

# Cutaneous Sarcoidosis: A Retrospective Clinico-Pathological Study from the Indian Subcontinent in Patients Attending a Tertiary Health Care Centre

## Abstract

**Context:** Sarcoidosis is a systemic disorder characterized histologically by noncaseating granulomas. There is paucity of Indian data on cutaneous sarcoidosis. **Aims:** To describe the clinical, histopathological findings, and extracutaneous involvement in cutaneous sarcoidosis. **Materials and Methods:** A retrospective study was done in patients of cutaneous sarcoidosis who had attended the dermatology clinic of a tertiary health care center in India from May 2009 to April 2015. The clinical details, histopathological findings, treatment, and response were reviewed. **Results:** There were 38 patients with cutaneous sarcoidosis. Mean age was  $48 \pm 13$  years; 58% were female. Median duration of disease was 11 months (IQR 4–48 months). More than one morphology was seen in 28.9%, commonest being plaques (65.7%), and papules (50%). Erythema nodosum was rare. More than one site was involved in 55.3%, most commonly trunk (52.6%). Six patients had isolated cutaneous sarcoidosis. Commonest extracutaneous organs involved were lung (73.7%) and lymph nodes (68.4%). Histopathologically, classical naked sarcoïdal granulomas were found in only 55.3%. Angiotensin converting enzyme (ACE) levels were elevated in 74.3% (26/35) with significant association with extracutaneous disease. Treatment included topical and/or systemic corticosteroids, hydroxychloroquine, and tacrolimus. **Statistics:** Pearson's Chi-square test was done to analyze associations between the skin lesions, ACE levels, and systemic involvement;  $P < 0.05$  was considered significant. **Conclusions:** Cutaneous manifestations of sarcoidosis are varied, commonest being erythematous plaques. Even though most patients had systemic involvement, we found no significant association of the type and number of skin lesions with extracutaneous involvement or prognosis. Elevated ACE levels were significantly associated with systemic involvement.

**Keywords:** ACE levels, naked granulomas, sarcoidosis

Gauri D. Mahabal,  
Dincy C. V. Peter,  
Leni George,  
Meera Thomas<sup>1</sup>,  
Susanne A.  
Pulimood

Departments of Dermatology  
and <sup>1</sup>Pathology, Christian  
Medical College, Vellore,  
Tamil Nadu, India

## Introduction

Sarcoidosis is a multisystem disorder of unknown etiology characterized by noncaseating granulomas on histopathology.<sup>[1]</sup> Skin is the most accessible and second most common organ involved in sarcoidosis.<sup>[2]</sup> The reported prevalence of cutaneous sarcoidosis is 20–35%.<sup>[1,2]</sup> Most of the studies on cutaneous sarcoidosis are from the West with relative paucity of Indian data.<sup>[3–6]</sup> Hence, we undertook this study to describe the clinical and histopathological spectrum of cutaneous sarcoidosis in our population and to look for any association between the various cutaneous lesions, systemic involvement, serum angiotensin converting enzyme (ACE) levels and prognosis.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

## Subjects and Methods

A retrospective study on cutaneous sarcoidosis between 1 May 2009 to 30 April 2015 (6 years) was conducted in the dermatology department of a tertiary care setting in South India. Patients in whom cutaneous sarcoidosis was clinically suspected and the histopathology showed the presence of epithelioid granulomas were included in the study after exclusion of infective causes like cutaneous tuberculosis, atypical mycobacterial infections, leishmaniasis, and deep fungal infections, by special stains and cultures for bacteria, mycobacteria, and fungi and non-infectious granulomatous conditions like granuloma annulare. Their clinical details, laboratory investigations, and

**How to cite this article:** Mahabal GD, Peter DC, George L, Thomas M, Pulimood SA. Cutaneous sarcoidosis: A retrospective clinico-pathological study from the Indian subcontinent in patients attending a tertiary health care centre. Indian Dermatol Online J 2021;12:566-71.

