

Although the pathophysiologic relationship between mast cell proliferation and associated hematologic malignancies is not well established, some lineage distribution studies of the c-kit D816V mutation suggest the existence of a common pluripotent hematopoietic stem cell in most patients.² In some cases, however, it is possible that the 2 clonal hematologic disorders may develop coincidentally in the same patient.²

When we talk about SM, we tend to think of asymptomatic mast cell infiltration in bone marrow or the rare aggressive forms of mastocytosis. However, we must also be aware of the possibility of association with other hematologic malignancies, as the case of essential thrombocythemia in our patient illustrates. The prognosis of indolent mastocytosis associated with clonal hematologic non-mast-cell lineage disease depends on the type of associated hematologic disorder. Cutaneous manifestations of mastocytosis can therefore be considered possible markers of a more severe associated hematologic disorder that may require specific treatment.

All adult patients with mastocytosis should undergo a bone marrow study that includes mutational analysis and mast cell immunophenotyping. These patients require clinical follow-up not only because of the risk of developing aggressive forms of SM but also because of the risk of associated hematologic malignancies.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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J. Marcoval

Servei de Dermatologia, Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Barcelona, Spain

E-mail address: jmarcoval@bellvitgehospital.cat

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Dermatomyositis-like Eruption in a Woman Treated With Hydroxyurea[☆]



Erupción dermatomiositis-like en una paciente tratada con hidroxiurea

To the Editor:

Dermatomyositis is an idiopathic inflammatory myopathy that usually progresses with inflammation of the skin and skeletal muscle. However, there are hypomyopathic and amyopathic forms that progress without laboratory

abnormalities and/or muscle weakness, respectively.^{1,2} While the cause is not generally known, some forms can be induced or exacerbated by drugs.³ We report a case of dermatomyositis-like eruption with no muscle involvement associated with hydroxyurea and review specific immunological, clinical, and epidemiological findings.

The patient was a 63-year-old woman diagnosed with essential thrombocytopenia who had been receiving treatment with hydroxyurea since 2010. She was evaluated at the dermatology clinic for a 3-year history of erythematous, scaly lesions on the dorsum of the interphalangeal and metacarpophalangeal joints of the hands, dorsum of the feet, elbows, knees, and presternal area (Fig. 1). No muscular weakness or other remarkable cutaneous or mucosal manifestations were observed.

The histopathology findings are shown in Figure 2. The laboratory workup revealed normal results for inflammatory parameters and muscle enzymes. Negative results were recorded for myositis-specific antibodies (anti-Mi2, anti-MDA5, anti-SAE, anti-TIF, anti-NXP-2, anti-t-RNA-synthetase, anti-PMS, anti-SSA/Ro, anti-U1RNP, anti-Pm-Scl, and anti-Ku) and for antinuclear antibodies.

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Figure 1 A, Periorbital heliotrope rash. B, Prominent periungual telangiectases. C, Erythematous, scaly plaque on the knee. D, Erythematous, scaly lesions on the dorsum of the interphalangeal and metacarpophalangeal joints. E, Erythematous, scaly plaque on the buttocks. F, Erythematous, scaly lesions on the dorsum and lateral aspect of the feet.

Table 1 Main Differences Between Hydroxyurea-Associated DM-like Eruption and DM Caused by Other Drugs.

	Hydroxyurea-Associated DM	DM Associated With Other Drugs
Median age at diagnosis	61	50
Median time since administration of drug until onset of DM, mo	60	2
Positive ANA titer, %	16	54
Muscular symptoms, %	0	79
Underlying neoplasm, %	69	18
Treatment	Suppression of the drug	Suppression of the drug ± immunosuppressant

Abbreviations: ANA, antinuclear antibodies; DM, dermatomyositis. Source: Seidler and Gottlieb.⁵

On the basis of these findings, the patient was diagnosed with dermatomyositis-like eruption secondary to treatment with hydroxyurea, and, given the hematology report, we opted to suspend treatment. The lesions were in remission at 3 months, although the increased platelet count obliged us to reintroduce the medication, thus exacerbating the lesions again.

