Interferon alfa–induced sarcoidosis resolving without drug withdrawal

José María Ortiz Salvador, MD,[a] Ana Mercedes Victoria Martínez, MD,[a] Daniela Subiabre Ferrer, MD,[a] Victor Alegre de Miquel, MD, PhD,[a,b] and Amparo Pérez Ferriols, MD, PhD[a,b]
Valencia, Spain

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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

From the University General Hospital Consortium of Valencia[a] and the University of Valencia.[b]

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Correspondence to: José María Ortiz Salvador, MD, Avenida Tres Cruces n2, 46014 Valencia. E-mail: Josema.ortiz.salvador@gmail.com.

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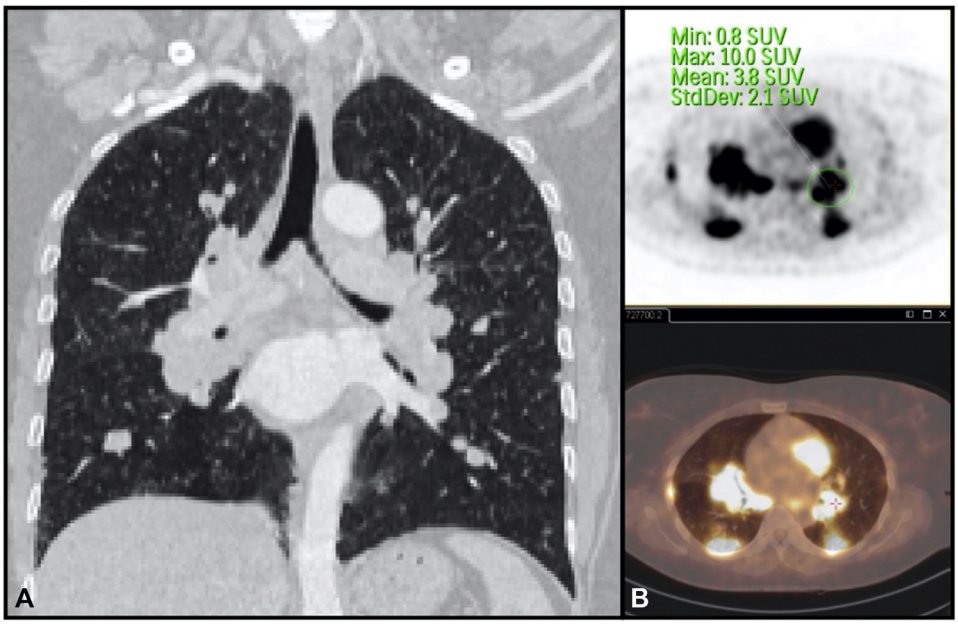

Fig 1. Pulmonary sarcoidosis. **A**, CT scan shows gross bilateral hilar lymphadenopathy. **B**, PET-CT shows absorption of fluorodeoxyglucose in the lymph nodes and lung parenchyma.

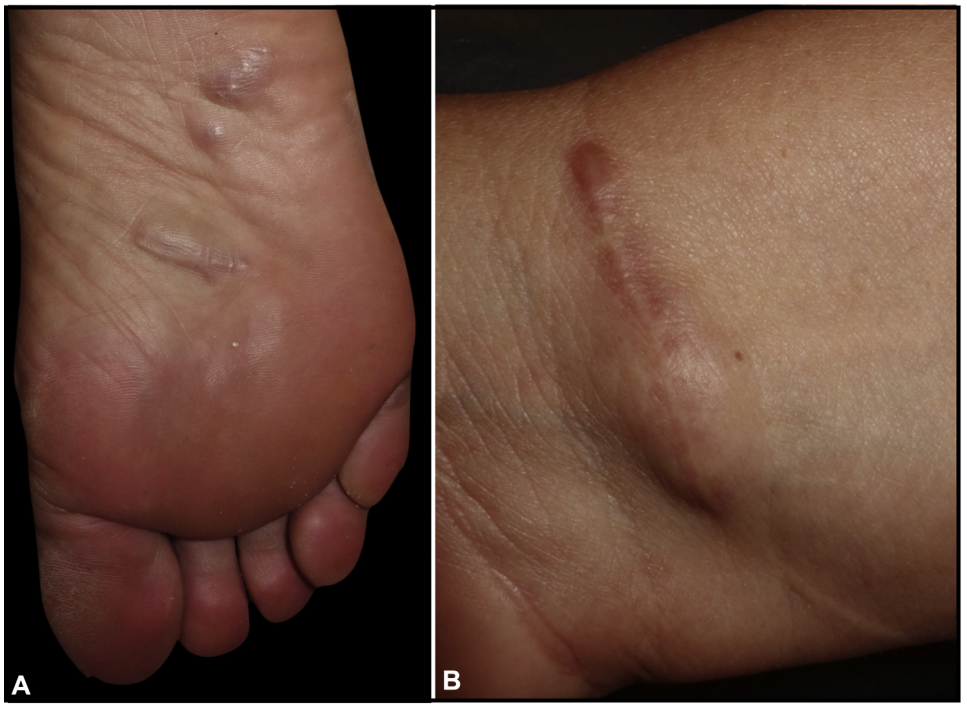

Fig 2. Cutaneous sarcoidosis. **A**, Skin-colored papules and nodules in the sole of the patient. **B**, Nodule developed in the scar of a previous surgery.

