

Cutaneous sarcoidosis as upsurging mimicking granulomatous diseases

Khalifa E. Sharquie, Thamir A. Kubaisi*, Inas K. Sharquie**

Department of Dermatology, College of Medicine, University of Baghdad, Center of Dermatology, Medical City Teaching Hospital, Baghdad, Iraq.

* Department of Dermatology, College of Medicine, University of Anbar; Ramadi, Anbar, Iraq.

** Department of Microbiology & Immunology, College of Medicine, University of Baghdad, Baghdad, Iraq.

Abstract

Background Cutaneous manifestations of sarcoidosis are seen in around 25% of patients with sarcoidosis and that usually accompanies systemic involvement. Non-caseating granuloma is the classical histopathological picture. Sarcoidosis shares many clinical and histopathological features with many granulomatous diseases.

Objective To do full clinical and histopathological evaluation of all cases that were diagnosed with cutaneous sarcoidosis, trying to find clinical limitations and borders between sarcoidosis and other granulomatous mimicking diseases.

Methods This is a descriptive study where all patients that were diagnosed with cutaneous sarcoidosis during the period from 2014-2023 were assessed regarding dermographic features, clinical pictures and histopathological examination. An appropriate general physical examination as well as investigative techniques were implemented to detect the presence or absence of systemic involvements.

Results This study included 24 patients, whose ages ranged from 27-70 years with a mean of 47.8 years with 16 (66.7%) females and 8 (33.3%) males. All patients had shiny smooth, skin colored or dusky red papules, nodules or plaques but rarely scaly. No obvious systemic involvements were detected by physical examination or investigative techniques. The histopathological assessment showed marked granulomatous reaction consisting of multiple non-caseating non-necrotizing granuloma formations.

Conclusion Sarcoidosis is emerging as not a rare cutaneous disease that can mimic and compete with other granulomatous diseases. There is no specific available test for this disease but identifying the full cutaneous and pathological features is mandatory and might lead us to the correct diagnosis, hence it is an exclusion disease.

Key words

Cutaneous sarcoidosis; Granulomatous disease; Lupus pernio-like; Tuberculosis-like; Naked granuloma.

Introduction

Sarcoidosis is a multisystem problem of unknown causes that may involve nearly any body part.¹ Skin is the most common part of extra-thoracic involvement. Cutaneous sarcoidosis (CS) is present in up to one-third of the sarcoidosis, while it might be pure CS in

25%.² Sarcoid-specific lesions typically exist histologically with granulomatous alignment in the tissue.³⁻⁵ There were no significant variations in skin manifestation between those who established isolated sarcoidosis of the skin and those who had systemic sarcoidosis associated with skin manifestations.⁶

Clinically, CS has female predominance and can present with red or red-brown plaques, subcutaneous nodules or maculopapular lesions, and less frequently as ulcers or alopecia. The skin changes could also be limited to preexisting scars. There may be single or multiple cutaneous lesions. The well-recognized clinical pictures of sarcoid-specific skin involvement include lupus pernio (nodules/plaques of the face), subcutaneous nodules, and scar-related sarcoidosis.^{3,7}

Sarcoid antigens are captured by resident dendritic cells (DCs) and alveolar macrophages in the airways for presentation via major histocompatibility complex II (MHC Class II) to CD4+ T-cells, whose activity is upregulated in Sarcoidosis. MHC-Class II receptors interact with the T-cell receptor's variable portion in conjunction with the affinity between CD28 and CD86 on T-cell and DC's surfaces, respectively, interacting with Toll-like receptor 2 (TLR2). Secretion of pro-inflammatory cytokines by macrophages, neutrophils and invariant natural killer cells (NKT cells) aid in CD4+ cell activation which will differentiate into effector T-cells depending on the cytokines present in the local surroundings.^{8,9} The Th1 phenotype is strongly linked with granuloma formation in the lung and skin with IL-2 and IFN- γ , IL12 and IL-18 cytokines upregulated in the lungs with Th2 cytokines reduced. Moreover, chemokine (CX-C motif) ligand (CXCL)10 which recruits neutrophils and lymphocytes is upregulated as is

the transcription factor for T-bet which increases gene expression of IFN- γ and CXC receptor (CXCR)3.¹⁰

