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Case Report

Cutaneous Mastocytosis: Case Report

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SUMMARY

Introduction: Mastocytosis is a group of rare diseases characterized by the infiltration and abnormal proliferation of mast cells in various tissues. The disease can have either a benign or malignant form. Symptoms result from the excessive degranulation of mast cells and the release of inflammatory mediators, which can cause hypotension, anaphylaxis, diarrhea, and other systemic symptoms. The clinical picture varies, cutaneous mastocytosis (CM) more commonly occurring in children and often spontaneously regressing, while adults are more likely to develop more aggressive forms of the disease.

Case Report: We present a 22-year-old female patient with livid-brown macules that appeared four years ago and progressively spread. Initially, she was diagnosed with acute urticaria and treated with antihistamines and topical corticosteroids without improvement. Due to the persistence of symptoms, in 2024, she consulted a dermatologist, after which she was hospitalized for further diagnostics. The clinical examination indicated a positive Darier sign. Laboratory findings, bone densitometry, chest X-ray, and ultrasound of the upper abdomen were all normal. A skin lesion biopsy revealed mast cell infiltration with an immunohistochemical profile consistent with mastocytosis. Bone marrow biopsy did not indicate systemic mastocytosis. During hospitalization, no medications were prescribed, and the symptoms improved with the application of general measures.

Conclusion: CM can also occur in adulthood without the development of the systemic form of the disease. The initial difficulties in recognizing and treating mastocytosis highlight the need for further education of healthcare providers, given the rarity of the disease. With proper education of patients on avoiding triggers and regular use of antihistamines, the disease can be effectively controlled.

Keywords: Mast Cells, Rare Diseases, Antihistamines, c-KIT, Mutations

INTRODUCTION

Mastocytosis is a group of rare diseases characterized by the infiltration and abnormal proliferation of mast cells in various tissues. The epidemiology of mastocytosis remains incompletely understood. A Dutch study based on 48 patients reported a prevalence of 13 per 100,000 of the most common type of SM (ISM and SSM) [1]. However, no epidemiologic studies have precisely defined the incidence, point prevalence, or cumulative prevalence of mastocytosis in the general population. This disease can present in a benign form, with lesions that spontaneously resolve, or a malignant form, with infiltration of internal organs and/or medullary dysplasia According to the World Health Organization

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(WHO) classification from 2022, mastocytosis is divided into three categories: cutaneous mastocytosis (CM), systemic mastocytosis (SM), and mast cell sarcoma (MCS) [2], while CM mastocytosis is further divided into: 1) maculopapular cutaneous mastocytosis (MPCM), also known as urticaria pigmentosa; 2) diffuse cutaneous mastocytosis (DCM); and 3) mastocytoma of the skin [3]. Symptoms result from excessive mast cell degranulation and the release of chemical mediators (heparin, histamine, and prostaglandins) into the bloodstream, which consequently causes systemic symptoms such as hypotension, anaphylaxis, weakness, diarrhea, and loss of appetite. Involvement of the liver and spleen can result in portal hypertension and splenomegaly. Infiltration of the bone marrow leads to pancytopenia, an increased risk of infections, and the development of osteopenia, which is a result of enhanced osteoclast activity and decreased osteoblast function [4]. The clinical presentation of mastocytosis shows significant variability. In children, CM is most commonly observed and often spontaneously regresses during puberty. In contrast, in adults, more aggressive forms, such as SM, are more frequently developed, which can be accompanied by severe organ dysfunction and a shortened life expectancy [5]. A characteristic feature is a positive Darier sign—the appearance of redness, itching, and swelling upon rubbing or irritating a skin lesion [6]. Mastocytosis is often associated with comorbidities. The most significant comorbidities include IgE-dependent allergies, vitamin D deficiency, as well as psychiatric or mental disorders [2]. In a study conducted in 2011, which included 101 children, a group of European researchers found that CM was diagnosed in 73% of the participants by the sixth month of life, while 97% of the children developed the disease by the second year [7]. In adults, mastocytosis most commonly develops during the third or fourth decade of life [8]. This disease is present among all races and affects both sexes, with recent studies showing a slight male predominance [9].

