


# Subcutaneous sarcoidosis (Darier–Roussy sarcoidosis) with extensive disease on positron emission tomography: A case report and review of the literature

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## Abstract

Cutaneous manifestations of sarcoidosis are common, but subcutaneous nodules are rare, originally described in 1904 by Darier and Roussy and thought to represent isolated skin disease. We present a 61-year-old male who presented with 3 months of subcutaneous nodules on the forearms and knees. Biopsy confirmed sarcoidosis. An [F-18] fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) showed confluent uptake in the skin of forearms and knees, along with thighs and buttocks, mediastinal, hilar and upper abdominal lymph nodes, and multiple bones. He was well and treated with hydroxychloroquine 400 mg/day. The nodules resolved and a repeat FDG PET/CT at 5 months showed a significant decrease in the uptake at all involved sites. Although a PET scan can demonstrate extensive disease in a patient presenting with subcutaneous nodules, the literature suggests prognosis is good and treatment should start simply with the least toxic approach, such as with hydroxychloroquine therapy.

## KEYWORDS

hydroxychloroquine, PET, prognosis, sarcoidosis, subcutaneous

## INTRODUCTION

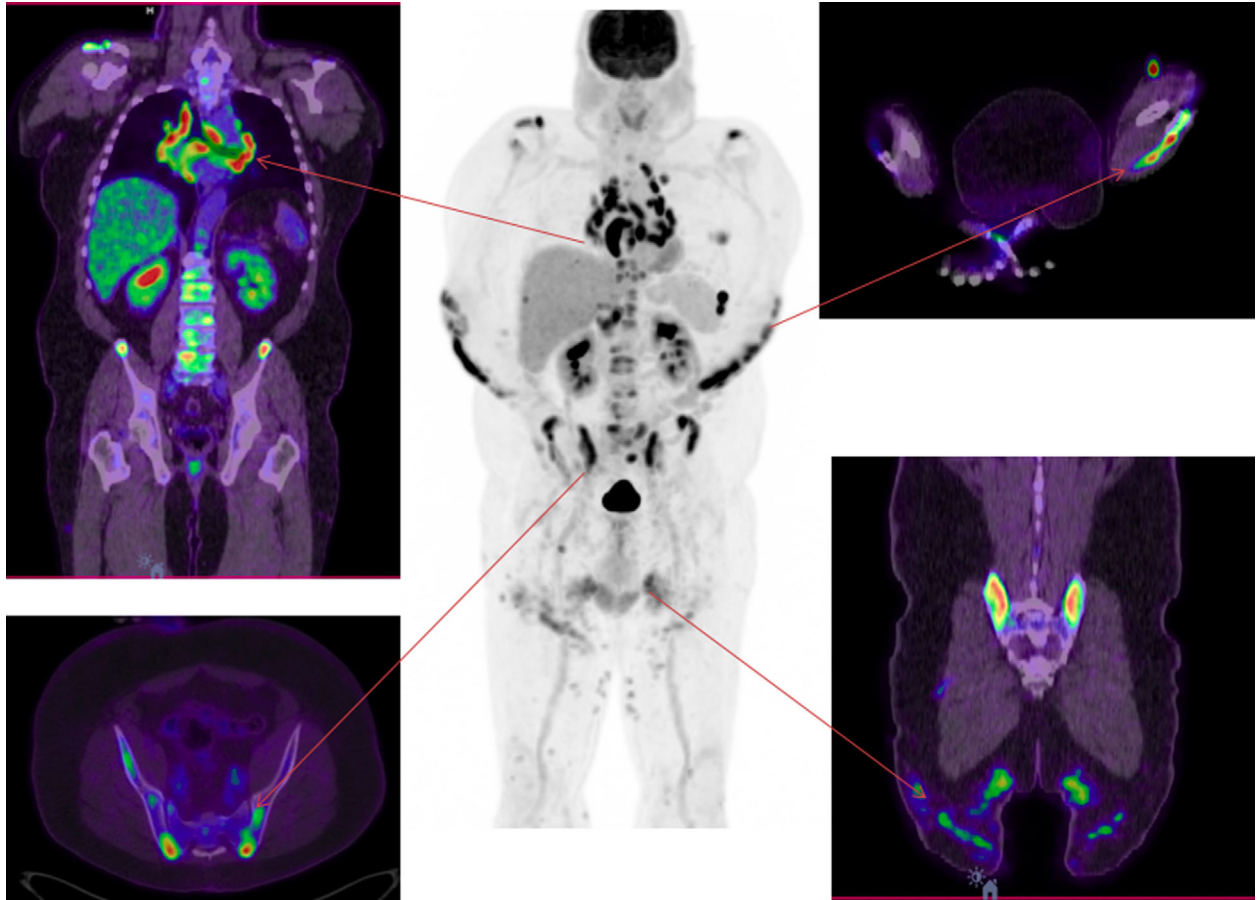
Sarcoidosis is a heterogenous, systemic inflammatory disease, characterized by non-caseous epithelioid cell granulomas with no evidence of an infectious aetiology. The prevalence ranges from 10 to 20 cases per 100,000 persons.<sup>1</sup> The aetiology of sarcoidosis is unclear, but it is hypothesized that both environmental and genetic influences play a role in the immunopathogenesis.<sup>2</sup> Sarcoidosis is frequently isolated to symmetric involvement of hilar and mediastinal lymph nodes, with the lungs being the next most common organ involved, with beading or irregular thickening of the bronchovascular bundles and upper zone ground-glass opacities seen on computed tomography (CT). Calcium metabolism, heart, liver, nervous system and the eye are frequently involved as is the skin (25%–30%).<sup>1,3</sup> Presentation and outcome in sarcoidosis vary greatly and phenotypic and staging systems continue to be developed, aiming to understand prognosis and guide therapy. The original staging was based on the chest x-ray (Wurm–Scadding) and was related to the

