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Case report

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### Cutaneous Mastocytosis in a 61-year-old Female from a Dermatological and Histopathological Perspective

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#### Abstract

First described by Nettleship et al. in 1869 [1], mastocytoses are a heterogeneous group of disorders characterized by the pathologic accumulation of mast cells in various tissues [2-5]. Mastocytosis can be confined to the skin as in cutaneous mastocytosis (CM), or it can involve extracutaneous tissues such as the liver, spleen, bone marrow and lymph nodes, as in systemic mastocytosis [6]. Mastocytosis is a World Health Organization-defined clonal mast cell disorder characterized by significant clinicopathologic heterogeneity [7].

**Keywords:** Cutaneous mastocytosis; Systemic mastocytosis; Systemic involvement; Mast cells; Mastocytosis.

#### Introduction

The organ most frequently involved in mastocytosis is the skin. Cutaneous mastocytosis is classified according to clinical presentation and is further defined by onset of disease [8]. Cutaneous mastocytosis tends to appear early in life but adult onset can occur. Over 55% of cases occur in patients under the age of two years, and another 10% of cases appear in patients between the ages of 2 and 15 years [9]. Males and females are affected equally and is most common in whites. Historically, CM was described by Nettleship and Tay in 1869 as a symmetrical maculopapular eruption with urtication of the lesions after rubbing [10]. Mastocytosis is characterized by expansion of clonal mast cells in different organs, often related to KIT mutations [8,11-13]. Whether mastocytosis is a

hyperplastic reaction to an unknown stimulus or a neoplastic condition remains unknown. More than 80% of all patients with mastocytosis exhibit characteristic brown-red macular skin lesions [14]. The diagnosis of CM is based on clinical features, histopathologic analysis and the absence of systemic mastocytosis. Darier's sign, which is defined by whealing and reddening of lesions upon mechanical stroking or rubbing, is a classic diagnostic hallmark of mastocytosis [15,16]. Blistering or bullous mastocytosis represents an exaggerated Darier's sign, more commonly seen in pediatric patients.

### Case presentation

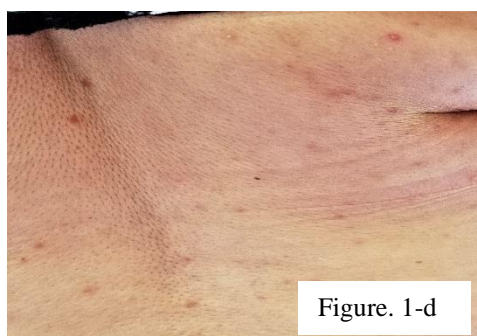
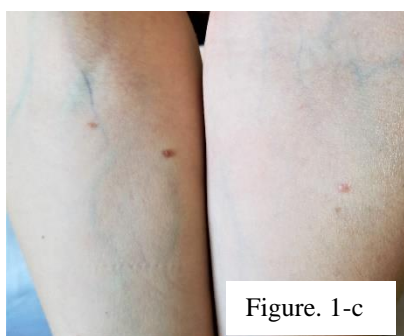
A 61-year-old female presented to the Department of Dermatology with multiple pigmented macules in the chest area, arms and shoulders. Several years ago, it started as few papular elements, distributed in a non-symmetrical order, that appeared initially on the legs. The lesions were accompanied by an itch and general discomfort feeling, especially when she was exposed to heat and during emotional

stress. Physical examination revealed numerous red-brown macules measuring 2-3 mm in diameter and a positive Darier's sign. The rest of the findings were unremarkable and no evidence of systemic mastocytosis was seen.

