

Subcutaneous sarcoidosis localised to sites of previous desensitizing injections

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Summary

Subcutaneous sarcoidosis is a specific cutaneous lesion of systemic sarcoidosis that is rarely reported. Clinically, it is characterized by multiple, asymptomatic subcutaneous nodules mainly located on the forearms. Adverse effects of desensitization injections mostly consist of local transient reactions. Nodular lesions may also develop at the site of injection; these have been attributed to the aluminium hydroxide contained by many vaccines. We report a 49-year old woman with a history of two outbreaks of acute sarcoidosis (Löfgren syndrome) in 1994 and 1999, who developed lesions of subcutaneous sarcoidosis in the upper part of both arms, at the sites of desensitization injections for extrinsic asthma immunotherapy.

Sarcoidosis is a multisystemic disease defined by the formation of noncaseating granulomas in various organs.¹ Types of sarcoidosis are usually classified on the basis of specific cutaneous lesions as maculopapular, plaque, scarring or subcutaneous sarcoidosis, and lupus pernio.² Subcutaneous sarcoidosis is the least common of these forms and usually presents with nontender nodular subcutaneous lesions mainly involving the forearms.^{3,4}

We report a patient with sarcoidosis who developed granulomatous subcutaneous lesions predominantly located under the inoculation site of desensitization vaccines for extrinsic asthma administered 3 years earlier.

Report

A 49-year-old woman presented with subcutaneous lesions on the upper part of her arms. Her family history was unremarkable. She had presented with two outbreaks of acute sarcoidosis (Löfgren syndrome) in 1994 and 1999, which spontaneously remitted without

corticosteroid therapy. She also had extrinsic asthma and had received immunotherapy with subcutaneous allergen extracts injected into the upper part of her arms between 1999 and 2001. Over 3 years after the immunotherapy she developed a subcutaneous nodular lesion 80–90 mm in diameter on the upper part of each arm. These nodular lesions were painless, more evident upon palpation, and showed minute erythematous macules grouped in the overlying skin (Fig. 1). Two weeks later the patient developed 2–3 similar nontender subcutaneous lesions, 10–20 mm in diameter, on both knees. There were no associated symptoms.

Laboratory tests showed that the patient's serum angiotensin-converting enzyme (ACE) level was raised (0.96 μ kat/L; normal range 0.13–0.87); the other tests were normal or negative. Chest X-ray showed bilateral hilar lymphadenopathy. A cutaneous biopsy from the left arm showed a nodular inflammatory infiltrate limited to the subcutaneous tissue. The infiltrate was composed of sarcoid granulomas with sparse lymphocytic components and few giant cells (Fig. 2 and 3). Examination under polarized light did not show the presence of foreign bodies. The lesions spontaneously remitted within 2 months.

The adverse effects of vaccines mostly consist of mild transient reactions at the site of injection.⁵ The development of persistent painful subcutaneous nodules at

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Figure 1 Subcutaneous nodular lesion 80–90 mm in diameter located on the left upper arm. The overlying skin shows minute erythematous macules that might represent the points of injection of the desensitizing agent administered 3–4 years earlier.

the site of vaccination or desensitization injections with allergen extracts has also been reported. In most cases, these reactions have been attributed to the aluminium hydroxide used as an adsorbing agent in many of these preparations. A nonallergic direct toxic effect of aluminium or a delayed hypersensitivity reaction to aluminium has been postulated.⁶ In early lesions, a pure foreign-body reaction to deposits of an extracellular basophilic material is observed, whereas some lesions show a massive lymphoid inflammatory infiltrate with lymphoid follicles and abundant eosinophils in addition to a variable foreign-body reaction.⁶ In other patients with subcutaneous nodular lesions appearing at a vaccination site, cutaneous lymphocytic hyperplasia or pseudolymphoma can only be detected histologically, and in these cases the presence of aluminium has also been shown.^{7,8} It has been postulated that aluminium hydroxide could sequentially induce a histiocytic

