Cutaneous Sarcoidosis- A not so Rare Entity in Pakistan

Sana Siddiqui[1], Humaira Talat[1], Afza Naureen[1], Mutaher Zia[2], Muhammad Irfan Anwar[3]

ABSTRACT

Objective: To study the demographic characteristics, clinicopathological features and radiological stage of cutaneous sarcoidosis in a public sector tertiary care hospital of the largest metropolitan city of Pakistan.

Methods: A case series was conducted from August 2014 to July 2017 at the Dermatology department of Civil Hospital Karachi. Case records of cutaneous sarcoidosis patients with a histopathological diagnosis of noncaseating sarcoidal granuloma on skin biopsy were reviewed. Diagnosis was done based on clinical manifestations, radiologic examinations and pathologic data.

Results: Mean age at the time of diagnosis was 35.8 years, while the mean duration of disease was 31.6 months. Plaques were found in five patients (50%), one of whom had coexistent plaques and nodules. Three patients (30%) displayed subcutaneous lesions, whereas two patients (20%) had maculopapules. Extracutaneous involvement occurred in six patients (60%), affecting mainly lungs and lymph nodes. Skin biopsy revealed typical sarcoid non-caseating granulomas in nine cases (90%). Radiological evaluation revealed Stage 0 in six patients (60%), Stage 1 and 3 in one patient (10%), while two patients (20%) showed Stage 2 involvement. The mainstay of treatment was topical or systemic corticosteroids to which a good response was achieved.

Conclusion: Our study concurred with the literature in that sarcoid plaques are the most common lesions while the involvement of the lungs and lymph nodes are the commonest extracutaneous features. Moreover, since cutaneous sarcoidosis leads to a diverse range of presentation, diagnosis in countries like Pakistan, where tuberculosis is endemic can be overlooked. Therefore, further studies are needed to overcome this diagnostic dilemma.

Key words: Cutaneous sarcoidosis, Sarcoid plaques, non-caseating granuloma

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1. *Department of Dermatology, Civil Hospital Karachi, Dow University of Health Sciences Karachi, Pakistan.*
2. *Department of Dermatology, Marie Adelaide Leprosy Centre (MALC) Karachi, Pakistan.*
3. *Department of Dermatology, PNS Shifa Karachi, Pakistan.*

Correspondence:
Dr. Sana Siddiqui
Department of Dermatology, Civil Hospital Karachi,
Dow University of Health Sciences Karachi, Pakistan. sid.sanaa@gmail.com
Email: sid.sanaa@gmail.com

INTRODUCTION

Sarcoidosis is an antigen mediated disease of unknown etiology, characterized by the presence of non-caseating epitheliod cell granulomas in multiple organs.[1,2] The most frequently affected organs are the lungs and the mediastinal lymph nodes, followed by the eyes and skin. Less frequently, but usually severe manifestations can occur in the liver, spleen, central nervous system, heart, upper respiratory tract and bones.[3] The skin lesions of sarcoidosis exhibit a vast variety of clinical morphology, hence making it 'a great imitator'.[4]

The incidence of sarcoidosis varies widely throughout the world.[5] It is not uncommon in Pakistan, but rarely reported. Data is scanty because of the more prevalent and recognized granulomatous diseases, like tuberculosis, leprosy, fungal infections, which obscure its recognition.[6]

The main purpose of this study was to assess the demographics, as well as the various clinical, radiological and histopathological features of cutaneous sarcoidosis in Pakistan, where due to lack of published data, delays in prompt diagnosis and management often result.

METHODS

A total of ten cases of cutaneous sarcoidosis were enrolled in the study conducted at the Department of Dermatology, Civil Hospital Karachi, Pakistan, from August 2014 to July 2017. Case records of patients with a histopathological diagnosis of noncaseating sarcoidal granuloma on skin biopsy were reviewed. A thorough physical examination was performed, including skin as well as systemic examination. Diagnosis was done based on clinical manifestations, radiologic examinations and pathologic data. Other investigations, including routine blood and urine test, biochemical tests, detection of erythrocyte sedimentation rate (ESR), C reactive protein (CRP), antinuclear antibodies (ANA), blood calcium and serum angiotensin-converting enzyme (sACE), PPD (purified protein derivative) skin test, chest computed tomograms (CT), lung function, bronchoscopy, abdominal and thyroid ultrasonography, electrocardiography, bone and joint X-ray and ophthalmic examination were also performed where required. The study was approved by the Ethics Committee and informed consent obtained.

