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Hydroxyurea - Induced Non-Healing Leg Ulcer in a Patient with Essential Thrombocythemia: A Case Report

Dr. Aman Kumar

D.N.B Medicine, Sardar Vallabh Bhai Patel Hospital, New Delhi,India
Email:masteramankumar@gmail.com

Abstract

Hydroxyurea is a first-line cytoreductive agent for high-risk essential thrombocythemia (ET) due to its efficacy in reducing thrombotic events. Although generally well tolerated, long-term use may lead to rare cutaneous complications, notably non-healing leg ulcers. We report the case of a 52-year-old female with triple-negative ET who developed a painful ulcer above the left lateral malleolus after three years of hydroxyurea therapy. Initial evaluation, including venous Doppler, ruled out vascular pathology. Despite standard wound management, the ulcer progressed, prompting suspicion of a drug-induced etiology. Hydroxyurea was discontinued, and anagrelide was initiated, resulting in complete ulcer healing within three months. Hydroxyurea-induced ulcers are thought to result from cytotoxic damage to keratinocytes and endothelial cells, impairing microvascular function and delaying healing. Clinicians should maintain a high index of suspicion for drug-induced ulcers in ET patients on long-term hydroxyurea therapy to avoid unnecessary interventions. Early withdrawal of hydroxyurea and initiation of alternative agents such as anagrelide can ensure favorable outcomes.

Keywords: Hydroxyurea,Essential Thrombocythemia,Leg ulcer , Anagrelide, Drug -Induced ulcer

1. Introduction

Hydroxyurea is widely used as a first-line cytoreductive agent in high-risk essential thrombocythemia (ET), owing to its effectiveness in reducing thrombotic risk. While generally well tolerated, it may rarely lead to cutaneous adverse effects such as non-healing leg ulcers, especially with long-term use. We present a case that highlights the importance of recognizing this uncommon complication to prevent delayed healing and unnecessary interventions.

A 52-year-old female with triple-negative ET was initially prescribed hydroxyurea 500 mg twice daily, later increased to three times daily, along with low-dose aspirin (75 mg daily) for three years. Her platelet counts remained well controlled during this time. The patient presented with a painful ulcer located just above the left lateral malleolus.[Figure 1]. Initial assessment suggested a venous ulcer; however, a venous Doppler study showed no abnormalities.

Despite standard wound care, the ulcer worsened and became increasingly painful. Given the chronic course, localization over a pressure point, and normal vascular studies, a drug-induced etiology was considered. Hydroxyurea was discontinued, and anagrelide 0.5 mg twice daily was initiated. Over the following three months, the ulcer progressively healed and eventually resolved completely. The patient remained symptom-free with stable hematologic control on anagrelide.

Hydroxyurea-induced leg ulcers are a recognized but infrequent complication, affecting approximately 5–10% of long-term users [1,2]. The proposed pathogenesis involves cytotoxic injury to keratinocytes and endothelial cells, leading to microvascular compromise and impaired wound healing [3]. These ulcers often localize near pressure zones such as the malleoli, resist conventional wound care, and may be complicated by secondary infection if recognition is delayed.

Recognition of this adverse effect is vital, particularly when vascular and neuropathic causes have been excluded. Early withdrawal of hydroxyurea typically leads to complete resolution. In ET patients, anagrelide serves as an effective alternative, especially in those intolerant to hydroxyurea [4].

This case underscores the need for clinicians to maintain a high index of suspicion for drug-induced ulcers in patients on long-term hydroxyurea therapy. Timely recognition and substitution with agents like anagrelide can lead to complete ulcer resolution and prevent morbidity [Figure 2].

Figure 1: Ulcer over the left lateral malleolus.