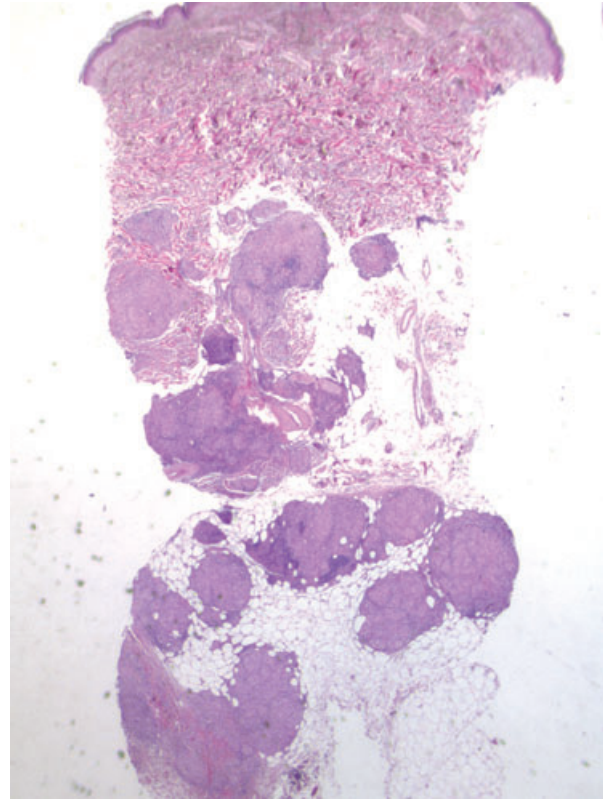


Figure 2 Sarcoid granulomas limited to the hypodermis. The granulomas are small, with sparse lymphocytes and a few giant cells (haematoxylin and eosin; original magnification $\times 20$).

foreign body reaction, a granuloma mixed with follicular infiltrates, and, finally, follicular infiltration.⁸ Although we could not perform a test to detect aluminium, our patient did not show any of the histological features associated with an aluminium reaction; only sarcoid granulomas were observed and the subcutaneous lesions developed simultaneously with hilar adenopathy and raised serum ACE levels.

Although the aetiology of sarcoidosis remains unknown, it has been suggested that in patients with systemic sarcoidosis, the presence of foreign bodies in the dermis may induce the development of granulomas.⁹ This hypothesis might explain the predilection of sarcoidosis to involve old scars, where foreign bodies and exogenous antigens are expected to be more abundant. Specific lesions of sarcoidosis have also been observed in inoculation sites, most commonly the sites of Mantoux tests, and scar sarcoidosis was also reported on the posterolateral side of the upper left arm of a patient who had previously undergone desensitization injections.¹⁰ Foreign bodies were also detected by polarized light in 2 of 10 patients with subcutaneous

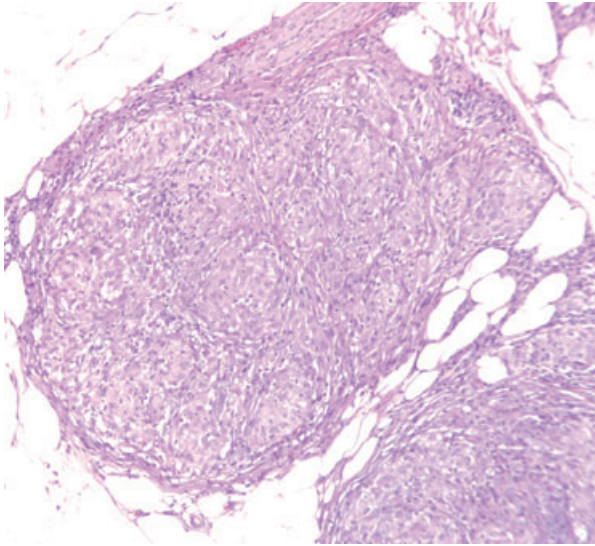


Figure 3 Sarcoid granulomas in the hypodermis at higher magnification (haematoxylin and eosin; original magnification $\times 100$).

sarcoidosis.³ Our patient developed subcutaneous sarcoidosis on both upper arms, at sites where she had received desensitization injections for asthma 3–4 years earlier. The lesions appeared when she experienced a new recurrence of sarcoidosis. We believe that our patient developed a granulomatous reaction when she developed a new recurrence of sarcoidosis, which was induced by antigens (aluminium or others) inoculated into the subcutaneous tissue by the desensitization injections. This case suggests that if pure sarcoid granulomas are demonstrated at the inoculation site of vaccines or desensitization injections, the diagnosis of sarcoidosis must be considered and the patient must be followed up clinically. We should also bear in mind that

in patients with sarcoidosis, the inoculation of antigens such as desensitization injections may induce granulomatous lesions at the inoculation site.

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