Cutaneous mastocytosis: diagnostic challenges and dietary influences

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Abstract

Cutaneous mastocytosis (CM) is a rare condition characterized by abnormal mast cell proliferation in the skin. We present the case of a 65-year-old man with recurrent urticaria-like rashes persisting for more than eight years. Despite multiple misdiagnoses as insect bites, examination and biopsy revealed mast cell infiltration. The patient's unique lifestyle, particularly his frequent seafood consumption, adds an intriguing dimension to the case. Treatment with systemic antihistamines and corticosteroids provided symptomatic relief, but long-term follow-up showed the persistence of clinical lesions, indicating that the treatment did not adequately address the underlying cause of the disease. A notable improvement in disease control was observed when the patient's diet was adjusted, suggesting a potential link between food and cutaneous mastocytosis. To our knowledge, this is the first documented case of maculopapular cutaneous mastocytosis in Syria.

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Introduction

Mastocytosis is a rare disease characterized by the abnormal accumulation of mast cells across multiple organs, primarily the skin.[1,2] Mature mast cells derive from hematopoietic progenitors in designated locations and display unique traits as local effector cells, which differ according to the tissue environment.[3] Historically, mast cells were believed to primarily react to various external stimuli, such as allergens, pathogens, and physical or inflammatory factors. However, recent research has uncovered a more proactive role for these cells, particularly in individuals with conditions involving the proliferation of mast cells in the bone marrow.[3] Cutaneous mastocytosis (CM), a subtype of mastocytosis, presents with diverse clinical manifestations, including maculopapular CM (MPCM), also known as urticaria pigmentosa (UP), diffuse CM (DCM), and localized mastocytoma.[2] MPCM causes small brown spots that may be flat or raised. Scratching these spots can result in reddened, itchy skin, a reaction known as Darier's sign. In adult patients, these lesions tend to be more prominent in areas of the skin exposed to pressure or friction.[4] Diagnostic criteria include characteristic skin lesions, histologically confirmed mast cell infiltrates, and activating KIT mutations.[5] The etiology of CM remains poorly understood, and the rarity of the disease presents significant diagnostic challenges. Patients with mastocytosis must avoid triggers that activate mast cells. We present a unique case highlighting the challenges in diagnosis, the significance of lifestyle factors, and the complexities of managing CM over an extended period.

Case Report

A 65-year-old male ship captain presented to the dermatology department with recurrent urticaria-like rashes on his back, persisting for eight years despite various treatments (Figure 1). His lifestyle includes frequent seafood consumption (three times per week). The patient reported an increased frequency of rashes during travel. He has no history of specific seafood allergies, prior allergies, family history of mast cell disorders, or other significant

dermatological conditions. A dermatological exam revealed multiple pale red papules and macules (fewer than 100) limited to the back, with well-defined margins, abrasions, and itching. Darier's sign was positive, indicating possible CM. Lab tests were normal except for elevated triglycerides. A skin biopsy showed mild dermal edema and diffuse perivascular accumulation of small fusiform and spindle mast cells (Figures 2 and 3).

Immunohistochemistry with CD45 and CD117 confirmed the presence of mast cells, leading to a diagnosis of CM. Skin tests were negative, and the serum tryptase level was normal. An abdominal ultrasound and CT scan showed no liver or spleen enlargement. A bone marrow biopsy revealed no mast cell infiltration, excluding systemic mastocytosis. The patient was treated with systemic antihistamines and corticosteroids, including oral prednisolone (1 mg/kg for one month) and ketotifen (1 mg in the evening). Topical corticosteroids and antibiotics were also administered. While prednisolone was gradually discontinued, ketotifen was maintained long-term. The patient experienced partial improvement, with a reduction in the severity of rashes and itching, though the frequency of episodes and the characteristics of the lesions remained unchanged. We noticed that the episodes occurred more frequently after consuming fish. Accordingly, a low-histamine diet was introduced, restricting fermented foods, cured meats, and fish. This dietary change helped reduce the frequency of attacks. After two years on the diet, the frequency of episodes decreased, although the number of lesions remained unchanged. The patient underwent biannual follow-ups for five years, which included blood tests to monitor serum tryptase and other mast cell mediators. Treatment adjustments were made as needed. Five years post-diagnosis, the patient's condition remained stable, with no new lesions observed.

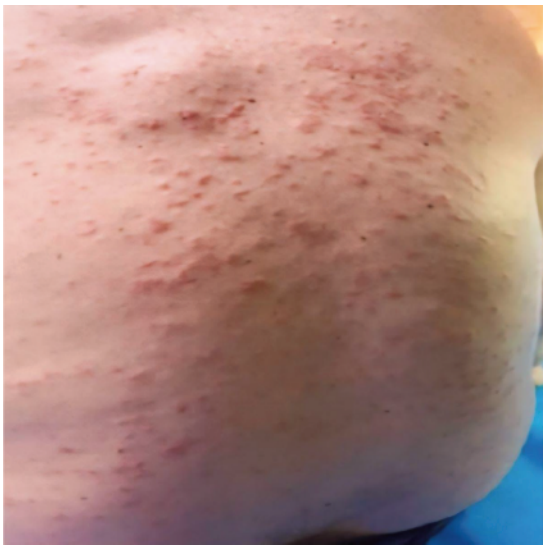

Figure 1. Patient's back with numerous reddish-brown macules and papules, resembling urticaria. The lesions are slightly raised and clustered in some areas.