**Received:** 04-Aug-2020. **Revised:** 12-Sep-2020.  
**Accepted:** 01-Mar-2021. **Published:** 14-Jul-2021.

## Address for correspondence:

Dr. Susanne A. Pulimood,  
Department of Dermatology,  
Christian Medical College,  
Vellore, Tamil Nadu - 632 004,  
India.  
E-mail: sapulimood@gmail.com

## Access this article online

**Website:** www.idoj.in

**DOI:** 10.4103/idoj.IDOJ\_606\_20

## Quick Response Code:



histopathology were reviewed. Histopathologically, sarcoidosis was diagnosed based on non-caseating granulomatous inflammation and the features looked for were type of granulomas, whether naked or non-naked, discrete or confluent, and their location and depth and necrosis, if present.<sup>[7]</sup> Reticulin and mucin stain, if done, were also reviewed. The symptoms, clinical features, and systemic involvement were noted from the hospital records. Investigations like Mantoux test (performed using 2TU tuberculin), chest radiography, and ACE levels were reviewed. Chest X-ray staging was done based on the Siltzbach classification system.<sup>[8]</sup> Serum ACE levels more than 52 U/L were taken as elevated. The treatment given and the response to treatment were recorded and classified as complete resolution, persistent lesions, and relapse of lesions.

### Statistical methods

Frequencies and percentages were reported for qualitative variables. Pearson's Chi-square test was used to analyze associations between the type and extent of skin lesions with systemic involvement and elevated ACE levels. The *P* value less than 0.05 was considered as statistically significant. Analysis was done using SPSS version 16.0.

### Results

There were 38 patients of cutaneous sarcoidosis during the six-year study period. The patient details are shown in Table 1. Mean age was  $48 \pm 13$  years with a slight female preponderance (58%). Majority (51%) of our patients were from the eastern states, followed by the southern (30%) and north eastern states of India (5.2%), 4 patients from Bangladesh, and 1 from Nepal. More than one anatomical region was involved in 55.2% patients. The sites involved were trunk (52.6%), face (44.7%), and upper limbs (44.7%). Isolated cutaneous sarcoidosis was found in 6 (15.8%) patients. Erythematous plaques (65.7%) [Figure 1a and b] and papules (50%) [Figure 2a and b] were the commonest specific skin lesion seen. Rare cutaneous presentations [Figure 3a and b] were seen in 5 patients (13.1%). Erythema nodosum was seen in only 2 patients (5.2%) and both had lung involvement. Multiple (>3) skin lesions were seen in 28 patients (73.7%). Lungs (73.7%) were the most common extracutaneous organ system involved followed by the lymph nodes (68.4%). The chest X-ray staging was stage 0 in 23.6% (*n* = 9) patients, stage 1 in 2.6% (*n* = 1), stage 2 in 63.2% (*n* = 24), and stage 3 in 10.6% (*n* = 4). Eye involvement was found in 5 cases of which 3 had uveitis, 1 had conjunctival granulomas, while both uveitis and conjunctival granulomas were noted in 1 patient. Mantoux test was negative in all cases. There was no significant association of systemic involvement and type of skin lesions (*p* = 0.40) or number of skin lesions (*p* = 0.13) or of lesions over the face with involvement of the respiratory tract (*p* = 0.456).

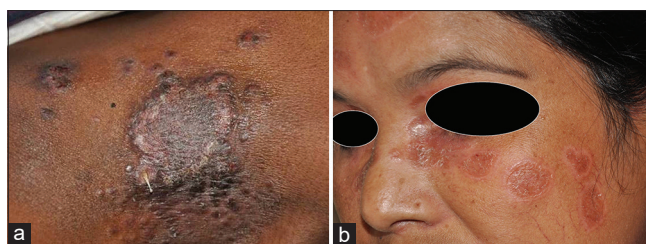


Figure 1: 1(a): Plaque lesions sarcoidosis on the lower limb. 1(b): Annular plaques of sarcoidosis on the face

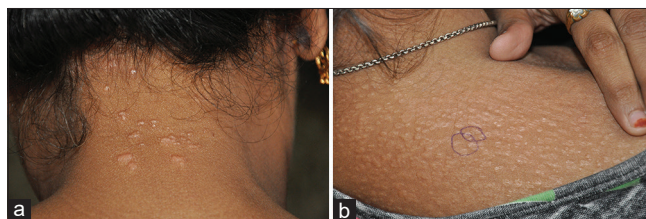


Figure 2: 2(a): Papular lesions of sarcoidosis on the nape of the neck. 2(b): Papular lesions of sarcoidosis on the upper back

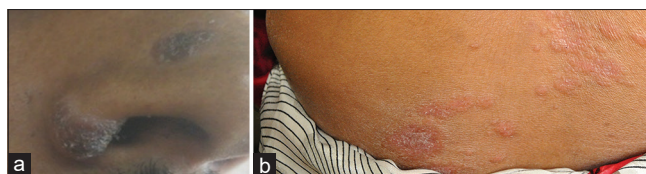


Figure 3: 3(a): Angiolupoid sarcoidosis. 3(b): Psoriasiform lesions of sarcoidosis on the lower back

Elevated ACE levels were found in 74.3% (26/35) of those tested and were significantly associated with systemic involvement (*p* = 0.00) (especially lung involvement [*p* = 0.00] and lymph node involvement [*p* = 0.013]). All the patients with isolated cutaneous sarcoidosis were found to have normal ACE levels.

