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## CORRESPONDENCE

# Sarcoidosis on the injection sites following treatment of interferon-alpha and ribavirin for hepatitis C

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Dear Editor,

Sarcoidosis is a systemic granulomatous disease of unknown origin commonly affecting the skin, lung, and lymphoid tissue. Some cases of sarcoidosis following treatment of interferon-alpha (IFN- $\alpha$ ) and ribavirin have been reported in the literature.<sup>1–4</sup> Herein we present a case of cutaneous sarcoidosis that developed on the intramuscular injection sites and venipuncture sites, as well as pulmonary involvement after treatment of IFN- $\alpha$  and ribavirin for hepatitis C.

A 70-year-old man with hypertension, diabetes mellitus, and chronic hepatitis B and C was started on a 48-week course of IFN- $\alpha$  and ribavirin. One year after finishing the treatment, some asymptomatic, erythematous, infiltrated papules developed on the intramuscular injection sites over bilateral deltoid regions (Fig. 1A) as well as the bilateral cubital fossae, where he had received venipuncture for a blood test (Fig. 1B). No lymphadenopathy or systemic symptoms such as fever, malaise, or cough were mentioned.

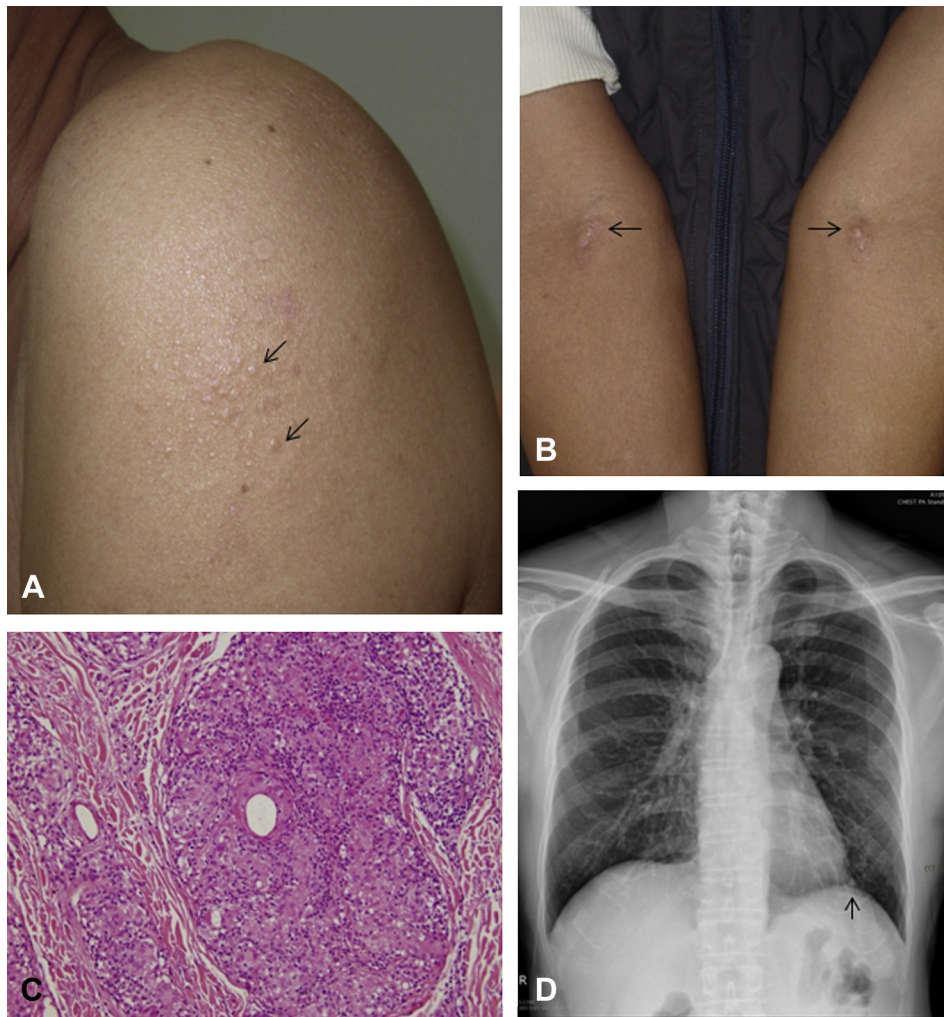
Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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The skin biopsies on both regions revealed multiple well-formed noncaseating granulomas with mainly epithelioid histiocytes, lymphocytes, and multinucleated giant cells in the dermis (Fig. 1C). No foreign material or microorganism was detected by polarization and special stain. Chest X-ray showed some small suspicious nodules over the left lower lung (Fig. 1D). Cutaneous and pulmonary sarcoidosis was diagnosed. The patient's laboratory data were all within normal limits. The patient then received oral prednisolone (5~10 mg/day) and intralesional triamcinolone acetonide injection on involved areas. The skin lesions improved after 1 month of therapy, and the pulmonary lesions were diminished on the following chest X-ray as well.

IFN- $\alpha$  is an immunomodulator commonly used in hepatitis C virus infection. Various dermatologic adverse effects have been associated with IFN- $\alpha$  therapy, including allergic reactions, lupus erythematosus, alopecia, psoriasis, extensive inflammation of actinic keratoses,<sup>5</sup> and sarcoidosis.<sup>1–4</sup> IFN- $\alpha$ -induced cutaneous sarcoidosis can appear before or concurrent with other organ involvement,<sup>2</sup> but its diagnosis can be easy and timely because of its distinct clinical and histopathological presentation. The time of onset varies from several days after the beginning therapy to 24 months after completing therapy.<sup>1</sup> The hypotheses of trauma-induced sarcoidosis under IFN- $\alpha$  use include: (1) repeated trauma of the skin, such as tattoos, surgical scars, and venipuncture sites may trigger the activity of dendritic cells and result in granulomas<sup>3,4</sup>; (2) IFN- $\alpha$  stimulates the Th1 type immune response, which leads to the formation of



**Figure 1** (A) Some asymptomatic erythematous infiltrated papules developed on the intramuscular injection sites of bilateral deltoid regions (arrows). (B) The same skin lesions also appeared on the bilateral cubital fossae (arrows), where the patient had received venipuncture for blood test. (C) The skin biopsies on both regions revealed multiple well-formed noncaseating granulomas with mainly epithelioid histiocytes, lymphocytes, and multinucleated giant cells in the dermis. No foreign material or microorganism was detected by polarization and special stain. (D) Chest X-ray showed some small suspicious nodular over the left lower lung (arrow).

granulomas<sup>1</sup>; (3) ribavirin is also able to stimulate Th1 lymphocytes by inhibiting Th2 response<sup>2</sup>; and (4) the hepatitis C virus itself exaggerates the expression of endogenous IFN- $\alpha$ .<sup>3</sup> Thus, the trauma area is more vulnerable to sarcoidosis under combined therapy of IFN- $\alpha$  and ribavirin, especially in patients with hepatitis C. The treatments include discontinuation of IFN- $\alpha$ , topical steroid, local triamcinolone acetonide injection, and systemic steroid.

In summary, because of the high prevalence of hepatitis C in Taiwan, we present a case of sarcoidosis on the injection sites following IFN- $\alpha$  and ribavirin treatment for hepatitis C to remind the physicians of this easily underdiagnosed cutaneous adverse reaction.

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