**Polymorphous cutaneous and chronic multisystem sarcoidosis**

D. Krasowska, R. A. Schwartz, D. Wojnowska, B. Mackiewicz, and D. Czelej

**Summary**

Sarcoidosis is a systemic disorder in which cutaneous findings are often prominent. These may be polymorphous to the extent that sarcoidosis may mimic many other cutaneous diseases. We describe a 56-year-old woman with involvement of the skin, eyes, bones, heart, and lung. After an initial presentation 10 years earlier of erythema nodosum with bilateral hilar adenopathy, there were three types of cutaneous changes: subcutaneous, nut-sized palpable nodules localized along the upper and lower extremities, annular plaques on the shins, and erythema nodosum-like palpable and slightly tender nodules. It is very unusual to have all three types of skin lesions, especially the erythema nodosum-like histologically specific cutaneous ones in this setting, which is what prompted this report.

**Introduction**

Sarcoidosis is a multisystem granulomatous disorder of unknown etiology characterized by epithelioid noncaseating granulomas in all affected organs. Specific skin manifestations of sarcoidosis are polymorphous, ranging from papules or plaques to nodules, lupus pernio, or ulcerations, with erythema nodosum a characteristic but nonspecific skin finding (1–7). Sarcoidosis frequently involves the lungs, mediastinal and peripheral lymph nodes, eyes, bones, and skin. The clinical course is progressive, although remissions and relapses often occur (8). Sarcoid granuloma formation begins with the presentation of as-yet unidentified infectious antigens or autoantigens to the T lymphocytes. Some observations suggest that the causes of sarcoidosis are occupational or environmental exposures. The two common target organs, the skin and lungs, are in permanent contact with environmental agents. Some inorganic antigens, such as beryllium, clay, talc, pine pollen, and oxalosis have been suggested as environmental triggers in the development of sarcoidosis (9, 10).

The preceding activation of macrophages participates in lymphocyte stimulation and recruitment. The exact point when sarcoidosis starts is usually unclear. We describe a patient with chronic sarcoidosis affecting the internal organs and accompanied by polymor-
Phous skin changes. She was remarkable in having both erythema nodosum and histologically specific cutaneous and subcutaneous sarcoidosis simultaneously.

**Case report**

A 56-year-old woman was seen in January 2005 for multiple painless subcutaneous nodules in a linear pattern and skin lesions on the extremities of 6 months' duration. She complained of weakness, dyspnea, and easy fatigability. She had had erythema nodosum 10 years earlier, associated with hilar lymphadenopathy in a chest X-ray. Mediastinoscopy with histologic examination of the hilar lymph nodes revealed noncaseating epithelioid cell granulomas. Spirometric examination performed at the same time showed normal pulmonary capacity. From 1996 to September 2004 she had no cutaneous findings suggestive of sarcoidosis. Her occupational history was noteworthy for 30 years of exposure to polyvinyl chloride (PVC) and tetrahydrofuran (THF). PVC is one of the most popular plastic materials. There is some evidence associating prolonged exposure to PVC with pulmonary impairment (11). THF is a heterocyclic organic compound that is used as a solvent of intermediate polarity in chemical reactions.
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and industrially to degrease metal parts. THF can also
be used as a component to produce polyurethane fi-
bbers (12). The patient did not report any skin injuries
on the sites of sarcoidosis lesions.

On examination, three different types of skin lesion
were observed. The first was subcutaneous, nut-sized
palpable nodules localized along the upper and lower
extremities with the overlying skin of normal color. Sec-
ond, the skin of both shins was covered by multiple
annular plaques with light surface scaling. Some larger
plaques showed central clearing with hyperpigmenta-
tion (Fig. 1). On diascopy these lesions exhibited an
apple-jelly color, indicating the presence of a sarcoïd
infiltrate. The third type of lesion was evident on the
skin of the knee joints as violaceous, palpable, and
slightly tender nodules, deeply placed in the skin (Fig.
2). The diagnosis of cutaneous sarcoidosis was con-
firmed by histological examination of the skin biopsy
specimens. The skin samples were obtained from two
different skin lesions: the first was taken from the firm,
red-brownish cutaneous plaque localized on the shin,
and the second was taken from the subcutaneous nodule
on the thigh. Histological examination of the samples
from the plaque and nodule revealed noncaseating
granulomatous infiltration. The granulomas were
well-circumscribed and consisted of epithelioid cells,
mononuclear cells, and rare Langhans-type giant cells.
A peripheral rim of sparse lymphocytes surrounded the
epithelioid histiocytes (Fig. 3). The specimen obtained
from the nodule revealed numerous granulomas ex-
tending through the entire thickness of the dermis, also
partially involving the subcutaneous adipose tissue.
Peripheral lymph nodes were not enlarged. The mu-
cous membranes, scalp, and nails were not involved.