### Histopathology

Table 2 illustrates comparison of histopathological findings with other studies. Naked granulomas [Figure 4a] were found in 55.3% (*n* = 21), while non-naked granulomas in 44.7% (*n* = 17). Cutaneous lesions in patients with non-naked granulomas included papules and plaques (*n* = 3), only plaques (*n* = 7), papules (*n* = 4), papules and plaques with depigmented lesions (*n* = 1), angiolupoid lesion (*n* = 1), and subcutaneous nodule (*n* = 1). Rare clinical presentations like depigmented lesions with plaques (*n* = 1), psoriasiform (*n* = 1), and scar (*n* = 1) showed naked granulomas. Perineural location of granulomas with special stains being negative for acid fast lepra bacilli was seen in 1 patient. Fibrinoid necrosis was seen in 15.7% (*n* = 6) and multinucleated giant cells [Figure 4b] in 94.7%. Foreign bodies were found in only 5 cases, under non-polarizing microscope. Reticulin staining [Figure 4c] was done in 23 patients, of which it was preserved or increased in 19 (82%). There was no clinicopathological correlation with systemic features.

**Table 1: Disease characteristics**

Characteristic	Number (%)
Gender	
Male	16 (42)
Female	22 (58)
Age (mean $\pm$ SD in years)	48 ( $\pm$ 13)
Age at onset (mean $\pm$ SD in years)	46 ( $\pm$ 13.5)
Duration of disease (median; interquartile range) (in months)	11 (4-48)
Type of skin lesion (More than 1 morphology in $n=11$ (28.9%))	
1. Plaques	25 (65.7)
2. Papules	19 (50)
3. Nodules	5 (13.1)
4. Others (Depigmented macules 2, Psoriasiform 1, Scar 1, Angiolupoid 1)	5 (13.1)
5. Non-specific (Erythema nodosum)	2 (5.2)
Number of skin lesions	
1. Up to three lesions	10 (26.4)
2. More than or equal to 4 lesions	28 (73.7)
Site of the lesion (More than 1 region involved in $n=21$ (55.3%))	
1. Torso	20 (52.6)
2. Face	17 (44.7)
3. Upper limb	17 (44.7)
4. Lower limb	14 (36.8)
Isolated cutaneous sarcoidosis	6 (15.8)
Systemic involvement (more than 1 organ involved in $n=29$ (76.3%))	32 (84.2)
1. Lungs	28 (73.7)
2. Lymph nodes (thoracic=19, extrathoracic=7)	26 (68.4)
3. Liver	7 (18.4)
4. Spleen	5 (13.2)
5. Eyes	5 (13.2)
5. Others (Neurologic 2, Cardiac 2, bone marrow 1, salivary gland 1)	6 (15.7)
ACE levels ( $n=35$ )	
ACE levels up to 52 U/L	9 (25.7)
ACE >52 U/L	26 (74.3)
Treatment	
Topicals (Steroids $\pm$ Tacrolimus)	38 (100)
Intralesional steroids	1 (2.6)
Systemic steroids alone	15 (39.4)
Systemic steroids + hydroxychloroquine	10 (26.3)
Hydroxychloroquine alone	6 (15.7)
Response to treatment (cutaneous lesions)	
Resolved	10 (26.3)
Improving	5 (13.2)
Persistent	3 (7.9)
Relapsed	4 (10.5)
Lost to follow up	16 (42.1)

Values are given as number (%) unless otherwise specified

### Treatment

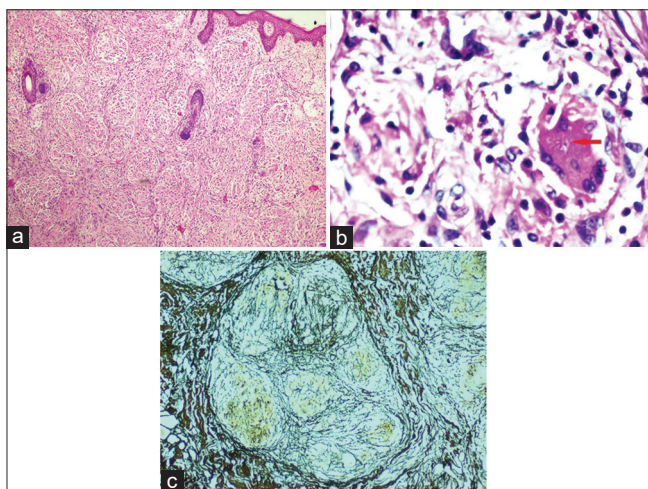
Topical steroids with or without tacrolimus was given for the cutaneous lesions in all patients. Systemic steroids were given in 25 patients, 1 of whom had only cutaneous

