CASE REPORTS

Rare presentation of subcutaneous sarcoid granulomas: A case report and review of the literature

First Authors: Andrea Matson*, D.O. PGY-3, Kelly Shortridge, D.O. PGY-2, Ashley Brown, D.O. PGY-1

Authors' affiliation:

Mountain Vista Medical Center, Department of Surgery, 10238 East Hampton Avenue Suite 301C, Mesa, AZ 85209, Phone: 541-660-8747, Fax: 480-993-3422
Email: Andrea_Matson@iasishealthcare.com

*** Corresponding author**

Second author: Raul Lopez, M.D.

Author's affiliation:

Mountain Vista Medical Center, Department of Surgery, Mesa, Arizona
10238 East Hampton Avenue Suite 301C
Mesa, AZ 85209
Phone: 480-257-2670
Fax: 480-993-3422
Email: Raul_Lopez@iasishealthcare.com

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Abstract

Few cases of Darier-Roussy type sarcoidosis have ever been presented in the literature due to the rarity of this condition. Sarcoidosis occurs in only 10-20 per 100,000 in the population and can be present throughout various organs and sites of the body. Skin manifestation as a broad category represent just 25-35% of these cases and even more rare is the Darier-Roussey type which has not had prevalence quantified. We report a new case of Darrier-Roussey sarcoidosis in a 59-year old Caucasian female with flesh colored, firm subcutaneous nodules on her bilateral forearms and hips that developed over 6 months time. Histopathology with special stains identified these nodules as noncaseating sarcoid granulomas. She was also found to have bilateral hilar lymphadenopathy. This is a literature review and case report of subcutaneous sarcoidosis in an adult patient with diagnosis confirmed by clinical exam, imaging, and histopathology who had successful treatment outcome with oral prednisone.

Keywords: sarcoidosis; Darier-Roussy type; nodules; naked granuloma

INTRODUCTION

Sarcoidosis is a well-known multi-system disorder most recognized by non-caseating granulomas throughout various organs and sites in the body [1,4,5]. Its etiology remains a mystery but research has shown a combination of genetic (HLA genes) and environmental factors are at play [6]. This disease occurs in 10-20 per 100,000 in the population. Although lungs are the most common site of presentation in this disease (90%), there are many different forms of cutaneous sarcoidosis [1,11]. It is the second most common manifestation at 25-30% [4,11]. Among the rarest is a form of skin manifestation known as Darrier-Roussy which manifests as subcutaneous nodules palpable just under the skin (See Table 1 for a complete list of skin manifestations) [1,2]. Due to the rarity of this form of sarcoid in an already infrequent disease only a handful of case presentations have been reported some dating back to the 1930's.

Table 1. Various cutaneous presentations of sarcoidosis [4,8,12]

Type	Skin manifestation
Papular sarcoid	Presents with papules on the skin
Lichenoid sarcoid	Presents as plaques
Nasal ala papules	Papules around nasal ala with scaling
Sarcoidal alopecia	Scarring and scaling areas with associated hair loss
Darier-Roussy type	Subcutaneous nodules most commonly extremities
Ichthyosiform sarcoid	Dry thickened scaling skin
Ulcerative sarcoidosis	Ulcerative skin lesions
Scar associated sarcoid	Granuloma formation/ fibrosis at scar sites
Tattoo-associated sarcoid	Similar to scar associated sarcoid
Lupus pernio	Extensive violaceous plaques with scales in perinasal region and mid face
Erythema Nodosum	Acute nodular erythematous eruptions

In 1904, Darier and Roussy reported the first case of subcutaneous sarcoidosis identifying it as a disease with numerous subcutaneous nodules on trunk and extremities [4, 10]. Because sarcoidosis is a diagnosis of exclusion many other causes of granuloma formation must be ruled out with a litany of tests and studies involving multiple specialties (as in this case). A punch biopsy should be used and will show noncaseating granulomas with central organized collections of epithelial macrophages and multinucleated giant cells surrounded by sparse lymphocytes [1]. This presentation with sparse lymphocytes is known as a naked granuloma and is a key feature of sarcoid lesions [1]. Gram stains on biopsy samples to rule out infectious organisms, imaging to rule out involvement of other organs, extensive history and physical exam, chest x-ray, pulmonary function tests, eye exams, CBC, CMP, EKG, UA, Tb skin test or interferon-*y* release assay, Thyroid testing, and Vitamin D25, and D1,25 are included in the workup. Also useful is the serum ACE which is elevated in 40-80% of patients with sarcoidosis [1].

