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Clinico-Pathological Study of Cutaneous Granulomatous Lesions- a 5 yr Experience in a Tertiary Care Hospital in India

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KEY WORDS

Granuloma
histopathology
skin biopsy

ABSTRACT

Background: Granulomatous dermatoses are common skin pathology, often need histopathological confirmation for diagnosis. Histologically six sub-types of granulomas found in granulomatous skin diseases- tuberculoid, sarcoidal, necrobiotic, suppurative, foreign body & histoid type. The aims of the present study were clinico-pathological evaluation of granulomatous skin lesions and their etiological classification based on histopathological examination.

Methods: It was a five years (Jan 2009- Dec 2013) retrospective study involving all the skin biopsies. Detailed clinical and histopathological features were analyzed and granulomatous skin lesions were categorized according to type of granuloma & etiology. Special stains were used in few cases for diagnostic purpose.

Results: Among 1280 skin biopsies, 186 cases (14.53%) were granulomatous skin lesions with a ratio 1:24. In histopathological sub-typing, tuberculoid granuloma was most common type (126 cases, 67.74%). Most common etiology of granuloma in the study was leprosy (107 cases, 57.52%). Other etiologies were cutaneous tuberculosis, foreign body granulomas, fungal lesions, cutaneous leishmaniasis, sarcoidosis and granuloma annulare.

Conclusion: Histopathology is established as gold standard investigation for diagnosis, categorization and clinico-pathological correlation of granulomatous skin lesions.

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ARTICLE INFO

Received 28 Oct 2014;

Accepted 15 Jan 2015;

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Introduction

Granulomatous skin lesions are distinctive pattern of chronic inflammatory response of skin due to reaction against various organic and inorganic antigens (1, 2). Granulomas are

characterized by focal collection of epithelioid cells or histiocytes, admixed with variable number of leucocytes (especially mononuclear cells) and multinucleated giant cells. Granulomatous reaction is a type IV hypersensitivity reaction evoked by poorly soluble reactive substances.

Six types of granulomatous skin lesions are identified according to cellular constituents and associated changes: 1) tuberculoid, 2) sarcoidal, 3) necrobiotic, 4) suppurative 5) foreign body and 6) histoid type granuloma (3,4).

Incidence and prevalence of different types of granulomatous dermatitis depend on geographic location. Granulomatous skin lesions are common in eastern India. Many granulomatous skin lesions have identical histomorphology and conversely a single pathology can produce varied histological features (5). They often lead to diagnostic confusion among Dermatologist & Pathologist due to variable morphology.

The present study was undertaken to determine the frequency and pattern of different granulomatous skin lesions and clinico-histopathological correlation of the lesions to reach correct etiological diagnosis.

Material and Methods

The present study was a retrospective analysis of all skin biopsies of granulomatous skin lesions received in the Department of Pathology, Bankura Sammilani Medical College & Hospital (Bankura, India), over a period of five yr from Jan 2009 to Dec 2013.

Ethical clearance was obtained from institutional ethical committee before undertaking the study. Written consents were taken from all patients included in the study.

Detailed history and clinical data were collected from patient's treatment sheet as well as from hospital's record section. Dermatological diagnosis was done by dermatologists. Skin biopsies were taken at Dermatology Department and specimens were sent to our histopathology laboratory for histopathological examination. The biopsy samples were undergone routine tissue processing and section cutting. All cases were stained with H&E stain and special stains (PAS, ZN stain, Giemsa, Fite-Faraco, and Reticulin) were applied as required. Histopathological diagnoses of skin biopsies were done by us in our laboratory. Only the histopathologically confirmed cases of granulomatous skin lesions were included in study group. The cases of non-granulomatous dermatoses and inadequate samples were excluded from study. All cases of granulomatous skin lesions were analyzed in respect to clinical information and histopathological examination of biopsy samples. Data analysis was done by use of statistical software SPSS.

Results

In the five years retrospective study, total 1280 skin biopsies were evaluated. Granulomatous skin lesions were diagnosed in 186 cases (14.42%). Among 186 cases, 103 cases (55.38%) were male and 83 cases (44.62%) were female. Age of the patients in the present study varied from four yr. to 77 yr. with the mean age of 30.45

Table 1
Distribution of the cases of granulomatous skin lesions according to age and sex distribution

Age	Male	Female	Total	(%) Percentage
0-10	4	1	5	2.68
11-20	29	28	57	30.65
21-30	31	22	53	28.49
31-40	15	17	32	17.20
41-50	13	7	20	10.75
51-60	6	5	11	5.91
61-70	3	2	5	2.68
70<	2	1	3	1.61
Total	103	83	186	100

years. Age & sex distribution of the cases in our study has been shown in the Table 1. Maximum numbers of cases were found among age group of 11-30 yr (110 cases, 59.14%).