likelihood of resolution of disease at 5 years.<sup>4</sup> More recent studies have explored combinations of clinical, radiological, genetic and other measures, but as yet there is no consensus as to a clinically useful model.

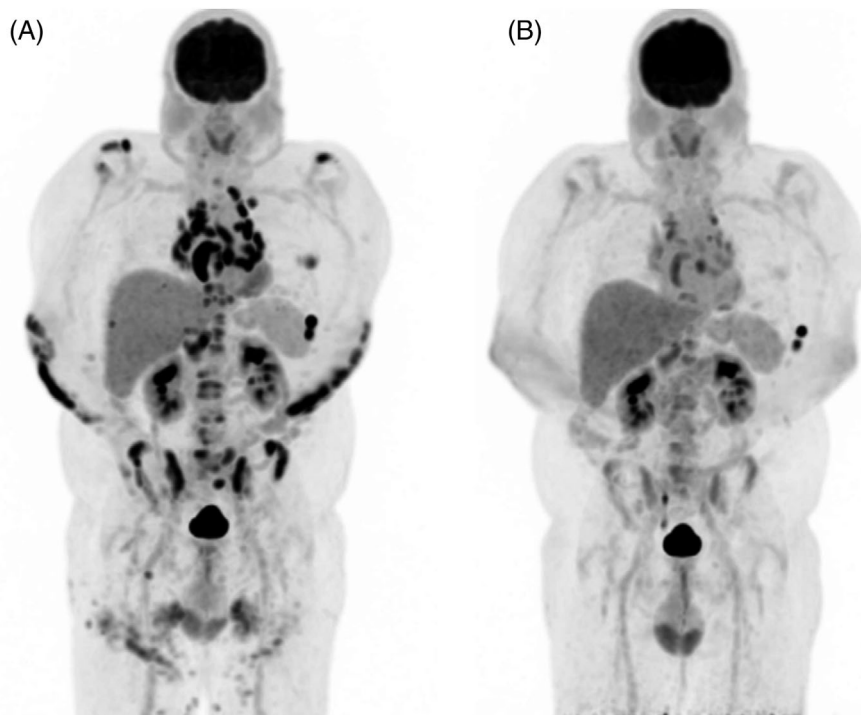
Skin manifestations vary and include papules, scar-associated sarcoidosis, erythema nodosum, lupus pernio, plaques and, rarely, subcutaneous nodules (so-called Darier–Roussy sarcoidosis).<sup>1</sup> We report a patient who presented with subcutaneous nodules, where imaging demonstrated extensive activity in the skin, nodes and musculoskeletal system, but which responded rapidly to hydroxychloroquine. We review the literature regarding manifestations and prognosis of Darier–Roussy sarcoidosis which, like in our case, suggests simple treatment may be sufficient despite the extent of disease.

