

# A Clinicopathological Analysis of Granulomatous Dermatitis : 4 Year Retrospective Study

Jyotsna Suri, Subhash Bhardwaj, Rita Kumari, Shailija Kotwal

## Abstract

The present study was carried out with an attempt to study the incidence of granulomatous dermatitis in hospital based population and to classify and compare the granulomatous dermatitis on the basis of histopathology and find the etiology. This is a four year retrospective study done on the data available in the dermatopathology section of department of pathology. The cases diagnosed as granulomatous dermatitis were retrieved, clinical data and the histopathological features compared to know the incidence of various etiologies of GD. Out of 310 cases of GD with male to female ratio 2.03:1, leprosy comprised major reported etiology (n-244) followed by tuberculosis (n-44), sarcoidosis (n-4), Leshmania Donovanii (n-14)) granuloma annulare (n-1) and 3 granulomatous lesions not further classified. Infections form the commonest form of GD out of which leprosy forms the major group. Role of histopathology(H&E and special stains) is very important in confirming the diagnosis of granulomatous dermatitis .

## Key Words

Granuloma, Dermatitis, Inflammatory, Tissue Injury

## Introduction

Granuloma is defined as a focal chronic inflammatory response to tissue injury, characterised by focal, compact collection of inflammatory cells, principally of the activated histiocytes, modified epitheloid macrophages & multinucleate giant cells that may or may not be rimmed by lymphocytes and show central necrosis. (1)

Granulomas are formed as an end result of complex interplay of inflammatory cells and chemical mediators in hypersensitive response to nondegradable product or antigen resulting in prolonged antigenaemia. Various chemoattractants secreted by activated macrophages, T cells, B cells attract monocytes macrophages which undergo transformation to form epitheloid cells and many fuse to form multinucleate giant cells. (2, 3)

CD4 helper cells and lymphocytes are necessary for development of the granulomas. The helper cells produce IL2, IFN gamma & TNF beta upon stimulation with antigen and delayed type of hypersensitivity reaction. Granulomas resulting from different infections have different immunoregulatory mechanisms governing their formation and resolution. On the basis of aetiology, granulomatous inflammation is classified into bacterial, fungal, viral, cat scratch fever, lymphogranuloma venereum, helminthic, foreign body type and unknown cause. In the dermatology and dermatopathology granulomatous

dermatitis presents a diagnostic challenge, many a times. The granulomatous dermatitis comprise a large family sharing the common histological denominator of granulomas formation. Rightly said that in granulomatous dermatitis, an identical histologic picture may be produced by several causes & conversely a single cause may produce varied histologic patterns. (3) This makes it cumbersome to classify granulomatous dermatitis in a satisfactory way. The present study was carried out with the aim of classifying granulomatous dermatitis on the basis of aetiology and morphology and to study the incidence of different aetiologies of granulomatous dermatitis in hospital based population of Jammu region.

## Material and Methods

A retrospective 4 year analysis of skin biopsies reported in dermatopathology section of the department of pathology GMC Jammu and the cases diagnosed as one or other form of granulomatous dermatitis were retrieved. Detailed information's like age, sex and clinical diagnosis were recorded. In each case, haematoxylin and eosin stained paraffin sections along with special stains like PAS, Ziehl-Neelsen (ZN), Giemsa, etc. were studied.

## Results

In the four year retrospective study, out of total 1081 cases reported in the dermatopathology section of

From the Department of Pathology, Govt. Medical College Jammu- J&K India 180001

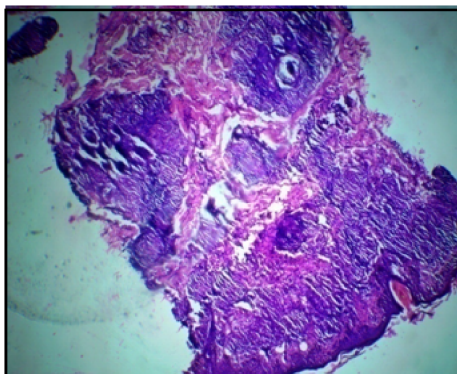
Correspondence to : Dr Jyotsna Suri , Associate Professor, Department of Pathology , Government Medical College, Jammu J&K India 180001

department of pathology, 310 cases of granulomatous dermatitis were retrieved. The age of the patients ranged from 4-80 years with male to female ratio of 2.03:1(208:102).

