Interferon alfa–induced sarcoidosis resolving without drug withdrawal

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INTRODUCTION

Sarcoidosis is an uncommon systemic granulomatous disease of unknown origin affecting lung, skin, liver, and other tissues. Noncaseating granulomas in the involved organs are the hallmark of this disease. An exaggerated immune response to an unknown antigenic stimulus could play a role in sarcoidosis development.

Lung is one of the most frequently involved organs.[1] Manifestations range from alveolitis to granulomatous infiltration of alveoli, bronchi, and blood vessels. The end stage of lung sarcoidosis is development of interstitial fibrosis with "honeycombing" of lung parenchyma.

Interferon alfa in association with ribavirin is the treatment of choice for hepatitis C. Early treatment of acute hepatitis C with interferon alfa-2b will prevent the development of hepatic cirrhosis, but adverse effects are frequent and often can result in discontinuation of treatment.[2]

Most frequent adverse effects related to interferon are malaise, fever, arthralgia, and cough. Pulmonary events such as bronchial asthma, bronchiolitis obliterans, and interstitial pneumonitis have been reported.

Interferon alfa is also used in the treatment of malignant melanoma, multiple myeloma, hairy-cell leukemia and HIV-associated Kaposi's sarcoma.[3]

Some cases of sarcoidosis after treatment with interferon alfa have been reported in the literature.[4-6] Improvement of sarcoidosis has been reported with discontinuation of treatment, but in other cases an independent course of disease has been proposed, raising the belief that interferon discontinuation is unnecessary in mild-to-moderate cases of interferon-related sarcoidosis.[7]

Abbreviation used:

CT: computed tomography

We present the case of a patient with hepatitis C treated with interferon in whom pulmonary sarcoidosis developed. The sarcoidosis was initially believed to be a pulmonary neoplasm, but skin lesions developed that indicated the diagnosis of systemic sarcoidosis. The sarcoidosis finally resolved without discontinuation of interferon alfa.

CASE REPORT

A 50-year-old Romanian woman who was an intravenous drug user and an active smoker had hepatitis C and was started on a 48-week course of interferon alfa-2a plus ribavirin. Thirty weeks after initiating treatment, she presented to pneumology department with a 3-week history of progressive shortness of breath and hemoptysis. A chest radiograph showed bilateral hilar lymphadenopathy. A lung neoplasm was suspected and computed tomography (CT) was performed showing enlarged hilar lymph nodes and diffuse nodules affecting both lungs (Fig 1, *A*). A positron emission tomography-CT scan showed active absorption of fluorodeoxyglucose at the lymph nodes and lung parenchyma (Fig 1, *B*).

Subsequently, the patient had asymptomatic papules and nodules on the soles (Fig 2, *A*) and on a past surgery scar (Fig 2, *B*). Biopsy of the skin lesions was performed and showed epithelioid macrophages converging in noncaseating naked granulomas devoid of a conspicuous infiltrate of lymphocytes

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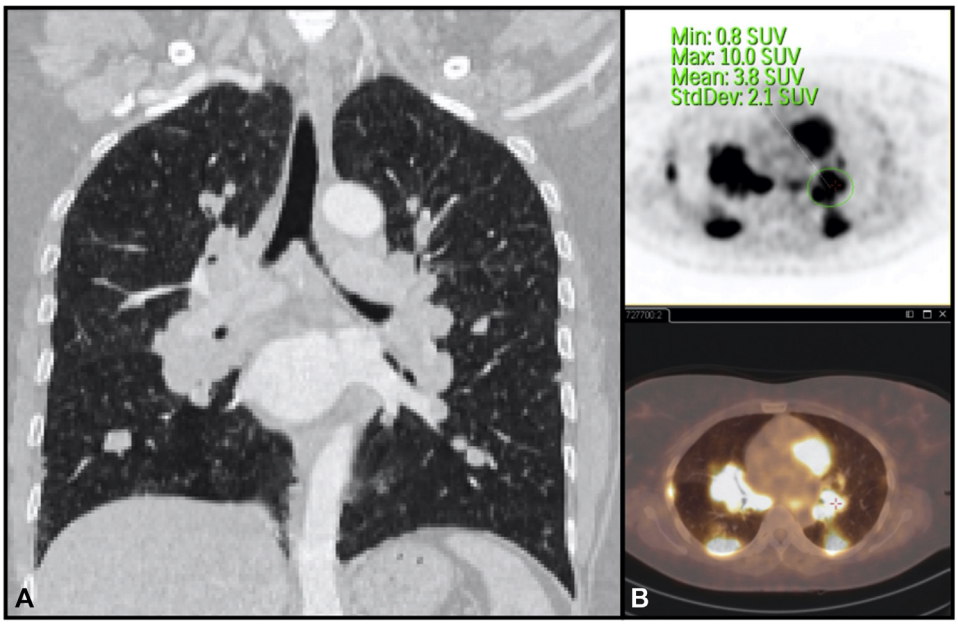

