**Objectives:** To assess the presence of foreign material in the granulomatous cutaneous lesions of patients with systemic sarcoidosis.

**Design and Setting:** Observational study reevaluating histological specimens at a university referral hospital.

**Patients:** Sixty-five patients diagnosed as having sarcoidosis who developed granulomatous cutaneous involvement.

**Main Outcome Measures:** To detect the presence of polarizable foreign particles in cutaneous biopsy specimens and to evaluate the association with clinical features of the patients.

**Results:** Granulomatous cutaneous involvement was demonstrated in 65 (15.3%) of 425 patients with systemic sarcoidosis. In 14 (22%) of the 65 patients, the cutaneous biopsy specimen showed foreign particles in polarized light. The skin lesions corresponded to 3 different clinical patterns: an admixture of papules and infiltration of previously undetected minute scars (n=6); scar sarcoidosis (n=4); and subcutaneous nodules (n=4). The lesions were located most frequently in the extremities, involving the knees in 10 patients.

**Conclusions:** The presence of polarizable foreign body material in granulomatous cutaneous lesions is not infrequent in patients with systemic sarcoidosis. Inoculation of foreign matter from a previous inapparent minor trauma may induce granuloma formation in individuals with sarcoidosis.

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SARCOIDOSIS is a multisystemic granulomatous disease of unknown etiology that involves mainly the lungs, mediastinal and peripheral lymph nodes, eyes, and skin. The liver, spleen, salivary glands, heart, nervous system, muscles, bones, and other organs may also be involved. The diagnosis is well established when clinical and radiological findings are supported by histological evidence of widespread noncaseous granulomas in 1 or more tissues or positive results of a Kveim test. Because of its easy accessibility, the skin biopsy is of great value as a less-invasive diagnostic procedure. The finding of polarizable foreign matter in cutaneous epithelioid granulomas traditionally permits the exclusion of the diagnosis of sarcoidosis. However, some cases have been reported in which foreign particles were present in granulomatous cutaneous lesions in patients with well-demonstrated systemic sarcoidosis. These findings questioned the significance of the presence of foreign bodies in granulomatous skin lesions of patients with sarcoidosis. With these considerations in mind, we reviewed the data in a series of patients with systemic sarcoidosis and granulomatous cutaneous involvement to ascertain the presence of foreign body material in the skin biopsy specimens and to reevaluate the clinical aspects.

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Of 425 patients diagnosed as having systemic sarcoidosis, the biopsy specimens in 65 (15.3%) patients showed granulomatous cutaneous involvement. In 15 biopsies obtained from 14 (22%) of the 65 patients, foreign particles were observed under polarized light. Of these 14 patients, there were 13 women and 1 man (mean age, 50.3 years; range, 33-70...
PATIENTS AND METHODS

During a 26-year period (1974-1999), 425 patients were diagnosed as having sarcoidosis at the Sarcoid Clinic of the Hospital de Bellvitge, a 1000-bed teaching institution in Barcelona, Spain. The diagnosis of sarcoidosis was made according to the classic criteria: a compatible clinical and radiological picture; histological demonstration of noncaseous granulomas involving 1 or more tissues, with stains and cultures negative for mycobacteria and fungi or positive results of the Kveim test; and exclusion of other granulomatous diseases. In patients whose tissue biopsy specimens did not provide histological confirmation, the diagnosis of sarcoidosis was accepted if the purified protein derivative of tuberculin test results were negative, other diseases were excluded, and the clinical course was consistent with sarcoidosis.  

We also accepted a diagnosis without a biopsy specimen when the intrathoracic gallium citrate Ga 67 uptake showed a lambda pattern (image resembling the Greek letter produced by gallium uptake in the right paratracheal and bilateral hilar lymph nodes), with or without the panda image (image of the face of a panda produced by gallium uptake in the symmetrical lacrimal and parotid glands). All patients with systemic sarcoidosis who had cutaneous lesions were evaluated at the Department of Dermatology. Skin biopsies were performed when granulomatous cutaneous involvement was clinically suspected. Those patients with histologically demonstrated granulomatous skin lesions were included in this study. We collected data about the stage of baseline radiograph and extrathoracic sarcoidosis and the history concerning inoculation of exogenous material into the skin from all patients. Cutaneous biopsy specimens with granulomatous involvement were reexamined under polarized light to detect foreign particles. We excluded asteroid bodies, Schaumann bodies, and the small refractive crystals of calcium carbonate usually encountered in sarcoidosis.

Clinical Data of the Patients*

<table>
<thead>
<tr>
<th>Patient No./ Age, y/Sex</th>
<th>Extrathoracic Involvement</th>
<th>Chest Radiograph Stage</th>
<th>Cutaneous Lesions</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/45/F 2/54/F 3/70/F 4/37/M 5/43/F 6/60/F 7/42/F 8/58/F 9/53/F 10/70/F 11/33/F 12/33/F 13/53/F 14/53/F</td>
<td>Erythema nodosum... Axillary adenopathy... Erythema nodosum, cutaneous plaques Erythema nodosum Uveitis Erythema nodosum... Erythema nodosum Erythema nodosum Erythema nodosum Uveitis</td>
<td>II I II I 0†</td>
<td>Papules, scars Nodules Nodules Nodules Nodules Nodules</td>
<td>Knees Face Arms Arms Arms Arms</td>
</tr>
</tbody>
</table>

* Ellipses indicate that there was no extrathoracic involvement.
† Micronodular pattern shown in the results of high-resolution computed tomography.

