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Systemic mastocytosis associated with chronic myelomonocytic leukemia and xanthogranuloma

Philipp Tschandl, M.D.[1], Leonhard Müllauer, M.D.[2], Harald Kittler, M.D.[1]

[1] Department of Dermatology, Division of General Dermatology, Medical University of Vienna, Austria
[2] Department of Pathology, Medical University of Vienna

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Corresponding author: Harald Kittler, M.D., Department of Dermatology, Division of General Dermatology, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria. Tel. +43.40400.7700; Fax. +43.1.408.1928. E-mail: harald.kittler@meduniwien.ac.at.

ABSTRACT A patient with a history of non-diagnostic bone marrow biopsies presented with a red to brown maculopapular rash on the back. Biopsies confirmed multiple xanthogranulomas as well as a mastocytosis. A consequently performed bone marrow biopsy verified a systemic mastocytosis and a chronic myelomonocytic leukemia (CMML) type I.
Here, we describe for the first time in the literature a patient with three diseases occurring synchronously: CMML, xanthogranulomas and systemic mastocytosis. Two of them at a time are known to be associated and may be indicative of a common progenitor cell.

Introduction

Xanthogranulomas, mastocytoses and chronically myelogenous leukemias are known to be associated with each other. We herein report a case where all three entities are diagnosed within a single patient synchronously.

Case report

The patient presented is a 61-year-old man with several past bone marrow biopsies that never confirmed a suspected hematologic neoplasm. During diagnostic work-up of diabetes insipidus the patient was presented to our department with a rash that had been persistent and undiagnosed for about a year. The rash spread over the whole back and showed red-to-brown macular and papular eruptions with a few small nodules (Figure 1A). The Darier's sign was positive (Figure 1B). Histopathology confirmed the clinical suspicion of a mastocytosis (Figure 2). Additionally, a biopsy of a papular lesion (Figure 3) showed a xanthogranuloma (Figure 4). Several other papules were also identified as xanthogranulomas (Figure 3A, B), as they had exactly the same dermatoscopic appearance. Auxiliary studies raised the suspicion of systemic involvement of the mast cell disorder: a significant amount (>10%) of CD20-positive cells in the biopsied mastocytosis,