## CASE REPORT

A 61-year-old male with a past medical history of psoriasis and primary hypertension presented with a 3-month history



**FIGURE 1** F-18 fluorodeoxyglucose (FDG) positron emission tomography scan images at diagnosis showing intense FDG activity in the forearms and thighs/buttocks, as well as mediastinal, hilar and upper abdominal lymph nodes, and extensive skeletal/marrow



**FIGURE 2** F-18 fluorodeoxyglucose (FDG) positron emission tomography scan images. (A) Image taken at the time of diagnosis. (B) Image taken after 5 months of hydroxychloroquine therapy, showing much less significant FDG accumulation in sarcoid lesions

**TABLE 1** Reports of subcutaneous sarcoidosis with pulmonary parenchymal infiltrates demonstrated by computed tomography from 2000 onwards (including the current case)

| Author                              | Year | Site of subcutaneous lesion   | Treatment   | Outcome   |
|-------------------------------------|------|---|---|---|
| This report                         | 2022 | Upper and lower limbs   | Hydroxychloroquine 400 mg once daily  | Complete recovery   |
| Zendah et al. <sup>7</sup>          | 2020 | Arms, elbows, hands, right thigh and the legs   | 1 mg/kg/day prednisone  | Complete recovery   |
| Kim et al. <sup>8</sup>             | 2017 | Chin and right fourth toe   | Local excision. No systemic treatment   | Not reported  |
| Janegova et al. <sup>9</sup>        | 2016 | Left foot—plantar area  | Local and systemic corticosteroid therapy (not specified)   | Not reported  |
| Dulguerov et al. <sup>10</sup>      | 2015 | Right paranasal region  | Excision of the paranasal mass. No systemic treatment   | Complete recovery   |
| Yamaguchi et al. <sup>11</sup>      | 2013 | Upper limbs and buttocks  | Oral prednisolone 10 mg/day   | Complete recovery   |
| Kim et al. <sup>12</sup>            | 2013 | Right arm and leg   | No treatment  | Complete recovery   |
| Dalle Vedove et al. <sup>13</sup>   | 2011 | Two cases:<br>(1) Lateral and extensor surface of both forearms and thighs, buttocks and the dorsal surface of the hands<br>(2) Extensor surface of the upper and lower limbs | (1) Oral prednisone 0.3 mg/kg/day<br>(2) Oral prednisone 0.4 mg/kg/day  | (1) Complete recovery<br>(2) Complete recovery  |
| Moscattelli et al. <sup>14</sup>    | 2011 | Left hand—thenar eminence   | No treatment  | Complete recovery   |
| Meyer-Gonzalez et al. <sup>15</sup> | 2011 | Three cases:<br>(1) Upper and lower extremities<br>(2) Both elbows and right thigh<br>(3) Forearms  | (1) and (2) Oral prednisone 1 mg/kg/day + hydroxychloroquine 400 mg/day<br>(3) Oral prednisolone 1 mg/kg/day + methotrexate 12.5 mg once a week | Partial recovery over 12 months. Reduced in number and size gradually, persisting in a small number |
| Celik et al. <sup>16</sup>          | 2010 | Left foot—plantar surface   | Two intralesional triamcinolone acetonide injections, 10 mg/ml (once a month)   | Complete recovery   |
| Miida and Ito <sup>17</sup>         | 2009 | Right forearm   | Oral corticosteroid. Dose not reported  | Complete recovery   |

of subcutaneous nodules on the forearms and knees. The patient had no respiratory symptoms and was otherwise well. There was no environmental or drug exposure. Physical examination demonstrated nodules, coalescing in areas, on the side of the hands extending onto the extensor surfaces to the elbows with a few small lesions medial to the knees. The remainder of the examination was unremarkable. A biopsy of a nodule demonstrated non-caseating epithelioid granulomas consistent with sarcoidosis, with no evidence of organisms on culture or staining. Blood examination showed a normal angiotensin-converting enzyme (ACE) level and no lymphopenia. CT chest revealed hilar and mediastinal lymphadenopathy and fissural beading, in keeping with sarcoidosis. Lung function was normal. Whole-body [F-18] fluorodeoxyglucose (FDG) positron emission tomography (PET) scan was performed on Siemens Biograph 64 mCT PET-CT, following administration of 341 MBq [F-18] FDG, with imaging from vertex to below knees. This showed extensive uptake in the nodules of the forearms and around the knees and subcutaneous uptake around the thighs and buttocks (Figure 1). Intense uptake was seen in mediastinal, hilar and upper abdominal lymph nodes, and multiple areas of the skeleton including the left orbit, C5, multiple midthoracic

and all lumbar vertebrae, pelvis, sternum, scapulae, left clavicle and acromioclavicular regions, right humeral head and multiple ribs. No sclerotic or lytic lesions in bone were seen on the low-dose scan. The clinical, radiological and histopathological findings supported sarcoidosis. The patient was well and treated with hydroxychloroquine 400 mg daily. The cutaneous nodules regressed and treatment was ceased at 6 months with no subsequent relapse. A repeat FDG PET scan showed a significant decrease in the size of subcutaneous nodules in the upper and lower limbs and an excellent metabolic response elsewhere (Figure 2).

