

# UC Davis

## Dermatology Online Journal

### Title

Hydroxyurea-induced amyopathic dermatomyositis presenting with heliotrope erythema

### Permalink

<https://escholarship.org/uc/item/2r11f768>

### Journal

Dermatology Online Journal, 20(8)

### Authors

Ito, Eri  
Muro, Yoshinao  
Shibata, Akitaka  
[et al.](#)

### Publication Date

2014

### DOI

10.5070/D3208023534

### Copyright Information

Copyright 2014 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

**Case Presentation**

**Hydroxyurea-induced amyopathic dermatomyositis presenting with heliotrope erythema**

**Eri Ito MD, Yoshinao Muro MD PhD, Akitaka Shibata MD, Kazumitsu Sugiura MD PhD, Masashi Akiyama MD PhD**

**Dermatology Online Journal 20 (8): 10**

**Department of Dermatology, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550, Japan**

**Correspondence:**

Yoshinao Muro, MD, PhD

Division of Connective Tissue Disease & Autoimmunity, Department of Dermatology,  
Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku,  
Nagoya, 466-8550 Japan

Tel: 81-52-744-2314 / Fax: 81-52-744-2318

E-mail: [ymuro@med.nagoya-u.ac.jp](mailto:ymuro@med.nagoya-u.ac.jp)

**Abstract**

Hydroxyurea (HU) is a chemotherapeutic agent used for the treatment of myeloproliferative disorders such as chronic myeloid leukemia, polycythemia vera, and essential thrombocytosis. We describe a 69-year-old man who had essential thrombocytosis and developed amyopathic dermatomyositis after long-term HU therapy. He presented with Gottron papules and heliotrope erythema. The former has been described in all cases of HU-induced dermatomyositis; the latter has been seen in a few cases of that disorder.

**Keywords: dermatomyositis, Gottron papule, heliotrope erythema, hydroxyurea**

**Case synopsis**

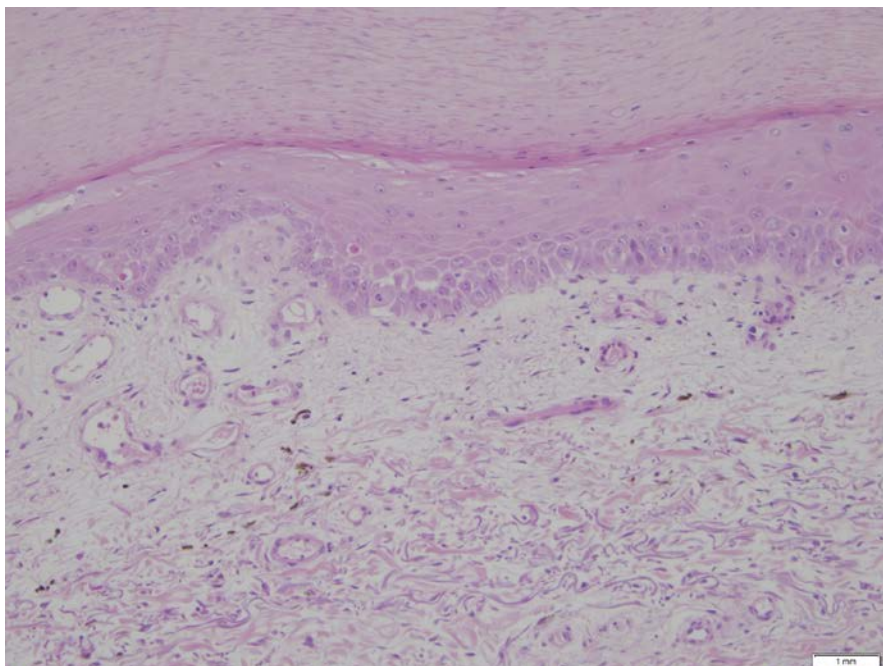
Hydroxyurea (HU) is a chemotherapeutic agent used for treating myeloproliferative disorders such as chronic myeloid leukemia, polycythemia vera, and essential thrombocytosis. It inhibits DNA synthesis by deactivating ribonucleoside diphosphate reductase [1]. Predominant adverse reactions associated with HU include bone marrow suppression and gastrointestinal tract symptoms. Cutaneous adverse reactions have been reported in 10-35% of patients treated with HU [2]. We report a patient with essential thrombocytosis who developed a dermatomyositis (DM)-like eruption after long-term HU therapy.

A 69-year-old man was referred to our department from our hospital's department of general medicine for evaluation of an eruption on his hands and an external condyle ulcer. He had received oral HU at 1-1.5 g/day for treatment of essential thrombocytosis that had been diagnosed ten years previously. For five years, non-pruritic scaling erythema on the dorsa of the hands had gradually increased. Six months before the referral, the patient had complained of painful ulcers on his foot that interfered with walking. There was no history of muscle weakness, dysphagia, or joint pain. He had received no other drugs that could induce a DM-like illness, such as statins.