Th17 cells which induce secretion of IL-17A have been found upregulated in lungs and peripheral circulation with chemokine (C-C motif) ligand (CCL) 20 enhancing Th17 cell infiltration in the lungs. While cytotoxic T-lymphocyte antigen 4 (CTLA4) expression is impaired causing Th17 activation promulgating the inflammatory response.¹⁰ IFN- γ producing Th17.1 cells (a subset of Th17 cells numbers is also increased in the lungs) blood and lymph nodes and have been speculated to be the main contributors of IFN- γ release, contradicting the consensus that TH1 cells were largely responsible for this role. However, the role of Th17.1 cells requires further study with some suggesting their role may be protective and others implicating them in sarcoidosis pathogenesis.¹¹ Treg cells dampen the Th immune response, with their numbers reduced in the lung and blood in sarcoidosis, whilst others have noted increased Treg presence but with reduced immunosuppressive capabilities with functional resolution linked to clinical remission.^{8,9}

Monocytes in the periphery will migrate into the affected organ, commonly lung and other systems like skin, and then differentiate into activated macrophages which in turn form aggregate to form sarcoid granulomas. In later sarcoidosis there is a transition from M1 to M2 macrophages although how this contributes to sarcoidosis is poorly understood as are the roles of B-cells NK cells and NKT cells in disease pathogenesis.^{8,9}

Histopathological principle for an accurate diagnosis of CS is the evidence of sarcoidotic granulomas, which are characterized by a non-caseating granulomatous reaction of clustered

Manuscript

Received on: August 12, 2023

Accepted on: April 19, 2024

Address for correspondence

Professor Khalifa E. Sharquie

Iraqi and Arab Board of Dermatology and

Venereology, Center of Dermatology and

Venereology, Baghdad Teaching Hospital, Medical

City, Medical Collection Office, P.O.BOX 61080,

Postal code 12114, Baghdad, Iraq.

Ph: 009647901468515

Email: ksharquieprof@yahoo.com

epithelioid histiocytes, besides few giant cells, and frequently an outer layer of few lymphocytes surrounded by dermal fibrosis.¹² Furthermore, the diagnosis of the isolated CS requires the presence of histopathologic features of sarcoidotic granuloma and the exclusion of other diseases that could be presented with a granulomatous reaction. These share many clinical and histopathological features like granuloma annulare, granulomatous rosacea, granulomatous secondary syphilis, tuberculoid leprosy, tuberculosis and foreign body granuloma (mainly as a result of silica) which are still endemic in many countries. In addition, there was an absence of additional signs of systemic sarcoidosis or other organ involvement.^{3,13,14}

This present study attempts to do a full clinical and histopathological evaluation of all cases that were diagnosed as sarcoidosis, which is a rare and not well-established disease in countries of the middle east including Iraq. Trying to find clinical limitations and borders between sarcoidosis and other granulomatous diseases.

Methods

This is a descriptive study where all patients were diagnosed with cutaneous sarcoidosis, at a private clinic (KES) and Baghdad Teaching Hospital, Baghdad, Iraq during the period from January 1, 2014, to March 31, 2023. Established cases of CS were recorded regarding name, age, sex, address, disease onset, lesion morphology, site of involvement, and number of lesions. All dermographic features and histopathological assessments as sarcoid granulomas on cutaneous biopsy were documented. In addition, almost all cases with granuloma-forming infections such as granulomatous secondary syphilis, tuberculoid leprosy, mycobacterial and fungal infections and leishmaniasis were excluded. As well as all other granulomatous mimicking diseases like granuloma annulare, granulomatous rosacea,

necrobiosis lipoidica diabetorum and foreign body granuloma (mainly as a result of silica) were fully examined, investigated and excluded.

A compatible clinical characteristic and its classifications of the different morphology such as maculopapular, plaque, alopecia, scar, and subcutaneous nodules were done.

A thorough history of non-specific features such as fever, fatigue, and weight loss with an appropriate physical examination was achieved, as well as investigative techniques were carried out to detect the presence or absence of any systemic involvements. Continuous follow-up for eligible individuals with skin sarcoidosis was done to assess the appearance of systemic involvement from their diagnosis up to March 31, 2023. The Ethical Approval Committee reviewed and accepted the study. All participating subjects gave informed consent for the publication of data and their digital photographs.

Results

This study included 24 patients, whose ages ranged from 27-70 years with a mean of 47.8 year, 16 (66.7%) females and 8 (33.3%) males with a ratio of 2:1. The mean (range) disease duration was 14.5 (6-30) months (**Table 1**). The different clinical data and case series of CS are described in **Table 2**. All patients had shiny smooth lesions and the color of the rash could be red, dusky red, skin-colored, or even pigmented. It was usually asymptomatic or there was slight itching in 14 (58.3%) and 10 (41.7%) patients, respectively. The frequent site of cutaneous involvement was the face in 17 (70.8%) cases, followed by lower limbs, upper limbs and trunk. The morphological picture of the rash was papular in 14 (58.3%) of cases, nodular 10 (41.7%), plaques (mainly annular) 13 (54.2%), tumors 3 (12.5%) but seldom scaly. A rare skin presentation was lumps, or scarring alopecia of

Table 1 The frequency rate of clinical manifestations of cutaneous sarcoidosis (n =24).

