

## CLINICAL STUDY

# Birefringent particles in granulomatous dermatitis, sarcoidal-type, as well as in other non-granulomatous skin disorders in patients without sarcoidosis

Fernandez-Flores A

Service of Anatomic Pathology, Hospital El Bierzo, Service of Cellular Pathology, Clinica Ponferrada, Ponferrada, Spain. [gpyauflowerlion@terra.es](mailto:gpyauflowerlion@terra.es)

**Abstract:** Silica granuloma (SG) is a rare entity in literature. The relationship between SG and sarcoidosis has not always been clear. We tried to find out how common birefringent particles are in cutaneous biopsies from patients with and without sarcoidal granulomas. We studied the most recent 200 skin biopsies that came to our service. We also studied 10 cases of sarcoid-type granulomatous dermatitis. All of them were studied under the polarized light. Quantification of particles was classified from negative to very abundant. We found birefringent particles in 39.5 % of the biopsies without a sarcoid-type granulomatous infiltrate. We found birefringent particles in 7 out of the 10 cases of the group with a sarcoid-type cutaneous dermatitis (70 %). 5 of the 10 cases presented with systemic sarcoidosis, and from these, 4 presented with birefringent particles (80 %). From the other 5 cases, we found birefringent particles in 3 cases (60 %). Birefringent particles can be evidenced in the skin biopsy of patients with systemic sarcoidosis in a higher percentage than in non-granulomatous skin biopsies of subjects without a history of sarcoidosis. Therefore, evidence of those particles does not exclude sarcoidosis (Tab. 1, Fig. 4, Ref. 23). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).

Key words: sarcoidosis, silica, granuloma, scar sarcoidosis.

Although silica is a nearly ubiquitous material, silica granuloma (SG) is a rare entity in literature. Moreover, the relationship between SG, scar granulomas and sarcoidosis has not always appeared clear in the different studies that mention the subject. While for some, the evidence of silica particles excludes sarcoidosis (1–3), others found that silica particles were commonly found in granulomas of patients with sarcoidosis (1, 4–6).

Therefore, it can be claimed that: either silica particles are not so common in the skin of humans (in spite of the many opportunities of entering our cutis during our life) or a granulomatous reaction to silica particles is less common than we had thought (and probably only happens in predisposed people or under predisposing conditions).

We designed this study to search for the evidence of cutaneous birefringent particles in patients with a granulomatous dermal response of sarcoidal type, as well as in skin biopsies of cutaneous biopsies of patients without such types of dermal infiltrate.

## Materials and methods

We evaluated the most recent 200 skin biopsies that came to our service of Anatomic Pathology. None of them was excluded

Service of Anatomic Pathology, Hospital El Bierzo, Service of Cellular Pathology, Clinica Ponferrada, Ponferrada, Spain

**Address for correspondence:** A. Fernandez-Flores, MD, PhD, S. Patología Celular, Clinica Ponferrada, Avenida Galicia 1, 24400 Ponferrada, Spain. Phone: +34.987.423732, Fax: +34.987.429102

from the study, in order not to have bias. All the biopsies corresponded to 4  $\mu$ m sections which had been stained with hematoxylin-eosin.

The cases were classified in 9 groups according to topographical rules: 1) non-specified (the site of the biopsy was not specified by the clinician); 2) the neck; 3) the trunk (excluding the back, but including the trunk, the abdomen, buttock, shoulder, chest, groin, axilla and the vulva); 4) the leg (including not only the leg but also the foot, sole and the thigh); 5) the arm (including not only the arm but also the forearm and elbow); 6) the face (including not only the face but also the eyelid, lip, nose, forehead and the eyebrow); 7) the back; 8) the scalp; and 9) the hand (also including the fingers).

We also evaluated 10 cases that we recovered from our archives, where a cutaneous granulomatous infiltrate of sarcoidal type was evidenced.

All the cutaneous biopsies were studied under the polarized light in order to search for the birefringent particles. Quantification of particles was classified into five groups: from negative (–) to very abundant (++++).

## Results

Figure 1 shows the percentages of cases included in each group from the 200 biopsies that did not present a sarcoidal-type granulomatous. We found the birefringent particles in 39.5 % of these biopsies.