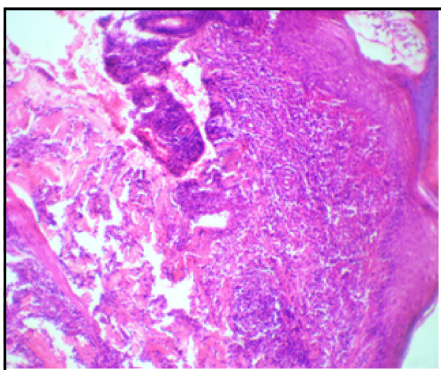
Leprosy comprised the major reported aetiology of the cases of granulomatous dermatitis in our study. These cases reported on histopathology as Leprosy were further categorised into tuberculoid, borderline tuberculoid, borderline, borderline lepromatous & lepromatous as per clinical & pathological criteria in Ridley & Jopling's classification. Some of the cases were reported as histioid variant of lepromatous leprosy. The cases which on microscopic examination were showing multiple well formed epithelioid cell granulomas with rim of lymphocytes and distribution throughout papillary and reticular dermis specially around the skin adnexae & neurovascular bundles and abutting the basal layer of epidermis (with absence of grenz zone) were reported as Tuberculoid leprosy (n=32), (Fig 1). The cases which on microscopic examination were showing few epithelioid cell granulomas with few lymphocytes and multinucleate giant cells and absence of grenz zone were categorised as Borderline Tuberculoid (n=63), (Fig 2). The cases showing granulomas rich in foamy histiocytes but admixed with

few epithelioid cells were categorised as Borderline Lepromatous (n=68), (Fig 3). The cases which on microscopic examination were showing diffuse sheets of foamy histiocytes with presence of grenz zone were classified as Lepromatous leprosy (n=52), (Fig 4). 20 cases were reported in these 4 years as Histioid variant of lepromatous leprosy and were showing presence of grenz zone under the microscope along with presence of numerous thin spindle-shaped cells, seen forming

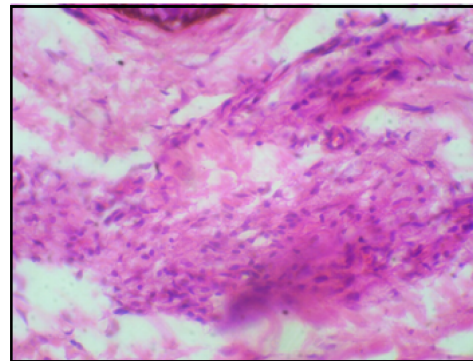
**Fig 1. Photomicrograph of Tuberculoid Leprosy [H&E X100]**



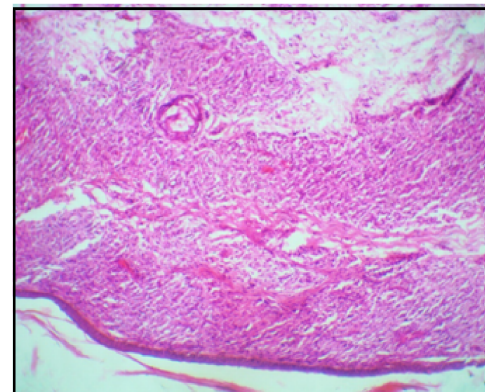
**Fig 2. Photomicrograph of Borderline Tuberculoid Leprosy [H&E X100]**



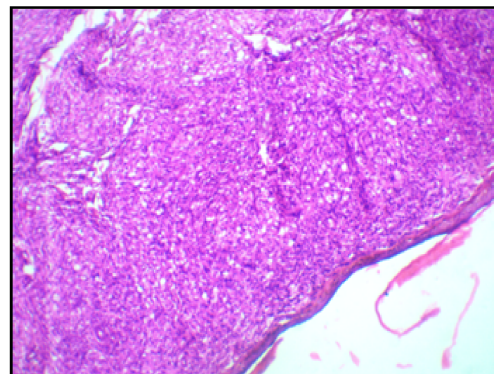
**Fig 3. Photomicrograph of Borderline Lepromatous Leprosy [H&E X400]**