Variables	Data
Females (n%)	16 (66.7%)
Age, mean (range)	47.8 (27-70) yrs.
Disease duration, mean (range)	14.5 (6-30) mon.
The distribution of skin involvement	
Localized	9 (37.5%)
Generalized	15 (62.5%)
Sites of cutaneous involvement	
Face	17 (70.8%)
Lower limbs	11 (45.8%)
Upper limbs	10 (41.7%)
Trunk	9 (37.5%)
Neck	2 (8.3%)
Scalp	1 (4.2%)
Clinical features	
Asymptomatic	14 (58.3%)
Itching	10 (41.7%)
Papules	14 (58.3%)
Plaques (mainly annular)	13 (54.2%)
Nodules	10 (41.7%)
Tumor	3 (12.5%)
Lump (profundus type)	1 (4.2%)
Alopecia	1 (4.2%)
Scar-related	1 (4.2%)
The color of rash	
Red	12 (50%)
Dusky red	10 (41.7%)
Skin-colored	4 (16.7%)
Pigmented	2 (8.3%)
Dermographic pictures	
Granuloma annulare-like	13 (54.2%)
Lupus pernio-like	11 (45.8%)
Granulomatous rosacea-like	4 (16.7%)
Tuberculosis-like	3 (12.5%)

the scalp in one (4.2%) patient for each.

The distribution of rash could be classified into localized affecting 9 (37.5%) individuals and generalized picture in 15 (62.5%) cases. Multiple lesions involvement was seen in 23 (95.8%) of the cases but solitary was only seen in one female.

The dermatological features of CS could be classified into the following common dermographic pictures: granuloma annulare-like in 13 (54.2%) patients, lupus pernio-like seen in 11 (45.8%) and uncommonly granulomatous rosacea-like in 4 (16.7%) or tuberculosis-like in

3 (12.5%) of cases.

Scar sarcoid reactions (**Figure 7E**) were reported in one (4.2%) female who had generalized skin-colored scaly nodules. Moreover, an adult man had generalized asymptomatic multiple shiny, dusky red infiltrated papules, nodules, annular plaques and tumors, presented with scalp lesions and ended with scarring alopecia (**Figure 1D**). An additional one (4.2%) female patient presented with peculiar deep nodular lumps on her hand, so-called profundus type (**Figure 3B**). Another unexpected presentation was the so-called sarcoidosis-lymphoma syndrome, that was detected in one patient, it ended with death and was published as a case report.¹⁵

The histopathological assessment showed a marked granulomatous reaction consisting of multiple non-caseating and non-necrotizing granuloma formation with little or no inflammatory reaction, so-called naked granuloma. These granulomas were loaded with foamy cells and there were different types of giant cells. Moreover, the query appearance of granulomatous diseases was undergoing frequent evaluation as an exclusion trial.

No obvious systemic involvements were detected by physical examination or any other investigative techniques at diagnosis or thereafter; except in one male patient who progressed into sarcoidosis-lymphoma syndrome and that unfortunately ended with death.

Discussion

Cutaneous sarcoidosis is the most common affected organ in sarcoidosis after the lung and it has been estimated to be around 25% presenting as pure cutaneous involvement and can exist in a variety of clinical presentations.^{2,7} However, there is no single diagnostic dependable test. Variable asymptomatic early presentations of sarcoidosis present a struggle in an initial and

Table 2 The clinical data of the 24 participants presented with cutaneous sarcoidosis.