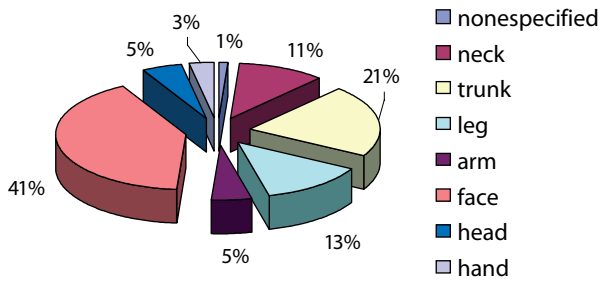


Fig. 1. The image shows the percentages of biopsies without the sarcoid-type granulomatous infiltrate that were studied, according to the location.

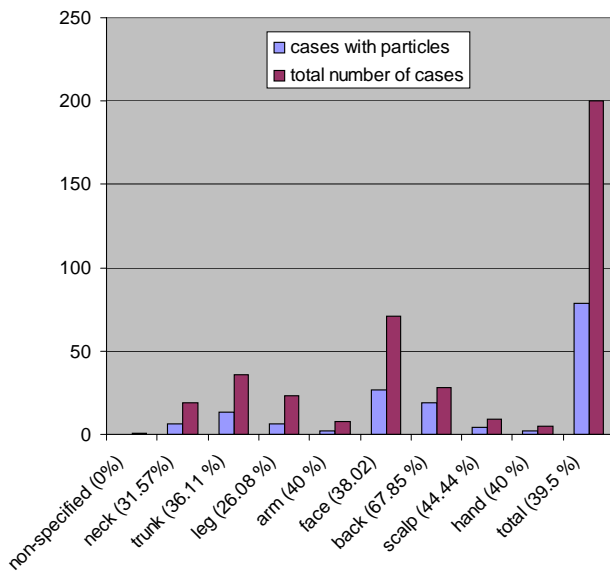


Fig. 2. Percentage of cases in each group of the biopsies without the sarcoid-like infiltrate, where the birefringent particles were evidenced.

Figure 2, on the other hand, shows the percentage of cases in which these particles were observed in each group. The particles were more frequent in biopsies from the back (67.85 %) than in other location (Fig. 3, top). In 14 cases, a foreign-body-type granulomatous response was seen. In 12 of these 14 cases, the diagnosis was infundibular cyst and the granulomatous response was apparently directed to keratin. 6 of these 12 cases presented with birefringent particles. Two of them were from the back, one from the elbow, one from the forehead, one from the eyelid and one from the nose. Another case with the granulomatous response was from the retroauricular area and was diagnosed as perifolliculitis capitis abscedens et suffodiens; it did not show any particles. The last case with the granulomatous response was pilomatricoma of the face and did not show any particles either.

Table 1 shows the details of the patients with the cutaneous granulomatosis of sarcoid type, from which the biopsies were

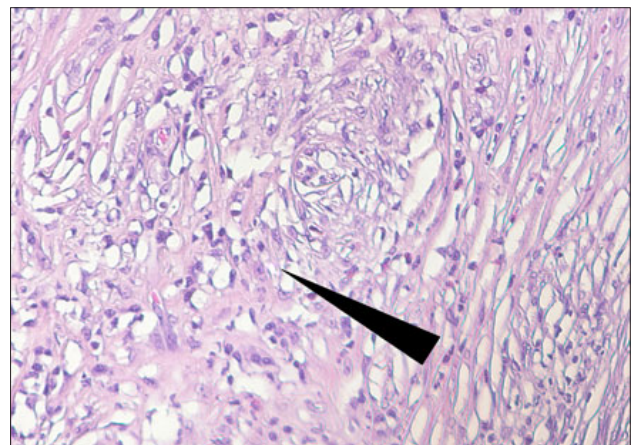
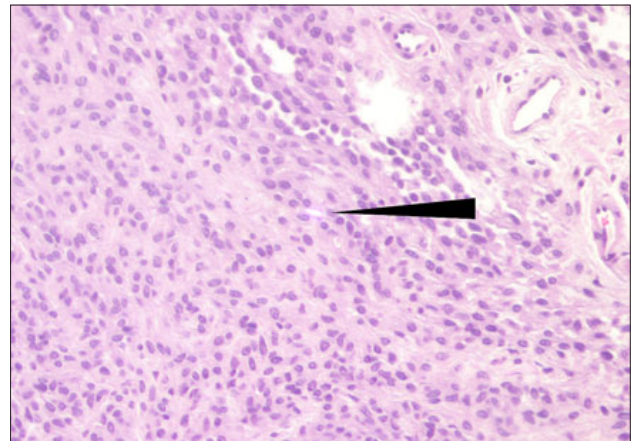