CASE REPORT

We confirm that we have obtained the patient's written consent for the anonymous publication of the case report in the scientific journal „Hospital Pharmacology – International Multidisciplinary Journal". We present the case of a 22-year-old female patient who came for examination due to livid-brown macules, approximately 2mm in diameter (Figure 1, B, C, D), which first appeared four years ago. The initial lesions were localized on the forearms and decolletage, and over the following months, they spread to the skin of the entire body. Initially, the diagnosis of acute urticaria was made, and she was treated with oral antihistamines and topical corticosteroids, but with no clinical improvement. The patient did not seek further medical attention during the following four years. Due to the persistence of existing lesions and the appearance of new ones, in March 2024, the patient consulted a dermatologist at the University Clinical Center of Vojvodina. During this visit, CM was suspected, and hospitalization was indicated for diagnostic and therapeutic procedures. In her medical history, the patient reported frequent respiratory infections during childhood, while since puberty, she has suffered from frequent headaches and intense menstrual pain, for which she regularly uses nonsteroidal anti-inflammatory drugs (NSAIDs), specifically „Caffetin Cold" (paracetamol, pseudoephedrine, dextromethorphan, ascorbic acid). The patient denies any of hereditary and chronic non-infectious diseases. Upon admission to the hospital, clinical examination revealed pale erythematous to hyperpigmented macules, approximately 2 mm in diameter, on the skin of the neck, trunk, and upper and lower extremitie. The Darier sign was subtly positive (Figure 1, A), while no other pathological changes were observed on the rest of the skin.

Relevant laboratory tests and diagnostic procedures were performed: complete blood count (CBC), C-reactive protein (CRP), urine analysis, blood glucose (BG); total and direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH); urea, creatinine were within reference ranges. Electrolytes: sodium (Na), potassium (K), chloride (Cl), total calcium, and ionized calcium were also within reference ranges. 5-hydroxyindoleacetic acid (5-HIAA): 25 umol/dU (10.4 - 31.2). For technical reasons, the serum tryptase level was not measured. Bone densitometry, chest X-ray, and ultrasound of the upper abdomen showed no abnormalities. A 6 mm punch biopsy of the skin lesion was taken for histopathological examination and immunohistochemical stain-

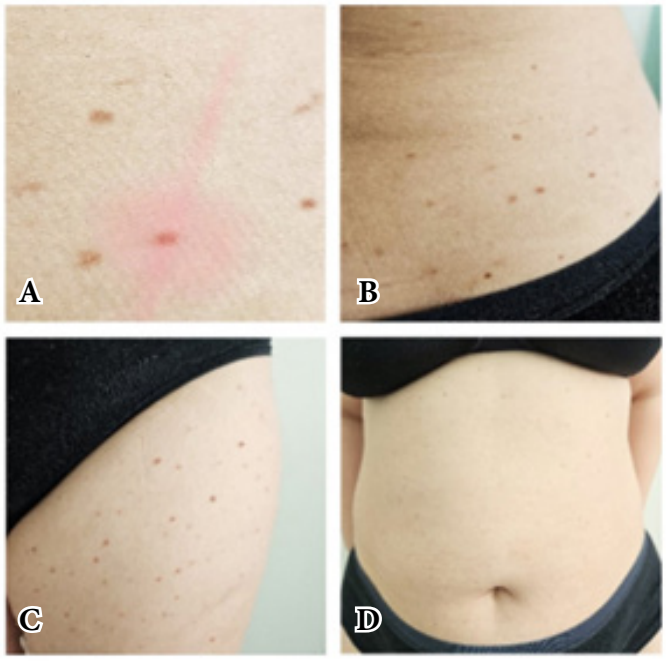

Figure 1. Discreetly positive Darier sign (A), hyperpigmented macules on the patient's skin (B, C, D)

ing. The skin histopathology revealed a flattened epidermis with a moderate perivascular infiltrate of lymphocytes and mast cells (Figure 2, A). The skin appendages were of normal morphology. Special May-Grünwald-Giemsa staining was used to highlight the presence of mast cells in the skin (Figure 2, B).

Immunohistochemical findings were consistent with mastocytosis: MCT+; CD117+; CD25-; CD2- (Figure 2, C). A hematology consultation was conducted, and a bone marrow biopsy was recommended and performed, which revealed mildly uneven cellularity around 70% (Figure 3, A, B, C). Elements of all three hematopoietic lineages were present in a normal ratio, with preserved maturation continuity and spatial organization. Megakaryocytes present as single cells, mildly polymorphic, some smaller in size, with appropriate morphology and spatial distribution. The erythroid lineage was represented by limited erythron consisting of cell forms in all stages of maturation (CD71+). Myelopoiesis was predominantly represented by mature cell forms. The blast count was not elevated (<5% CD34+/CD117+ cells). Interstitially, regular plasma cells, single small mature lymphocytes, and individual regular mast cells (CD117+/MCT+/CD2-/CD25-) were observed.