Case	Age (y)/ Gender	Duration in months	Site of involvement	The distribution	Clinical features	symptoms	Demographic pictures	Figure no./ Note
1	45/M	20	Scalp, trunk & lower limbs	Generalized	Multiple shiny, dusky red infiltrated papules, nodules, annular plaques, tumors and alopecia.	Asymptomatic	Granuloma annulare-like	1/ Scalp lesion ended with scary alopecia
2	50/F	15	Face & limbs	Generalized	Multiple red shiny papules & nodules	Itchy	Lupus pernio-like/ face. Eruptive granuloma annulare-like/ limbs	2
3	70/F	12	Face & hands	Localized	Multiple shiny, dusky skin-colored papules on the face & lumps on the hands	Asymptomatic	granulomatous rosacea-like of the face.	3
4	28/M	14	Lower limbs	Generalized	Multiple eroded pigmented or skin-colored nodules & plaques.	Itchy	Tuberculosis-like	4
5	55/F	9	Face & back	Generalized	Multiple shiny, red infiltrated papules & nodules	Itchy	Lupus pernio-like/ face Granuloma annulare-like/ back	5
6	56/F	14	Trunk & upper limbs	Generalized	Multiple shiny, dusky red papules & nodules	Itchy	Eruptive granuloma annulare-like	6
7	59/F	24	Face & neck	Localized	Multiple shiny, dusky red plaques	Asymptomatic	Lupus pernio-like	7A
8	45/F	6	Face	Localized	Multiple shiny, dusky red plaques	Asymptomatic	granulomatous rosacea-like	7B
9	50/F	7	Face, limbs & back	Generalized	Multiple shiny, dusky red plaques & tumors	Asymptomatic	Lupus pernio-like/ face Granuloma annulare-like/ back	7C
10	55/F	6	Face & thigh (old scar)	Generalized	Skin-colored scaly nodules	Asymptomatic	Lupus pernio-like in the face,	7D&E
11	47/F	8	Rt. cheek	Localized	Single red shiny infiltrated annular plaque	Asymptomatic	Granuloma annulare-like	7F
12	25/M	13	Trunk	Generalized	Multiple shiny, dusky red skin-colored papules	Itchy	Eruptive granuloma annulare-like	-
13	32/F	9	Face	Localized	Multiple red shiny papules	Itchy	Lupus pernio-like	-
14	45/F	15	Face	Localized	Multiple red shiny papules	Asymptomatic	Lupus pernio-like	-
15	60/M	8	Lower limbs	Localized	Multiple shiny, dusky red and skin-colored plaques	Asymptomatic	Granuloma annulare-like	-
16	30/M	19	Face, neck, limbs	Generalized	Multiple shiny, scaly, dusky red plaques	Itchy	Tuberculosis-like	-
17	65/M	7	Face & trunk	Generalized	Multiple shiny, scaly, red papules.	Itchy	Granulomatous rosacea-like / face Eruptive granuloma annulare-like/ trunk	-
18	60/M	30	Face, limbs & back	Generalized	Multiple pigmented and dusky red nodules and plaques	Itchy	Granuloma annulare-like	sarcoidosis-lymphoma syndrome/ patient died
19	55/M	20	Face, limbs & back	Generalized	Multiple shiny, scaly, red papules and plaques	Asymptomatic	Lupus pernio-like/ face Granuloma annulare-like/ limbs & back	-
20	38/F	15	Face & limbs	Generalized	Multiple red shiny papules & nodules	Itchy	Lupus pernio-like/ face. Eruptive granuloma annulare-like/ limbs	-
21	28/M	9	Face	Localized	Multiple red shiny papules	Asymptomatic	Lupus pernio-like	-
22	52/F	22	Face, trunk & limbs	Generalized	Multiple shiny, scaly, red papules, plaques and tumors	Asymptomatic	Lupus pernio-like/ face. Eruptive granuloma annulare-like/ limbs	-
23	45/F	18	Face	Localized	Multiple shiny, scaly, red papules, annular plaques	Asymptomatic	Granulomatous rosacea-like	-
24	51/F	28	Upper limbs	Generalized	Multiple eroded dusky red skin-colored nodules & plaques.	Itchy	Tuberculosis-like	-

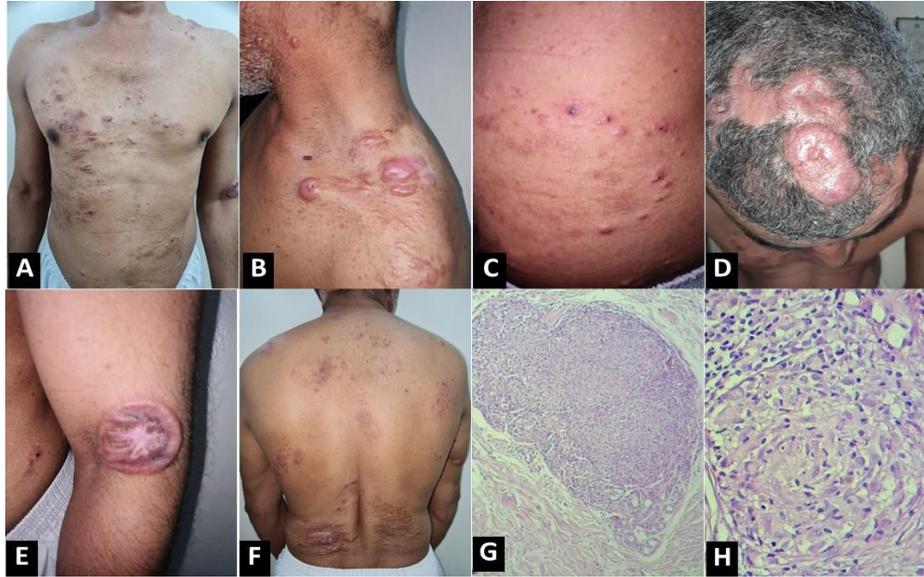


Figure 1 A 45-year-old male patient showing granuloma annulare-like involved the trunk (A, B, C& F); lower limbs (E), scalp (D); A low magnification view (G) shows naked granuloma, a non-caseating and non-necrotizing granuloma formation were loaded with foamy cells. Higher magnification (H); (Hematoxylin and eosin: G, X10; H, X40).