involvement while 24 had pulmonary involvement with or without other extracutaneous involvement. Ten patients received hydroxychloroquine in addition to systemic steroids, while 6 patients received hydroxychloroquine alone. Among the six patients with isolated cutaneous

**Table 2: Histopathological findings in our study and comparison with other studies**

Histopathological finding	Our study	Ball <i>et al.</i> , 2004 <sup>[19]</sup>	Cardoso <i>et al.</i> , 2009 <sup>[18]</sup>	Mangas <i>et al.</i> , 2006 <sup>[9]</sup>	Ishak <i>et al.</i> , 2014 <sup>[13]</sup>	García-Colmenero <i>et al.</i> , 2019 <sup>[16]</sup>
Number of specimens examined	38	28	31	42	81	48
Type of granulomas						
Naked granulomas	21 (55.3)	25 (89)	22 (71)	30 (71)	81 (100)	48 (100)
Naked (discrete)	13					
Naked (confluent)	5					
Naked (discrete + confluent)	3					
Non-naked (discrete)	6					
Non-naked (confluent)	5					
Non-naked (discrete + confluent)	6					
Depth of granulomas						
Superficial	11 (29)		5 (16)		4 (5)	21 (43.8)
Mid dermis	10 (26.4)		9 (29)		9 (11)	
Deep dermis	8 (21)		17 (54)		65 (80)	34 (70.8)
Subcutis	9 (23.6)		0 (0)		16 (20)	2 (41.7)
Distribution of granulomas						
Non-specific/Interstitial	19 (50)		17 (51)	34 (83)	27 (33)	
Perineural	1 (2.6)	7 (25)	4 (13)		15 (23)	6 (12.5)
Periadnexal	8 (21)		10 (32)	8 (19)	13 (16)	15 (31.3)
Perivascular	9 (23.6)		4 (13)		54 (66)	24 (50)
Associated inflammatory cells seen						
Neutrophils	3 (7.8)	7 (25)				
Eosinophils	0	9 (32)				
Plasma cells	12 (31.5)	10 (36)				
Multinucleate giant cells	36 (94.7)	28 (100)	30 (97)		90%	46 (95.8)
Foreign bodies	5 (13.1)	15 (53)	10 (32)	11 (26)		1 (2)
Necrosis	6 (15.7)	12 (43)	2 (6)	4 (9)	1 (1)	13 (27)
Mucin	2 (5.2)	5 (18)				
Reticulin	19/23					

Values are given as number (%) unless otherwise specified



**Figure 4:** 4(a): Multiple discrete naked granulomas (Hematoxylin and Eosin stain, 5 $\times$ ). 4(b): Granuloma with a multinucleate cell and ill-formed asteroid body (arrow), (Hematoxylin and Eosin stain, 400 $\times$ ). 4(c): Preserved reticulin fibers within the granuloma (Reticulin stain, 100 $\times$ )

sarcoidosis, 3 were treated with hydroxychloroquine alone while 1 received systemic steroids for unresponsive lesions and the remaining 2 were treated with topicals alone.

### Follow-up

The median follow-up period was 24 months (range: 3–120). Complete resolution of the cutaneous lesions was seen in 36.8% (n = 14) with relapse in 4 of these patients on tapering steroids, lesions were in resolving phase in 13.1% (n = 5), and persistent lesions were seen in 7.8% (n = 3). Of the patients who received hydroxychloroquine alone, 4 were lost to follow up, 1 had improving cutaneous lesions, while in another the skin lesions were persistent on follow up. Of the 6 patients with isolated cutaneous sarcoidosis, 3 patients were lost to follow up, 1 had persistent lesions, while 2 had complete resolution of their skin lesions. Lung function had improved in 33% (n = 13), 8% (n = 3) had worsening, and 13% (n = 3) had relapse after stopping the steroids. Sixteen patients did not review after primary evaluation. As the study was in a tertiary care center, and patients were from distant places, the patients preferred to follow up with their local physician once the diagnosis was established, and treatment plan was made.

