



# Clinicopathologic features, demographics, disease burden, and therapeutics in alopecic sarcoidosis: a case series and systematic review

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#### **ABSTRACT**

**Background:** Alopecic sarcoidosis is an uncommon cutaneous manifestation of sarcoidosis. Scarring and nonscarring alopecic sarcoidosis have been reported; however, information on the epidemiology, systemic disease associations, and treatment efficacy is limited.

**Objective:** To address these gaps, we conducted a retrospective chart review and systematic literature review of alopecic sarcoidosis cases.

**Methods:** Full-text English publications from PubMed, Scopus, and Google Scholar from inception to August 2023 were analyzed. Treatment evidence quality was assessed using the modified Oxford Centre for Evidence-Based Medicine rating scale. Three patients with biopsy-proven alopecic sarcoidosis were included as a case series, all demonstrating systemic sarcoidosis and 2 requiring multiple therapies. Among 1778 search results, 60 articles representing 77 cases of alopecic and scalp sarcoidosis were included. Patients were categorized into 4 distinct alopecic subgroups. Black patients constituted the majority of all subgroups.

**Results:** Extracutaneous sarcoidosis burden was high across all alopecic subgroups, with ocular disease appearing overrepresented. Topical and oral corticosteroids were the main treatments. Though scarring alopecia patients had poor outcomes despite receiving immunomodulators/cx, limited data suggest potential efficacy of tumor necrosis factor-alpha inhibitors.

**Limitations:** This study has a small sample size.

**Conclusion:** Our findings underscore the importance of evidence-based strategies for improving alopecic sarcoidosis management. Prompt diagnosis and systemic evaluation, especially for scarring alopecia, are essential for timely intervention to optimize patient outcomes.

Keywords: alopecia, cutaneous sarcoidosis, extracutaneous sarcoidosis, nonscarring, sarcoidosis, scarring, skin of color, treatment

#### Introduction

Sarcoidosis is a multisystem disease characterized by noncaseating granulomatous inflammation with an unknown etiology and variable disease course. 1-3 Sarcoidosis can impact any organ, potentially leading to chronic inflammation, fibrosis, organ dysfunction, or death. 1-3 The pathogenesis and prognosis of sarcoidosis are multifactorial, influenced by antigenic

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International Journal of Women's Dermatology (2024) 10:e181

Received: 29 April 2024; Accepted 9 August 2024

Published online 13 September 2024 DOI: 10.1097/JW9.000000000000181 triggers, genetics, gender, access to care, race, and income.<sup>1-3</sup> Approximately 30% of patients with systemic sarcoidosis in the United States develop skin manifestations.<sup>1,2</sup> Cutaneous sarcoidosis can serve as an initial indicator of systemic disease and may profoundly impact the quality of life.<sup>1-4</sup> Specific skin lesions, classified by the presence of granulomas on histology, may provide prognostic insights into systemic disease.<sup>1</sup> Certain specific skin lesions are chronic and occur more frequently among patients with skin of color, who also face a higher likelihood of developing severe extracutaneous disease.<sup>1,2,5,6</sup>

Alopecic sarcoidosis is an uncommonly reported cutaneous manifestation of sarcoidosis with limited literature suggesting a higher prevalence among Black patients. 1.2,7,8 Both scarring (SA) and nonscarring alopecic (NSA) sarcoidosis have been reported; however, data guiding evaluation and treatment of alopecic sarcoidosis are limited. 7,8 Considering the impact of SA on quality of life, and the potential prognostic implications of alopecic sarcoidosis on extracutaneous disease, it is important that dermatologists approach scalp disease in sarcoidosis comprehensively. Herein, we present a three-patient case series and systematic review of alopecic sarcoidosis to identify clinicopathologic features of SA and NSA, epidemiologic data, associations with cutaneous and extracutaneous disease, and response to therapy.

#### **Patients and methods**

# Case series

This case series included 3 patients with biopsy-proven alopecic sarcoidosis at NYU Langone Health between 2014 and 2024

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# What is known about this subject in regard to women and their families?

- Sarcoidosis, characterized by noncaseating granulomatous inflammation, demonstrates variable incidence and prevalence and may disproportionally impact women. While alopecia secondary to sarcoidosis is rare, it often manifests as scarring hair loss, particularly impacting Black women.
- The adverse psychosocial effects and impacts on quality of life in women caused by alopecia, especially when leading to scarring, may be profound. In addition to the burden of systemic sarcoidosis, women with alopecic sarcoidosis often experience increased levels of anxiety, depression, and social stigma, which can affect relationships and overall well-being.
- Despite its significant impact, there is limited literature on the epidemiology, systemic disease associations, and treatment efficacy of alopecic sarcoidosis.