Histopathological sub types of granulomatous lesions revealed 126 cases (67.74%) were tuberculoid type granulomas. Distributions of

different category of granulomatous lesions were exhibited in Table 2.

On histopathological examination and etiological typing of lesions, leprosy was the most common type of diagnosis (107 cases, 57.52%). Among the leprosy cases borderline tuberculoid was the most common sub-groups

Table 2

Distribution of cases according to histopathological types of granuloma

Type of Granuloma	Number	(%) Percentage
Tuberculoid type	136	73.12
Foreign body type	12	6.45
Suppurative	09	4.84
Necrobiotic	23	12.37
Sarcoidal	03	1.61
Histiocytic	13	6.99
Total	186	100

Table 3

Distribution of etiological diagnosis of granulomatous skin lesions on histopathological examination

Diseases	Number (n)	Percentage (%)
Leprosy	n- 107	57.52
-Tuberculoid	14	
-BT	62	
-BB		
-BL	07	
-Lepromatous	10	
-Indeterminate	13	
-Histoid	01	
Tuberculosis	n- 46	24.73
-Lupus vulgaris	29	
-Scrofuloderma	11	
-TVC	06	
Foreign body granuloma	n- 9	4.84
-Epidermal cyst	06	
-Xanthoma	02	
-Rhinosporidiosis	01	
Fungal infection	n- 7	3.76
-Actinomycosis	03	
-Maduromycosis	02	
-Pseudallescheria boydii	02	1.61
Sarcoidosis	n- 3	1.07
Cutaneous Leishmaniasis	n- 2	4.84
Granuloma annulare	n- 9	1.07
Helminthiasis	n- 2	

(62 cases, 57.94%). The distributions of different sub-types of cases have been shown in Table 3.

Cutaneous tuberculosis was diagnosed in 46 cases (24.73%), among which lupus vulgaris was the most common sub-types (29 cases, 63.04%); scrofuloderma (11 cases, 23.91%), and tubercular verruca cutis (6 cases, 13.04%) comprised rest of the cases of cutaneous tuberculosis.

Among the 12 cases of foreign body granulomatous skin lesions, seven were epidermal cyst, three were xanthoma & cutaneous rhinosporidiosis was diagnosed in two cases.

Among the 23 necrobiotic granulomatous lesions, 16 cases were tuberculous origin and seven cases were granuloma annulare. Histologically the cases of granuloma annulare show necrobiosis and palisaded granuloma with peripheral deposition of collagen mixed with lymphocytes, histiocytes and fibroblasts. Seven cases out of nine granuloma annulare were solitary lesion over extensor surface of extremities with female preponderance.

We diagnosed seven cases of fungal granuloma in our study. All the fungal skin lesions showed suppurative granuloma. Three cases were diagnosed as actinomycosis and diagnosis was confirmed by gram stain. Maduromycosis and *Pseudallescheria boydii* were diagnosed in two cases each.

Three cases of sarcoidosis and two cases of cutaneous leishmaniasis were diagnosed in the present study. Most of the histiocytic granulomas in our study were lepromatous leprosy (11 cases out of 13, 84.61%).

Discussion

Granulomatous inflammation is a type-IV hypersensitivity reaction to an antigen. Various infectious and non-infectious granulomatous dermatoses are frequent among the population of eastern part of India. Definitive etiological diagnosis is important for their management. Histopathology is a gold standard tool for

correct diagnosis of various granulomatous skin lesions. Microscopically, wide spectrum of histopathological features of different granulomatous lesions was observed in the present study. We classified the lesions based on histo-morphology and etiology of the granulomatous diseases.

In this study, we found male preponderance (103 cases among 186) with a sex ratio of 1.24. Our findings agreed with previous studies (1, 2, 6), but not with Zafar et al. (4).

Large number of cases in the present study were among 11-20 yr. (57 cases, 30.65%) and 21-30 yr. (53 cases, 28.49%); consistent with the findings of Pawale et al. (2).