correct diagnosis.¹⁶ The sarcoidosis-specific cutaneous disease shows specific skin manifestations that are well-matched with noncaseating granulomas without obvious causes.^{3,13,14}

No previous reports of systemic sarcoidosis were recorded in the Iraqi population, as the systemic manifestation are mixed up with many diseases, and the skin rash of sarcoidosis is either neglected and not mentioned by the patient, or doctors are not asking about it. The total clinical features of CS are not well-recognized as most of the previous studies were created on referral-based cohorts that did not purify the skin manifestation or add

classification of the disease.^{17,18} Consequently, documented sarcoidosis of the skin stays controversial and occasionally displays a great diagnostic task.^{1,4} The skin has variable clinical presentations of CS and imitates several common diseases. It is worth identifying the cutaneous features, which can offer clues to the disease scenario. The current research showed that sarcoid-specific skin involvement was female-dominant at 66.7%, with a mean age of 47.8 years; this finding is in line with preceding literature, which suggest that CS commonly affects adult women of about 50 years of age.^{2,19-21} Disease duration before the actual diagnosis ranged from 6 to 30 months and this long period may be related to the asymptomatic.

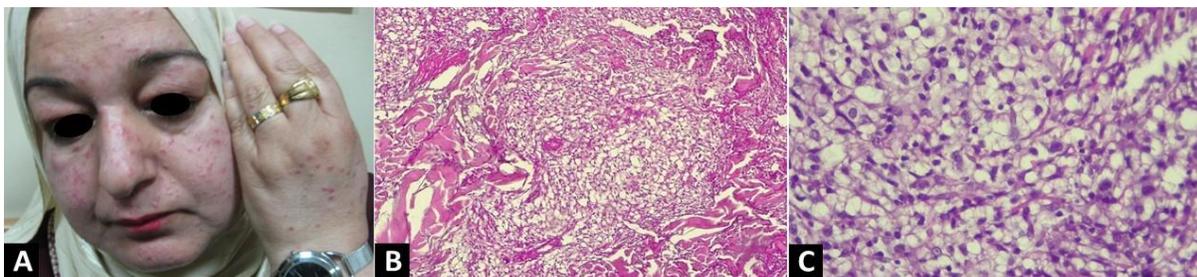


Figure 2 A 50-year-old female showing papulo-nodular lesions of face and limbs; A low magnification view (B) shows naked granuloma, a non-caseating and non-necrotizing granuloma formation loaded with foamy cells. Higher magnification (C); (Hematoxylin and eosin: B, X10; C, X 40).

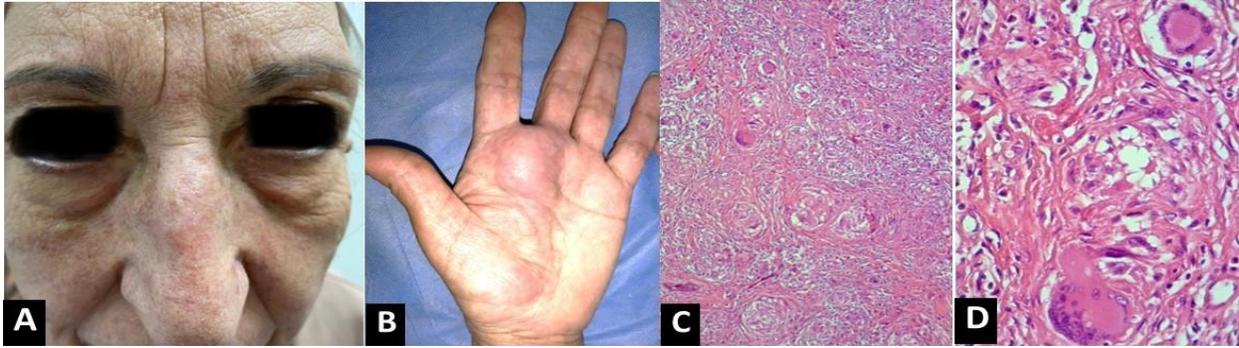


Figure 3 A 70-year-old female showing granulomatous rosacea-like (A); lumps on the hands (B); A low magnification view (C) shows naked granuloma, a non-caseating and non-necrotizing granuloma formation loaded with foamy cells. Higher magnification (D) there were giant cells. (HE stains: C, X10; D, X 40).