Fig. 3. Birefringent particles in a case of the melanocytic nevus from the back (top), as well as in the cutaneous granulomatous infiltrates (bottom). The images appear dark, because they were taken under polarized light.

studied. None of the patients were miners. We found the birefringent particles in 7 out of 10 cases (70 %) (Fig. 3 bottom). 5 of 10 cases presented with systemic sarcoidosis, and from these, 4 presented with birefringent particles (80 %). From other 5 cases (patients without systemic sarcoidosis but with cutaneous granulomatous infiltrate of sarcoid type) we found the birefringent particles in 3 cases (60 %). Figure 4 encapsulates our results observed in 10 cases of the granulomatous dermatitis.

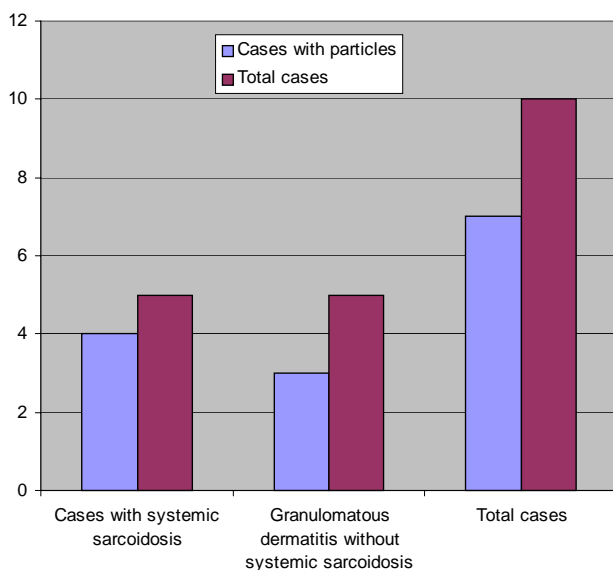
### Discussion

Cutaneous SG is alleged to be an underdiagnosed condition (1, 7), in spite of the fact that the condition has been known in literature for a long time (8).

The granulomatous response, which is associated with this condition, has usually been attributed to trauma (9), due to the inclusion of silica particles in the skin. Commonly, a large period of latency between the trauma and the granulomatous response has been described: up to 59 years in some cases (10), with a mean interval of 10 years (1). Therefore, the examination of any granulomatous infiltrate under the polarized light is

**Tab. 1. Details from the patients from which the biosies with a cutaneous granulomatous response sarcoidal-type were studied.**

Case	Age	Gender	Systemic sarcoidosis	Cutaneous lesions	Site from the one the biopsy was taken	Birefringent particles
1	33	Female	YES (Cutaneous and mediastinic involvement)	Maculae and papulae; face, legs trunk and arms	Leg	+/++++
2	43	Male	YES (Cutaneous and splenic involvement with several lymph node involvement)	Papulae and plaques; legs, forearms, back	Leg	+/++++
3	81	Female	NO	Plaque, Face	Face	+/++++
4	65	Male	YES (Cutaneous, pulmonary and ocular involvement)	Papulae; trunk, arms, legs.	Trunk	+/++++
5	65	Female	YES (Cutaneous, pulmonary and mediastinic-lumph-node involvement)	Nodule, Nose	Nose	–
6	82	Female	NO	Plaque, Arm	Arm	+/++++
7	54	Female	NO	Nodule, forehead	Forehead	+/++++
8	76	Female	NO	Nodules, leg	Leg	–
9	80	Female	NO	Nodule, face	Face	–
10	42	Female	YES (Cutaneous and pulmonary involvement)	Forehead and left knee	Knee	+/++++

**Fig. 4. Cases with the granulomatous dermal infiltrate of sarcoidal type. The diagram shows the percentage of cases where the birefringent particles were evidenced.**

mandatory, as some examples of re-established diagnosis have shown (11).

