CML. After an observation period of eight months following initiation of prednisone treatment, our patient is in partial remission of systemic sarcoidosis and maintains a complete cytogenetic remission of her pre-existing CML.

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Key words

Čhronic myelogenous leukemia, interferon- α *, side effect,* sarcoidosis, corticosteroids.

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References

- 1. Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med 1997; 336:1224-34.
- Pietropaoli A, Modrak J, Utell M. Interferon-α thera-2. py associated with the development of sarcoidosis. Chest 1999; 116:569-72
- Kikawada M, Ichinose Y, Kunisawa A, et al. Sarcoidosis induced by interferon therapy for chronic myelogenous leukaemia. Respirology 1998; 3:41-4. 4. Hoffman RM, Jung MC, Motz R, et al. Sarcoidosis
- associated with interferon- α therapy for chronic hepatitis C. J Hepatol 1998; 28:1058-63. Otte HG, Hartig C, Stadler R. Sarcoidosis in interfer-
- 5.
- on-alpha-therapy. Hautarzt 1997; 48:482-7. Yavorkovsky LL, Carrum G, Bruce S, Mc Carthy PL Jr. Cutaneous sarcoidosis in a patient with Philadelphia-6. positive chronic myelogenous leukemia treated with interferon-α. Am J Hematol 1998; 58:80-1
- 7. Krosi Z, Casassus P, Valeyre D, Paolaggi JA, Amouroux J, Battesi JP. Chronic myelocytic leukemia during the development of sarcoidosis. Rev Pneumol Clin 1988; 44:33-5
- 8. Banno S, Nitta M, Takada K, et al. Chronic myelogenous leukemia complicated with sarcoidosis. Rinsho Ketsueki 1993; 34:84-6.
- Wandl UB, Kloke O, Nagel-Hiemke M, et al. Combination therapy with interferon alpha-2b plus low-dose interferon gamma in pretreated patients with Ph-positive chronic myelogenous leukemia. Br J Haematol 1992; 81:516-9
- 10. Cheng DS, Kitahara M, Logan KH. Chronic granulocytic leukemia: long-term remission in a patient with familial sarcoidosis. South Med J 1979; 72:645-7.

Peri-lesional injections of granulocytemacrophage colony-stimulating factor in the management of chronic leg ulcers in type II mixed cryoglobulinemia

We report the good effects obtained with local injection of recombinant human granulocytemacrophage colony-stimulating factor (rhGM-CSF) in three patients with hepatitis C-virus related type Il cryoglobulinemia whose chronic leg ulcers, that caused pain and disability, would not heal despite the wide variety of treatments previously applied.

Sir

Mixed type II cryoglobulinemia is manifested as vascular purpura in all patients at some time during the course of the disease. Severe involvement around the malleoli often precedes the development of leg ulcers.1

Chronic leg ulcers in patients with type II cryoglobulinemia may represent a problem; the treatment is directed primarily at the underlying disease, the care of these patients is often disappointing and persistent leg ulcers often prove resistant to a plethora of local conservative measures.² Peri-lesional injections of recombinant granulocyte-macrophage colony-stimulating factor (rhGM-CSF) improved the healing of biopsy wounds in 35 patients with leprosy³ and induced the closure of Kaposi's sarcoma lesions in one patient;⁴ beneficial effects were obtained also in chronic leg ulcers of patients with hemoglo-binopathies.⁵ We report the effects of local injection of rhGM-CSF (Mielogen-Molgramostim; Schering-Plough) in three patients with hepatitis C virus (HCV)-related type II cryoglobulinemia whose chronic leg ulcers would not heal despite the wide variety of treatments applied.

Patient #1 was a 65-year old woman who had had a chronic painful ulcer on the left ankle $(3.2 \times 2.7 \text{ cm})$ for 6 months.

Patient #2 was a 62-year old woman who had had two deep ulcers, one on her left ankle $(3.7 \times 3.2 \text{ cm})$ and one on the dorsum of the left foot $(2.5 \times 2.2 \text{ cm})$, for 10 months.

Patient #3 was a 69-year old man; he had had two ulcers on his right leg (2.5×1.5 cm and 1.5×1.3 cm) for the past 3 years. All these patients had HCV-related type II cryoglobulins with non-Hodgkin's lymphoma: diffuse large cell lymphoma in complete remission (CR) for 3 years (patient #1), gastric MALT lymphoma in CR for 5 years (patient #2), immunocytoma in partial remission (patient #3).⁶ The three patients had an IgM- κ paraprotein which behaved like a cryoglobulin. Treatments with α -interferon (IFN) 3 MU three times a week for 3 months and subsequently intermediate doses of cyclophosphamide, prednisone and plasmapheresis were ineffective and the chronic ulcers caused pain and disability in all three patients. GM-CSF (Mielogen-Molgramostim; Schering-Plough) 300 mg was injected subcutaneously into four sites within the margins of the wounds, in approximately equal amounts, in the four quadrants of each ulcer, through a insulin syringe needle, twice a week for 2 months. In some instances, a small quantity of the solution was applied over the open ulcer. The injections were quite painful, but were well tolerated in all 3 patients; no other side effects were recorded and complete resolution of the ulcers was seen. In the first and second patients, the ulcers healed after 6 weeks (Figure 1); the ulcers of patient #3 required approximately 2 months to heal completely. We believe that subcutaneous peri-lesional injections of GM-CSF may play an important



Figure 1. The two chronic ulcers in patient #2 (A) before and (B) after treatment with peri-lesional injections of granulocyte-macrophage colony-stimulating factor.

role in the cure of chronic leg ulcers in patients with type II mixed cryoglobulinemia.

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Key words

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References

- Wintrobe's Clinical hematology. 9th ed. Philadelphia: 1. Lea and Febiger; 1993.
- Da Costa RM, Jesus FM, Aniceto C, Mendes M. Double-blind randomized placebo-controlled trial of the use of granulocyte-macrophage colony-stimulating factor in chronic leg ulcers. Am J Surg 1997; 173:165-
- Kaplan G, Walsh G, Guido LS, et al. Novel responses 3. of human skin to intradermal recombinant granulo-cyte-macrophage colony-stimulating factor: Langerhan's cell recruitment, keratinocyte growth and enhanced wound healing. J Exp Med 1992; 1175: 1717-28.
- 4.
- Boente P, Sampaio C, Brandao MA. Local peri-lesion-al therapy with rhGM-CSF for Kaposi's sarcoma. Lancet 1993; 341:1154-5. Voskaridou E, Kyrtsonis MC, Anagnostou AL, Loukopoulos D. Healing of chronic leg ulcers in the hemoglobinopathies with peri-lesional injections of granulocute macrophage colony stimulating factors. 5. granulocyte-macrophage colony-stimulating factors. Blood 1999; 93:3568-9.
- 6 Vallisa D, Bertè R, Rocca A, et al. Association between hepatitis C virus and non-Hodgkin's lymphoma and effects of viral infection on histologic subtype and clin-ical course. Am J Med 1999; 106:556-60.