## DISCUSSION

Sarcoidosis with subcutaneous nodules (Darier–Roussy sarcoidosis) is an uncommon variant, affecting between 1.4% and 6% of patients with systemic sarcoidosis.<sup>5,6</sup> Initially, the disease was thought to be isolated to the skin, but better imaging with CT and FDG PET, as with our patient, demonstrated disease can be widespread. To the best of our knowledge, there are approximately 30 case reports of subcutaneous sarcoidosis published in the last 20 years (2000–

2020) and of these, 15 cases, including ours, had pulmonary infiltrates on the CT chest (summarized in Table 1). In this group, the patients in whom outcomes were reported had partial or complete recovery, suggesting a good prognosis when subcutaneous disease is present.

The role of FDG PET in routine management of sarcoidosis is evolving with a clear benefit in identifying cardiac and other critical organ involvement and in determining response to treatment in complicated cases.<sup>18,19</sup> With regard to cardiac sarcoidosis, both FDG PET and cardiac magnetic resonance imaging (CMRI) have a role, and are often complementary in this setting. With FDG PET imaging in an adequately prepared patient, abnormal activity in the myocardium reflects active inflammation, and can be useful in monitoring disease response, whereas on CMRI late gadolinium enhancement represents myocardial fibrosis or scarring.<sup>20</sup> There are few cases reporting the use of FDG PET scanning when subcutaneous involvement is present. In one case report, an FDG PET scan was used to differentiate malignancy from sarcoidosis,<sup>12</sup> and the other two showed extensive skin involvement, like our patient, which were not clinically evident.<sup>21,22</sup> Our case demonstrates that FDG PET can show extensive disease not apparent on clinical examination. Although the CT chest showed mild beading suggesting pulmonary involvement, no activity was seen at this site on the FDG PET scan. He was asymptomatic and had normal lung function and there was no indication that he needed therapy for his lungs.

As shown in Table 1, treatment for subcutaneous sarcoid where there was pulmonary involvement varied from intralesional to systemic corticosteroids, to antimalarial medications. While systemic corticosteroids are widely accepted as standard therapy for symptomatic or deteriorating sarcoidosis or sarcoidosis involving critical organs, in cutaneous disease the focus is on disfiguring lesions with no guidelines for subcutaneous disease, but a suggestion treatment be reviewed on a case-by-case basis,<sup>19</sup> recognizing monitoring is appropriate as you can get spontaneous improvement.<sup>12</sup> The guidelines for disfiguring disease suggest that intralesional followed by oral corticosteroids should be the first approach followed by hydroxychloroquine if the former is not tolerated or effective. Treatment length is unknown but resolution is often the endpoint. As noted, the prognosis with subcutaneous sarcoidosis, as shown in Table 1 where there is additional pulmonary, or in our case extensive involvement elsewhere, is good. Given that chronic corticosteroid therapy carries a risk of complications, Marchetti et al.<sup>23</sup> have advocated for hydroxychloroquine as the first-line therapy for subcutaneous sarcoidosis. Our patient was successfully treated with 6 months of hydroxychloroquine, with no side effects or relapse. It is hypothesized that hydroxychloroquine alters antigen presentation to T-helper cells.<sup>23</sup> When used, baseline and follow-up ophthalmological reviews are recommended. Further study of the use of hydroxychloroquine is warranted, although it will be difficult because of the rarity of the condition.

In conclusion, this case demonstrates that clinically localized subcutaneous sarcoidosis can be associated with

extensive disease detected by FDG PET imaging. However, the literature suggests prognosis is good with subcutaneous disease and if the patient is well with no disfiguring skin lesion or other critical organ involvement, hydroxychloroquine therapy may be sufficient and safe.

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## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTION

Paul Youn wrote the original draft of the manuscript and Paul Youn and Fiona Lake revised the manuscript. Roslyn J. Francis prepared the scans and Henry Preston reviewed the pathology. All authors edited and approved the final version of the manuscript.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

## ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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