# What is new from this article as messages for women and their families?

- Alopecic sarcoidosis frequently presents with systemic involvement, requiring thorough evaluation and monitoring.
- Given the potential for scarring hair loss, early recognition and aggressive therapeutic approaches are essential to potentially prevent or halt scarring alopecia.
- Additional research is warranted to advance our understanding of sarcoid alopecia and optimize therapy, with a particular focus on investigating the potential benefits of tumor necrosis factor-alpha inhibitors.

and was deemed institutional review board exempt given fewer than 4 cases presented. Baseline characteristics are demonstrated in Table 1.

#### Systematic literature review

We performed a systematic literature review of alopecic sarcoidosis and scalp sarcoidosis without alopecia to describe clinicopathologic features of SA and NSA, epidemiologic data, co-existing cutaneous and extracutaneous disease, treatment modalities, and efficacy.

## Methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines. Since this study used publicly available data from published studies, it was deemed institutional review board exempt.

#### Information sources and search

Two authors (C.O. and M.S.) conducted independent searches of PubMed, Scopus, and Google Scholar from their inception through August 2023. Search terms used in various combinations included: sarcoid, sarcoidosis, alopecia, hair, scalp, cicatricle, scarring, and non-scarring. The full search strategy is available in the Supplementary Methods, http://links.lww.com/IJWD/A57.

#### Inclusion criteria

Publications that described at least 1 case of sarcoidosis alopecia or scalp sarcoidosis were included. Publications without full-text versions in English were excluded.

## Study selection, data extraction, and quality assessment

Two authors (C.O. and M.S.) independently screened the title and abstract of each retrieved record and reviewed 15 articles independently to test the inclusion criteria, all decisions were unanimous. Both authors independently reviewed full-text publications that met inclusion criteria and extracted descriptive and quantitative data into a standardized Excel (Microsoft) spreadsheet. Extracted data included: demographics, presentation, exam features, differential diagnosis, additional cutaneous

# Table 1 Summary of sarcoidosis alopecia case series

Case	Age at biopsy (y)	Sex	Race	Clinical description	Histopathological description	Other skin manifestations	Systemic features	Treatment	Follow-up
1	40s	Female	White	Cicatricial alopecia, patches, scaling, and erythema	Granulomatous dermatitis comprising well- circumscribed aggregates of epithelioid histiocytes with a sparse admixed infiltrate	Indurated plaques on the face and lower extremities	Hilar and paratracheal adenopathy, pulmonary	Fluocinonide 0.05 % ointment BID, IL TAC, HCQ 200 mg BID	At 7 months: stabilization of hair loss, no new lesions
2	70s	Female	Black	Cicatricial alopecia, ulcers, scaling, pink dyspigmentation, and raised borders	Granulomatous dermatitis comprising nodular and loose aggregates of epithelioid histiocytes with admixed lymphocytes and neutrophils	Papulonodules on the face raised plaque on the arm	Ocular	Clobetasol 0.05% solution daily, Mupirocin 2% ointment BID, Doxycycline 40 mg daily	Lost to follow-up
3	40s	Female	Black	Cicatricial alopecia, patches, annular plaques, atrophy, pink dyspigmentation, hyperpigmented borders, and scaling	Granulomatous dermatitis comprising epithelioid histiocytes with a few multinucleated forms and a scant accompanying lymphocytic infiltrate	Erythematous to hyperpigmented, indurated, scaly plaques on face, neck, trunk, and extremities	Pulmonary	Clobetasol 0.05% solution daily, Tacrolimus 0.1% ointment BID, Doxycycline 100 mg BID, HCQ 200 mg BID	At 9 months: significant improvement, with partial hair regrowth, thinning plaques

findings, extracutaneous disease, treatment, and reported efficacy. Quality assessment of reported treatments was performed by both authors using the modified Oxford Centre for Evidence-Based Medicine's Level of Evidence rating scale.<sup>9</sup>

#### **Data analysis**

Statistical analyses were performed using STATA V.18 (College Station, TX: StataCorp).

Continuous variables are reported as means with standard deviation and categorical variables are displayed as percentages. P values were calculated with Pearson  $\chi^2$  for categorical variables and Student's t test or analysis of variance for continuous variables as appropriate. P values <.05 were considered statistically significant.

#### Results

#### Case series

#### Case 1

A White female in her 40s presented with a 20-year history of an eruption initially limited to her legs but progressing over 6 months to involve her scalp. She noted scalp redness, itch, and hair loss accompanied by fatigue and persistent cough. Physical examination of the scalp revealed a scarring alopecic, pink and yellow, scaly patch (Fig. 1A). Indurated plaques on the face and lower extremities were also noted.