### Discussion

Sarcoidosis has a worldwide distribution, with varying presentations and outcomes across ethnic and geographic



**Table 3: Comparison with other studies**

Characteristic	Present study	Mahajan et al., 2007 <sup>[3]</sup>	Collin et al., 2009 <sup>[14]</sup>	Ishak et al., 2014 <sup>[13]</sup>	Esteves et al., 2015 <sup>[15]</sup>	Garcia et al., 2019 <sup>[16]</sup>
Number of patients	38	23	32	76	41	40
Region/Ethnicity	Indian sub-continent	Indian	White (57%), South Asian (28%), Afro-Caribbean (15%)	Lebanese	Spain	Caucasian (77.5%), African (12.5%), Caribbean (5%), Asian (5%)
Mean age ( $\pm$ SD in years)	48 ( $\pm$ 13)	44(range 31-78)	49 (range 27-84)	48 (range: 19-74)	52 (+/-10)	54 (range 26-79)
Females (%)	58	65	74	79	83	82.5
Types of lesion in cutaneous sarcoidosis (%)		Combination of papules, nodules, and plaques				
Plaques	65		44	49	22	30
Papules	50		29	29	56	50
Nodules	13.2			18	39	30
More than 1 morphology	28.9				34	35
Distribution of lesions (%)		Widespread distribution (22/23)				
More than 1 region	55.3			40	31	57.5
Torso	52.6			14	14	35
Face	44.7			50	46	42.5
Upper limbs	44.7			25	25	67.5
Lower limbs	36.8			21	21	47.5
Isolated cutaneous sarcoidosis (%)	15.7		29	71	41.5	17.5
Systemic involvement(%)	84.2		71	29	58.5	82.5
Extra-cutaneous organs involved (%)						
Lungs	73.7		52	73	53.6	80
Lymph-nodes	68.4		14		24.3	17.5
Liver	18.4					
Spleen	13.2					
Eyes	13.2			18		
Joints						15

groups. Most studies on cutaneous sarcoidosis are from the West with very little data from the other regions.<sup>[9-13]</sup> Though previously considered less common, it is being increasingly recognized in Indian patients.<sup>[3,5,6]</sup>

In our study, the mean age of presentation was 48 years, consistent with that of existing literature.<sup>[3,13,14]</sup> Females constituted only a little more than half of our patients even though most studies have shown strong female preponderance.<sup>[13,15,16]</sup> This could be due to the gender differences in health seeking behavior in our population.

The clinical features of our patients have been compared with other studies [Table 3]. There is a wide variation in the distribution as well as types of lesions across races. Majority of our patients (55.3%) had lesions over more than 1 body region, including the torso. The commonest cutaneous lesions in our study were plaques and papules as has been previously reported.<sup>[13,16]</sup> Consistent with previous Indian data,<sup>[3]</sup> erythema nodosum was uncommon in our study. The other rarer types seen were psoriasiform, hypopigmented macules, scar, and angiolupoid. Owing to

the polymorphic nature of cutaneous sarcoidosis lesions, it is important to be aware of the varied clinical presentations including the rarer types.

The prevalence of systemic involvement in cutaneous sarcoidosis varies from 29–82%.<sup>[13,16]</sup> Majority (85.2%) of our patients had systemic involvement, most commonly lungs and lymph nodes, similar to that reported in a few studies.<sup>[16,17]</sup> As our study was conducted in a tertiary care center, it is likely that the patients with systemic symptoms were over-represented. There was no association of the type, distribution, or number of cutaneous lesions with extracutaneous involvement or disease prognosis as reported in a previous Indian study.<sup>[3]</sup>

Cutaneous sarcoidosis also has a significant variation in its histopathological findings. In contrast with existing literature,<sup>[9,18]</sup> classical naked granulomas described in sarcoidosis were found in only 55%. Necrosis in granuloma points toward an infective etiology, and is not classically described in sarcoidosis; however, it has been rarely reported.<sup>[9,16,18,19]</sup> Perineural localization of granulomas (seen

in 1 of our cases) necessitating the exclusion of Hansen's disease, has also been noted previously in sarcoidosis.<sup>[9,10,18]</sup> Preserved or increased reticulin staining (in 82%) is useful in diagnosing sarcoidosis since disruption of reticulin network can be found in infectious processes.<sup>[20]</sup>

Even though ACE levels are neither very sensitive nor specific for the diagnosis of sarcoidosis, our study corroborated previous studies, that elevated ACE levels correlate with systemic involvement.<sup>[14,15]</sup>

This is the largest series of cutaneous sarcoidosis from the Indian subcontinent. The commonest clinical presentation was plaques and papules, involving more than 1 body region, including the torso. A multidisciplinary approach is important in the holistic management of this multisystem disorder.