The presence of foreign particles in granulomatous cutaneous lesions was demonstrated in 14 (22%) of 65 patients with systemic sarcoidosis and skin involvement. The systemic character of the disease was well documented in all patients by the demonstration of intrathoracic and/or extrathoracic disease, in addition to specific (granulomatous) skin involvement. These results agreed with previous reports by Walsh et al and Val-Bernal et al and corroborated the observation that foreign body granuloma and sarcoidosis are not mutually exclusive.
In our series, we identified 3 different clinical forms of cutaneous sarcoidosis associated with the presence of foreign bodies: papular sarcoidosis of the knees, scar sarcoidosis, and subcutaneous sarcoidosis. Papular sarcoidosis of the knees was the most frequently occurring form in this series, and it was usually associated with acute sarcoidosis, particularly Löfgren syndrome. Clinically, it consisted of minute granulomatous papules grouped over the knees; some of the papules were linearly arranged, and, in some cases, the papules coexisted with infiltrated minute scars not previously noted by the patient. Of the 4 patients with scar sarcoidosis (granulomatous infiltration of previously known scars), we observed an association with Löfgren syndrome in 3 patients. In contrast, subcutaneous nodules were not associated with erythema nodosum but were observed in chronic forms of the disease.

Based on a large series of patients with cutaneous sarcoidosis, Veien et al reported that foreign material was sometimes found in old cutaneous scars probably introduced as a consequence of the initial injury. The propensity of cutaneous sarcoidosis to localize in tattoos has also been reported. More infrequently, specific (granulomatous) cutaneous sarcoidosis involved areas of long-term trauma, surgery, venipuncture, vaccination or inoculation, purified protein derivative of tuberculin skin test, and long-standing scarification marks. In all these cases, contamination by foreign matter, such as talc and ash, was suspected. In the present series, the granulomatous cutaneous lesions with foreign bodies were located, in most of the cases, on the knees or forearms of middle-aged women. The knees and forearms are easily exposed to trauma, and prior minor injury in these areas may be imperceptible. Consequently, a history of accidental inoculation of foreign particles cannot be elicited in the majority of cases; we were able to obtain this information in only 1 of our patients.

As in previous reports, our results suggested that the presence of polarizable matter in a cutaneous granuloma does not exclude the diagnosis of sarcoidosis, particularly when systemic features of the disease are present. Moreover, the presence of foreign bodies in 22% of our patients with systemic sarcoidosis and granulomatous skin involvement suggested that it is not a rare event.
in specific cutaneous lesions of sarcoidosis. This finding may contribute to the understanding of the pathogenesis of the disease. The cause of sarcoidosis remains obscure. It has been hypothesized that the disease occurs when a genetically susceptible host is exposed to a specific environmental antigen(s). In this event, an exaggerated inflammatory response takes place, characterized by large numbers of activated macrophages and T lymphocytes bearing the CD4 helper phenotype, with a pattern of cytokine production consistent with a Th1-type immune response. As a consequence, granulomas develop in the involved organs.\(^2\)\(^3\)\(^7\) In addition, it has also been hypothesized that sarcoidosis is a disease in which the immune system’s capacity to handle particulate foreign matter is altered and that the presence of foreign bodies, which are often not apparent and remain undetected, in the skin and other organs might provide the stimulus necessary for granuloma formation.\(^3\) Therefore, the presence of foreign bodies in some tissues may contribute to defining the patterns of organ involvement and the distribution of the lesions in the skin.

In summary, in our results, the presence of polarizable matter in granulomatous cutaneous lesions was not infrequent in patients with systemic sarcoidosis. Accordingly, foreign bodies and sarcoidosis were not mutually exclusive. The clinical pattern of the lesions observed in our patients suggested that previously undetected minor traumas may provide a nidus for granuloma formation in individuals with sarcoidosis.

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REFERENCES

Farber spearheaded and assumed leadership positions in many dermatological societies and organizations. He was on the board of directors of the American Academy of Dermatology, the American Dermatological Association, the Association of Professors of Dermatology, the Pacific Dermatologic Association, and the Society for Investigative Dermatology. In addition, he held editorial positions on many publications, including the *Journal of Investigative Dermatology*, *Scientific American*, *Skin and Allergy News*, and *Cutis*. He also served as president of the Association of Professors of Dermatology, the Pacific Dermatology Association, and the Society for Investigative Dermatology.

On retiring from his post at Stanford University in 1986, he assumed the presidency of the Psoriasis Research Institute, a unique nonprofit foundation, established by Russell Smith, Alejandro Zaffaroni (founder of ALZA Pharmaceuticals, Mountain View, Calif), and himself. They created a skin biology unit with a focus on the etiology, epidemiology, and treatment of psoriasis. Scholars from nearly a dozen countries outside the United States have studied at the Psoriasis Research Institute on fellowships or during sabbatical leaves.

While in high school and college, in addition to being an exceptional student, he was an excellent athlete, having performed as a champion hurdler and basketball player. He remained a loyal supporter of Stanford sports throughout his life.

He was also a devoted family man, marrying his life’s companion and best friend, Ruth, in 1944. They remained together for 56 years, raising 4 children and many large animals at their Portola Valley, Calif, home. He is survived by his wife; a son, Donald; daughters Charlotte and Nancy; grandchildren Elinor and Ben; and his great-grandchild Henry.

He will be dearly missed by many who were influenced or cared for by him, including 2 generations of fellow physicians and students and thousands of grateful patients.

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**Correction**

**Error in Placement of Figures.** In the study titled “Foreign Bodies in Granulomatous Cutaneous Lesions of Patients With Systemic Sarcoidosis,” published in the April issue of the ARCHIVES (2001;137:427-430), Figure 4 and Figure 5 were accidentally transposed in the article and on the cover, where they are referred to as parts B and C.