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CLINICO-HISTOLOGICAL SPECTRUM OF CUTANEOUS GRANULOMATOUS DERMATOSES AT A TERTIARY CARE CENTRE

Pathology

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ABSTRACT

Granulomatous Dermatoses comprise a large family having various etiologies but sharing the common denominator of granuloma formation. Aim of the present study was to classify granulomatous dermatoses based on histological pattern. Total 300 skin punch biopsies were studied, and diagnosed under 6 categories – Leprosy (222 cases), TB (34 cases), foreign body granuloma (27 cases), Sarcoid (1 case), fungal (8 cases) and Granuloma Annularae (08 cases). Clinical correlation with Dermatologist is important along with proper site of biopsy. Special stains should be performed. Early diagnosis and proper treatment would certainly help WHO's mission to eliminate TB by 2025 and Accelerating Towards Leprosy Free World.

KEYWORDS

Granulomatous Dermatoses, Leprosy, Tuberculosis, Histopathology

INTRODUCTION:

Granulomatous Dermatoses comprise a large family having various etiologies but sharing the common denominator of granuloma formation.[1] Granulomatous Dermatoses are distinctive pattern of chronic inflammatory response of skin as a reaction to variety of organic and inorganic antigens.[2,3] Granulomatous reaction is a type IV hypersensitivity reaction evoked by poorly soluble antigens.[4,5] Granulomas are very tiny, 0.5 – 2 mm lesions characterized by focal collection of epitheloid cells (modified histiocytes) admixed with variable number of lymphocytes and multi-nucleated giant cells. The word 'granuloma' is derived from 'granule', meaning circumscribed granule-like lesion and '-oma' is a suffix.[6] It is a protective defense reaction by the host, but eventually causes tissue destruction.[6] Granulomas may be hard as seen in Crohn's disease and Sarcoid, or soft as classically seen in Tuberculosis (TB). Six types of granulomatous dermatoses are known in literature – 1) Tuberculoid, 2) Sarcoidal, 3) Necrobiotic, 4) Suppurative, 5) Foreign body and 6) Histoid, according to the cellular constituents.[4,5]

Prevalence of types of granulomatous dermatoses differs according to geographic location. In Western countries, non-infectious granulomatous conditions like Crohn's and Sarcoid are common, while in developing countries of Asia like India, infectious granulomatous conditions like leprosy and tuberculosis are common. In India, granulomatous dermatoses are common in Eastern India.[7]

Many granulomatous skin lesions have identical histo-morphology and conversely a single lesion can present with variety of morphological features.[8] Advanced granulomas with well-formed sheets of epitheloid macrophages and giant cell are easily recognized but early lesions with only few epitheloid macrophages still qualify a granuloma. Many times, this diagnostic confusion between Dermatologist and Pathologist demands for acumen of the Histopathologist at microscopic level and diagnostic dilemmas are thereby solved. Thus, histopathology is the gold standard for diagnosis and categorization of cutaneous granulomas.

Granulomas are caused by variety of Mycobacteria, fungus, parasites as well as non-infectious conditions like Sarcoid, Crohn's, foreign body reactions and Granuloma Annulare.[6] There is not a single histologic feature to differentiate infectious and non-infectious granulomas.[9] However, special stains like Ziehl-Neelsen (ZN), Fite Faraco (FF), culture, Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and In-situ Hybridization can be performed to solve the diagnostic dilemma.[9]

Granulomatous dermatoses are a diagnostic challenge for both, Dermatologists and Histopathologists. The microscopic differences are very subtle and it requires knowledge and skill of histopathologist. Recognition of correct granulomatous pattern after clinical correlation is of utmost importance, as treatment modality is disease specific.

AIMS:

1) To classify granulomatous dermatoses based on histological pattern.
2) To determine prevalence of granulomatous infectious dermatoses like tuberculosis and leprosy in this part of Western Vidarbha.
3) To determine prevalence of granulomatous non-infectious dermatoses.
4) To highlight importance of clinical correlation between Dermatologist and Pathologist.

METHODS AND MATERIAL:

Present study was a retrospective study carried over 2 years period from June 2017 to June 2019 in the Department of Pathology, Government Medical College, Akola in collaboration with the Department of Dermatology. A total of 709 skin punch biopsies were received during this tenure, out of which 300 belonged to granulomatous category. All new cases, clinically suspected of granulomatous dermatoses were included in the present study. However, inadequate dermal biopsies were excluded.

