figure 1) on his body and also elevated tryptase levels (Tryptase levels 5,32 ng/mL at 2019; 10,35 ng/mL at 2022; 31.7 ng/mL at 2023; normal values <11.4 ng/mL). Serum tryptase level was found to be elevated from time to time.

Skin prick test with lidocaine did not show significant change from negative control due to dermatographism occurred. However, intradermal test with lidocaine 1:1 and 1:10 dilutions were found to be negative. Lidocaine was administered subcutaneously at incremental dose for drug allergy provocation test and the patient did not develop any reaction. Intradermal tests with midazolam and bupivacain were negative as well. No early or late reaction with any of them occurred. This patient was expected to undergo surgery shortly after our tests, but his family postponed circumcision for social reasons unrelated to his disease.

DISCUSSION

Mastocytosis is a rare disorder characterized by an excessive number of mast cells in tissues and the release of mast cell mediators. It is more commonly seen in childhood, and in pediatric cases, over 90% of childhood CM patients exhibit skin lesions known as urticaria pigmentosa (maculopapular CM). The other subtypes of CM are DCM and mastocytoma of skin. Our patient has a subtype of DCM, confirmed by a skin biopsy.

Mastocytosis can result in flushing, anaphylaxis, or an anaphylactoid reaction triggered by various factors, such as anesthesia, trauma, stress, temperature changes, and drugs. Degranulation of mast cells can lead to itching, erythema, bronchospasm, cardiovascular collapse, and even death. Individuals with mastocytosis may also experience gastrointestinal symptoms like diarrhea and abdominal pain, as well as bone pain, headache, and mild cognitive

Figure 1: Skin findings at the time of active disease of the case. Multiple tense vesicles and bullae filled with serous fluid and few large flaccid bullae over the abdomen.

changes. Overall, mastocytosis is a complex condition with diverse symptoms that can pose serious health risks (4,5). Such symptoms can be caused by different triggers, such as medication. As in our patient, this type of drug can be general anesthetics. Therefore, in case of suspicion, medications may need to be tested beforehand.

Perioperative immediate hypersensitivity in patients with CM can manifest as IgE-mediated hypersensitivity, but it may go undiagnosed without further investigation. Skin testing should be conducted with all drugs and latex used prior to the onset of immediate hypersensitivity, based on the patient's clinical history. A suggestive clinical history, usually indicating severe immediate hypersensitivity, coupled with an increased tryptase concentration compared to the patient's baseline level and a positive skin test to one of the suspected agents, confirms the diagnosis of IgE-mediated hypersensitivity. However, the absence of an elevated tryptase level does not rule out the diagnosis. On the other hand, a suggestive clinical history, which may or may not be severe and may or may not be accompanied by an elevated tryptase level, along with a negative skin test to the suspected medications, indicates non-IgE mediated hypersensitivity (6,7).

There are many case reports and studies on drug allergy in patients with CM (8-11). However, there are differences of opinion and thought between studies. For example, skin tests are considered important in some studies, but not in others. We report drug allergy testing in a patient with pediatric DCM using commonly used anesthesia regimens. It is recommended that patients with mastocytosis awaiting surgery be evaluated in advance by an allergist who can discuss appropriate management with the anesthesiologist and general practitioner before surgery. Routine skin tests against anesthetic drugs, muscle relaxants or opioids before general anesthesia are not mandatory but are an option. However, the test results may be difficult to interpret as in our patient. In addition, dermatographism may accompany some of these patients, as in our patient. Therefore, the usual skin prick tests performed in allergy clinics can give unreliable results (7). Since it is also known that some drugs can directly degranulate mast cells in vivo, skin tests (prick or intradermal) may be inadequate to show adverse reactions to the drug for these reasons (12). Nevertheless, some authors recommend that intradermal testing be performed before the procedure (13). Skin test applications performed in our case confirm the literature. When skin prick test failed, intradermal test and drug provocation test were performed in our patient.