CASE REPORT

This is the case of a 59-year old female who came to our clinic in March of 2017 with a 5-week history of bilateral indurated cutaneous lesions. They were firmly fixed to the skin, mobile, and nontender ranging in size from 1-6cm. She also reported lesions on her bilateral upper thighs. She had no history of any trauma to the regions, skin cancer, or skin infections. Her past medical history was notable for myocardial infarction, hypertension, hyperlipidemia, hypothyroid, pulmonary embolism, and gout. She had complained of a chronic dry cough that had occurred after moving to Arizona from California and denied history of smoking. Also noteworthy was a change in her medications upon arriving in Arizona. She had discontinued steroid injections for her hips upon arriving in Arizona (see Table 2 for a full list of medications). The decision was made to remove a lesion from each arm and send it to pathology. She had operative resection of the arm lesions on 3/30/17. She had no complications or recurrence and path showed non-necrotizing granulomata negative for neoplasia. Gram stains and anaerobic and aerobic cultures were negative. She was also sent to a pulmonologist for appropriate work up of her cough. On pulmonary function studies the patient had a mild restrictive lung defect with normal diffusion capacity. Suspecting sarcoidosis, further testing was requested by the pulmonologist including, repeat biopsies of the lesions with special stains, and a CT of the chest revealing multiple bilateral nonpathologically enlarged mediastinal lymph nodes.

On 4/25/17 the patient underwent repeat biopsies of the arm lesions and these were tested for AFP and GMS stains both of which returned negative along with negative repeat anaerobic and aerobic cultures. The pathology again showed non-necrotizing granuloma. A quantiferon gold level was negative ruling out a mycobacterial infection. ACE levels are elevated in approximately half of all sarcoidosis patients according to one source. However, in our patient it was found to be within normal limits [1]. The test results were discussed with the patient's pulmonologist who decided to do a bronchoscopy and right lower lobe lavage on 5/1/17. Lavage fluid was sent to pathology and returned with no sign of infection or malignancy. It was determined after ruling out all other possibilities of infectious, malignant, and foreign body reactions that the patient most likely had an undiagnosed sarcoidosis related illness. The patient was started on high dose steroids 3 weeks after her forearm biopsies to allow appropriate time for surgical wound healing. The steroids were then tapered to the lowest effective dose to suppress the cough and skin nodules. Shortly after beginning the steroids the nodules completely resolved. It was hypothesized that the nodules and cough were being suppressed while the patient was in California due to the steroid injections she had been receiving for her hips.

Table 2. Complete list of patient medications and doses.

Medication	Dose	Frequency
Fenofibrate	54mg tablet PO	QD
Furosemide	20mg tablet PO	QD
Levothyroxine	50mcg tablet PO	QD
Prednisone*	30mg 20mg tablet PO 8/16-10/14, 10mg tab PO 7/3-8/13	QD
Klor-Con Sprinkle	10mEq capsule PO	QD
Metformin	500mg tablet PO	QD
Atorvastatin	20mg tablet PO	QD
Allopurinol	100mg tablet PO	QD
Valsartan	320mg tablet PO	QD
Clonidine HCl	0.1 mg tablet PO	QD
Nifedipine ER	60 mg tablet PO	QD
Xarelto	20 mg tablet PO	QD
Breo Ellipta	100 mcg-25 mcg/ dose powder	1Puff QD

**New medications given after the patient developed her nodules*

DISCUSSION

Sarcoidosis is a diagnosis of exclusion typically presenting in patients between 20 and 60 years of age [1]. It most frequently involves the lungs (over 90%) commonly presenting with upper respiratory symptoms and cough [1]. On imaging, bilateral hilar adenopathy is often noticed as in this patient [13]. Other similar granulomatous skin diseases have characteristic findings that were not seen in our patients work up (see Table 2).