In the present study, largest group of lesions were tuberculoid granulomas (136 cases, 73.12%). Similar findings were seen in previous studies with the amount of 77.3% (1, 6), and 87.7% (7). (Majority of the cases in the present study were leprosy (107 cases, 57.62%). Our findings were consistent with Pawale et al. (2) (56.6%) but incidence of leprosy was lower than the others, 79.7% and 72.4% (1, 7). We classified the leprosy cases according to Ridley and Jopling classification. The largest subgroup of leprosy in our study was borderline tuberculoid (62 cases, 57.94%) similar to the findings of Gautam et al. (46.7%) and Bal et al. (55.2%)(1,7). All the tuberculoid leprosy and most of the borderline tuberculoid cases were similar to non-caseating granulomas of tuberculosis and sarcoidosis (8,9). Modified ZN stain revealed lepra bacilli only in seven cases of borderline tuberculoid leprosy and in none of the tuberculoid leprosy. Location of the granulomas around the neurovascular bundles and involvement of arrector pili muscle and adnexa in the background of proper clinical presentation cues to diagnose tuberculoid and borderline tuberculoid leprosy (Fig. 1). However, most of the borderline lepromatous (BL) and all the lepromatous leprosy (LL) cases exhibit histiocytic granulomas (Fig. 2), and were strongly positive for lepra bacilli in modified Z-N stain.

Lepra bacilli were seen in 30 cases (14 cases of lepromatous leprosy, six borderline lepromatous, seven cases of borderline tuberculoid, two cases of erythema nodosum leprosum and one case of histoid leprosy), 28.03% of all the leprosy cases. Bal et al. found AFB in 36.4% of their cases, slightly higher than our study (7).

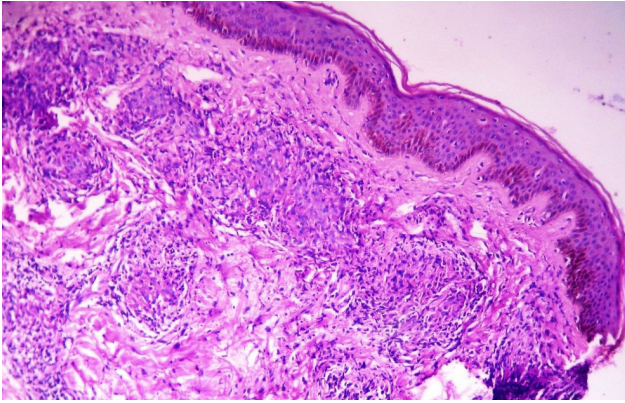


Fig. 1

Photomicrograph reveals many epithelioid granulomas around neurovascular bundles, not encroaching to epidermis in a case of borderline lepromatous leprosy (H & E stain, 10X view)

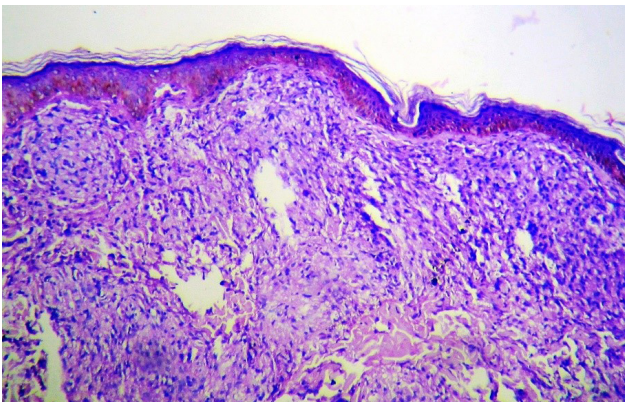


Fig. 2

Photomicrograph shows atrophic epidermis, large expansile macrophage granulomas (sheets of foam cells) in dermis in a case of lepromatous leprosy (H & E stain, 10X view)

Tuberculosis was the second most common cause of granulomatous skin lesions in our study, accounting 24.73% of all the granulomatous skin lesions. Incidence of cutaneous tuberculosis in the present study (3.59% of all the skin biopsies) is higher than the worldwide incidence (0.1 to 1%

of all cutaneous lesions) (1,2,6). The incidence of cutaneous tuberculosis has been found as 3.7% in Pakistan (4). Possible reasons of higher incidence of cutaneous tuberculosis in our study were poor nutrition and poverty, poor personnel hygiene in the tribal population of the district.

Cutaneous tuberculosis was more prevalent in female than male (1.3:1) in the present study, supporting the finding of previous studies (1,4,10,11). Lupus vulgaris (Fig. 3) was the most common type of cutaneous tuberculosis in our study (29 cases, 63.04%) similar to the previous investigations (4,6,12,13). But few other studies revealed scrofuloderma as the commonest type of lesion, particularly in childhood (1,14,15). However, in the present study scrofuloderma was diagnosed in 11 cases (23.91%); 2nd common tubercular skin lesion.