Dermatomyositis secondary to drugs is an uncommon condition. The drugs involved include hydroxyurea, statins, terbinafine, and anti-tumor necrosis factor agents.^{3,4} With no distinctions between drugs, the forms induced by medications carry a 39% risk of muscle involvement, which is lower than in the classic forms, and up to 50% of patients also have cancer or an underlying autoimmune disease. Furthermore, the disease usually affects patients taking multiple medications for their underlying condition.⁵ Consequently, diagnosis is truly challenging for 2 reasons: it is difficult to determine which drug is involved and it is complicated to determine whether dermatomyositis is related to the drug or

to the underlying cancer or rheumatic disease. In addition, given that paraneoplastic dermatomyositis is amyopathic in almost 60% of cases⁶ and that muscle involvement in drug-related forms is uncommon, the differential diagnosis is, if anything, somewhat more complex.

In the first place, it is important to know which drug is responsible. Hydroxyurea is the most commonly involved drug (50% of cases)⁴ and presents specific features with respect to other drugs, as shown in Table 1.⁵ In clinical terms, in addition to the typical cutaneous manifestations of classic dermatomyositis, the presence of cutaneous-mucosal manifestations associated with hydroxyurea (eg, xerosis, atrophy, stomatitis, ulceration, and melanonychia) is habitual.³⁻⁵ Histopathology findings are indistinguishable from those found in classic dermatomyositis, although, in some cases, there have been reports of changes suggestive of hydroxyurea-induced squamous dysplasia, such as keratinocyte atypia and overexpression of p53. According to some authors, the condition carries a risk of progression to

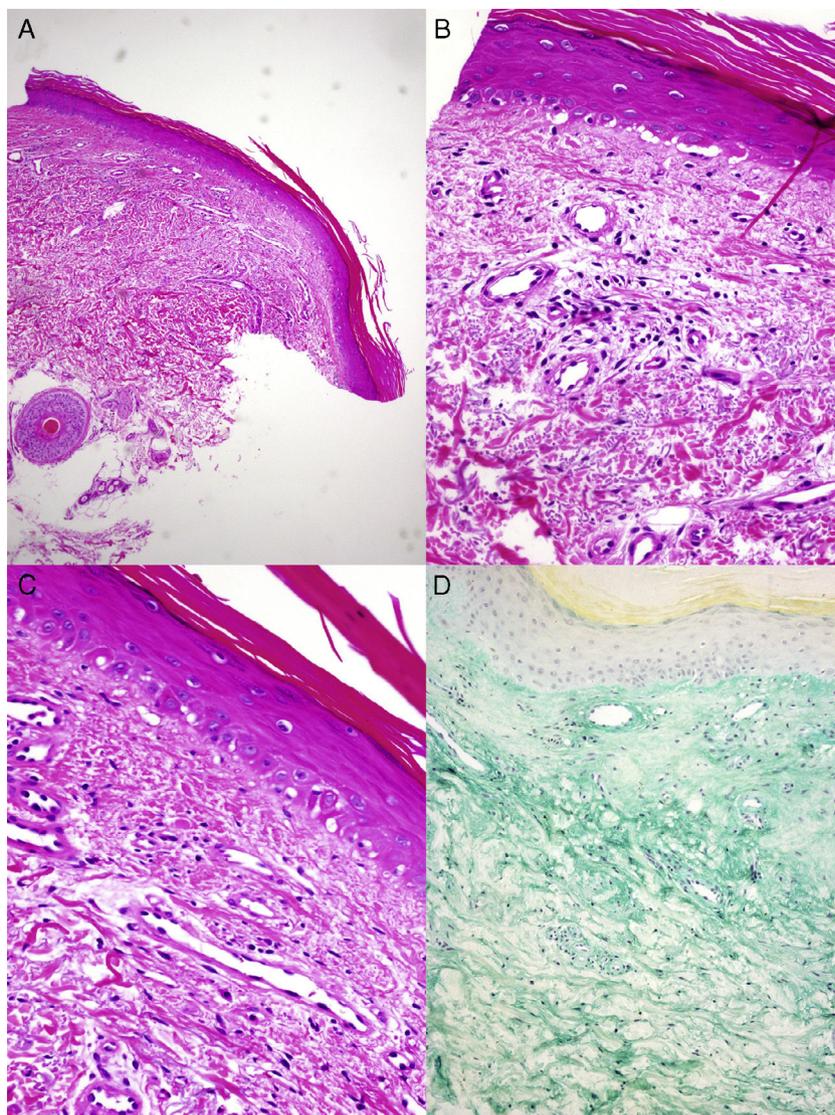


Figure 2 A and B, Histopathology reveals parakeratosis, mild epidermal atrophy, lymphocytic exocytosis, and foci of vacuolization in the basement layer, with occasional apoptotic keratinocytes (hematoxylin-eosin, original magnification $\times 4$, $\times 10$). C, Vascular proliferation and mild fibrosis in the dermis. No keratinocyte atypia or overexpression of p53 is observed (hematoxylin-eosin, original magnification $\times 20$). D, Abundant interstitial acid mucin deposits can be observed (colloidal iron, original magnification $\times 10$).