Skin examination of the dorsa of the hands revealed atrophy, depigmentation, and scaly erythematous plaques on the dorsa of all finger joints (Figure. 1A). Such lesions were indistinguishable from Gottron papules, pathognomonic lesions of classic DM. There was also periorbital erythema resembling "heliotrope erythema" (Figure. 1B). Laboratory tests revealed normal levels of creatine phosphokinase; the anti-nuclear antibody test was negative. Histopathological examination of a skin biopsy taken from one of the violaceous papules on the dorsal hand revealed hyperkeratosis, parakeratosis, atrophy of the epidermis, individual cell keratinization, and mild inflammatory cell infiltrates (Figure. 2). Although the dose of HU was reduced to 0.5 g/day, the Gottron papules and heliotrope erythema lesions persisted; the refractory leg ulcer improved slightly after half a year.



**Figure 1. Clinical images of the dorsal hands and face.** A: Scaly erythematous plaques on the dorsa of all joints; Gottron papules B: Heliotrope erythema around the eyes and photosensitivity



**Figure 2. Histological image of a skin biopsy specimen.** The specimen was taken from the dorsal hand (hematoxylin & eosin ×200). Hyperkeratosis, parakeratosis, atrophy of the epidermis, individual cell keratinization, and mild inflammatory cell infiltrates are observed.

## Discussion

HU appears to affect DNA synthesis and cell replication by inhibiting the conversion of ribonucleotides to deoxyribonucleotides. The major adverse reaction, bone marrow suppression, is reversible and dose-dependent [3]. Cutaneous eruptions of patients who undergo HU treatment include pigmentation, ulcerations, ichthyosis, alopecia, skin atrophy, and palmoplantar keratoderma [4]. Various drugs, including D-penicillamine, NSAIDs, and anti-infectious agents, as well as HMG-CoA reductase inhibitors, are known to cause DM-like skin lesions [5]. HU-induced DM is basically differentiated from classic DM by the absence of muscle weakness and by the normal levels of muscle enzymes. The latency of onset and slow progression, together with subsequent healing after withdrawal of the culprit drug, are suggestive of chronic cumulative damage to the basal layer of the epidermis [2, 6].

Clinical features of HU-induced DM-like eruptions are varied. Gottron papules are frequently seen, although heliotrope-like erythema has rarely been reported in the literature [7, 8]. Jenerowicz *et al.* [2] described erythema on the dorsal hand and reddish-purple periorbital erythema resembling “heliotrope erythema” in a 74-year-old man treated with HU for less than 2 years for polycythemia vera. Oskay *et al.* [9] described reddish-purple patches of the eyelids and erythema on the dorsal hands of a 69-year-old man treated with HU for 2 years for polycythemia vera. In our case, the 5-year latency from the beginning of HU treatment to the onset of the skin lesions was much longer than those in previously reported cases. The fact that the reduction in HU dose produced only moderate improvements in the eruptions may be attributable to the more intensive damage to the epidermis resulting from the longer period of HU intake.

It is often difficult to differentiate drug-induced amyopathic DM from idiopathic DM, even with histopathological study. We should keep in mind delayed adverse reactions of HU, including DM-like pathognomonic eruptions. Although the concept of hydroxyurea ‘causing’ dermatomyositis is certainly not new, we should occasionally remind practitioners of cases such as the one in this report.

## References

1. Nofal A, El-Din ES. Hydroxyurea-induced dermatomyositis: true amyopathic dermatomyositis or dermatomyositis-like eruption? *Int J Dermatol.* 2012 May;51(5):535-41. [PMID:22515579]
2. Janerowicz D, Czarnecka-Operacz M, Stawny M, Silny W. Dermatomyositis-like eruption induced by hydroxyurea: a case report. *Acta Dermatovenerol Alp Panonica Adriat.* 2009 Sep;18(3):131-4. [PMID:19784527]
3. Senet P, Aractingi S, Porneuf M, Perrin P, Duterque M. Hydroxyurea-induced dermatomyositis-like eruption. *Br J Dermatol.* 1995 Sep;133(3):455-9. [PMID:8547004]
4. Oh ST, Lee DW, Lee JY, Cho BK. Hydroxyurea-induced melanonychia concomitant with a dermatomyositis-like eruption. *J Am Acad Dermatol.* 2003 Aug;49(2):339-41. [PMID:12894095]
5. Seidler AM, Gottlieb AB. Dermatomyositis induced by drug therapy: a review of case reports. *J Am Acad Dermatol.* 2008 Nov;59(5):872-80. [PMID:18625537]
6. Haniffa MA, Speight EL. Painful leg ulcers and a rash in a patient with polycythaemia rubra vera. Diagnosis: hydroxyurea-induced leg ulceration and dermatomyositis-like skin changes. *Clin Exp Dermatol.* 2006 Sep;31(5):733-4. [PMID:16901329]

7. Vassallo C, Passamonti F, Merante S, Ardigò M, Nolli G, Mangiacavalli S, Borroni G. Muco-cutaneous changes during long-term therapy with hydroxyurea in chronic myeloid leukaemia. *Clin Exp Dermatol*. 2001 Mar;26(2):141-8. [PMID:11298103]
8. Varma S, Lanigan SW. Dermatomyositis-like eruption and leg ulceration caused by hydroxyurea in a patient with psoriasis. *Clin Exp Dermatol*. 1999 May;24(3):164-6. [PMID:10354169]
9. Oskay T, Kutluay L, Ozyilkan O. Dermatomyositis-like eruption after long-term hydroxyurea therapy for polycythemia vera. *Eur J Dermatol*. 2002 Nov-Dec;12(6):586-8. [PMID:12459535]