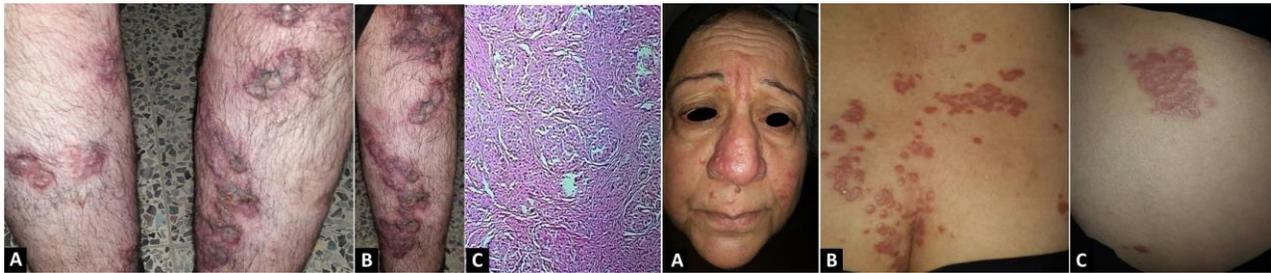


Figure 4 A 28-year-old male showing tuberculosis-like, eroded pigmented or skin-colored nodules & plaques (A & B); A low magnification view (C) shows naked granuloma, a non-caseating and non-necrotizing granuloma formation loaded with foamy cells. (HE stains: C, X10).



Figure 5 A 55-year-old female patient showing papulo-nodular rash with lupus pernio of the face (A); Granuloma annulare-like/ back (B & C).

condition or mild pruritus of illness, apart from skin lesions The patient frequently self-treated with over-the-counter topical steroids and oral antihistamines with different responses. This could also be related to misdiagnosis, since there are no clinical limitations and at borders between an upsurging CS that imitates the common granulomatous diseases like granuloma annulare, granulomatous rosacea, leprosy and tuberculosis. The authors recommended that CS be at mid of list of the differential diagnosis.

Interestingly, the present research showed that almost all cases had isolated CS and that did not associate with further systemic involvement, even during the period of the follow-up; apart from the man who progressed into sarcoidosis-lymphoma syndrome. This fact is not in line with earlier published reports which demonstrated that 62% of patients with CS developed sarcoidosis of systemic organs.^{2,21}

This could be explained by the fact that all patients in the present study mostly had only cutaneous manifestations. Other studies illustrated that approximately 40% of patients initially diagnosed with cutaneous sarcoidosis are found to have hidden asymptomatic sarcoidosis involving other organ systems.^{22,23} This finding is well explained by an earlier study, after years of following up on cases with CS, which showed that about 20% developed systemic involvement as they had elevated serum levels of C- reactive protein, angiotensin-converting enzyme, and interleukin-2. Thus, these lab studies might indicate or predict the presence of general organ involvement.² Accordingly, patients identified as CS need to rule out organ involvement and systematic follow-up is also suggested to monitor disease activity and to allow early recognition of widespread sarcoidosis.



Figure 6 A 56-year-old female patient showing papulo-nodular lesions, eruptive granuloma annulare-like involved the trunk & upper limbs (A, B & C); A low magnification view (D) shows naked granuloma, a non-caseating and non-necrotizing granuloma formation were loaded with foamy cells. (HE stains D, X10).



Figure 7 Showing different cases; lupus pernio-like (A, C & D), granulomatous rosacea-like (B); sarcoid reaction of old scar (E); single annular plaque / lupus pernio-like of the cheek (F).

The clinical skin manifestations, in the present study, showed that all patients had shiny smooth lesions, usually asymptomatic but slight itching was reported in 41.7% of patients. The color of the rash was red, dusky red, in 91.7%, and skin-colored, or pigmented in 25.1% of subjects. These are comparable to the clinical comprehensive update and review which showed that CS might present with a red, red-brown or violaceous-colored skin lesion and could be single or multiple.^{3,7}

The morphological pictures of presented cases were either papular, annular plaques, nodular, or mixed in about half of cases. Furthermore, 12.5% and 4.2% of patients showed tumors-like and scarring alopecia of the scalp, respectively. Also, an additional one woman (4.2%) presented with peculiar deep nodular lumps on her hand, so-called the profundus type. CS is a systemic problem, consequently, it can involve any part of

the skin as around two-thirds involved the face, followed by the lower extremities, upper extremities and trunk. Additionally, the disease appeared to be generalized in 62.5% of cases with multiple lesions seen in nearly all cases, except one female who had solitary infiltrated annular plaque.