Four-millimeter punch biopsies from the scalp and lower extremity demonstrated granulomatous inflammation with epithelioid histiocytes throughout the dermis. Stainings for periodic acid-Schiff and acid-fast bacilli were negative. Polarizing microscopy revealed no foreign material. Evaluation by pulmonology revealed mediastinal and right hilar lymphadenopathy with numerous pulmonary nodules, but normal pulmonary function tests. Cardiac and ophthalmologic workups were negative.

The patient's hair loss persisted despite topical and intralesional steroids. Subsequently, the patient was started on hydroxychloroquine 400 mg daily. At her 7-month follow-up, she reported stabilization of hair loss. Her follow-up scalp examination demonstrated loss of follicular ostia without erythema or scaling.

## Case 2

A Black female in her 70s was referred to dermatology for a 3-year history of progressive hair loss with painful and pruritic scalp lesions. Physical examination revealed SA, ulcers with light pink dyspigmentation, and diffuse scaling. Raised plaques





Fig. 1. Alopecic sarcoidosis. (A) Scarring alopecic, pink, and yellow, scaly patchy on the scalp. (B) Atrophic, pink plaques of scarring alopecia with hyperpigmented borders found to be late-stage scarring alopecic sarcoidosis.

on the left cheek and upper extremities and papulonodules at the medial canthi were observed. A scalp punch biopsy demonstrated a noncaseating granulomatous dermatitis with epithelioid histiocytes in the dermis. Ophthalmologic examination demonstrated bilateral intermediate uveitis consistent with ocular sarcoidosis. While undergoing further workup, the patient was lost to follow-up.

#### Case 3

A Black female in her 40s presented with a 12-year history of a widespread eruption extending to her scalp, causing progressive hair loss for several years. She reported arthralgia, palpitations, and dyspnea. She reported that prior skin biopsies were consistent with sarcoidosis. Previous treatments included topical steroids, oral steroids, and hydroxychloroquine. Physical exam was notable for atrophic, pink plaques of SA with hyperpigmented borders (Fig. 1B). Flesh-colored to hyperpigmented nodules on the right nasal ala and large indurated plaques on the face, neck, trunk, and extremities were observed. A 4-mm punch biopsy of an alopecic plaque on the scalp demonstrated aggregates of epithelioid histiocytes in the dermis. Stainings for periodic acid-Schiff and acid-fast bacilli were negative.

Pulmonary evaluation revealed mild hilar lymphadenopathy and normal pulmonary function tests. Due to extensive cutaneous involvement, the patient was started on hydroxychloroquine 400 mg daily and doxycycline 200 mg daily. At the 9-month follow-up, she reported significant improvement with thinning plaques, minimal inflammation, and partial hair regrowth (Table 1).

#### Systematic review

Of 1778 search results, 171 were duplicates and 1529 were excluded by title and abstract screening (Supplemental Material, http://links.lww.com/IJWD/A57). Among 78 full-text articles that were assessed, 60 met inclusion criteria, representing 77 patients.<sup>7,8,10-68</sup> About 58 of 60 publications were either case series or case reports. Most studies received poor-quality levels of evidence ratings. (Table 2 and Supplemental Material, http://links.lww.com/IJWD/A57). Cases were categorized as SA, NSA, scalp sarcoidosis without alopecia, or undefined if alopecia type was not specified.

#### Scarring alopecia

A total of 47 SA cases secondary to sarcoidosis were identified (mean age: 52.8 years, female: 86% [37/43]) (Table 3).  $^{7,8,10,11,13-19}$ ,  $^{23-25,27,28,30,31,33,35,37-39,41,44,46,48,52,53,56-58,60-64,66-68}$  Black patients were the most affected racial group (75.9% [22/29], P < .001). Common physical exam descriptors were scaly, atrophic, and indurated plaques with raised borders that were shiny, erythematous, yellow, or dyspigmented. Scalp ulceration was less commonly reported.  $^{5,11,13,44,57,61,64}$ 

Trichoscopy of scalp sarcoidosis demonstrated perifollicular and follicular yellow-orange, pale spots with perifollicular scaling, telangiectasias, and dystrophic hairs (Fig. 2).<sup>48</sup> Before the biopsy, a wide differential diagnosis of cicatricial alopecia was suggested, including discoid lupus erythematosus (DLE), necrobiosis lipoidica, lichen planopilaris, scleroderma, frontal fibrosing alopecia, psoriasis, central centrifugal cicatricial alopecia, and morphea. Most patients underwent scalp punch biopsies (87.2% [41/47]), which demonstrated dermal nodular infiltrates of noncaseating granulomas invading hair follicles with sparse lymphocytic infiltrates (Fig. 3). Complete follicular destruction (7.3% [3/41]), necrobiotic collagen (14.6% [6/41]), and loss of elastic fibers (2.4% [1/41]) were uncommonly reported. Special stains and polarized light examination were reported in 46.3% of biopsies (19/41), with no micro-organisms or foreign bodies found.