The reticular structure of the bone marrow is focally and mildly expressed (G1). Morphological and immunohistochemical findings suggest reactive changes in the bone marrow. Currently, there are no clear morpho-

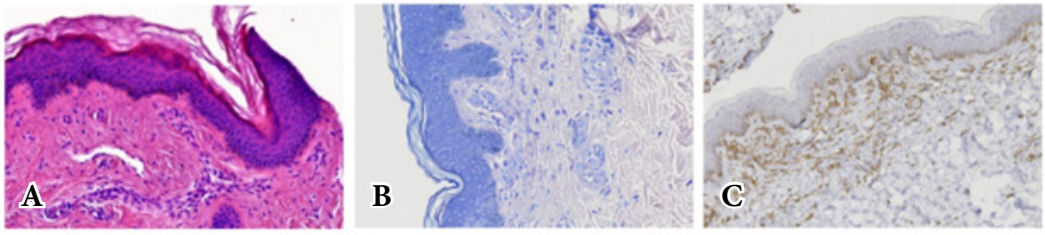

Figure 2. Mast cell hyperplasia of the skin, H&E x200 (A), May-Grünwald-Giemsa x200 (B), immunohistochemically positive mast cells with CD117 antibody (C).

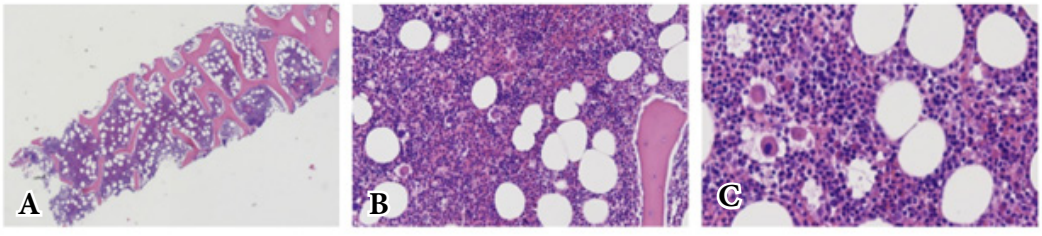

Figure 3. Bone marrow: H&E x25 (A), H&E x200 (B), H&E x400 (C)

logical indicators of lymphoproliferative, myeloproliferative, or myelodysplastic processes, nor are there signs of SM.

During hospitalization, the patient was not prescribed antihistamines or any other medications. Instead, consistent application of general measures—such as avoiding intense physical activity and NSAIDs, adhering to a hygienic-dietary regimen, and gently patting the skin dry after showering instead of rubbing—led to symptom improvement without the need for long-term antihistamine use.