**Fig 4. Photomicrograph of Lepromatous leprosy [H&E X 100]**



**Fig 5. Photomicrograph of Histioid Leprosy [H&E X 100]**



**Table 1. Distribution of Cases of Granulomatous Skin Lesions According to Age Group Distribution**

Age Range	No of patients	Percentage
0-10	3	0.97
11-20	40	12.9
21-30	88	28.39
31-40	76	24.51
41-50	33	10.66
51-60	36	11.61
61-70	25	8.06
71-80	9	2.90

**Table 2. Distribution of Case According to Etiological Diagnosis of Granulomatous Skin Lesions on Histopathological Diagnosis**

Distribution of case according to Histopathological types of granuloma Diagnosis	No of patients Total no =310	%
<b>Leprosy</b>	<b>244</b>	<b>78.7</b>
A;Tuberculoid Leprosy	32	
B;Borderline Tuberculoid	63	
C;Borderline lepromatous	68	
D;Lepromatous leprosy	52	
E; Histoid Leprosy	20	
F;ENL	4	
G;Down/Upgrading reaction	5	
<b>Tuberculosis</b>	<b>44</b>	<b>14.2</b>
A; Lupus Vulgaris	29	
B; Scrofuloderma	7	
C; TVC	8	
Sarcoidosis	4	1.3
Leishmania Donovanii	14	4.51
Granuloma Annulare	1	0.3
Granulomatous Dermatitis ( not further classified)	3	0.9

interlacing bands, whorls & tight clusters. Such structures were indistinguishable histologically, from a neurofibroma or a dermatofibroma. However, palisading of the nuclei was not observed and no giant cells were seen. The constituent spindle-shaped cells had a moderate amount of cytoplasm with nuclei that were oval and lightly stained. Foamy macrophages were not seen. The histioid lesions contained an unusually large number of acid-fast bacilli, very much more than were seen in the conventional lepromatous lesions in the same case. The organisms were packed tightly into bundles and groups completely occupying the entire extent of the cell, without, however, disturbing its normal contour. This arrangement has been designated by Wade as histioid habitus & is characteristic

of histioid leprosy. (Fig 5) The outstanding clinical features which distinguish the lesions of histioid leprosy are that they appear as cutaneous or sub-cutaneous nodules or occasionally as plaques, and they are sharply circumscribed. The lesions are either surrounded by normal skin or by conventional lesions of lepromatous leprosy. Cases were also diagnosed as Type 1 & Type 2 reactions Erythema nodosum leprosy (n=4) & downgrading & upgrading reactions in (n=5) cases.

Tuberculosis comprised the second major aetiology of granulomatous dermatitis in our study (n=44). Lupus vulgaris was diagnosed in 29 cases and microscopic examination showed well formed epithelioid cell granulomas with or without caseation necrosis in the dermis. Diagnosis of scrofuloderma was given in (n=7) cases, showing surface ulceration and admixture of neutrophilic abscesses and tuberculosis verrucosa cutis (8 cases) with marked epidermal hyperplasia and neutrophilic abscesses in the epidermis. Ziehl-Neelsen (ZN) stain for acid fast bacilli was positive in 6 cases (5%), only 3 cases (5%) of lupus vulgaris and 3 cases (6.5%) of scrofuloderma.

Sarcoidosis was diagnosed in (n=4) cases with presence of non-caseating naked epithelioid cell granulomas in skin biopsy and one of the case showed presence of inclusions in giant cell. Suggestion of sarcoidosis as clinical diagnosis, a compatible clinical picture and absence of evidence of known causes of local granulomatous reactions or of other generalised granulomatous diseases are required for making a definitive diagnosis. Out of all the 18 cases clinically diagnosed as cutaneous leishmaniasis and biopsy sent for histopathology in these four years, 8 cases showed the presence of the parasite leishmania Donovanii on microscopy and the parasite could be appreciated with Giemsa stain, whereas 6 cases showed post Kala Azar dermal leishmaniasis showing lymphohistiocytic and plasma cell infiltrate on microscopic examination. Only one case was reported as granuloma annulare. 3 cases showed epithelioid cell granulomas on microscopic examination, out of which one was biopsied as fungal dermatitis but the special stains were noncontributory. Other 2 cases were reported as granulomatous, necrosis absent. They were not served a specific diagnosis and were lost to follow up. (Table-1&2)