Table 2

#### Effectiveness of reported treatments for alopecic sarcoidosis with quality of evidence ratings

		Study supports potential effectiveness	Study does not support effectiveness
Treatment	Quality level of evidence <sup>a</sup>	(No. studies)	(No. studies)
Corticosteroids			
Oral	4	215,23	38,15,17
	5	1411,14,21,34,35,37,40,43,45,54,57–59,61	1113,16,20,33,41,48,52,55,56,63,65
Intralesional	3	118	0
	4	1 <sup>23</sup>	3 <sup>7,15,17</sup>
	5	431,43,48,64	$2^{22,56}$
Topical	4	1 <sup>23</sup>	3 <sup>7,8,47</sup>
	5	714,35,37,49,54,58,68	713,20,22,29,33,46,56
Intravenous	5	0	<b>1</b> <sup>41</sup>
Intramuscular	5	1 <sup>68</sup>	0
Antibiotics			
Tetracycline	4	0	27,17
	5	231,61	
Clarithromycin	4	0	<b>1</b> <sup>17</sup>
Clindamycin	4	0	1 <sup>7</sup>
Rifampin	4	0	1 <sup>7</sup>
Cephalosporin	4	17	0
обришооронн	5	0	1 <sup>61</sup>
Linezolid	5	1 <sup>61</sup>	0
Ciprofloxacin	5	1 <sup>61</sup>	0
Immunomodulators/immunosuppressants	Ŭ	•	ŭ
Hydroxychloroquine	4	0	28,17
Trydroxyomoroquino	5	331,37,64	213,39
Chloroquine	4	1 <sup>23</sup>	215,60
Methotrexate	4	1 <sup>23</sup>	1 <sup>17</sup>
IVICTI IOTI CACIC	5	235,58	213,39
Mycophenolate Mofetil	5	0	113
Infliximab	4	1 <sup>17</sup>	0
Topical tacrolimus	4	0	1 <sup>17</sup>
Topical tacrollinus		1 <sup>56</sup>	0
Doptovifulling	5 5	0	1 <sup>56</sup>
Pentoxifylline Miscellaneous	5	U	In
	5	4 21	0
Ketoconazole shampoo	5	1 <sup>31</sup>	0
Allopurinol	4	0	117
Topical minoxidil	5	135	0
Carpronium	5	0	1 <sup>29</sup>
Fusidic acid	5	145	0
Potassium permanganate compresses	5	<b>1</b> <sup>45</sup>	0

\*Quality defined by the JAMA Dermatology Quality Rating Scheme for Studies and Other Evidence (modified Oxford Centre for Evidence-Based Medicine, 2011 criteria): level 1, systematic review with meta-analysis, properly powered and conducted randomized clinical trial (not included in this analysis); 2, well-designed controlled trial without randomization; prospective comparative cohort trial (not included in this analysis); 3, case—control studies; retrospective cohort study; 4, case series with or without intervention, cross-sectional study; and 5, case reports, opinion of respected authorities.

Most patients (57.4% [27/47]) had additional cutaneous sarcoidosis findings with a statistically significant predominance of facial involvement (59% [16/27], P = .040). Involvement of the extremities (upper: 29.6% [8/27], lower: 33.3% [9/27]) and trunk (18.5% [5/27]) was reported. Plaques (44% [12/27]) and papules (33% [9/27]) were common morphologic findings. Nodules (11.1% [3/27]), ulcers (7.4% [2/27]), and infiltrative scar sarcoidosis (7.4% [2/27]) were uncommon.

Most patients had systemic sarcoidosis (66.6% [31/47], P=.03) with a predominance of lung involvement (87.1% [27/31]). Other organs impacted included the heart (6.5% [2/31]), liver (6.5% [2/31]), vasculature (6.5% [2/31]), bone (6.5% [2/31]), spleen (3.2% [1/31]), kidneys (3.2% [1/31]), eyes (3.2% [1/31]), and mucosa (3.2% [1/31]). Three patients developed severe hypercalcemia.