The relationship between the sarcoidosis and SG is more controversial. Elusive concepts, regarding the subject, are found in literature, such as scar sarcoidosis (3, 12). For instance, it was admitted by some authors in past, that the presence of silica particles in the cutaneous sarcoid-type granulomas excluded sarcoidosis (1–3). Others, on contrary, admitted that the cutaneous

sarcoidosis should only be diagnosed when systemic manifestations of sarcoidosis were present (13). Nevertheless, some patients with clear examples of SG presented with some laboratory characteristics of sarcoidosis (14). On the other hand, it has been demonstrated that the cutaneous granulomas in patients with systemic sarcoidosis frequently contain silica particles (1, 4–6), and some reported pulmonary sarcoidosis in relation to inhalation of silica particles (15).

Many of these facts, together with the ubiquity of the silica, made us think that the granulomatous reaction would develop in predisposed patients (16), and probably under predisposing conditions as well. The latter hypothesis meant to demonstrate the presence of silica particles as a common fact in skin biopsies from our daily practice, which were not suspicious of sarcoidosis. A previous report already showed the presence of inorganic particles in normal skin of patients living in volcanic areas (17). In this latter study, the authors demonstrated the presence of inorganic particles in 100 % of the cutaneous biopsies of healthy individuals. The biopsies were all taken from the arm. It is necessary to say that they studied 20  $\mu\text{m}$  sections when they looked for these particles (4  $\mu\text{m}$  sections are commonly used in the laboratories of histopathology, like the ones we used in our study). In the same report, they also stated that in normal individuals studied, silica and aluminium were *not* the predominant elements in the birefringent particles (17).

Our institutions cover an area of approximately 150 000 people. This area has a certain level of activity in coal and slate-mining. This latter fact might determine a higher presence of silica particles in the area, but it should be remembered that silica is an almost ubiquitous material (1, 18). Nevertheless, none of our patients were miners.

It caught our attention that the preferential location of the particles was the back (64.28 %), a fact for which we do not have any explanation.

In literature, SG has mainly been reported in extremities (6, 7, 16, 19–21), the face (1, 11, 12, 18, 22) and the forehead (5). This was also our experience with the cutaneous sarcoid granulomas. The percentage of the granulomatous cases, where we found the birefringent particles (70 %), was similar to the one, which has been found by other authors (23), i.e., high, but not 100 %. The latter fact supports the concept that the presence of the particles is not a sufficient condition to develop the granulomas, and that it must be triggered by certain predisposing conditions.

In conclusion, the following can be stated: 1) Birefringent particles can be evidenced in the cutaneous granulomatous responses in patients with systemic sarcoidosis; 2) Therefore, the evidence of those particles does not exclude sarcoidosis; 3) Inorganic particles are evidenced in the non-granulomatous skin biopsies of people without a history of sarcoidosis in a high percentage of cases, although still lower than in cases with granulomatous dermatitis of sarcoidal type (with or without systemic sarcoidosis); 4) Some areas of the skin, such as the back, are more prone to present inorganic particles than others.

Therefore, it can be hypothesized that the particles act as a triggering factor in the formation of the cutaneous granuloma in patients with a predisposing condition, such as sarcoidosis. The reports, where it was thought to be an isolated cutaneous phenomenon at the beginning (cutaneous granuloma), progressed later to the systemic sarcoidosis (12), support this point.