### *Financial support and sponsorship*

Nil.

### *Conflicts of interest*

There are no conflicts of interest.

### **References**

- Haimovic A, Sanchez M, Judson MA, Prystowsky S. Sarcoidosis: A comprehensive review and update for the dermatologist: Part I. Cutaneous disease. *J Am Acad Dermatol* 2012;66:699.e1-18; quiz 717-8.
- Mañá MJ, Marcoval J. Skin manifestations of sarcoidosis. *Presse Méd* 2012;41:e355-74.
- Mahajan VK, Sharma NL, Sharma RC, Sharma VC. Cutaneous sarcoidosis: Clinical profile of 23 Indian patients. *Indian J Dermatol Venereol Leprol* 2007;73:16-21.
- Kumar R, Goel N, Gaur SN. Sarcoidosis in north Indian population: A retrospective study. *Indian J Chest Dis Allied Sci* 2012;54:99-104.
- Mohanty R, Singh SN, Bhattamishra AB. Cutaneous sarcoidosis without systemic manifestations. *Indian J Dermatol* 2009;54:80.
- Reddy RR, Shashi Kumar BM, Harish MR. Cutaneous sarcoidosis-a great masquerader: A report of three interesting cases. *Indian J Dermatol* 2011;56:568-72.
- Kumar V, Abbas AK, Aster JC, editors. *Robbins Basic Pathology*. 10<sup>th</sup> ed. Philadelphia: Elsevier; 2018. p. 512.
- Siltzbach LE. Sarcoidosis: Clinical features and management. *Med Clin North Am* 1967;51:483-502.
- Mangas C, Fernández-Figueras M-T, Fité E, Fernández-Chico N, Sàbat M, Ferrándiz C. Clinical spectrum and histological analysis of 32 cases of specific cutaneous sarcoidosis. *J Cutan Pathol* 2006;33:772-7.
- Jacyk WK. Cutaneous sarcoidosis in black South Africans. *Int J Dermatol* 1999;38:841-5.
- Chong W-S, Tan H-H, Tan S-H. Cutaneous sarcoidosis in Asians: A report of 25 patients from Singapore. *Clin Exp Dermatol* 2005;30:120-4.
- Tong C, Zhang X, Dong J, He Y. Comparison of cutaneous sarcoidosis with systemic sarcoidosis: A retrospective analysis. *Int J Clin Exp Pathol* 2014;7:372-7.
- Ishak R, Kurban M, Kibbi A-G, Abbas O. Cutaneous sarcoidosis: Clinicopathologic study of 76 patients from Lebanon. *Int J Dermatol* 2015;54:33-41.
- Collin B, Rajaratnam R, Lim R, Lewis H. A retrospective analysis of 34 patients with cutaneous sarcoidosis assessed in a dermatology department. *Clin Exp Dermatol* 2010;35:131-4.
- Esteves TC, Aparicio G, Ferrer B, Garcia-Patos V. Prognostic value of skin lesions in sarcoidosis: Clinical and histopathological clues. *Eur J Dermatol* 2015;25:556-62.
- García-Colmenero L, Sánchez-Schmidt JM, Barranco C, Pujol RM. The natural history of cutaneous sarcoidosis. Clinical spectrum and histological analysis of 40 cases. *Int J Dermatol* 2019;58:178-84.
- Wu MC, Lee JY-Y. Cutaneous sarcoidosis in southern Taiwan: Clinicopathologic study of a series with high proportions of lesions confined to the face and angiolupoid variant. *J Eur Acad Dermatol Venereol* 2013;27:499-505.
- Cardoso JC, Cravo M, Reis JP, Tellechea O. Cutaneous sarcoidosis: A histopathological study. *J Eur Acad Dermatol Venereol* 2009;23:678-82.
- Ball NJ, Kho GT, Martinka M. The histologic spectrum of cutaneous sarcoidosis: A study of twenty-eight cases. *J Cutan Pathol* 2004;31:160-8.
- Ko CJ, Glusac EJ. Non infectious granulomas. In: Elder DE, editor. *Lever's Histopathology of the Skin*. 11<sup>th</sup> ed. Philadelphia: Wolters Kluwer; 2015. p. 438.