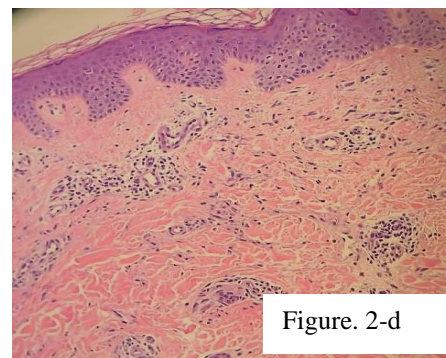
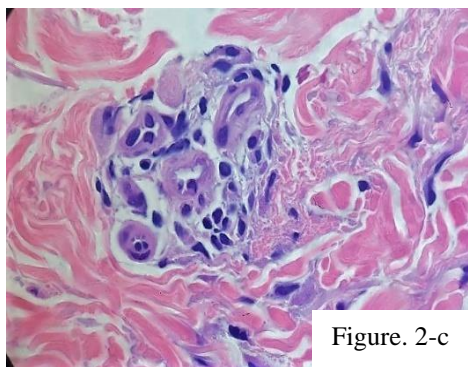
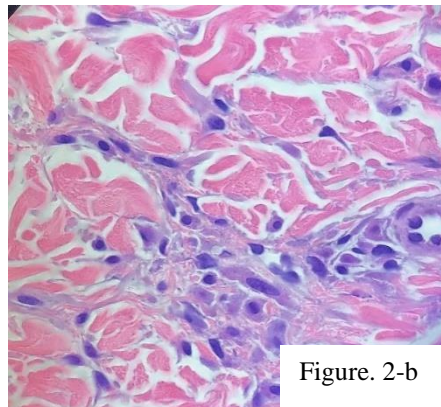
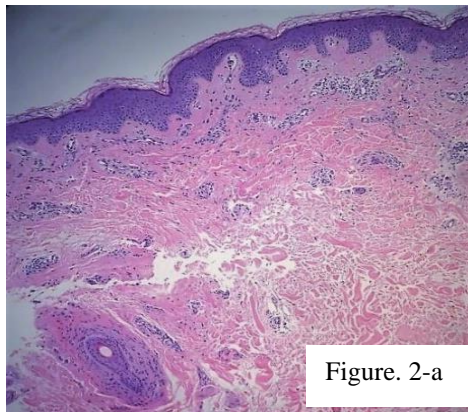
### The following tests were performed:

Abdominal ultrasonography: no hepatosplenomegaly. Several complete blood counts: within normal limits. Liver and renal function tests and lipid profile: within normal limits. Urine analyses: within normal limits. VDRL: negative. X-ray of long bones: unremarkable.

The differential diagnosis included histiocytosis, mastocytosis, Grover's Disease and autoimmune disease. After excision of the skin lesion, the morphologic and immunophenotypic findings were suggestive of CM. Thus, the occurrence of the skin lesion with no initial visceral involvement suggested the diagnosis of primary cutaneous mastocytosis.