cutaneous squamous cell carcinoma, which would require close follow-up of patients in the long term and withdrawal of the drug when dermatomyositis appears.⁴

Immunosuppressive treatment is not usually necessary, and suspension of hydroxyurea is generally sufficient to achieve remission of the clinical condition. However, immunosuppressive treatment is necessary in cases secondary to other drugs.

The second challenge is to determine whether the underlying neoplasm itself or a drug is responsible for the clinical condition. This is especially difficult with hydroxyurea, since it is not associated with muscle involvement and, as we have already said, paraneoplastic dermatomyositis is amyopathic in most cases.⁶ The most indicative parameter for differentiating this condition seems to be the time between onset of dermatomyositis and diagnosis of the

tumor. Paraneoplastic symptoms generally appear during the first 2 years after diagnosis of the tumor, especially during the first 7 months. In the case of drug-associated cases, only 37% are diagnosed during the first 3 years, whereas 78% appear during the first 5 years.⁵ In the present case, the interval was 40 months, which is far from the mean time reported for paraneoplastic cases.

In conclusion, dermatomyositis-like eruption associated with hydroxyurea is not a true myopathy for 2 reasons: first, it is not an immune-mediated condition, as seen in the low frequency of antinuclear antibodies; and second, it is not associated with muscle weakness. While the etiology is unknown, some authors defend the presence of factors other than those of the drug itself, such as the tumor in which the drug is used as treatment and the potential role of the interaction between UV radiation and hydroxyurea, which

could indicate a phototoxic reaction.^{4,5} Similarly, it is worth pointing out the risk of developing cutaneous squamous cell carcinoma.⁴ Lastly, it is important to distinguish the eruption from amyopathic paraneoplastic dermatomyositis owing to its better prognosis and different therapeutic management.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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E. Moreno-Artero,^{a,*} J.J. Paricio,^b J. Antoñanzas,^c A. España^a

^a *Departamento de Dermatología, Clínica Universidad de Navarra, Universidad de Navarra, Instituto de Investigación Sanitaria de Navarra, Pamplona, Navarra, España*

^b *Departamento de Anatomía Patológica, Clínica Universidad de Navarra, Universidad de Navarra, Pamplona, Navarra, España*

^c *Departamento de Dermatología, Clínica Universidad de Navarra, Universidad de Navarra, Pamplona, Navarra, España*

* Corresponding author.

E-mail address: emartero@unav.es (E. Moreno-Artero). 1578-2190/

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Allergic Contact Dermatitis Due to Methyl Glucose Dioleate in a Balm Cream[☆]



Eczema alérgico de contacto por metil glucosa dioleato contenido en una crema balsamo

To the Editor:

Methyl glucose dioleate (MGD) is a polyethylene glycol used as an emulsifier or surfactant that is considered nonirritant and nonsensitizing on healthy skin.

We report the case of a 12-year-old girl referred to the dermatology clinic with very pruriginous lesions that had first appeared on the axillas and, in just a few days, spread to the arms, trunk, neck, and face. Her parents reported that 3 days previously they had applied a balm cream (Mustela) on the axillas for erythema that had appeared after application of a depilatory cream.

The physical examination revealed erythematous, scaly plaques on both axillas. They affected the skin folds and spread less intensely to the areas described above (Fig. 1).

The lesions disappeared after 10 days with the application of topical corticosteroids.

We performed a use test with both the depilatory cream and the balm cream that the patient had used, by applying

both products twice daily at the same site on the forearm. The only reaction observed was with the balm cream 3 days after application.

We performed patch tests with the standard series of the Spanish Contact Dermatitis and Skin Allergy Research Group



Figure 1 Erythematous, scaly plaques on the axillas.

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