Fig 1. Pulmonary sarcoidosis. **A**, CT scan shows gross bilateral hilar lymphadenopathy. **B**, PET-CT shows absorption of fluorodeoxyglucose in the lymph nodes and lung parenchyma.

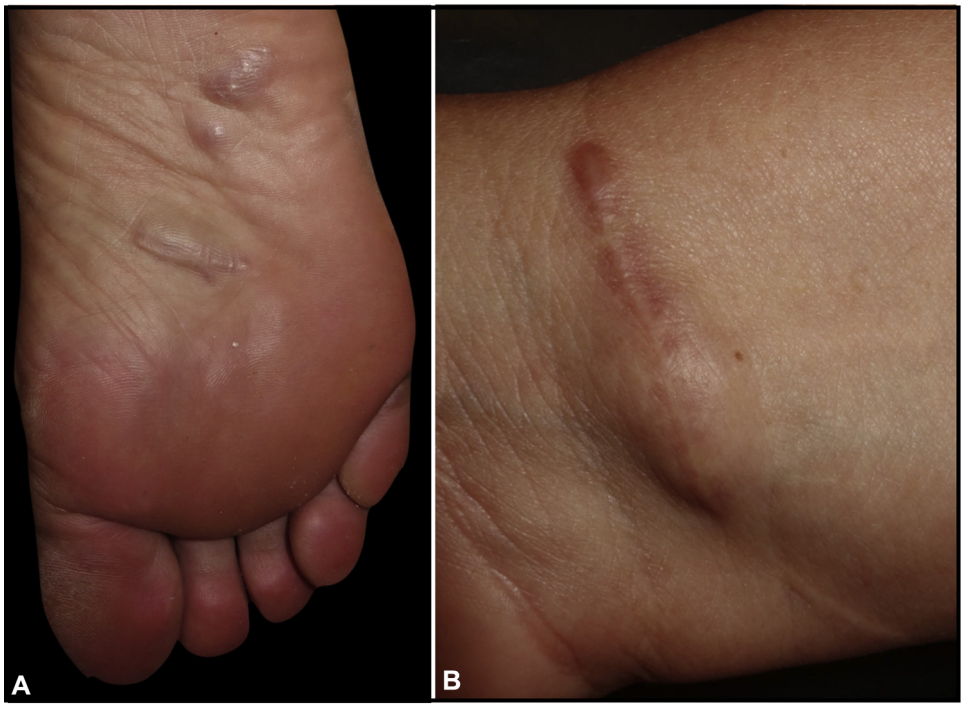

Fig 2. Cutaneous sarcoidosis. **A**, Skin-colored papules and nodules in the sole of the patient. **B**, Nodule developed in the scar of a previous surgery.

and multinucleated giant cells of the Langhans type with the nuclei arranged in a peripheral circular fashion (Fig 3). Special stains for acid-fast bacilli and fungus were negative. No foreign material was found with polarized light. No monoclonal proteins were detected on serum protein electrophoresis. Angiotensin-converting enzyme level was elevated at 128 IU/L. A transbronchial biopsy of the hilar lymph nodes also found naked noncaseating sarcoidal granulomas.

The patient was started on 30-mg daily of prednisone for 8 weeks with progressive tapering.