RESULTS

Out of the ten patients with the diagnosis of cutaneous sarcoidosis, five (50%) were male and five (50%) were female (ratio 1:1). At presentation, the ages ranged from 19 to 52 years, with a mean age of 35.8 years. The duration of skin lesions ranged from six months to eight years. Six patients (60%) had cutaneous involvement on sites except the face, which was also the most common location. Three patients (30%) presented with cutaneous lesions on the face as well as on the other sites, whereas only one patient (10%) had skin lesion that was confined to the face. Sarcoid plaques were seen in four cases (40%) (Fig 1, fig 3) while one patient had co-existent plaques and nodules. (Patient 7, Figure 4) Subcutaneous sarcoidosis was present in three patients (30%). Two patients (20%) had maculopapular lesions (fig 2). The presence of acute lesions such as erythema nodosum was not seen in any patient included in the case series. Majority of the patients (n=7, 70%) were asymptomatic, whereas 3 patients (30%) complained of slight itching. (Table 1)

Table 1: Basic demographic characteristics and clinical findings of patients (n=10)

CHARACTERISTSICS	n	%
Age, in years		
Range	19-52	Not
Mean	35.8	applicable
Sex		
Male	5	50%
Female	5	50%
Duration, in months		
Range	06- 96	Not
Mean	31.6	applicable
Cutaneous lesion		
Maculopapules	2	20%
Plaques only	4	40%
Plaque + Nodules	1	10%
Subcutaneous sarcoidosis	3	30%
Lesion Distribution		
Face only	1	10%
Face and other sites	3	30%
Other sites only	6	60%
Symptoms		
Asymptomatic	7	70%
Pruritic	3	30%
Painful	0	0
Extracutaneous involvement	6	60%

n: number

Extracutaneous systemic involvement was seen in six patients (60%). Pulmonary involvement was seen in four patients (40%), while two (20%) had lymph node enlargement, one (10%) had bone and eye involvement, presenting with flexion deformity and uveitis respectively. One patient had neurological features, with carpel tunnel syndrome. (Table 2) ESR was increased in two patients (20%), whereas serum ACE levels were elevated in four patients (40%).

Other blood tests were normal. Associated hypercalcaemia or hypercalciuria was seen in none of the patients.Skin biopsy revealed classical, back to back, non-caseating naked epithelioid granulomas in the dermis in nine patients (90%). Whereas only one patient (10%) showed the presence of numerous small granulomas with variable degree of lymphocytic infiltration.

Oral glucocorticoids were given in the majority of patients (n=6, 60%) due to systemic involvement or in isolated cutaneous sarcoidosis unresonsive to topical treatment.. Patient 10 was misdiagnosed as leprosy initially and received antileprosy multidrug treatment. Oral steroids were started once the diagnosis of sarcoidosis was made. Those with

Table 2: Clinical details, pathological features and treatment outcomes of patients with cutaneous sarcoidosis (n=10)

Patient	Age/Sex	Lesion Morphology	Duration	Pulmonary Involvement	Other Extra Cutaneous Involvement	Histology	Treatment	Response
1	39/M	Plaques on trunk + limbs	96 Months	Stage 2	Lymphadenopathy Uveitis Flexion deformity Gynecomastia	Non-caseasting ephtheliod granulomas	Prednisolore + Azathioprine	Improved
2	28/M	Subcutaneous Nodules on arms	15 Months	Stage 0	No	Non-caseasting ephtheliod granulomas	Intralesional steroids + topical steroids	Improved
3	35/F	Papules on neck +legs	7 Months	Stage 2	No	Non-caseasting ephtheliod granulomas	Prednisolore	Improved
4	37/M	Papules + Plaques on face + limbs +trunk	12 Months	Stage 0	Lymphadenopathy	Non-caseasting ephtheliod granulomas	Prednisolore	Improved
5	19/F	Macules on face + neck+ back	18 Months	Stage 0	Carpal tunnel syndrome	Non-caseasting ephtheliod granulomas	Prednisolore Referred to Neurology	Improved
6	36/M	Subcutaneous Nodules on fingers	24 Months	Stage 0	No	Non-caseasting ephtheliod granulomas	Intralesional steroids + topical steroids	Improved
7	52/F	Infiltrated plaques + nodules on vulva + perianal	36 Months	Stage 0	No	Numerous small granulomas	Prednisolore	Improved
8	30/F	Subcutaneous nodules on forearm	12 Months	Stage 1	No	Non-caseasting ephtheliod granulomas	Intralesional steroids + topical steroids	Improved
9	32/M	Annular plaques on face	48 Months	Stage 0	No	Non-caseasting ephtheliod granulomas	Topical Steroids + hydroxychloroquine	Improved
10	50/F	Plaques on face + back	48 Months	Stage 3	Nasal obstruction and deformity	Non-caseasting ephtheliod granulomas	Prednisolore + hydroxychloroquine Referred to ENT	Improved