Table 3. Histopathology was used to differentiate and confirm the diagnosis of subcutaneous sarcoidosis based on presence or absence of the above findings. [3]

Skin manifestation	Differentiating findings
Sarcoidosis	Noncaseating granulomas
Granuloma annulare	Mucin and collagen surrounding granulomas
Necrobiosis lipoidica	Granulomas with collagen between histiocytes
Necrobiotic xanthogranuloma	Xanthogranulomas, cholesterol clefting
Foreign body	Multinucleated giant cells, polarization
Infections	Postitive stains for microorganisms
Crohn's disease	Dermal granulomatous infiltrate composed of epithelioid histiocytes
Siliconosis	Fibrotic nodules with onion skinned arrangement of collagen fibers

In the case report by Plana et al, a 40-year old female with common variable immune deficiency (CVID) there was the similarity of sarcoidal granulomas of the skin. However in CVID there will frequently be synovial membrane involvement, history of recurrent infections, cytopenias, and autoimmune conditions [6]. Our patient had a normal cbc, and no history of recurrent infections making this diagnosis unlikely.

Vedove and colleagues—In contrast—present two confirmed cases of subcutaneous sarcoidosis which manifest with many similarities to this case presentation, following a similar work-up and treatment protocol to ours with successful results[1].

In the first case reported an 81-year old male presented with nontender firm nodules of bilateral forearms and thighs that appeared in 6 months time [1]. Biopsies, and special stains confirmed noncaseating granulomas of sarcoid origin [1]. He did also have an elevation in ACE which is common with sarcoidosis but not required for diagnosis [1]. He responded very well to prednisone [1].

In the second case a 69-year old woman presented with multiple large erythematous nodules appearing over 2 months time. Her biopsy results also confirmed noncaseating granulomas with negative staining and cultures ruling out foreign body particles, fungi, or infectious organisms. This patient also had bilateral hilar adenopathy on CT of the chest consistent with sarcoidosis[1].

During a review of 85 cases of subcutaneous sarcoidosis the majority presented with cutaneous nodules as their initial symptom[1]. Sixty-seven cases out of 85 presented with symmetric subcutaneous nodules on the extremities and the majority of them were subsequently found to have enlarged hilar lymph nodes.[1]

To confirm the diagnosis of sarcoidosis, supporting physical exam findings, histopathology, and imaging must be present. On balance, diseases with similar presentation must have been effectively ruled out. All criteria listed were met in our patient. Therefore, we can say with certainty that she had systemic sarcoidosis as evidenced by the hilar adenopathy seen on CT of her lungs, as well as subcutaneous sarcoidosis discovered by biopsy results and special staining performed on the specimen.

As for the trigerring event leading to the sarcoidal granuloma formation, historically research has shown that a variety of genetic mutations in HLA type genes combined with environmental exposures lead to the formation of sarcoid type granulomas [7]. Frequently infectious organisms, scars, polarized material such as tattoos, or foreign bodies have been required to trigger the inflammatory cascade leading to granuloma formation. In many cases the cause of granuloma formation remains unknown. Upon questioning our patient thoroughly there was no obvious identifiable exposure that led to the formation of the sarcoid granulomas seen on her forearms and hips [7]. Current treatments in the literature reflect a constantly evolving approach. One approach that has remained constant and with the best results is corticosteroids either systemic or locally injected [9]. Topical or intralesional steroids have been shown to have good outcomes as well in isolated cases without systemic symptoms [9].

