

Intertriginous maculopapular mastocytosis in a patient with acute myeloid leukemia



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INTRODUCTION

Maculopapular cutaneous mastocytosis (MPCM) is the clinical variant of cutaneous mastocytosis (CM) most frequently observed in adults, usually within the context of an indolent systemic mastocytosis (SM). Few cases of an unusual form of MPCM affecting the intertriginous areas have been described. Here, we present a case of SM with intertriginous cutaneous involvement in a woman with hematologic disease.

CASE

A 68-year-old woman presented with a 1-year history of slowly developing asymptomatic persistent exanthema in the intertriginous areas, affecting first the axillae and then months later the groins and submammary region. Clinical examination revealed numerous symmetrically distributed red-to-brown macules, up to 1 cm in diameter in the axillae, groins, and submammary regions (Figs 1 and 2). Darier sign was negative.

The patient was being followed in the hematology department for 3 years for chronic myelomonocytic leukemia (CMML), which transformed into acute myeloid leukemia M5 four months before our clinical evaluation.

Skin biopsy was performed showing mild acanthosis and perivascular infiltrates in the superficial dermis consisting of wide granular cytoplasmic cells identified as mast cells. In the reticular dermis, mild fibrosis and vascular proliferation were found. Immunohistochemical studies revealed positivity of CD117, CD2, and tryptase (Fig 3).

Abbreviations used:

AHNMD:	associated clonal hematologic non-mast cell lineage disease
CM:	cutaneous mastocytosis
CMML:	chronic myelomonocytic leukemia
MPCM:	maculopapular cutaneous mastocytosis
SM:	systemic mastocytosis

Bone marrow biopsy showed signs of progression of the disease but no clear mast cell infiltrates, so serum tryptase levels were not measured. Finally, the presence of the D816V mutation in *c-KIT* was assessed, and cells in the bone marrow and peripheral blood were found positive.

After completing a first chemotherapy cycle, reinduction, and consolidation chemotherapy, the patient underwent complete remission of the acute leukemia, and the cutaneous lesions gradually faded (Fig 4).

DISCUSSION

Only 6 cases of MPCM limited to intertriginous areas have been described.^{1,2} Four of these cases, like ours, occurred in elderly women with scattered multiple symmetrical small macules and papules in these areas. The other 2 reported cases were in a Chinese adolescent with lesions in groins and axillae² and an infant with few large lesions exclusively present in one axilla, which was consistent with multiple mastocytoma.³ Only 1 of these cases showed extracutaneous disease with discrete bone marrow involvement.¹

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Fig 1. Numerous erythematous-to-brown macules grouped at the axilla.



Fig 2. Intertriginous maculopapular mastocytosis affecting the submammary region.

None of the previously reported cases was associated with hematologic disease. In our case, the patient was suffering from a CMML, which transformed into acute myeloid leukemia months after the initiation of the CM.

In a recent consensus, CM has been classified into 3 categories: solitary CM, diffuse CM, and MPCM. This last one is subdivided in 2 variants: polymorphic, typically observed in children, and

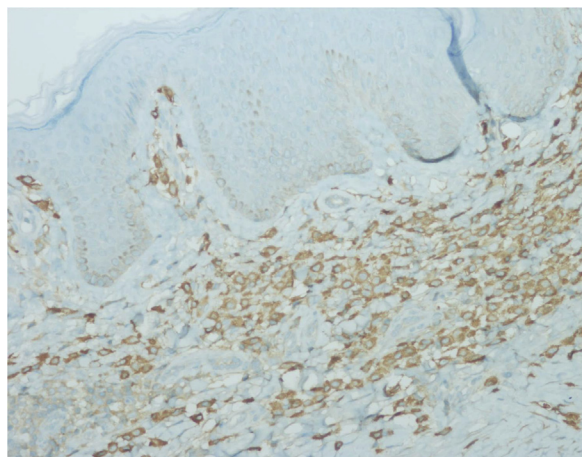


Fig 3. Histochemical staining of region affected by intertriginous maculopapular mastocytosis. There is mild acanthosis and a perivascular infiltrate in the superficial dermis staining positive for tryptase. (Original magnification: $\times 40$.)



Fig 4. Reduction in maculopapular mastocytosis lesions at the axilla after 5 months.

monomorphic, in adults.⁴ Adult-onset MPCM usually manifests as SM, most frequently indolent SM. It has been observed that in advanced SM (namely SM with an associated clonal hematologic non—mast cell lineage disease [AHNMD] or aggressive SM) the cutaneous lesions tend to show confluence,⁴ as our patient did in the intertriginous areas. The reason why the lesions were limited to these areas remains obscure. A possible explanation is that in

these areas friction would cause a certain degree of inflammation, with release of cytokines that would be chemotactic for mast cells.

Concerning the diagnosis of SM, it has been shown that the highly sensitive *KIT* D816V mutation analysis in peripheral blood might be especially useful in patients that do not fulfill the required diagnostic criteria for the recognition of SM with a low mast cell burden.^{5,6} By this method, some studies have found that nearly all patients with adult-onset CM had, in fact, systemic mastocytosis with cutaneous involvement.^{6,7}

In approximately 5% to 40% of SM cases, concomitant AHNMD is diagnosed⁸ and in most of them a myeloid malignancy is found, as in our patient. The mast cell aggregates in the bone marrow might become obscured by the non—mast cell proliferation but later become more apparent after therapy-induced aplasia or repopulation of the marrow by normal hematopoietic elements. A high frequency of D816V *KIT* mutations in the non—mast cell component has been observed in patients with SM associated with CMML.^{9,10} This suggests that these patients might have mast cells and myeloid cells that arise from a chromosomally altered, *KIT*-mutated stem cell that retains a degree of lineage plasticity, making it capable of differentiating into both cell lineages.

To conclude, we present a rare case of intertriginous MPCM in a patient with CMML, which transformed into acute myeloid leukemia M5.

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