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.

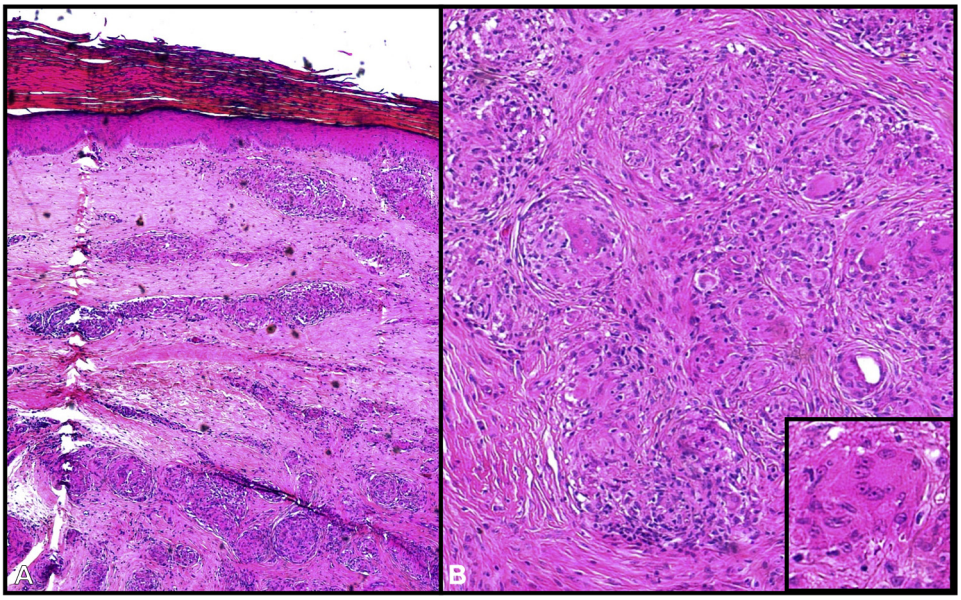

Fig 3. Cutaneous sarcoidosis. Skin biopsy. **A**, Granulomatous infiltrate affecting the whole dermis. **B**, Naked noncaseating granulomas without peripheral rim of lymphocytes (sarcoidal granuloma). **Inset,** Langhans type multinucleated giant cell. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×20; **B**, ×40.).

Interferon alfa and ribavirin were not interrupted. The skin lesions rapidly improved, and the dyspnea resolved gradually. Interferon alfa and ribavirin treatment was finished at week 48 with undetectable hepatitis C virus RNA in her serum. The patient was followed up for 6 months after finishing treatment, and no recurrence of hepatitis C was noted. Skin lesions and pulmonary symptoms did not recur.

DISCUSSION

Several cases of interferon-induced sarcoidosis have been reported in the medical literature. This type of sarcoidosis can present from several days after initiating treatment to years after completing therapy.[8,9]

Diagnosis of sarcoidosis is given by the concurrence of characteristic skin findings or radiologic findings and histopathologic findings of noncaseating granulomas. Differential diagnosis of lung sarcoidosis should be made with tuberculosis, some fungal infections, berylliosis, and other interstitial lung diseases.[10] Skin lesions must be differentiated from cutaneous Crohn's disease, foreign body reactions, leprosy, and cutaneous tuberculosis, among others. Special stains and polarized light examination must be performed to exclude other entities, as sarcoidosis is a diagnosis of exclusion.[10,11]

The prognosis of interferon-induced sarcoidosis is very good.[2,7,11] Some investigators recommend discontinuation of interferon therapy,[4] but cases resolving in several months regardless of interferon course have also been reported.[7]

Our patient responded very well to systemic corticosteroids allowing treatment with interferon to continue. This method of treatment can be crucial in severe diseases that require interferon for treatment such as hepatitis C or malignant melanoma.

CONCLUSION

Sarcoidosis should be suspected in a patient with lung or skin disease while undergoing interferon alfa therapy. Most cases are mild and prognosis is good. Interferon alfa should be continued if there is no life-threatening disease.

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