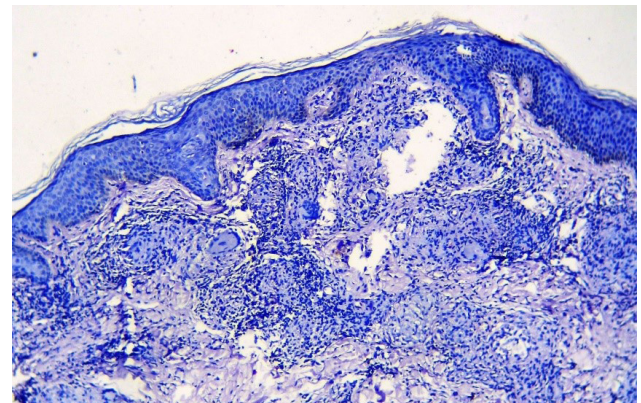


Fig. 3

Photomicrograph reveals hyperplastic epidermis; epithelioid granulomas and Langhans type giant cells in dermis in a case of lupus vulgaris (H & E stain, 10X view)

Twelve cases (6.45%) of foreign body type granuloma were identified in the present study. Most common type foreign body granuloma was epidermal cyst (six cases), correlating the findings of Gautam et al. (1). Granulomatous reaction occurs against the ruptured keratin material of epidermal cyst resulting in numerous multinucleated giant cells and keratin granuloma formation surrounding the cyst wall (1). Cutaneous xanthoma was diagnosed in two cases; where histopathology revealed aggregates

of foamy histiocytes and touton giant cells and cholesterol clefts. Another study by Pawale et al. found cutaneous xanthoma as the most common type foreign body type cutaneous granulomatous lesions (2).

We found two cases of cutaneous rhinosporidiosis in the present study, both the cases were young male patients, had nodular skin lesion at neck region. Extra-nasal rhinosporidiosis is common at ocular and head neck region and present as nodular skin lesions with granular reddish surface (16). Granuloma formation and giant cells are very common inflammatory reaction against the chettenious wall of sporangium and spores (Fig. 4) (17).

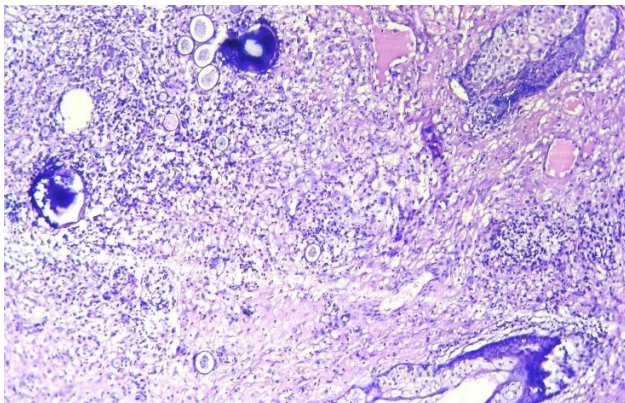


Fig. 4
Photomicrograph reveals many sporangia with endospores in dermis with foreign body reaction of cutaneous rhinosporidiosis (H & E stain, 10X view).

We diagnosed seven cases (3.76%) of fungal cutaneous granuloma in the present study. Our observation is similar to other studies with the amount of 3.2% and 3.3% (4,7). Pawale et al. found 11.32% fungal lesions in their study (2). Distribution of the fungal lesions in the present study was mostly on the extremities over chest wall. Three cases were actinomycetes, two cases were maduromycosis and *P. Boydii* was diagnosed in another two cases.

Cutaneous leishmaniasis was diagnosed in two cases (1.07%) in our series. Incidence varies in different tropical areas like (1.16%) in the study by Bal et al., whereas Qureshi R et al

found 56.7% in Pakistan (3,7). Our findings are consistent with other studies in India (1.16%) (7). Both the cases of cutaneous leishmaniasis were male and presented with itchy nodulo-ulcerated skin lesions at upper extremities and face. Microscopy of cutaneous leishmaniasis revealed heavy plasma cell infiltration at sub epithelial tissue and macrophages containing amastigote forms in case of early lesions (3). Leishman Donovan (LD) bodies were demonstrable in both the cases in our study. Bal et al. found LD bodies in 50% of the leishmaniasis cases in their series (7). Leishmania skin test and staining of the exudates by Giemsa & Wrights stain are the ancillary tests for diagnosis (1).

We diagnosed two cases of cutaneous sarcoidosis in the present study. Both the cases exhibited non-caseating epithelioid granuloma devoid of inflammatory cells and Langhans giant cells. Incidence of sarcoidal lesions in the present study was 1.07%, quite similar to Gautam et al. (1.88%) (1). Both the cases in our study were female and diagnosis also correlated with the findings of chest x-ray and serum calcium level.