DISCUSSION

Cutaneous mastocytosis (CM) is a rare condition characterized by the proliferation of mast cells in the skin. This proliferation is primarily driven by mutations in the tyrosine kinase receptor c-KIT (CD117), which activate molecular signaling pathways that promote autonomous mast cell growth and differentiation, thereby increasing their lifespan and number [10, 11]. CM most commonly occurs in childhood, with the highest incidence observed by the second year of life. In adults—particularly during the third or fourth decade—systemic mastocytosis (SM), involving both cutaneous and systemic manifestations, is more frequently diagnosed. However, the present case illustrates a relatively rare clinical scenario: CM occurring in adulthood as an exclusively cutaneous form without systemic involvement. In our patient, CM was suspectedat the age of 22, although the symptoms had been present for four years. Diagnosis of CM is often challenging because CM can mimic other dermatological conditions, especially in patients who do not respond to standard therapy. Our patient was initially diagnosed and treated as having acute urticaria, and due to the lack of therapeutic response, mastocytosis (CM) was considered as a possible differential diagnosis. Although urticaria treatment, including antihistamines, often provides symptom relief in CM, in this case, the patient's medical history — including frequent colds, headaches, dysmenorrhea, and the frequent use of NSAIDs and dextromethorphan — contributed to the poor response to therapy. Our patient was initially diagnosed and treated as having acute urticaria, and due to the lack of therapeutic response, CM was considered as a possible differential diagnosis. Although antihistamines are often effective in managing CM symptoms, our patient's clinical course was influenced by factors in her medical history—specifically, frequent respiratory infections, dysmenorrhea, recurrent headaches, and regular use of NSAIDs and dextromethorphan—which may have contributed to therapeutic resistance. Laboratory tests, including CBC, CRP, liver enzymes, and electrolytes, were within reference values, which is expected in patients with CM. It is important to note that the histopathological examination of the skin sample showed a perivascular infiltrate of mast cells and positive immunohistochemical staining for mast cell markers (MCT+; CD117+), thus confirming the diagnosis of CM. Bone marrow biopsy findings were crucial in excluding systemic mastocytosis (SM). The negativity of CD2 and CD25 markers in immunohistochemical staining supported the diagnosis of cutaneous mastocytosis (CM). Management of CM focuses on reducing and controlling the release of mediators from mast cells, or avoiding triggers [11-14]. These triggers fall into two major categories: environmental and pharmacologic. [12, 13]. Environmental triggers include extreme temperatures, fever, infections, stress, exercise, skin friction, allergens, and certain foods such as seafood, chocolate, tomatoes, pineapple, caffeine, alcohol, synthetic dyes, and flavor enhancers in food [12-16]. Although drug-induced mast cell activation is rare, medications such as NSAIDs, opioids, contrast agents, dextromethorphan, and specific antibiotics (e.g., quinolones) should be avoided when possible [12, 13, 15, 16]. When general measures are insufficient to control symptoms, the therapeutic approach is expanded to include antihistamines that block H1 receptors. These medications have shown significant efficacy in alleviating redness, itching, urticaria, and the sensation of burning on the skin. Consistent implementation of general measures in our patient led to symptom improvement, without the need for long-term antihistamine use. In accordance with current guidelines, follow-up visits with both a hematologist and dermatologist are planned, highlighting the importance of continuous monitoring of patients with CM and the need for early recognition of potential progression to systemic disease (SM).

CONCLUSION

CM can also occur in adulthood without pro-

gressing to thesystemic form of the disease. The initial challengesin recognizing and treating CM underscore the need for increased awareness and education among general practitioners and dermatologists, given the rarity of the condition. With proper patient education on how to avoid triggers, regular use of antihistamines, and consistent monitoring, the disease can be effectively controlled. Ongoing follow-up of patients with CM is crucial for the timely recognition of potential progression to SM.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Kožna mastocitoza: prikaz slučaja

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KRATAK SADRŽAJ

Uvod: Mastocitoza predstavlja grupu retkih bolesti koje karakteriše infiltracija i abnormalna proliferacija mastocita u različitim tkivima. Bolest može imati benignu ili malignu formu. Simptomi su posledica prekomerne degranulacije mastocita i oslobađanja medijatora inflamacije, što može izazvati hipotenziju, anafilaksu, dijareju i druge sistemske simptome. Klinička slika varira, pri čemu se KM češće javlja kod dece i spontano regredira, dok odrasli češće razvijaju agresivnije oblike bolesti.
Prikaz slučaja: Prikazujemo 22-godišnju pacijentkinju sa lividno smeđim makulama koje su se pojavile pre četiri godine i progresivno se širile. Inicijalno je dijagnostikovana akutna urtikarija i lečena antihistaminicima i topikalnim kortikosteroidima bez poboljšanja. Zbog perzistiranja simptoma, 2024. godine se javlja dermatologu, nakon čega je hospitalizovana radi dalje dijagnostike. Klinički pregled je ukazao na pozitivni Darier znak. Laboratorijski nalazi, denzitometrija kostiju, rendgen grudnog koša i ultrazvuk gornjeg abdomena bili su uredni. Biopsija kožne lezije je pokazala infiltraciju mastocita sa imunohistohemijskim profilom koji odgovara KM. Biopsija koštane srži nije ukazala na sistemsku mastocitozu. Tokom hospitalizacije pacijentkinji nisu bili ordinirani lekovi, a simptomi su se poboljšali primenom opštih mera.
Zaključak: KM se može javiti i u odrasloj dobi, bez razvoja sistemske forme bolesti. Početne teškoće u prepoznavanju i lečenju KM ukazuju na potrebu za dodatnom edukacijom lekara, s obzirom na retkost bolesti. Pravilnom edukacijom pacijenata o izbegavanju okidača i redovnom primenom antihistaminika bolest se može efikasno kontrolisati.

Ključne reči: mastociti, retke bolesti, antihistaminici, c-KIT, mutacije

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