#### Nonscarring alopecia

Fewer cases of NSA were identified (n=18) (Table 3).  $^{7,8,27,29,32,34,40,42,43,45,47-51,65}$  On average, NSA patients were over 10 years younger than SA patients (40.1 years NSA vs 52.8 years SA, P=.02) with a more equal sex distribution

(female: 47.1%, P < .001). No significant difference in race was observed between alopecia subgroups (P = .39).

NSA was described as scaly, erythematous plaques, or patches. Most cases were confined to the scalp; however, 3 patients developed nonscalp alopecia involving the lower extremities. <sup>32,50,65</sup> One patient presented with total alopecia of the scalp and body, with 2 biopsies demonstrating granulomatous inflammation.<sup>34</sup>

Differential diagnoses prior to biopsy were alopecia areata, lichen planopilaris, DLE, necrobiosis lipoidica, follicular mucinosis, folliculitis decalvans, or tinea capitis. Scalp punch biopsies were performed in 94.4% (17/18) of cases, revealing dermal noncaseating granulomas adjacent to pilosebaceous units. Loss of hair follicles was described in 3/17 (17.6%) cases. Few cases reported completion of special stains and polarized light microscopy (23.5% [4/17]).

Notably, 44.4% (8/18) of NSA patients had additional cutaneous manifestations. Unlike SA patients, involvement of the extremities (upper: 37.5% [3/8], lower: 62.5% [5/8]) was more common than facial involvement (25% [2/8]), but not statistically significant (upper extremities P = .52, lower extremities P = .22). Plaques and subcutaneous nodules were the most described cutaneous findings.

Table 3
Characteristics of cases of sarcoidosis alopecia and scalp sarcoidosis

	All cases	Scarring alopecia	Nonscarring alopecia	Scalp sarcoidosis without alopecia	<b>Undefined alopecia</b>	<i>P</i> value
Characteristics, n (%)	N = 77	n = 47	n = 18	n = 6	n = 6	
Demographics	-					
Age (y), mean (SD) Sex	48.9 (16.2)	52.8 (15.1)	40.1 (16.3)	54.7 (19.3)	40.8 (8.84)	.02 <.001
Female Male	51 (70.8%) 21 (29.2%)	37 (86%) 6 (14%)	8 (47.1%) 9 (52.9%)	1 (16.7%) 5 (83.3%)	5 (83.3%) 1 (16.7%)	
Not stated	5	4	1	0	0	
Race						.39
Black White	32 (71.1%) 9 (20%)	22 (75.9%) 5 (17.2%)	5 (55.6%) 3 (33.3%)	1 (50%) 0	4 (80%) 1 (20%)	
Asian	4 (8.8%)	2 (6.9%)	1 (11.10%)	1 (50%)	0	
Not stated Sarcoidosis information Cutaneous sarcoidosis elsewher	32	18	9	4	1	
Yes	42 (54.5%)	27 (57.4%)	8 (44.4%)	3 (50%)	4 (66.7%)	.73
No/not stated Systemic sarcoidosis	35 (45.5%)	20 (42.6%)	10 (55.6%)	3 (50%)	2 (33.3%)	.75
Yes	55 (71.4%)	31 (66%)	13 (72.2%)	6 (100%)	5 (83.3%)	.32
No/not stated	22 (28.6%)	16 (34%)	5 (27.8%)	0	1 (16.7%)	.02
Systemic sarcoidosis organs involve		(- (- (- (- (- (- (- (- (- (- (- (- (- (	- (=: := /=/	-	. ( , . ,	
Pulmonary	49 (89.1%)	27 (87.1%)	12 (92.3%)	6 (100%)	4 (80%)	.23
Cardiac	3 (5.5%)	2 (6.5%)	1 (7.7%)	0`	0 ′	.88
Hepatic	5 (9.1%)	2 (6.5%)	2 (15.4%)	0	1 (20%)	.48
Splenic	3 (5.4%)	1 (3.2%)	1 (7.7%)	0	1 (20%)	.33
Bone	4 (7.3%)	2 (6.5%)	0	0	2 (40%)	.01
Muscular	1 (1.8%)	0	1 (7.7%)	0	0	.35
Arthritic/arthropathy/joint	1 (1.8%)	0	1 (7.7%)	0	0	.35
Neurologic	2 (3.6%)	0	2 (15.4%)	0	0	.08
Ocular/ophthalmic	11 (20%)	1 (3.2%)	5 (38.5%)	3 (50%)	2 (40%)	.001
Extrathoracic lymphadenopathy	1 (1.8%)	0	1 (7.7%)	0	0	.35
Mucosal	3 (5.5%)	1 (3.2%)	1 (7.7%)	0	1 (20%)	.34
Glandular	1 (1.8%)	0	0	0	1 (20%)	.007
Vasculitis (arteritis)	2 (3.6%)	2 (6.5%)	0	0	0	.72
Renal	1 (1.8%)	1 (3.2%)	0	0	0	.89
Other: hypercalcemia	3 (5.5%)	3 (9.7%)	0	0	0	.72

Reported P values compare values between alopecia subgroups using Pearson  $\chi^2$  for categorical variables and analysis of variance for continuous variables as appropriate.

