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### OBJECTIVE

To highlight a case of lower extremity ulceration in the setting of long term therapeutic use of hydroxyurea in order to identify this common place consequence of hydroxyurea therapy

### INTRODUCTION

Hydroxyurea is a cytostatic agent that inhibits DNA synthesis and is a standard drug in the treatment of chronic myeloproliferative disorders including polycythemia. However, long-term hydroxyurea use has been implicated in the development of ulcerations, with lower extremities being one of the most common areas [1]. It has been reported that individuals can develop ulcers on the lateral malleolus 5 years or more after treatment initiation [2]. The recognition of ulcers with chronic usage of hydroxyurea is of significant relevance.

Another pathologic mechanism is the increase in mean corpuscular volume seen after hydroxyurea treatment, increasing hyperviscosity and the risk of ulceration formation. Additionally, hydroxyurea has also been shown to damage basal keratinocytes and affect collagen synthesis, which could explain some of the other dermatologic side effects of continued treatment.

### CASE

57-year-old with history of polycythemia vera managed by hematology with hydroxyurea presented with a solitary ulcer located on the lateral malleolus. The patient had been taking hydroxyurea for six years. Physical exam revealed well-circumscribed ulcer with a hyperpigmented border and central white-yellow exudative tissue. In consultation with hematology, his hydroxyurea was discontinued. He was subsequently initiated on anagrelide, a platelet-lowering substitute. Local wound care was initiated with topical antibiotic mupirocin, along with topical Vaseline. In addition, Mepilex bandage was applied and compression hosing was recommended. After initial improvement with resolution of yellow crusted debris, mupirocin was discontinued. After 3 months, his ulcer fully re-epithelialized.



**Figure 1 and 2: Clinical Presentation** Relatively well-circumscribed ulcer on the left lateral malleolus with a hyperpigmented border around central white-yellow granulation tissue with associated swelling of the left ankle

### DISCUSSION

Hydroxyurea (HU) is a cytostatic agent that inhibits DNA synthesis and is a standard drug in the treatment of chronic myeloproliferative disorders, including polycythemia. Long-term hydroxyurea use has been implicated in the development of cutaneous ulcers [1]. These ulcerations are usually found in the perimalleolar region, but are occasionally found on the forearms, hands, and face [4]. Ulcer development is associated with chronic, cumulative exposure to hydroxyurea; prior studies suggest that the median duration of HU therapy before ulcer formation is about 51 months [5]. The recognition of ulcers with chronic hydroxyurea use is of significant relevance, as cessation of the drug is typically indicated. Megaloblastic changes in deformability due to hydroxyurea may prevent RBCs from easily traversing capillaries, resulting in ischemia in the basal layer of skin [6,7].

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