Detailed clinical history including age, sex, duration, site of disease and family history. were noted. Punch biopsies were fixed in 10% formalin, processed and slides were stained with Hematoxylin and Eosin (H&E) stain. Special stains like ZN, FF, Periodic acid-Schiff (PAS), Reticulin, Congo red and Giemsa stains were performed wherever indicated. Deeper sections were also studied.

Morphological features of epidermal changes like atrophy, hypertrophy with hyperkeratosis, destruction of basal cell layer were studied. Location of granulomas in the dermis, predominant cell type in the form of histiocytes, lymphocytes, giant cells, neutrophils were noted. Micro-organisms like Actinomycosis, Mycetoma, Chromoblastomycosis were studied with special stain PAS. For suspected cases of Hansen's, FF and for tuberculosis cases ZN stains were studied. Bacteriological Index (BI) and Morphological Index (MI) was taken from FF smears for Hansen's disease.

RESULTS:

Total 300 skin punch biopsies were studied, and diagnosed under 6 categories – Leprosy (222 cases), TB (34 cases), foreign body granuloma (27 cases), Sarcoid (1 case), fungal (8 cases) and Granuloma Annularae (08 cases). Out of total 300 cases, males predominated with total of 191 cases (63.6%), and females were 109 (36.3%), as shown in table no.1. Tuberculoid type of granuloma outnumbered on histopathology, with a total of 184 (61.3%) and only 01 case (0.3%) showed Sarcoidal type of granuloma, as shown in figure no.1. Maximum cases belonged to age group of 21 years to 30 years, with a total of 63 cases (21%) and predominantly were diagnosed as Leprosy (57 cases – 19%), as shown in table no.2. Minimum age was found to be 03 years female with Scrofuloderma and the oldest case in the study was 82 years male diagnosed as BTH. Histological changes were as mentioned in table no.3, with maximum of 267 cases (89%) showing granuloma on microscopic examination. As shown in table no.4, most common site of the lesion was found to be back (87 cases – 29%), out of which maximum belonged to Leprosy (77 cases). Least common site was abdomen (3 cases – 1%), again all diagnosed as leprosy. The site of lesion of 01 Sarcoid case was found to be face.

Table no.1: Sex-wise distribution according to etiology on histopathology (n = 300)

Diagnosis		No. of cases (%)	Male	Female	Total
Leprosy	BTH	113 (37.6%)	141	81	222
	LL	38 (12.6%)			
	TT	21 (7%)			
	Histoid	18 (6%)			
	Mid-Borderline	11 (3.6%)			
	BLH	10 (3.3%)			
	Indeterminate	05 (1.6%)			
	Type I reaction	05 (1.6%)			
	Type II reaction	01 (0.3%)			
TB of skin	Lupus Vulgaris	18 (6%)	22	12	34
	Scrofuloderma	06 (2%)			
	TBVC	06 (2%)			
	Papulo-necrotic TB	02 (0.6%)			
	TB cutis Orofacialis	02 (0.6%)			
Fungal	Actinomycosis	03 (1%)	08	00	08
	Madura Mycetoma	03 (1%)			
	Chromoblastomycosis	02 (0.6%)			
Foreign Body granuloma	Calcinosis cutis	09 (3%)	13	14	27
	Fat necrosis	08 (2.6%)			
	Epidermal cyst	07 (2.3%)			
	Xanthoma	03 (1%)			
Granuloma Annulare		08 (2.6%)	06	02	08
Sarcoid		01 (0.3%)	01	00	01
Total		**300 (100%)**	**191 (63.6 %)**	**109 (36.3%)**	**300 (100 %)**

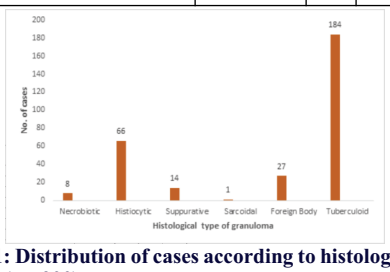

Figure no.1: Distribution of cases according to histological type of granuloma (n = 300)

Table no.2: Age-wise distribution of cases (n = 300)