Extracutaneous features:

* Pulmonary involvement seen in patients 1, 3, 8 and 10
* Lymph node involvement seen in patients 1 and 4
* Bone & eye involvement in patient 1
* Neurological involvement in patient 5

only cutaneous involvement received topical or intralesional corticost-eroids (n=3, 30%). Patients 9 and 10 also received hydroxychloroquine along with topical and oral steroid respectively. One patient (patient 1) was given azathioprine in addition to oral steroids. Patient 7 received anti tuberculous treatment initially. After no response was seen, oral steroids were commenced. In most patients both the cutaneous lesions and the extra cutaneous involvement improved within 3 to 6 months of starting treatment. Patient 5 was referred to Neurology department for the management of carpal tunnel syndrome, while Patient 10 was referred to ENT for nasal obstruction and deformity. (Table 2)

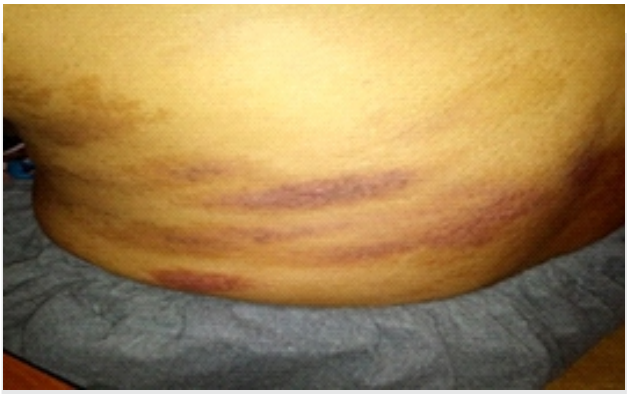

Figure 1
Multiple eryhtematous, infiltrated plaques involving th trnk (Patient 1)

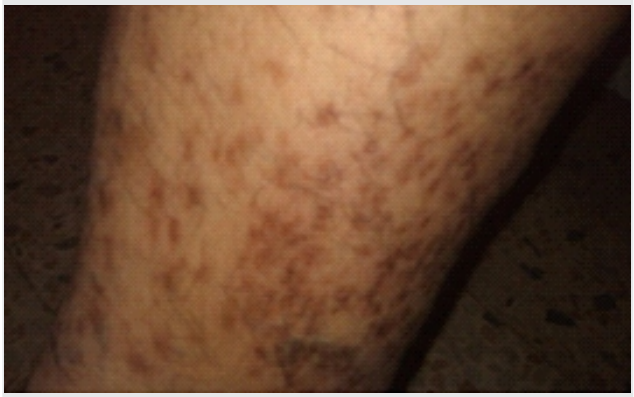

Figure 2
Numerous brown flat topped papules seen on the extensors in Patient 3

DISCUSSION

Sarcoidosis is a non-caseating granulomatous disease of unknown etiology.[7] It occurs throughout the world, with the highest incidence being reported in the Northern European countries with 5-40 cases/million registered annually.[8] The true incidence and prevalence of sarcoidosis in Pakistan is unknown because of the small number of cases reported. It can affect all ages and both sexes.[9] Although a female predominance is seen in most studies[10], our case series showed an equal gender distribution with the male to female ratio 1:1. The mean age of patients at the time of diagnosis was 35.8 years, which was lesser than that observed in a Lebanese population and in a study done in Taiwan.[10]

Around 30% of systemic sarcoidosis patients have skin lesions, but isolated cutaneous