Granuloma annulare was diagnosed in nine cases (4.83%) in our series. Gautam K et al, Pawale J et al and Qureshi R et al found 3.7%, 3.77% and 5.4% respectively (1-3). Our findings were consistent with the previous studies. Most of the cases were young female and seven cases showed localized lesions on dorsal aspect of extremities similar to findings of other authors (1, 3). However, Mohan H et al found male preponderance in their series (18).

All the granulomatous skin lesions were correlated with clinical history, examination findings and ancillary investigations.

Conclusion

Histopathology is gold standard for diagnosis & categorization of granulomatous skin lesions. Our study gives a prevalence of important granulomatous skin diseases in this region, which

will help in implicating health programmes and management of the individual cases.

Conflict of interest

The authors declare that there is no conflict of interests.

References:

1. Gautam K, Pai RR, Bhat S. Granulomatous lesions of the skin. *Journal of Pathology of Nepal*. 2011;1(2):81-6.
2. Pawale J, Belagatti SL, Naidu V, Kulkarni MH, Puranik R. Histopathological study of cutaneous granuloma. *Ind J Public Health Res Develop* 2011 July;2(2):74-9.
3. Qureshi R, Sheikh RA, Haque AU. Chronic granulomatous inflammatory disorders of skin. *Int J Pathol* 2004; 2(1):31-4.
4. Zafar MNU, Sadiq S, Menon MA. Morphological study of different granulomatous lesions of the skin. *J Pak Assoc Dermatol* 2008;18(1):21-8.
5. R Singh, K Bharathi, R Bhat, C Udayashankar. The histopathological profile of non-neoplastic dermatological disorders with special reference to granulomatous lesions - study at a tertiary care centre in pondicherry. *Internet J Pathol* 2012; 13(3):14240
6. Dhar S, Dhar S. Histopathological features of granulomatous skin diseases: an analysis of 22 skin biopsies. *Indian J Dermatol* 2002;47(2):88-90.
7. Bal A, Mohan H, Dhami GP. Infectious granulomatous dermatitis: a clinico-pathological study. *Indian J Dermatol* 2006;51(3):217-20.
8. Hirsh BC and Johnson WC. Concepts of granulomatous inflammation. *Int J Dermatol* 1984 March;24 (2):90-9.
9. Young RJ 3rd, Gilson RT, Yanase D, Elston DM. Cutaneous sarcoidosis. *Int J Dermatol* 2001 April;40(4):249-53.
10. Khan Y, Anwar J, Iqbal P, Kumar A. Cutaneous tuberculosis: a study of ten cases. *J Pak Asso Dermatol* 2001;11(3):6-10.
11. Yasmeen H, Kanjee A. Cutaneous tuberculosis: a three year prospective study. *J Pak Med Assoc* 2005 Jan;55(1):10-2.
12. Kumar B, Muralidhar S. Cutaneous tuberculosis: a twenty year prospective study. *Int J Tuberc Lung Dis* 1999 Jun;3(6):494-500.
13. Puri N. A clinical and histopathological profile of patients with cutaneous tuberculosis. *Indian J Dermatol*. 2011;56(5):550-2.
14. Farina MC, Gegundez MI, Pique E et al. Cutaneous tuberculosis: a clinical, histological and bacteriologic study. *J Am Acad Dermatol* 1995 Sep;33(3):433-40.
15. Kumar B, Rai R, Kaur I, Sahoo B, Muralidhar S, Radotra BD. Childhood cutaneous tuberculosis: a study over 25 years from northern India. *Int J Dermatol* 2001;40(1):26-32.
16. Saha J, Basu AJ, Sen I, Sinha R, Bhandari AK, Mondal S. Atypical presentation of rhinosporidiosis: A clinical dilemma? *Indian J Otolaryngol Head Neck Surg* 2011 July;63(3):243-6.
17. Arseculeratne SN. Recent advances in rhinosporidiosis and *Rhinosporidium seeberi*. *Indian J Med Microbiol* 2002;20(3):119-31.
18. Mohan H, Bal A, Dhami GP. Non-infectious granulomatous dermatitis: a clinicopathological study. *J Cutan Pathol* 2006;33(12):767-71.

How to cite this article:

Chakrabarti S, Pal S, Biswas B, Bose K, Pal S, Pathak S. Clinico-Pathological Study of Cutaneous Granulomatous Lesions- a 5 yr Experience in a Tertiary Care Hospital in India. *Iran J Pathol* 2016; 11(1): 54 - 60.