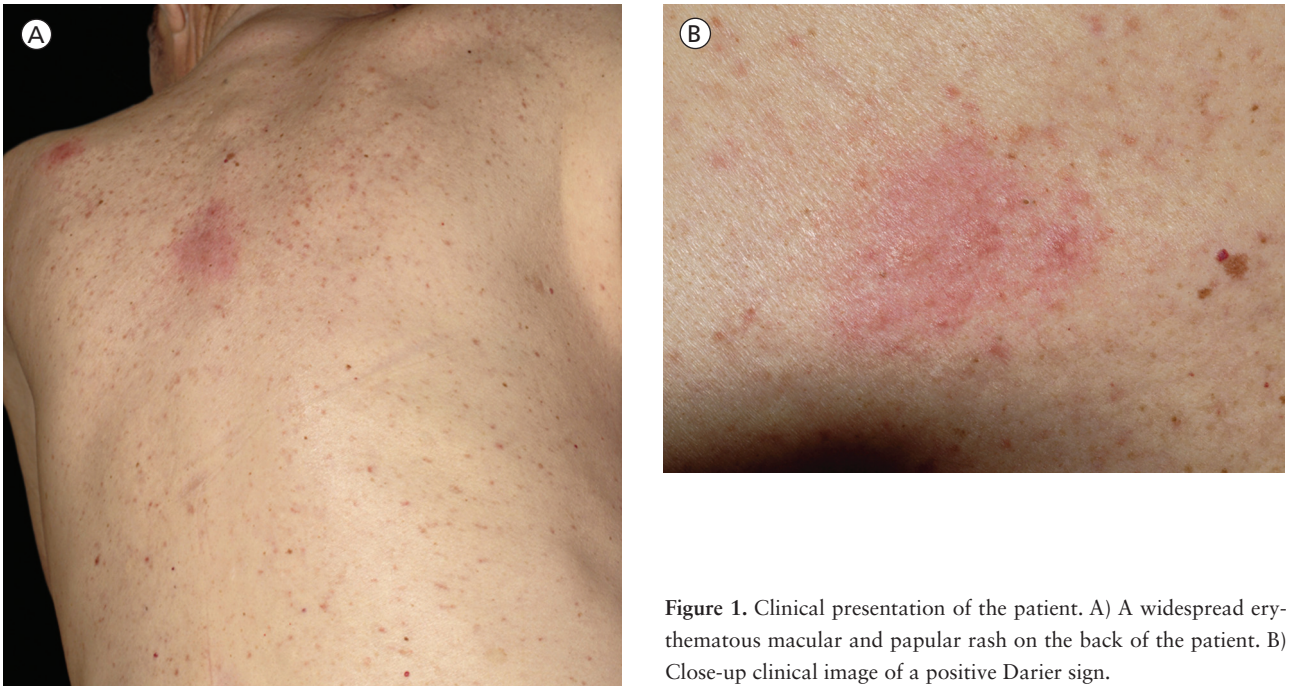

Figure 1. Clinical presentation of the patient. A) A widespread erythematous macular and papular rash on the back of the patient. B) Close-up clinical image of a positive Darier sign.

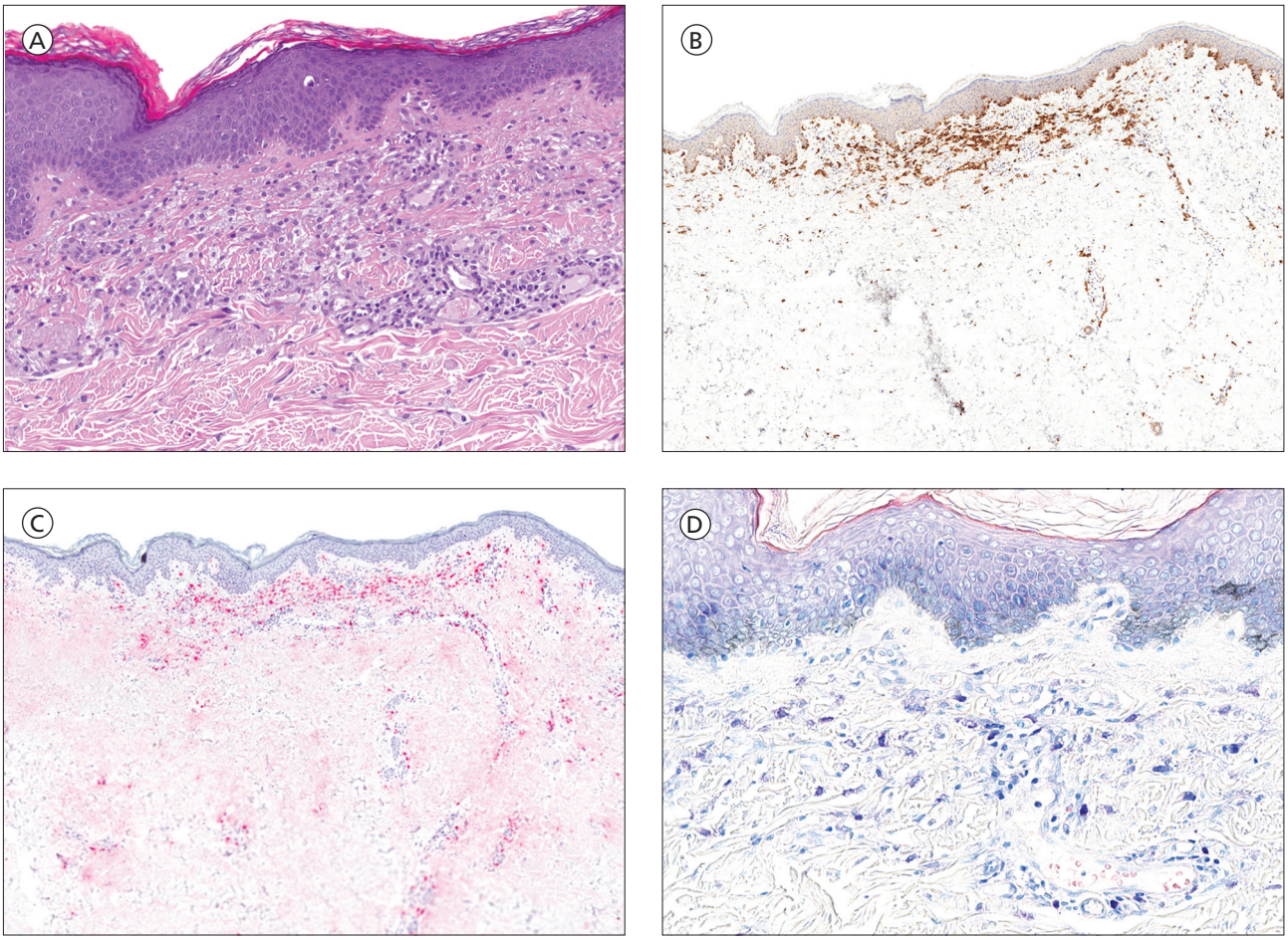

Figure 2. Histopathologic images of the mastocytosis. A) Hematoxylin and eosin (H&E). B) CD117 / c-KIT—Immunohistochemistry. C) Tryptase. D) Giemsa.