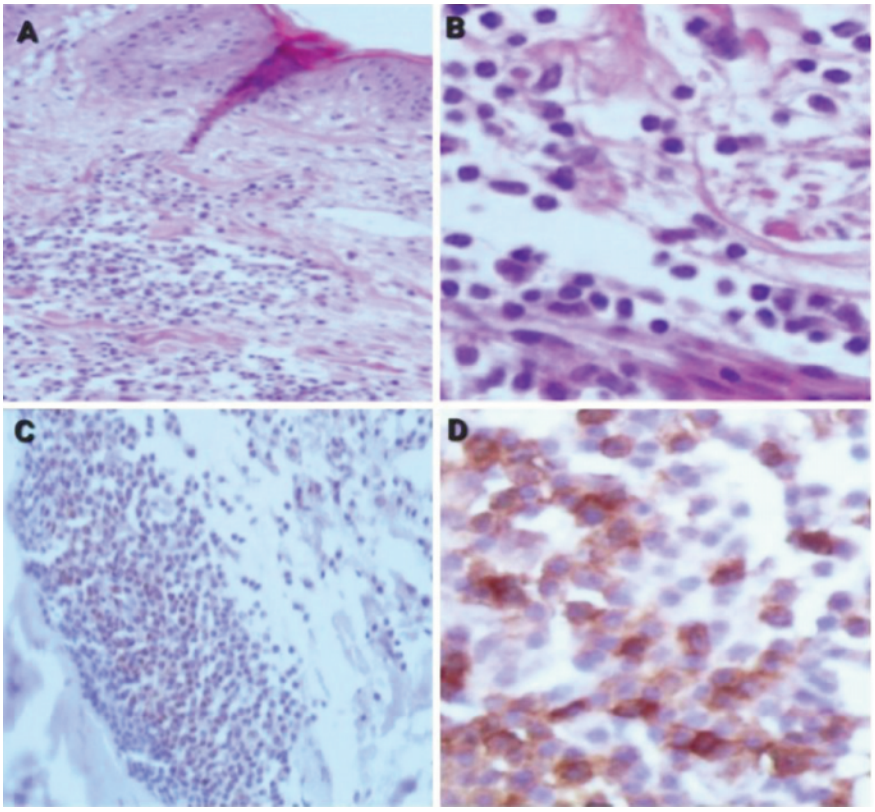

Figure 2. A) Nodular accumulation of mast cells in the dermis, as seen under hematoxylin and eosin (H&E) stain at 40x magnification. The nodules are dense and well-defined. **B**) Mast cells with a round or spindle shape, featuring eosinophilic cytoplasm and large, oval, centrally located nuclei. This is observed under H&E stain at 100x magnification, highlighting the distinct cellular morphology characteristic of mast cells. **C**) Positive immunostaining for CD45. **D**) Immunostaining positive for CD117.

Discussion

Mastocytosis is a rare disorder characterized by the proliferation and accumulation of clonal mast cells in various organs, including the skin, bone marrow, spleen, lymph nodes, and gastrointestinal tract. The prevalence of mastocytosis is estimated to be 1 in 10,000 people, with an annual incidence of 1 per 100,000 people.[6] CM, marked by the abnormal accumulation of mast cells in the skin, is a rare and enigmatic disorder that poses diagnostic challenges and requires a nuanced approach to management. Our case report sheds light on the complexities of CM, focusing on the patient's prolonged and recurrent urticaria-like lesions and the intriguing association with frequent seafood consumption. The rarity of CM has led to a limited understanding of its etiology and management. Most studies highlight the necessity of a multidisciplinary approach for the successful diagnosis and treatment of this condition.[1,7] Our case exemplifies this principle, as the collaboration of various specialists was crucial for an accurate diagnosis and effective treatment of the patient.

The extended presence of urticaria-like lesions in our patient posed a diagnostic challenge, as repeated misdiagnoses as insect bites impeded the commencement of suitable treatment.[7] This case serves as an educational example, emphasizing the need for awareness and a comprehensive approach. The positive Darier's sign observed in our patient, characterized by urtication and erythema upon rubbing or scratching the skin, indicates mast cell degranulation in response to mechanical stimuli.[8] These clinical manifestations align with previous reports that Darier's sign is a valuable tool for diagnosing mastocytosis. Our case introduces an intriguing element: the patient's lifestyle, characterized by frequent consumption of seafood, which is known to contain high levels of histamine, a potent mast cell activator.[9]

The diagnosis of MPCM is usually straightforward. However, differential diagnoses such as chronic urticaria, Langerhans cell histiocytosis (LCH), or idiopathic anaphylaxis should be considered.[10] LCH shares clinical similarities with mastocytosis, but LCH is diagnosed through a CD1a-positive immunohistochemistry test, whereas mastocytosis is confirmed by CD117 positivity.