Most NSA patients had systemic sarcoidosis (72.2% [13/18]) with a predominance of pulmonary sarcoidosis (92.3% [12/13]). Patients also exhibited involvement of the eyes (38.5% [5/13]), liver (15.4% [2/13]), central nervous system (15.4% [2/13]), heart (7.7% [1/13]), spleen (7.7% [1/13]), muscle (7.7% [1/13]), joints (7.7% [1/13]), nose (7.7% (1/13)), larynx (7.7% (1/13)), and extrathoracic lymph nodes (7.7% (1/13)).

# Scalp sarcoidosis without alopecia and undefined alopecia

Scalp sarcoidosis without concomitant alopecia was reported in 6 cases (male:83.3% [5/6], mean age: 54.7 years) and described as erythematous, infiltrated scaly plaques (Table 3).<sup>20,21,36,54,55,59</sup> A biopsy was obtained in all cases and demonstrated sarcoidal features.

A total of 50% (3/6) of patients had additional cutaneous sarcoidosis findings with papules, plaques, and nodules found on the face, trunk, and extremities. All 6 patients had evidence of systemic sarcoidosis with pulmonary sarcoidosis seen in all cases and ocular involvement was reported in 3 patients.

In 6 cases, alopecia subtype was not defined by authors (female: 83.3% [5/6], mean age: 40.8 years, Black race: 80% [4/5]) (Table 3). 8,12,22,26 Biopsies were obtained in 83.3% (5/6) and demonstrated granulomatous inflammation. Most patients had additional cutaneous manifestations of sarcoidosis (66.7% [4/6]) and systemic disease (83.3% [5/6]).

## **Treatment**

Treatment was reported in 48/77 cases (Table 4).  $^{7.8,11,13-18,20-23,29,31,33-35,37,39-41,43,45-49,52,54-61,63-65,68}$  The average number of treatment agents given across all cases was 2.3. Topical and oral corticosteroids were the most reported treatment. SA patients commonly received oral corticosteroids (SA: 66.7% [20/30] vs NSA: 41.7% [5/12], P = .02). SA and NSA patients received similar amounts of topical corticosteroids (SA: 40% [12/30] vs NSA: 41.7% [5/12]; P = .92).

SA patients were additionally treated with hydroxychloroquine (26.7% [8/30]), chloroquine (10% [3/30]), methotrexate (20% [6/30]), mycophenolate mofetil (3.3% [1/30]), and tetracycline antibiotics (16.7% [5/30]). Two SA patients were treated with infliximab (6.7% [2/30]). 17

SA patients had poor treatment outcomes (Supplemental Material, http://links.lww.com/IJWD/A57). Of patients receiving oral corticosteroids, only 10% (2/20) reported partial or complete hair regrowth while 30% (6/20) had stabilization of hair loss and 40% (8/20) had no improvement. Most SA patients receiving topical (58.3% [7/12]) or intralesional steroids (66.6% [6/9]) similarly reported no improvement of alopecia. SA patients who received hydroxychloroquine (50% [4/8]) or methotrexate (33.3% [2/6]) did not have improvement in hair loss. Both patients treated with infliximab had hair regrowth. Notably, their biopsies demonstrated superficial and deep granulomatous inflammation without comment on scarring or follicular destruction.<sup>17</sup>

NSA patients generally had better treatment outcomes (Supplemental Material, http://links.lww.com/IJWD/A57). About 60% (3/5) of NSA patients given oral corticosteroids



**Fig. 2.** Trichoscopy of scalp sarcoid demonstrating yellow globules, telangiectasias, and perifollicular scale. Representative image obtained from an NYU Langone Health patient.

reported a complete response of their hair loss to treatment. And 80% of patients (4/5) who received topical corticosteroids had no improvement, while only 20% (1/5) reported a complete response. Some patients with scalp sarcoidosis without alopecia had complete (20% [1/5]) or partial (40% [2/5]) response with oral corticosteroids.