Direct ophthalmologic examination showed the pres-
ence of 3 mm papules on the lower right palpebral conjunctiva that may correspond with granuloma. Other
ocular involvement was not established. X-ray exami-
nation of the hand bones showed multiple cystic les-
sions (Fig. 4). Chest X-ray revealed bilateral hilar lymph-
adenopathy and disseminated small nodules. Com-
puted tomography showed parenchymal infiltration,
thickened interlobular septa, and early fibrosis. Cardiac
ultrasonography demonstrated enlargement of the right
ventricle and maximum pressure in the pulmonary ar-
tery of about 40 mm Hg. Spirometry showed decreased
diffusing capacity, obstruction, and a restrictive pattern:
FEV₁ = 1,160 ml (47% of pred. value), VC = 1,860 (62%
of pred. value), MEF₂₅ = 440 l/s (31% of pred. value),
MEF₅₀ = 980 l/s (26% of pred. value), and MEF₇₅ = 2,530 l/s (46% of pred. value). Laboratory findings included
an ESR of 20; white and red blood cell counts and urin-
alysis were normal. Liver enzymes and kidney param-
eters were normal. Calcium metabolism was normal.

The sputum was examined and a standard mycobacte-
rial culture was performed to exclude tuberculosïs.
Stains for acid-resistant bacilli and cultures for fungi
were negative. The tuberculin skin test result was nega-
tive.

In 1995 the patient was initially treated with aspirin
for a few months because of erythema nodosum and bi-
ilateral hilar lymphadenopathy, but the gradual exac-
teration of pulmonary changes led to the beginning of
oral corticosteroid therapy. An initial dose of prednisone
of 60 mg per day was given. The pulmonary lesions
markedly improved, but 3 months later a perforated
peptic ulcer occurred. After a short break in the sys-
temic steroid treatment, prednisolone injections and
then oral prednisone (40 mg daily) were prescribed.
The chest radiographs markedly improved for almost 5
years. In March 2003, after a 5-year period of systemic
corticosteroid therapy, the patient stopped prednisone
intake. In September 2004 she developed polymor-
phous superficial and deep cutaneous lesions associ-
ated with progressive pulmonary symptoms. Accord-
ingly, the very potent topical corticosteroid clobetasol
and oral naproxen were started. However, both were
ineffective, and so additional treatment with chloro-
quine phosphate (500 mg daily) and topical 0.1%
tacrolimus ointment twice daily was initiated. After 2
weeks’ therapy with topical tacrolimus, the beginning
of the resolution of the plaques on the shins was ob-
erved.

Discussion

Sarcoidosis is a granulomatous disease of unknown
etiology that is suspected to be the product of a combi-
nation of genetic, immunologic, and environmental fac-
tors (10). The most common sites involved in sarcoïd-
osis are the lungs, skin, and eyes (13). Nearly one-fourth
of sarcoïdosis patients have skin lesions (8). They may
be divided into two groups: specific skin involvement
with typical sarcoïd granulomas on histologic exami-
nation and nonspecific skin lesions. The most frequent
lesion classified as nonspecific is erythema nodosum,
which is characteristic of acute sarcoïdosis. An erythema
nodosum-like eruption with the histological changes
of sarcoïdosis has also been described (14). Our pa-
tient had typical erythema nodosum at the begin-
ing of the disease. The presence of erythema nodosum
is the best predictor of a good prognosis in patients with
sarcoïdosis, but some patients with it do develop chronic
sarcoïdosis (15). An association with the development
of chronic, progressive disease in subjects over 40 has
been observed, as is the case with our patient (16–18).

The frequency of various skin lesions in sarcoïd-
osis may be present: erythema nodosum (20.5%), cuta-
neous plaques (4.3%), subcutaneous nodules (4.3%),
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maculopapular rash (3.7%), scar lesions (2.9%), lupus pernio (2.7%), and psoriasiform lesions (0.9%) (19).

We describe a patient with pulmonary established sarcoidosis and erythema nodosum at the beginning of disease. She had been given long-term therapy with systemic steroids because of the progression of the pulmonary involvement. A year and a half after the cessation of corticosteroids, marked exacerbation of pulmonary symptoms and new polymorphous skin lesions appeared. On examination there were three types of lesions: subcutaneous painless nodules on the upper and lower extremities, cutaneous tender nodules around the knee joints (erythema nodosum-like lesions), and multiple small plaques on the front and back aspects of the shins. As opposed to erythema nodosum, which is typical for the acute stage of sarcoidosis, these types of skin lesions are characteristic for the chronic stage of disease. More than one type of chronic skin lesions may exist at the same time. Nevertheless, subcutaneous sarcoidosis is rare, especially in white people (20, 21).

Subcutaneous sarcoidosis is usually accompanied by hilar lymphadenopathy, but in our patient subcutaneous sarcoidosis appeared after the progression of the pulmonary changes. These plaques were accompanied by the tender nodules around the knee joints, which were persistent and difficult to treat. The plaques on the shins are responding well to topical tacrolimus. This case is unusual due to the coexistence of polymorphous superficial and deep skin lesions. Our patient’s exposure to prolonged and regular occupational contact with PVC and THF should be considered a possible causative agent inducing a cell-mediated immune response in the skin and internal organs.

REFERENCES