In a study; 22 cases with CM were anesthetized for 29 diagnostic and surgical procedures. Routine anesthetic techniques were utilized, the peri-operative courses were uncomplicated and without severe adverse events (6). Contrary to adults, the authors found no reports of anesthesia-related deaths and several reports of serious anesthesia-related complications in cases with CM (8-14). The experience of 29 general anesthetics in 12 children with urticaria pigmentosa and 3 with solitary CM was reviewed. No major complications were encountered and the 4 minor problems seen were self-limiting. The data from this study suggest that urticaria pigmentosa or solitary CM patients are not at increased risk of life-threatening complications under general anesthesia (15).

Effective teamwork between anesthesiology, pediatric allergy, and surgical teams is crucial in pediatric cases involving CM. While drug restrictions are usually followed, prophylactic antihistamines and steroids can be administered before interventions to prevent potential reactions. However, caution is still exercised to avoid drugs that may trigger hypersensitivity reactions. It is important to note that certain drugs used during anesthesia may directly or indirectly activate mast cells. Opioids like codeine, morphine, meperidine, and pethidine can cause mast cell degranulation while fentanyl, sufentanil, and remifentanil do not. Histamine release has been observed with d-tubocurarine, tubocurarine, pancuronium, gallamine, and atracurium. Succinylcholine and cisatracurium lead to mild histamine release, while vecuronium, rocuronium, and pancuronium activate mast cells moderately. Atracurium and mivacurium cause strong mast cell degranulation based on in vitro studies. Despite drug restrictions, no severe complications have been reported in pediatric cases of CM (6,16). In a study, detailed tables summarizing reports of selected anesthetic medications used for 57 patients with CM undergoing anesthesia, reported side effects, and suggested prophylaxis regimens are included (17). Ahmad et al. evaluated perioperative management of 6 patients with CM presenting for general anesthesia and demonstrated none of the complications (18).

Propofol and thiopental have been known to cause histamine release, but propofol is considered safe to use in cases where histamine release is a concern. Ketamine has a minimal effect on histamine release. Volatile anesthetics do not cause mast cell degranulation and are safe to use. Diazepam, a benzodiazepine, has been associated with anaphylactic reactions (6-8,19). In a particular anesthesia case, intubation was performed without muscle relaxants after sevoflurane induction, propofol was administered to maintain depth, and no complications were observed (14). Intraoperative anaphylaxis can be the first presenting sign of mastocytosis. In a study including adult 113 patients with mastocytosis who used chronic anti-mediator therapy and/or preoperative prophylactic drugs had an uneventful surgical course (20). Since the literature data are contradictory in patients like our case, we think that premedication may not necessarily be required, but it is useful to be cautious.

In addition, studies have not reported serious side effects related to routine medications used during general anesthesia / surgery (6,9,12,13). Anesthesia planning for patients with mastocytosis should prioritize avoiding triggers for mediator release and taking precautions for potential anaphylaxis. Identifying the cause of anaphylaxis is crucial to prevent attacks, and careful premedication should be done to assess any previous drug reactions and evaluate the risk. Omitting previous reactions may lead to more severe reactions. Preoperative sedation and postoperative analgesia are advised to reduce anxiety and pain-induced mast cell degranulation. Detailed records of the procedures should be kept for reference. Cross-reacting drugs should be avoided if the patient is known to be sensitive to certain drugs. During anesthesia, cardiovascular and cutaneous symptoms are more common than bronchospasm (15-18,20).

In conclusion; the risk of severe systemic reactions after drugs intake seems to be extremely low and in general lower in children than in adults (19). We report that amide group local anesthetics (lidocaine and bupivacaine) and midazolam, one of the general anesthetics, can be used without any problem in a patient with DCM according to intradermal test results. However, all precautions should be taken against the possibility of anaphylaxis in these patients. In addition, it is appropriate to consult again 24 hours before surgery regarding the use of prophylactic drugs.

Acknowledgment

None.

Author Contributions

Author contributions are equal.

Conflicts of Interest

Authors declare no conflict of interest.

Financial Support

None.

Ethical Approval

This study is'nt a experimental and clinical research. Because of it was a case report, the ethical approve wasn't needed. Informed consent was given by parents and legal representatives for this report.

Review Process

Externally and extremely peer-reviewed.

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