Currently, emerging scar sarcoid reaction characterized by asymptomatic skin-colored scaly nodules over an old scar has been reported in one (4.2%) female. Another man presented with scalp lesions that ended with scarring alopecia, his condition was associated with generalized asymptomatic CS characterized by multiple shiny, dusky red infiltrated papules, nodules, annular plaques and tumors involving the scalp, trunk and lower limbs. This is in line with the preceding published studies that revealed the most commonly encountered finding of cutaneous sarcoidosis was papules in

43%, whereas 24% of the patients demonstrated plaques and nodules. The subcutaneous variant, alopecic and scar-related sarcoidosis were reported in one patient for each condition.^{2,24} Another large cohort study noticed that the most commonly detected skin lesions in patients with isolated CS were plaques (35%), papules (31%), and scar lesions (12%). While the subcutaneous nodules (33%) were the most frequent type of skin lesions seen in cases with systemic sarcoidosis. Consequently, the affected areas were lower limbs (38%), head/neck (35%) and upper limbs (31%).⁶

Regarding the dermographic pictures in the present work, the most frequent cutaneous features of CS were granuloma annulare-like, and lupus pernio-like seen in 54.2% and 45.8% of patients respectively. Granulomatous rosacea-like was observed in 16.7%, or tuberculosis-like was detected in 12.5% of cases. This ideal classification of sarcoid skin lesions makes the clinical diagnosis of CS simple when facing similar cases sharing both clinical and histopathological manifestations of sarcoidotic granulomas and after excluding the other known causes of granulomatous diseases. This vision, to some degree agrees with published studies that recognized the lupus pernio as characterized by bluish-red nodules/plaques over cheeks, nose, and ears; subcutaneous nodules; and scar-like sarcoidosis.^{3,7,24} Moreover, the commonest types of cutaneous lesions detected in both large cohort studies of isolated CS and specific skin lesions of systemic sarcoidosis were the subcutaneous nodules while scar/ tattoo sarcoidosis and lupus pernio were uncommonly observed.⁶

On the other hand, Sharquie *et al.* reported a case of sarcoidosis-lymphoma syndrome with a distinguished clinical and histopathological picture.¹⁵ Accordingly, this association with malignancy should always be part of the general assessment. This observation was supported by

recent research that noticed that sarcoidosis may herald, follow, or occur alongside of several malignancies, particularly lymphomas, adding a diagnostic challenge in the differential between them.²⁵

The pathological findings of all cases of the present study revealed marked granulomatous reactions made up of multiple non-caseating and non-necrotizing granuloma formations called naked granuloma. These granulomas were loaded with foamy cells, and there were different types of giant cells. For confirmatory evidence, the histopathological appearance of granulomatous diseases was undergoing further evaluation by special stains for microorganisms and cultures as exclusion strategies. Many foregoing researchers agreed with the results of the present work and defined CS as compatible clinical skin lesion plus the presence of noncaseating granulomas after elimination of other granulomatous causes, as well as no evidence of systemic contribution or infection.^{3,12,13,26}

Conclusion

This is the first research study documenting that sarcoidosis is emerging as a not rare cutaneous disease in Middle East countries including Iraq and imitating what is happening in Western countries. The mechanism behind this dramatic change and upsurge in cases of sarcoidosis could not be well explained but we can speculate that life changes simulating Western life, including diet behavior, might give the answer. Additionally, multiple wars and using depleted uranium might be another possible cause for this increase. Cutaneous sarcoidosis can mimic and compete with other granulomatous diseases like tuberculosis, leishmaniasis, granuloma annulare, granulomatous rosacea, leprosy and foreign body reaction. There is no specific available test for CS but the full clinical and pathological

features might offer clues to the disease scenario; so, it is an exclusion problem. The finding of noncaseating granulomas and suggestive skin manifestations are considered CS until proven otherwise.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship None.

Conflict of interest Authors declared no conflict of interest.

Authors' contribution

KES, TAK, IKS: Identification, diagnosis and management case, manuscript writing, critical review, final approval of the version to be published.