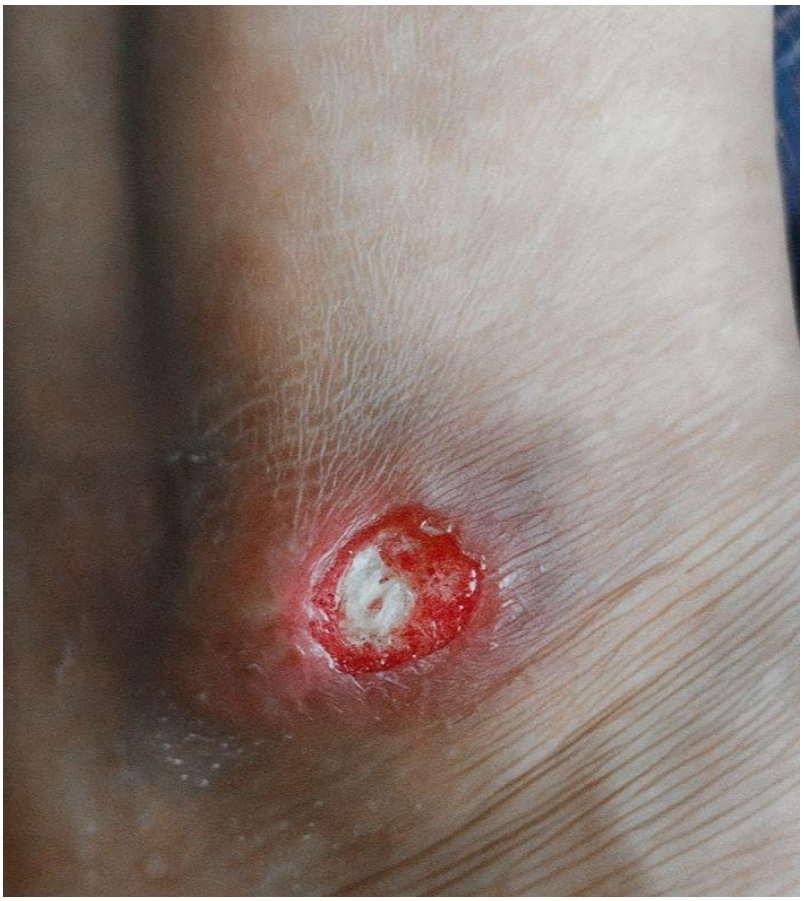
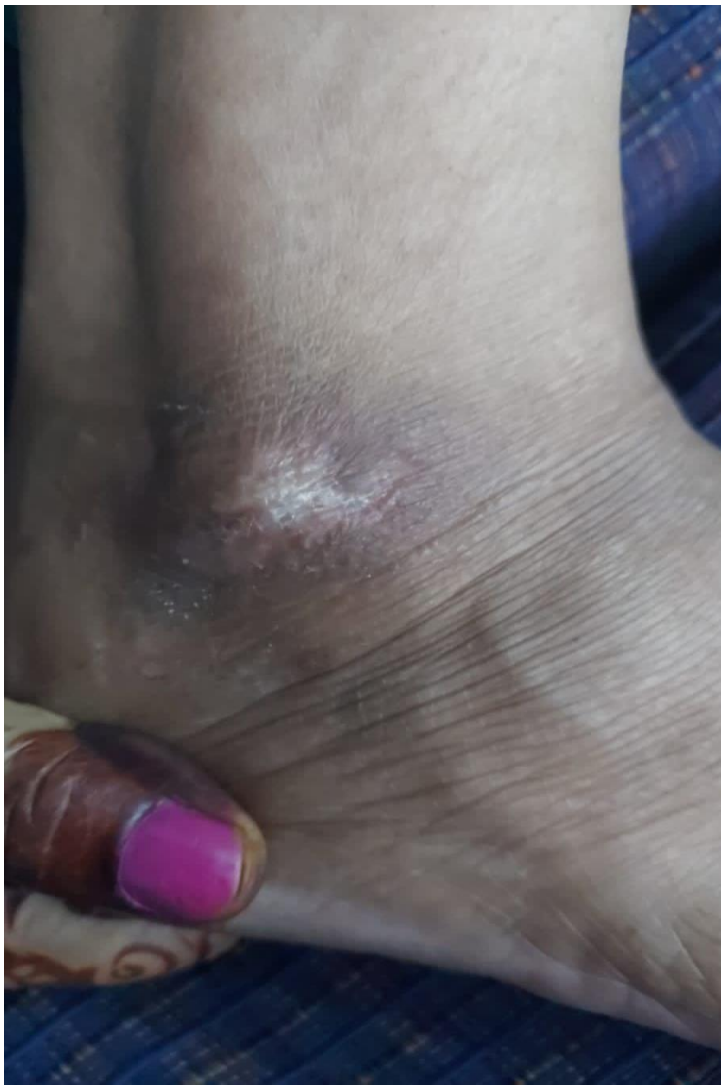


Figure 2: Healed ulcer over the left lateral malleolus following hydroxyurea cessation and initiation of anagrelide.



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Declaration of patient consent

Written informed consent was obtained from the patient for publication of th clinical information and images.