a raised serum-tryptase level (27,4µg/ml), and chronic diarrhea [1]. The consequently performed bone marrow biopsy showed a neoplastic mast cell infiltrate confirming the diagnosis of systemic mastocytosis and an increase of neoplastic monocytes consistent with the diagnosis of a chronic myelomonocytic leukemia type I (images not shown). The patient was transferred back to the hemato-oncology department, where he received a treatment with 5-azacitidine.

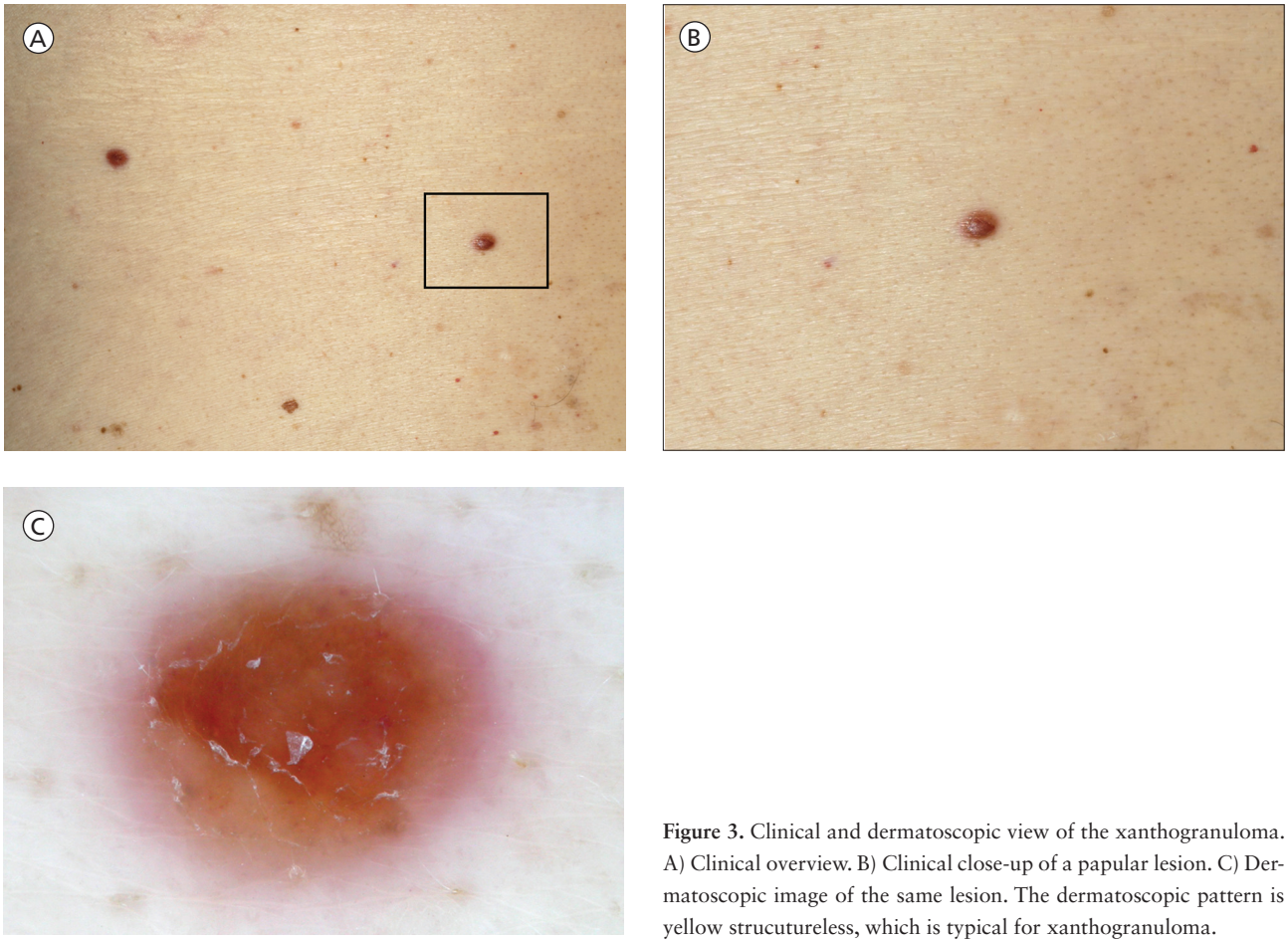

Figure 3. Clinical and dermatoscopic view of the xanthogranuloma. A) Clinical overview. B) Clinical close-up of a papular lesion. C) Dermatoscopic image of the same lesion. The dermatoscopic pattern is yellow strucutureless, which is typical for xanthogranuloma.