References

1. Drent M, Crouser ED, Grunewald J. Challenges of sarcoidosis and its management. *New Eng J Med.* 2021;**385(11)**:1018-32.
2. Boch K, Langan EA, Zillikens D, Ludwig RJ, Kridin K. Evaluation of clinical and laboratory characteristics of patients with cutaneous sarcoidosis: A single-center retrospective cohort study. *Front Med.* 2022;**9**:980507.
3. 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(5)**:e691-699.
4. Grunewald J, Grutters JC, Arkema EV. Publisher correction: sarcoidosis. *Nat Rev Dis Primers.* 2019;**5**:45.
5. Ezeh N, Caplan A, Rosenbach M, Imadojemu S. Cutaneous Sarcoidosis. *Dermatol Clin.* 2023;**41(3)**:455-70.
6. Ungprasert P, Wetter DA, Crowson CS, Matteson EL. Epidemiology of cutaneous sarcoidosis, 1976–2013: a population-based study from Olmsted County, Minnesota. *J Eur Acad Dermatol Venereol.* 2016;**30(10)**:1799-1804.
7. Caplan A, Rosenbach M, Imadojemu S. Cutaneous sarcoidosis. Seminars in respiratory and critical care medicine: Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA. 2020:689-99.
8. Zhang H, Costabel U, Dai H. The role of diverse immune cells in sarcoidosis. *Frontiers Immunol.* 2021;**12**:788502.
9. Loke WSJ, Herbert C, Thomas PS. Sarcoidosis: immunopathogenesis and immunological markers. *Int J Chron Dis.* 2013;**2013**:928601.
10. Facco M, Cabrelle A, Teramo A, Olivieri V, Gnoato M, Teolato S, et al. Sarcoidosis is a Th1/Th17 multisystem disorder. *Thorax.* 2011;**66(2)**:144-50.
11. Chen ES. Reassessing Th1 versus Th17. 1 in sarcoidosis: new tricks for old dogma. *Eur Respirat Soc.* 2018;**51**:1800010.
12. Rosen Y. Four decades of necrotizing sarcoid granulomatosis: what do we know now? *Arch Pathol Laboratory Med.* 2015;**139(2)**:252-62.
13. Ishak R, Kurban M, Kibbi AG, Abbas O. Cutaneous sarcoidosis: clinicopathologic study of 76 patients from Lebanon. *Int J Dermatol.* 2015;**54(1)**:33-41.
14. Noe MH, Rosenbach M. Cutaneous sarcoidosis. *Curr Opin Pulm Med.* 2017;**23(5)**:482-6.
15. Sharquie KE, Al-Hayani RK, Abdulwahhab WS, Mohammed A. Sarcoidosis-Lymphoma Syndrome: A Spectrum of One Disease. *J Cosmet Dermatol Sci Appl.* 2015;**5(03)**:181.
16. Lundkvist A, Kullberg S, Arkema EV, Cedelund K, Eklund A, Grunewald J, et al. Differences in disease presentation between men and women with sarcoidosis: a cohort study. *Respirat Med.* 2022;**191**:106688.
17. Thomas K, Hunninghake G. Sarcoidosis JAMA, 289 (2003). View in Scopus.3300-3.
18. Chen ES, Moller DR. Etiology of sarcoidosis. *Clin Chest Med.* 2008;**29(3)**:365-77.
19. Wu M, Lee JY. 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(4)**:499-505.
20. Liu K-L, Tsai W-C, Lee C-H. Cutaneous sarcoidosis: A retrospective case series and a hospital-based case-control study in Taiwan. *Medicine.* 2017;**96(40)**:e8158.
21. Paolino A, Galloway J, Birring S, Brex P, Larkin G, Patel A, et al. Clinical phenotypes and therapeutic responses in cutaneous-predominant sarcoidosis: 6-year experience in a tertiary referral service. *Clin Exp Dermatol.* 2021;**46(6)**:1038-45.

22. Byrne B, Goh A, Izham NF, Porter E, Field S. Systemic evaluation of cutaneous sarcoidosis: 15-year dermatology experience at University Hospital Limerick. *Clin Exp Dermatol*. 2022;**47(5)**:850-7.
23. Mañá J, Marcoval J. Skin manifestations of sarcoidosis. *La Presse Médicale*. 2012;**41(6)**:e355-e374.
24. Abed Dickson M, Hernández BA, Marciano S, Mazzuocolo LD. Prevalence and characteristics of cutaneous sarcoidosis in Argentina. *International J Women's Dermatol*. 2021;**7(3)**:280-4.
25. Lococo F, Muoio B, Chiappetta M, Nachira D, Petracca Ciavarella L, Margaritora S, *et al*. Diagnostic performance of PET or PET/CT with different radiotracers in patients with suspicious lung cancer or pleural tumours according to published meta-analyses. *Contrast Media Mol Imaging*. 2020;**2020**:5282698.
26. Wanat KA, Rosenbach M. A practical approach to cutaneous sarcoidosis. *Am J Clin Dermatol*. 2014;**15**:283-97.