spinal paralysis due to fungal infection. Rinsho Ketsueki 1979; 20:268-72.

Systemic sarcoidosis associated with interferon-α treatment for chronic myelogenous leukemia

We describe a patient with chronic myeloid leukemia (CML) on low-dose treatment with interferon (IFN) who developed systemic sarcoidosis, a rare IFN-related side effect, while in complete cytogenetic remission. We chose to continue IFN and to treat the sarcoidosis with prednisone. After eight months, the CML is still in complete cytogenetic remission and the sarcoidosis is almost completely resolved.

Sir,

Sarcoidosis is a systemic non-caseating granulomatous disorder of unknown etiology.1 Sarcoidosis can develop as a consequence of IFN-α therapy.2,3 The role that IFN plays in the pathogenesis of sarcoidosis is not known. Probably, it stimulates T-cells and macrophages, which produce interleukins, promoting a cascade of inflammation culminating in a granuloma.

A 49-year old female was diagnosed as having CML Ph+ in early chronic phase. The patient was started on IFN-α 3 MU/daily in August 1996. The dosage was not increased because of lack of tolerance. The patient achieved a complete hematologic remission with minor cytogenetic improvement in February 1997. The cytogenetic response was complete in May 1999. In July 1999 the patient developed cough, dyspnea on exertion and some 1-2 cm subcutaneous nodules on her right knee (Figure 1). Skin biopsy revealed non-caseous epithelioid granulomas. Chest X-ray and CT of the thorax showed non-caseous epithelioid granulomas. Cultures for fungi and Tuberculosis mycobacteria, performed on broncoalveolar lavage, were negative. A bone marrow biopsy showed epithelioid granulomas (Figure 2).

These findings led us to the conclusion that the patient was suffering from symptomatic sarcoidosis and we started oral prednisone without interrupting the IFN therapy. At the last follow-up visit, after eight months of prednisone therapy, CML was still in complete cytogenetic remission. The skin nodules were reduced, chest X-ray and marrow biopsy showed, respectively, disappearance of hilar opacities and epithelioid granulomas.

Pulmonary or cutaneous sarcoidosis that resolved after oral cortisone or after IFN-α dose reduction has been reported in patients treated with IFN-α for hepatitis C and non-Hodgkin’s lymphoma.4,5 There have been only three cases of sarcoidosis developing during IFN-α therapy in CML patients.2,3,6 In all three patients sarcoidosis resolved after discontinuation of IFN therapy. Four other cases of sarcoidosis with CML are reported; three patients had underlying sarcoidosis when CML was diagnosed.7-9 In the fourth both diseases were diagnosed simultaneously.10

Our patient developed cutaneous, pulmonary and bone marrow sarcoidosis. This type of involvement was not described in the previously reported cases. Considering that the 5-year survival rate of CML patients in complete cytogenetic remission is 90%, we chose to continue IFN treatment and to treat the sarcoidosis with oral corticosteroids. The IFN dose could not be reduced because it was already very low, near to the minimum value necessary to maintain complete cytogenetic remission.

We would like to emphasize there is no evidence of the impact of cortisone on the cytogenetic response of CML. In the other three patients who developed sarcoidosis during IFN therapy, the drug was interrupted or reduced with clinical resolution of the sarcoidosis. For only one of the three patients is information available about hematologic remission of
CM L. 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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References
7. Krosi Z, Casassus P, Valeyre D, Paolaggi JA, Amouroux J, Batteux JP. Chronic myelocytic leukemia during the course of the disease. Severe involvement around the malleoli often precedes the development of leg ulcers. The chronic leg ulcers would not heal despite the wide variety of treatments applied.

Peri-lesional injections of granulocyte-macrophage 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 granulocyte-macrophage colony-stimulating factor (rhGM-CSF) in three patients with hepatitis C virus related type II 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.

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. Peri-lesional injections of recombinant granulocyte-macrophage colony-stimulating factor (rhGM-CSF) improved the healing of biopsy wounds in 35 patients with leprosy and induced the closure of Kaposi’s sarcoma lesions in one patient; beneficial effects were obtained also in chronic leg ulcers of patients with hemoglobinopathies. We report the effects of local injection of rhGM-CSF (Mielogen-M-oilranostim; 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 (3.2×2.7 cm) for 6 months.

Patient #2 was a 62-year-old woman who had had two deep ulcers, one on her left ankle (3.7×3.2 cm) and one on the dorsum of the left foot (2.5×2.2 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), immuno-lymphoma in partial remission (patient #3). 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-M-oilranostim; 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 role in the healing of ulcers.