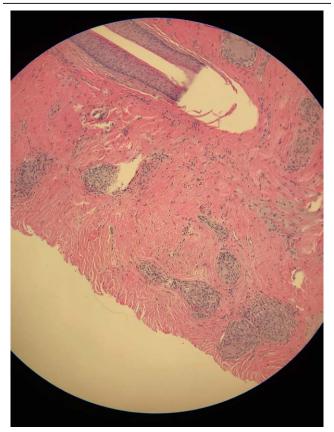


Fig. 3. Dermal nodular infiltrates of noncaseating granulomas surrounding hair follicle with sparse lymphocytic infiltrate (hematoxylin and eosin). Representative image obtained from the Section of Dermatopathology in NYU Langone Health's Ronald O. Perelman Department of Dermatology.

#### **Discussion**

This case series and systematic review highlight important clinical and pathologic features of alopecic sarcoidosis. While there was a wide range of clinical descriptions of scalp disease, both SA and NSA often presented as scaly, atrophic, erythematous, or dyspigmented plaques or patches. The wide range of differential diagnoses considered before biopsy underscores the potential for cutaneous sarcoidosis to mimic several conditions, highlighting the importance of obtaining a biopsy in the evaluation of alopecia, especially when scarring or systemic disease is a consideration.

The pathophysiology of alopecic sarcoidosis remains unclear. While a high burden of scarring alopecic sarcoidosis was described in this review, cutaneous sarcoidosis rarely involves scarring or ulceration. This raises the possibility that patients with alopecic sarcoidosis may have a primary concomitant alopecia that initiates inflammation and scarring, to which granulomas hone to in the setting of sarcoidosis. To highlight this hypothesis, one case series demonstrated patients with alopecic sarcoidosis with histologic evidence of co-existing DLE and alopecia areata.<sup>27</sup> However, definitive conclusions cannot be drawn and further research is required as to why alopecic sarcoidosis can scar.

Black patients constituted a significant proportion of patients who developed alopecia secondary to sarcoidosis. Though it remains unclear why alopecic sarcoidosis appears to be more common among Black patients, this disproportionate impact may point to underlying environmental exposures or barriers to care and delayed care as contributing factors. Statistically significant differences in age and sex were observed between SA and NSA. The greater involvement of SA among older patients may reflect the longevity of the disease process or delayed diagnosis, suggesting the importance of early treatment to prevent scarring hair loss.

Most patients with alopecic sarcoidosis had additional manifestations of cutaneous sarcoidosis; however, the distribution of cutaneous disease varied among subtypes. All forms of alopecic and scalp sarcoidosis were associated with high rates of systemic involvement, aligning with established prevalence patterns of extracutaneous sarcoidosis. Pulmonary sarcoidosis predominated across all groups, as expected, given this is the most impacted organ in sarcoidosis. For Considering reported rates of ocular sarcoidosis, ocular involvement was overrepresented in this systematic review, possibly influenced by the high representation of female and Black patients, who have an established increased burden of ocular sarcoidosis. Yet this illustrates for dermatologists that referring patients for eye screening is imperative.

In general, alopecic sarcoidosis had poor treatment outcomes. Most patients received corticosteroids. 70,71 NSA patients had moderate treatment responses with topical and oral corticosteroids. In addition to receiving corticosteroids, SA patients typically received corticosteroid-sparing immunomodulators and immunosuppressants. Two cases illustrated the response of hair loss secondary to SA with infliximab.<sup>17</sup> This is consistent with prior literature demonstrating infliximab's benefit for severe, chronic, and cutaneous sarcoidosis, 72 highlighting for dermatologists that when treating alopecic sarcoidosis, rapid deployment of tumor necrosis factor inhibitors may be required. Treatment with other immune therapies can also be considered. While azathioprine and leflunomide have been described as treatments for sarcoid, neither were reported as therapies for alopecic sarcoidosis. Moreover, azathioprine has demonstrated low efficacy in treating cutaneous sarcoid.<sup>73</sup> The role of Janus Kinase inhibitors for alopecic sarcoidosis is underexplored; however, prior data suggests potential benefits for cutaneous sarcoidosis. 74-76

Interpreting this data comes with several limitations including heterogeneity in patient characteristics, variability in treatment and treatment response measures, small sample size, and the absence of blinding, randomization, or control groups in

Table 4
Treatment is given to patients with sarcoidosis alopecia/scalp sarcoidosis, stratified by alopecia subtype