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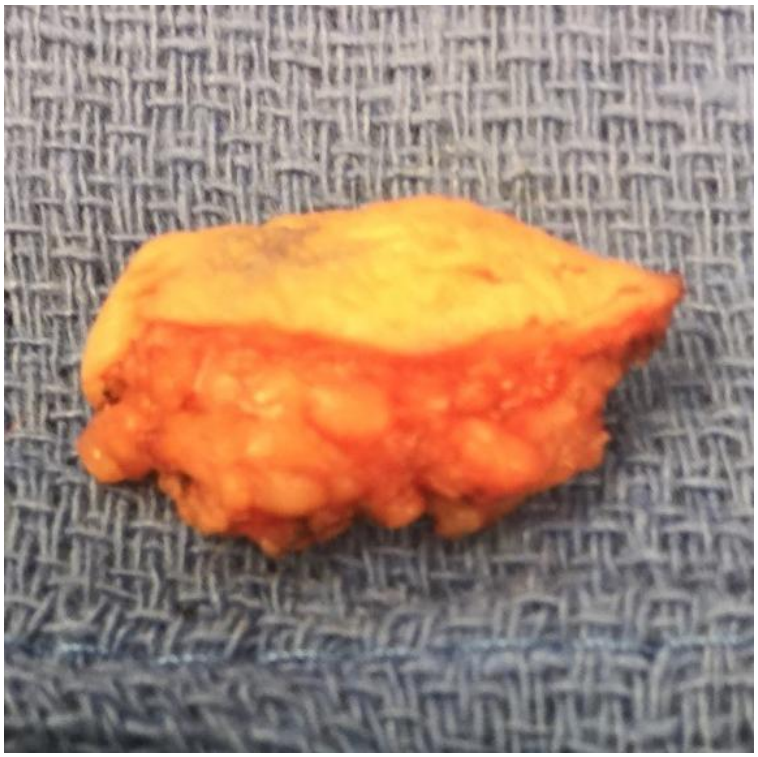

Figure 1. Right sided 1cm nodule removed from forearm.

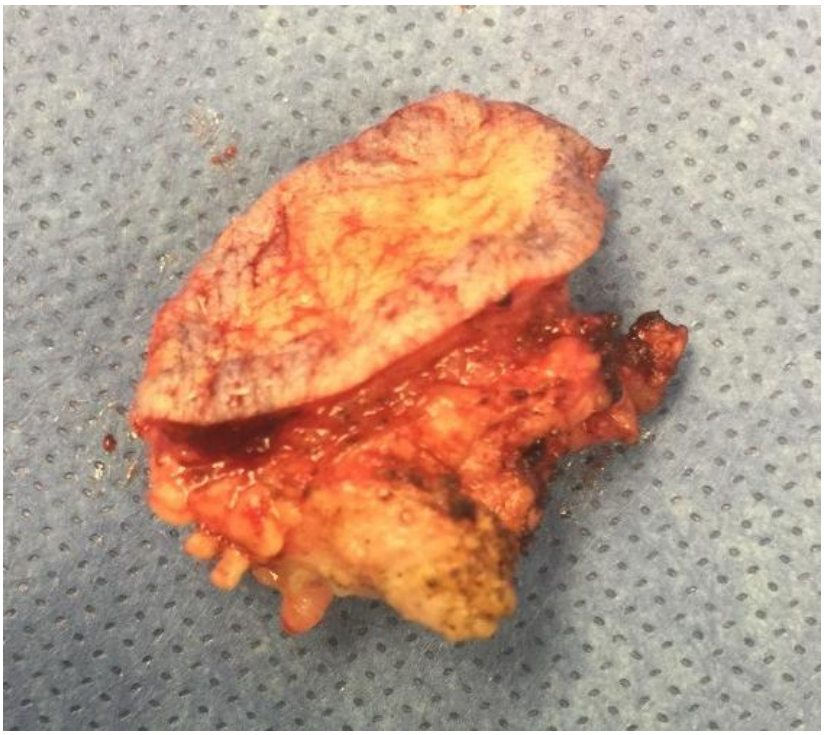

Figure 2. Left sided 2cm nodule removed from forearm.