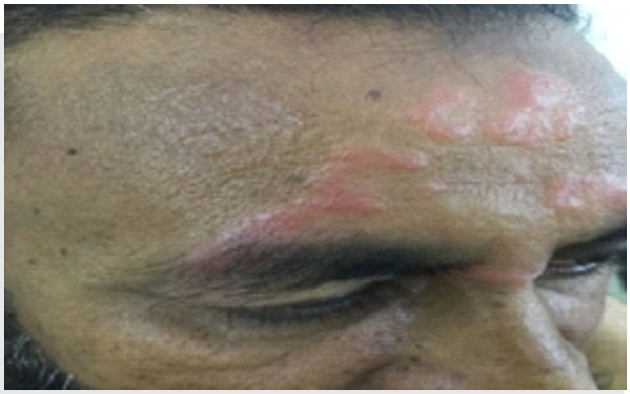

Figure 3
Annular Erythemarous plaques on the face of Patient 9

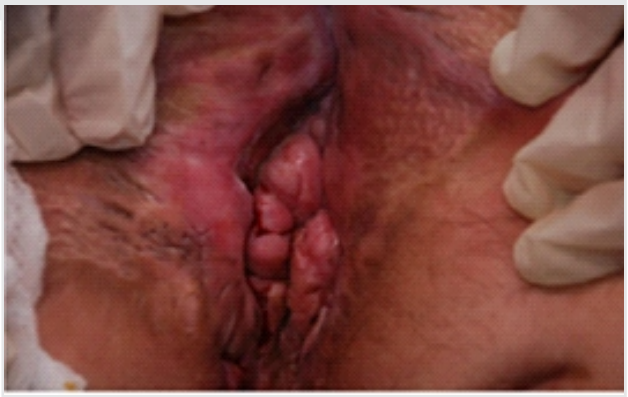

Figure 4
Patient 7 showing the presence of infilt-rated plaque and modules in valve and perianal region.

sarcoidosis can also occur, seen in approximately 10% of patients.[10,11] The skin lesions of sarcoidosis can be classified as specific and non-specific. The specific skin lesions include maculopapules, plaques, subcutaneous

nodules, scar sarcoidosis and lupus pernio, which display typical non-caseating granulomas. Non-specific lesions like erythema nodosum show reactive processes without granuloma formation.[12] Other rare types, such as angiolupoid, hypopigmented, icthyosiform, annular, ulcerated variants are also reported.[6]
In our study, sarcoid plaques were the most common cutaneous lesion, which was consistent with the findings of a study of 76 patients in Lebanon by Ishak et al.[13] In contrast, a Taiwanese series reported the angiolupoid variant as the most common form.[10]
Extracutaneous involvement is commonly seen involving the lungs, eyes, lymph nodes and heart.[14] We found pulmonary involvement to be the commonest (40%), followed by the lymph nodes (20%), which was in accordance to the literature. In the chest radiological examination, the majority (60%) had normal findings (Stage 0). This was in contrast to other series reported in Hong Kong, where the finding of bilateral hilar lymphadenopathy (Stage1) was the most common.[8]
Histologically, the typical granulomas of sarcoidosis are non-caseating, with few or no inflammatory cells (naked granulomas). Our study did not differ from these findings. Infective granulomas which may result in confusion were excluded by testing tissue specimens for Gram-stain, Grocott, Ziehl Nelson and Wade-fite stains.[15] Culture and polymerase chain reaction for M.tuberculosis was also negative.
The usual treatment of sarcoidosis is with steroids. Potent topical steroids or intralesional steroids can be prescribed for isolated cutaneous sarcoidosis. Systemic corticosteroids at 0.5mg/kg with gradual tapering are deemed effective for extensive and those unresponsive to topical therapy. Other drugs, which also give a steroid sparing effect, include hydroxychloroquine, minocycline, thalidomide, methotrexate, azathioprine, infliximab and adalimimab.[16] The majority of patients in our series responded well to prednisolone and intralesional steroids. They are currently doing well on follow up.
The major drawback of our study is the small sample size. Studies done on a larger population are needed in order to achieve a more objective result.
The strength of this study is that there is no published case series dedicated to the presence of cutaneous sarcoidosis in Pakistan done in the last five years.

CONCLUSION

In conclusion, this case series suggests that sarcoid plaques are the most commonly seen lesions. While the lungs and lymph nodes are the most frequent extracutaneous manifestations of cutaneous sarcoidosis. Other systemic involvement was also seen although less frequently. Therefore, cases of cutaneous sarcoidosis need regular surveillance for any new systemic feature that may develop in the future. In addition, sarcoidosis in our setups may have been under diagnosed. Clinicians need to keep sarcoidosis in their differential diagnosis in appropriate clinical and radiological settings. The main diagnostic dilemma with sarcoidosis is in countries such as Pakistan, where tuberculosis and leprosy are endemic. Patients receive multiple course of anti-mycobacterium therapies while organ damage continues to progress. Further studies are hence required in Pakistan, where due to scanty data, diagnosis and management remains a challenge.

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