	All patients	Scarring alopecia	Nonscarring alopecia	Scalp sarcoidosis without alopecia	<b>Undefined alopecia</b>	
	N = 77	n = 47	n = 18	n = 6	n = 6	P value
Treatment given						
Yes	48 (62.3%)	30 (63.8%)	12 (66.7%)	5 (83.3%)	1 (16.7%)	.08
No/not stated	29 (37.7%)	17 (36.2%)	6 (33.3%)	1 (16.7%)	5 (83.3%)	
Total number of treatments	2.3 (1.6)	2.6 (1.8)	1.8 (1.4)	1.4 (0)	2	.29
given, mean (SD)	, ,	, ,	, ,	. ,		
Number of systemic treatments	1.4 (1.4)	1.8 (1.5)	0.75 (1.1)	1 (0)	0	.097
given, mean (SD)	,	,	,	· /		
Treatment class						
Corticosteroids						
Oral	30 (62.5%)	20 (66.7%)	5 (41.7%)	5 (100%)	0	.02
Intralesional	13 (27.1%)	9 (30%)	3 (25%)	0	1 (100%)	.75
Topical	20 (41.7%)	12 (40%)	5 (41.7%)	2 (40%)	1 (100%)	.92
Intravenous	1 (2.1%)	1 (3.3%)	0 ′	0 ′	0 ′	.89
Intramuscular	1 (2.1%)	1 (3.3%)	0	0	0	.89
Antimicrobials	(/	()				
Tetracycline	6 (12.5%)	5 (16.7%)	1 (8.3%)	0	0	.64
Clarithromycin	1 (2.1%)	1 (3.3%)	0 ′	0	0	.89
Ketoconazole (topical)	1 (2.1%)	1 (3.3%)	0	0	0	.89
Clindamycin	1 (2.1%)	0` ′	1 (8.3%)	0	0	.35
Rifampin	1 (2.1%)	0	1 (8.3%)	0	0	.35
Cephalexin	1 (2.1%)	0	1 (8.3%)	0	0	.35
Cefepime	1 (2.1%)	1 (3.3%)	0	0	0	.89
Linezolid	1 (2.1%)	1 (3.3%)	0	0	0	.89
Ciprofloxacin	1 (2.1%)	1 (3.3%)	0	0	0	.89
Immunomodulators/immunosu	ippressants					
Chloroquine	3 (6.3%)	3 (10 %)	0	0	0	.57
Hydroxychloroquine	8 (16.6%)	8 (26.7%)	0	0	0	.13
Methotrexate	6 (12.5%)	6 (20 %)	0	0	0	.25
Mycophenolate mofetil	1 (2.1%)	1 (3.3%)	0	0	0	.89
Tacrolimus (topical)	3 (6.3%)	3 (10%)	0	0	0	.57
Allopurinol	1 (2.1%)	1 (3.3%)	0	0	0	.89
Pentoxifylline	1 (2.1%)	1 (3.3%)	0	0	0	.89
Biologics						
Infliximab	2 (4.2%)	2 (6.7%)	0	0	0	.73
Other						
Minoxidil (topical foam)	1 (2.1%)	1 (3.3%)	0	0	0	.89
Carpronium	1 (2.1%)	0`	1 (8.3%)	0	0	.35
Fusidic acid (topical)	1 (2.1%)	0	1 (8.3%)	0	0	.35
Potassium permanganate	1 (2.1%)	0	1 (8.3%)	0	0	.35
compress						

Reported P values compare values between alopecia subgroups using Pearson  $\chi^2$  for categorical variables and analysis of variance for continuous variables as appropriate.

these case reports. Additionally, considering the high likelihood of publication bias with the use of case report data, the rate of systemic associations is likely an overestimation. Despite these limitations, given the importance of early recognition of specific signs of cutaneous sarcoidosis, and as SA adversely affects quality of life,<sup>77</sup> dermatologists should understand and recognize alopecic sarcoidosis and consider aggressive therapy to prevent scarring hair loss.

In conclusion, this review highlights the multifaceted nature and significant impact of alopecic sarcoidosis, especially among patients with skin of color, and the associations with cutaneous and extracutaneous disease. The heterogeneity in the presentation, clinical features, and treatment outcomes of SA and NSA in sarcoidosis underscores the need for further research to investigate the underlying factors that drive these differences. Additionally, challenges in treating and diagnosing sarcoidosis highlight the need for clinical trials and standardized treatment approaches to provide evidence-based guidance for clinicians.

#### **Conflicts of interest**

None.

#### **Funding**

None.

#### Study approval

N/A

## **Author contributions**

All authors participated in the writing of this manuscript. CO, MS, SI, and ASC participated in the research design and data analysis.

#### **Patient consent**

Informed written consent was received from all patients for whom photographs are present in the manuscript.

#### **Data availability**

Template data collection forms, extracted data from included studies, and data used for all analyses are available from the corresponding author (A.C.) upon request.

#### Supplementary data

Supplementary material associated with this article can be found at http://links.lww.com/IJWD/A57.

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