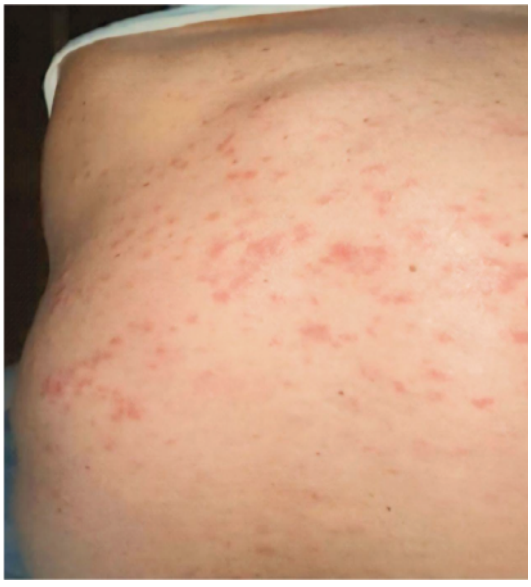

Figure 3. The shape, nature, and number of the lesions have remained unchanged despite the patient's condition stabilizing.

Chronic urticaria is characterized by recurrent, transient, pruritic wheals, which can be distinguished from the fixed, pigmented lesions observed in mastocytosis. Additionally, idiopathic anaphylaxis is diagnosed by excluding other causes and is characterized by recurrent, unexplained episodes of anaphylaxis without an identifiable trigger.[11] CM and paraneoplastic pemphigus also share similar skin manifestations. Paraneoplastic pemphigus is a rare autoimmune disorder that affects the skin and mucous membranes and is often associated with underlying lymphoproliferative disorders.[12]

Studies have implicated histamine-rich diets in exacerbating mast cell disorders, suggesting a potential link between dietary habits and the clinical course of CM.[13] This warrants further investigation into the role of dietary modifications in managing mast cell disorders. Dietary considerations in mastocytosis management have gained attention in recent years, with research exploring the impact of histamine content in food items, including seafood, on mast cell activation.[14] The variability in individual responses to dietary histamine highlights the need for personalized dietary management in patients with mast cell disorders.[15] While our patient's regular seafood consumption is noteworthy, more studies are needed to establish definite links between specific dietary components and the progression of CM. The treatment approach for our patient included systemic antihistamines and corticosteroids, resulting in symptomatic relief and improved itching. However, the persistence of clinical lesions raises questions about the long-term effectiveness of these conventional treatments in altering the natural course of CM. The current literature acknowledges the challenges in achieving complete resolution of lesions, emphasizing the need for individualized treatment plans based on symptomatology.[5,16] When antihistamines and corticosteroids are insufficient to fully treat CM, the role of diet in managing this disorder becomes essential. A low-histamine diet that minimizes the frequency of acute attacks can achieve successful outcomes.

Long-term follow-up, spanning five years post-diagnosis, revealed a stable general condition in our patient with no deterioration or emergence of new lesions. The clinical inertia observed in lesion improvement echoes findings in the literature, where CM often exhibits a chronic course with persistent skin lesions. The chronicity of the condition prompts consideration of alternative or adjunctive therapeutic strategies to enhance lesion resolution and improve overall quality of life.[2] Elderly patients often experience significant delays in receiving a diagnosis for this rare disease, which may be attributed to gerontologists' lesser familiarity with the disease's typical symptoms compared to its cutaneous manifestations. This delay is compounded by the fact that the disease is more commonly recognized in younger individuals, as evidenced by the findings of this research.[17] Like in many other cases, patients can be negatively impacted by delayed diagnosis.

Currently, no known cure exists for any type of mastocytosis. Despite this, most patients' life expectancy remains unaffected, though their quality of life may be compromised. The primary goal of pharmacological treatment is to control symptoms by curbing the production and release of mediators and blocking their effects once released.[16,17] Under these specific conditions, the use of antihistamines, corticosteroids, and dietary modifications may be beneficial.

Limitations

We did not include the figures for the abdominal ultrasound, CT scan, and bone marrow biopsy, as these images were not archived in the dermatology department's records. However, the corresponding results of these procedures were provided. Only the

histopathological slides, which are directly related to the dermatology case, were retained in the patient records, in accordance with department policy. This limitation may affect the comprehensive visual documentation of the case.

Conclusions

This case demonstrates the importance of clinical examination and histopathologic studies in confirming the diagnosis of chronic dermatological disorders such as CM. We observed a link between histamine-rich food intake and the progression of CM, since our patient improved significantly after dietary changes. Clinical trials are required to prove this correlation. This points out the significance of customized management of this condition.

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