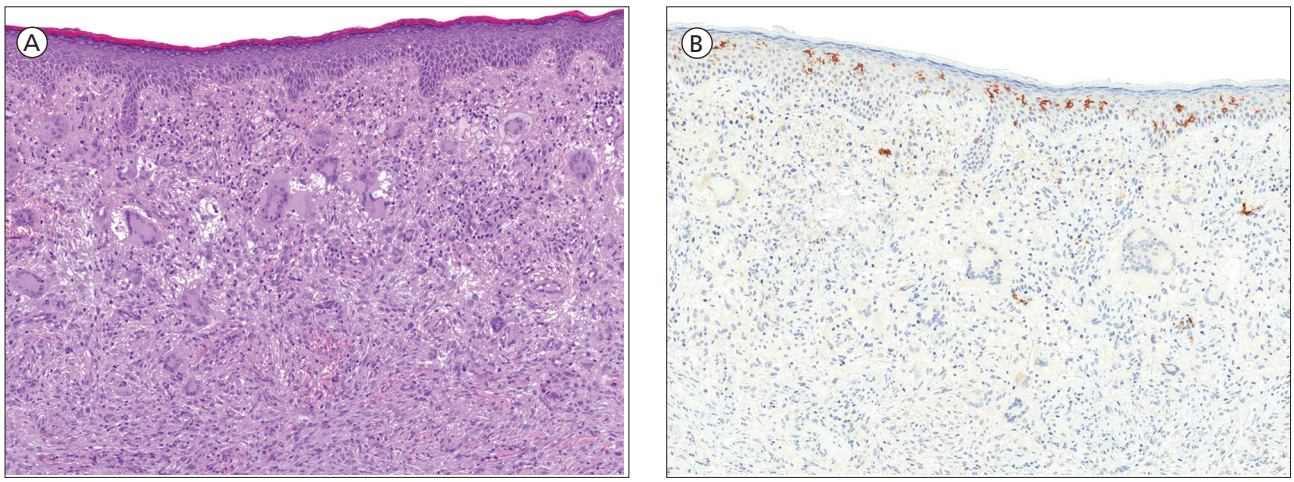

Figure 4. Histopathologic images of the lesion shown in Figure 3. A) H&E: A collection of lipid-laden macrophages and multinucleated giant cells, mostly of Touton type, in the dermis. B) Immunohistochemistry for CD1a: The macrophages were positive for CD68 (not shown) but negative for CD1a.

Discussion

Systemic mastocytosis is frequently associated with hematologic neoplasms not confined to the mast cell lineage [2,3], accompanied by a drastically reduced life expectancy [4,5]. Among these associated disorders, chronic myelomonocytic leukemia (CMML) is the most frequent with a median survival of 15 months [5]. Given these numbers, it is obvious that the diagnosis of an associated hematologic disorder should be made as early as possible to deliver proper therapy to these patients. Unfortunately the options for treating an associated CMML are limited. The patient received 5-azacitidine, a hypomethylating agent that has been tested in a small group of patients with good response [6,7].

Xanthogranulomas, especially of the juvenile type, have been reported to be associated with CMML, in particular,

when the patient also suffers from neurofibromatosis type I [8-10]. Mastocytosis can also be associated with xanthogranulomas and with CMML [11,12]. The challenge in this case was to sort out the different diagnoses clinically. The positive Darier sign (Figure 1B) helped to confirm the diagnosis of mastocytosis, but the clinical and dermatoscopic appearance of the papular lesion was not consistent with mastocytosis. On dermatoscopy the papule showed a yellow structureless pattern (Figure 3C). This pattern is typical for xanthogranulomas [13]. In metaphorical language it has also been termed "setting sun" pattern, but we consider this metaphor dispensable.

In this report we present a patient with three different diagnoses, namely xanthogranulomas, systemic mastocytosis and chronic myelomonocytic leukemia, occurring synchronously, which, to our knowledge, has never been described before. This could be a hint that monocytes and mast cells may share some kind of progenitor cell in hematopoiesis.

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