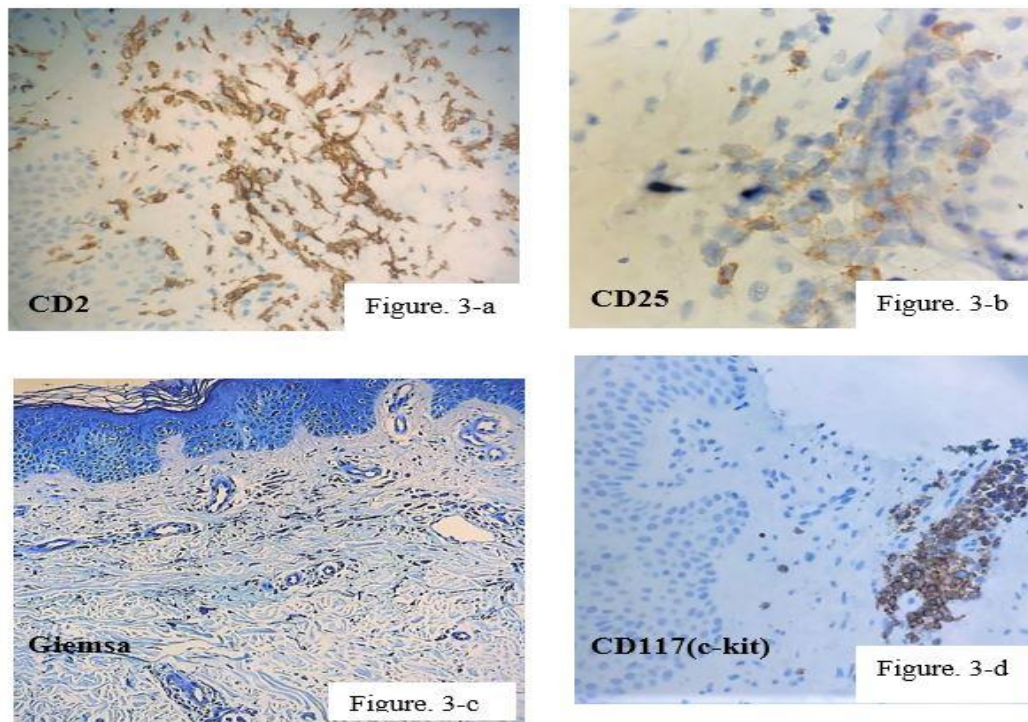


**Figure 1 (a-c):** Clinical presentation of maculopapular cutaneous mastocytosis with red-brown, ill-defined macules starting from the legs and expanding in random distribution involving the chest area and arms, bilaterally (c). Histopathological examination of the lesion showed a proliferation of spindled mast cells within the superficial dermis. The cells showed a granular eosinophilic to amphophilic cytoplasm and nuclei with dispersed chromatin without significant atypia.



**Figure 2:** Hematoxylin & eosin-stained sections from skin biopsy of the patient revealed numerous superficial dermal perivascular mast cells.





**Figure 3:** Immunohistochemical and special stains. Neoplastic mast cells show CD117 positivity with aberrant coexpression of CD2 and CD25. Giemsa stain highlights mast cells.

## Discussion

Mastocytosis refers to a rare group of disorders characterized by excessive mast cell accumulation and is subdivided into cutaneous and systemic mastocytosis. According to the World Health Organization, cutaneous mastocytosis is classified into (1) urticaria pigmentosa, also known as maculopapular cutaneous mastocytosis (MPCM); (2) diffuse cutaneous; (3) mastocytoma of the skin and (4) telangiectasia macularis eruptiva perstans (TMEP) [17,18]. Union-US consensus group also established criteria for cutaneous involvement in patients with mastocytosis [19]. These criteria include the presence of (1) a typical skin lesion (major criterion), (2) a histologically-confirmed infiltrate of mast cells in the dermis (minor criterion) and (3) KIT mutation at codon 816 in lesional skin (minor criterion). Urticaria pigmentosa, resulting from the accumulation of excessive numbers of mast cells in the skin, is the most common form of

cutaneous mastocytosis [20]. The classification of CM has been based on macroscopic features of skin lesions, their distribution and disease onset. Cutaneous mastocytosis typically has a benign course and may spontaneously regress. Commonly reported symptoms of cutaneous mastocytosis are generalized flushing and localized blistering. The laboratory tests performed should be chosen according to the symptoms displayed. The prognosis of patients with cutaneous mastocytosis depends on the existence of systemic involvement and disease onset. A bone marrow examination is recommended in all adult patients suspected of mastocytosis even if the serum tryptase is normal [21].

## Conclusion

Cutaneous mastocytosis poses a diagnostic challenge clinically, as it presents with diverse dermatological manifestations and clinical symptoms. Clinicians should be aware of the

various subforms and the overlapping features of the lesions with other possible etiologies such as endocrinologic, vasculopathies or immunologic. Assimilation of the clinical presentation, histologic findings and immunohistochemical and molecular studies may help to clarify the diagnosis. A multidisciplinary approach is recommended in the diagnosis and management of patients with mastocytosis. Although much progress has been made in understanding the pathogenesis of the disease and establishing diagnostic criteria and treatment recommendations, mastocytosis still remains a diagnostic challenge for physicians.

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