### Discussion

Granulomatous inflammation was recognised as a distinct entity in the early nineteenth century. (4) It is a common problem for which clinicopathological correlation is of help in arriving to a proper diagnosis so that the appropriate treatment can be given. Histopathology has always played an important role in establishing a definite diagnosis. (4, 5) Recently many studies on granulomatous dermatitis have been done in different regions. In our

institution, which is a tertiary care centre, no such study has been done. Our study is a retrospective 4 year study. In this we have done 4 year retrospective analysis of cases reported as one or other aetiology of granulomatous dermatitis, in the dermatopathology section of department of pathology. In our study group, the granulomatous dermatitis was more common in males as compared to females (2.03:1). This finding was in accordance with that of Dhar et al, who also found males to be involved more frequently than females. (6)

The majority of the cases in our study were of Leprosy (n=244; 78.7%), which were further classified on the basis of morphology of granulomas as Tuberculoid (n=32;13.11%); Borderline Tuberculoid (n=63;25.8%); Borderline Lepromatous (n=68;27.86%); Lepromatous (n=52;21.31%). Twenty cases were reported on microscopy as Histioid variant of Lepromatous Leprosy (n=20;8.19%) and nine cases were reported as ENL or Type 1 or Type 2 reactions (n=9;0.37%). (7, 8, 9)

The granulomas of Tuberculoid and Borderline Tuberculoid are well formed epithelioid granulomas with Langhans type of multinucleate giant cells and come in differential diagnosis of non-caseating granulomatosis as may be seen in tuberculosis without caseation necrosis and sarcoidosis. But in case of tuberculosis, the suggestive family history & clinical picture also suggest the diagnosis and other investigations also help in reaching to a definite diagnosis (10, 11). The granulomas seen in Sarcoidosis are discreet, noncaseating naked granulomas lacking a rim of lymphocytes and again the clinical details & immunological investigations also help in coming to a diagnosis (12). The ZN stain for *Lepra bacilli* is not of much help in differential diagnosis of these cases as BT & TT may show only sparse bacilli. However the cases of BT & TT show the granulomas around the skin adnexae and neurovascular bundles.

The granulomas in BL & LL are histiocytic granulomas, strongly positive for *lepra bacilli* on ZN staining. The next major group of granulomatous dermatitis was of cutaneous tuberculosis & were diagnosed on clinicopathological grounds as Lupus Vulgaris, scrofuloderma & Tuberculosis Verrucosa Cutis. The granulomas of tuberculosis, in vast majority of cases show epithelioid cell granulomas, Langhans type of giant cells & central caseation necrosis. But the absence of necrosis doesn't rule out the diagnosis of tuberculosis. ZN stain may show presence of acid fast bacilli. Clinical correlation may help in definite diagnosis. (13, 14)

When non-caseating discreet granulomas are present in the dermis, Reticulin stain helps in supporting the diagnosis of sarcoidosis. (12) Cutaneous Leishmaniasis can be confirmed as a cause of granulomatous dermatitis with the help of Giemsa stain to demonstrate LD bodies.

(15). With this study we conclude that infections are the commonest aetiology of granulomatous dermatitis and out of all these, granulomatous dermatitis because of leprosy forms the major category followed by tuberculosis, cutaneous leishmaniasis, sarcoidosis, fungal and other less common causes like foreign body type. The accurate diagnosis of cases of granulomatous dermatitis is very important as it decides the treatment and future course of the disease. (16).

### Conclusion

Infections form most common cause of granulomatous dermatitis, Leprosy being the commonest cause. The histopathological examination is important for forming the definite diagnosis of the granulomatous dermatitis and classification of the aetiology. Special stains also play an important supportive role in confirming the diagnosis of the infectious granulomatous dermatitis.

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