## References

1. Mowry RG, Sams WM Jr, Caulfield JB. Cutaneous silica granuloma. A rare entity or rarely diagnosed? Report of two cases with review of the literature. *Arch Dermatol* 1991; 127 (5): 692–694.
2. Walsh NM, Hanly JG, Tremaine R, Murray S. Cutaneous sarcoidosis and foreign bodies. *Amer J Dermatopathol* 1993; 15 (3): 203–207.
3. Kim YC, Triffet MK, Gibson LE. Foreign bodies in sarcoidosis. *Amer J Dermatopathol* 2000; 22 (5): 408–412.
4. Löfgren S, Snellman B, Nordenstam H. Foreign body granulomas and sarcoidosis. A clinical and histo-pathological study. *Acta Chir Scand* 1955; 108 (6): 405–418.
5. Val-Bernal JF, Sánchez-Quevedo MC, Corral J, Campos A. Cutaneous sarcoidosis and foreign bodies. An electron probe roentgenographic microanalytic study. *Arch Pathol Lab Med* 1995; 119 (5): 471–474.
6. Marcoval J, Mañá J, Moreno A, Gallego I, Fortuño Y, Peyrí J. Foreign bodies in granulomatous cutaneous lesions of patients with systemic sarcoidosis. *Arch Dermatol* 2001; 137 (4): 427–430.
7. Boztepe G, Rakhshanfar M, Erkin G, Ozkaya O, Sahin S. Cutaneous silica granuloma: a lesion that might be clinically underdiagnosed. *Eur J Dermatol* 2005; 15 (3): 194–195.
8. German WM. Lupoid-sarcoid reaction induced by foreign body (silica). *Amer J Clin Pathol* 1940; 10 (2): 245–250.
9. Kay S, Jackson HS. The possible role of silica in cutaneous granulomas. *Ann Surg* 1952; 136 (6): 1031–1033.
10. Eskeland G, Langmark F, Husby G. Silicon granuloma of the skin and subcutaneous tissue. *Acta Pathol Microbiol Scand* 1974; 248 Suppl: 69–73.
11. Kaya TI, Kokturk A, Polat A, Anadolu R, Tursen U, Ikizoglu G. Cutaneous silica granuloma in a child. *Pediatr Dermatol* 2003; 20 (1): 40–43.
12. Payne CMER, Thomas RHM, Black MM. From silica granuloma to scar sarcoidosis. *Clin Exper Dermatol* 1983; 8 (2): 171–175.
13. Constela Camba MI, Corbacho Abelaira MD, Mendez Pineiro MJ, Fernández Larranaga JR. La sarcoidosis cutánea cicatricial: el papel del sílice. *An Med Interna* 1996; 13 (3): 155.
14. Pucevich MV, Rosenberg EW, Bale GF, Terzakis JA. Widespread foreign-body granulomas and elevated serum angiotensin-converting enzyme. *Arch Dermatol* 1983; 119 (3): 229–234.
15. Bodokh I, Brun P, Mayaffre C, Majewrczyk N, Montagne M. Sarcoidosis following inhalation of insulation of insulation particles. *Ann Dermatol* 1998; 125 (3): 182–184.
16. Fernandez-Flores A, Montero MG. Does cutaneous silica granuloma develop mainly in predisposed patients? *Eur J Dermatol* 2006; 16 (3): 321–322.
17. Convit J, Ulrich M, Castillo J, De Lima H, Pérez M, Caballero N, Hung J, Arana B, Pérez P. Inorganic particles in the skin of inhabitants of volcanic areas of Central America: their possible immunomodulatory influence in leishmaniasis and leprosy. *Trans R Soc Trop Med Hyg* 2006; 100 (8): 734–739.
18. Finley J, Knabb J. Cutaneous silica granuloma. *Plat Reconstr Surg* 1982; 69 (2): 340–343.
19. Chun SI, Cho SW. Silica granulomas: scanning electron microscopy and energy dispersive X-ray microanalysis. *J Dermatol* 1991; 18 (2): 92–96.
20. Murphy M, Wiehe P, Barnes L. Silica granulomas: another cause of tennis elbow. *Brit J Dermatol* 1997; 137 (3): 477.
21. Pimentel L, Barnadas M, Vidal D, Sancho F, Fontarnau R, Alovera A. Simultaneous presentation of silicone and silica granuloma: a case report. *Dermatology* 2002; 205 (2): 162–165.
22. Riddle PJ, Font RL, Johnson FB et al. Silica granulomas of eyelid and ocular adnexal. *Arch Ophthalmol* 1981; 99 (4): 683–687.
23. Marcoval J, Moreno A, Maná J. Papular sarcoidosis of the knees: a clue for the diagnosis of erythema nodosum-associated sarcoidosis. *J Amer Acad Dermatol* 2003; 49 (1): 75–78.

Received November 3, 2008.

Accepted March 6, 2006.