Huge post-operative ulcer following hydroxyurea therapy in a patient with polycythemia vera

A 75-year old woman was referred to our hospital due to a worsening post-operative cutaneous ulcer. She had a history of polycythemia vera and had been treated with a daily dose of 500mg hydroxyurea (HU) for six years. She underwent a right hernioplasty in another hospital in September 2002. Two days after the hernioplasty, the skin around the wound became erythematous and necrosis was observed. Even with the administration of antibiotics and debridment was performed three times, her condition deteriorated and she was referred to our hospital. On admission, a 22x15cm ulcer was observed on the lower abdomen. With termination of HU, the cutaneous ulcer became smaller and with the withdrawal of other medication, the ulcer size continued to decrease. Although post-operative cutaneous ulcer complicated by HU administration has rarely been reported, our case clearly indicates that early termination of HU should be considered when patients develop symptoms preceding cutaneous ulcer.

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Introduction. Hydroxyurea (HU) is a relatively well-tolerated antimetabolite agent used for chronic myeloproliferative disorders. Adverse effects of long term HU therapy have been reported to involve the skin and mucocutaneous membranes.[1,2] Here we describe a patient who developed a huge post-operative ulcer following HU therapy for polycythemia vera (PV). To our knowledge, there are no previous reports describing ulcer formation in a surgical wound on the abdomen.

Case report. On Octorber 1, 2002, a 75-year old woman was referred to our hospital due to a worsening post-operative ulcer. In 1996, she was diagnosed as having PV and had been receiving 500mg hydroxyurea daily for six years. She underwent right hernioplasty at another hospital in September 2002. Two days after hernioplasty, the skin around the wound developed erythema and necrosis was observed. Despite administration of antibiotics and debridement, performed three times, the ulcer extended further. Her general condition worsened and she was transferred to our hospital. On admission, a 22x15 cm cutaneous ulcer was observed on the lower abdomen. (Figure 1) Computer-assisted tomography showed that the abscess was superficial and the muscle layer was intact. Initially, she was treated with antibiotics, heparin and hyperbaric oxygen (HBO) because possible embolism related to PV might have caused the erythemia and ulcer around the wound However, these treatments did not improve the ulcer. HU was terminated on October 5th and thereafter the cutaneous ulcer became smaller. Despite withdrawal of antibiotics, heparin and HBO, the size of the ulcer continued to reduce, and even with the withdrawal of HU the leukocyte count did not increase and the red blood cell count was below 400x10^{4}μL and platelet count was

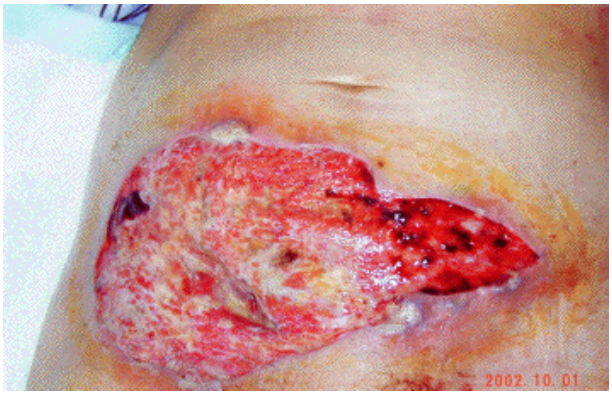

Figure 1. A 22x15 cm cutaneous ulcer was observed on the lower abdomen

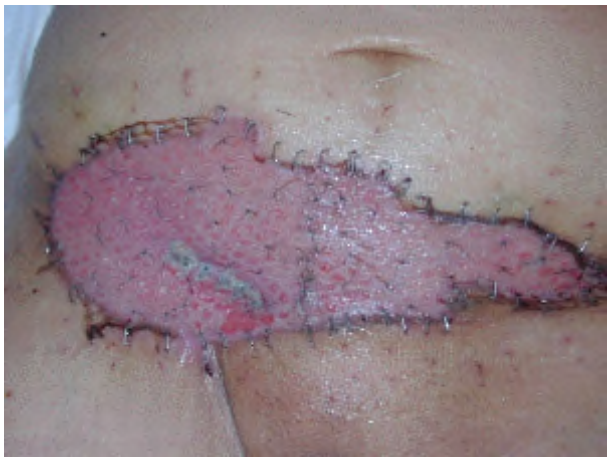

Figure 2. The size of the ulcer decreased remarkedly and it healed

100x10^4/μL. Therefore, no cytotoxic drug was administrated during the period that the patient was in our hospital. After epidermization was performed on October 18th, the ulcer was cured and she was discharged from our hospital on November 17$^{th.}$ (Figure 2) Three months after she discharged from our hospital, leukocytosis with a white blood cell count of 36600/μL and thrombocytosis of 148 x 104/μL was observed; since the control of PV became difficult without cytotoxic agents, the patient began treatment with busulfan instead of HU.

Discussion. The adverse dermatological effects of HU have been well documented. These include xerosis, diffuse hyperpigmentation, brown nail discoloration, stomatitis, erythema, and scaling of the face, hands and feet.[2,3] Since the first report by Stahl and Silber which reported bilateral leg ulcers induced by HU administration in two chronic myelogenous leukemia (CML) patients,[2] mucocutaneous ulcer has been a relatively frequently reported side effect of HU. In a prospective study, leg ulcers were reported to occur in 9% of patients taking HU medication.[6] These ulcers were completely refractory to topical or systemic therapy during hydroxyurea treatment, although the ulcers healed within variable periods of time after HU suspension.[9] Re-starting HU treatment

caused recurrence of cutaneous ulcers in patients with polycythemia vera and myeloproliferative disorders . Improvement and disappearance of these ulcers after suspension of HU strongly suggests that HU plays a crucial role in the pathogenesis of cutaneous ulcers, and the underlying hematological disorders are a less important cause of the changes.[7] There is currently no established specific treatment for HU-induced cutaneous ulcer and previous observations indicated that HU administration should be interrupted to allow healing of the ulcers.[8] Although post-operative cutaneous ulcers as a complication of the use of hydroxyurea have been reported rarely, our case clearly indicates that special attention should be paid when patients receiving HU undergo surgery. Early termination of hydroxyurea should be considered when such patients develop symptoms preceding a cutaneous ulcer.

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