Age Group (Years)	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	Total
Diagnosis										
Leprosy	02	27	57	43	44	26	19	03	01	222
TB	06	04	04	12	04	02	02	-	-	34
Granuloma Annularae	-	-	-	-	02	04	02	-	-	08
Fungus	-	-	-	01	02	03	02	-	-	08
Foreign Body type	-	-	02	02	02	04	10	07	-	27
Sarcoid	-	-	-	01	-	-	-	-	-	01
Total	**08 (2.6 %)**	**31 (10.3 %)**	**63 (21 %)**	**59 (19.6 %)**	**54 (18 %)**	**39 (13 %)**	**35 (11.6 %)**	**10 (3.3 %)**	**01 (0.3 %)**	**300 (100 %)**

Table no.3: Histological changes seen in different diagnosis (n = 300)

Changes	Leprosy	TB	Foreign Body type	Fungus	Granuloma Annularae	Sarcoid	Total
Epidermal atrophy	48	12	-	-	-	-	**60**
Epidermal hypertrophy	-	16	20	08	-	-	**44**
Basal layer destruction	21	30	21	08	-	-	**80**
Abscess	-	14	10	08	-	-	**32**
Normal	174	06	07	-	08	01	**196**
Granulomas	189	34	27	08	08	01	**267**
Giant cells	65	34	27	06	08	01	**141**
Caseation	-	20	-	-	-	-	**20**
Periadnexal granuloma	180	26	-	-	-	-	**206**

Table no.4: Distribution of cases according to site (n = 300)

Site	Leprosy	TB	Fungus	Foreign Body	Granuloma Annularae	Sarcoid	Total
Back	77	02	-	06	02	-	**87 (29%)**
Arm	28	06	-	-	01	-	**35 (11.6%)**
Face	23	02	-	-	-	01	**26 (8.6%)**
Forearm	21	02	-	-	01	-	**24 (8%)**
Hand	21	01	-	-	03	-	**25 (8.3%)**
Elbow	15	01	-	-	-	-	**16 (5.3%)**
Leg, Foot	15	16	08	04	01	-	**44 (14.6%)**
Trunk	11	02	-	03	-	-	**16 (5.3%)**
Gluteal	04	-	-	10	-	-	**14 (4.6%)**
Abdomen	03	-	-	-	-	-	**03 (1%)**
Head	02	-	-	04	-	-	**06 (2%)**
Neck	02	02	-	-	-	-	**04 (1.3%)**
Total	222	34	08	27	08	01	**300 (100%)**

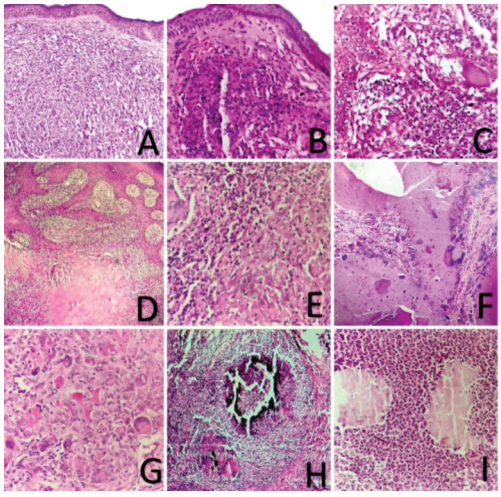

Fig A - Lepromatous Leprosy showing atrophic epidermis, grenz zone, and sheets of lepra bacilli. (H&E- 400X)

Fig B – Boderline Tuberculoid Leprosy showing multiple granulomas with giant cell not encroaching epidermis. (H&E-400X)

Fig C – Tuberculoid Leprosy showing multiple granulomas with giant cells encroaching base of epidermis. (H&E-400X)
Fig D - TBVC showing hyperkeratotic and hyperplastic epidermis with caseating granuloma in mid Dermis. (H&E-400X)
Fig E - Scrofloroderma showing granulomas with giant cells and lymphocytes. (H&E-400X)
Fig F - Foreign body granulomatous reaction seen in calcinosis cutis of skin. (H&E-400X)
Fig G – Granuloma Annulare showing mucosal and hyaline degeneration in the centre of granuloma with foreign body giant cell. (H&E-400X)
Fig H – Madhura Myecetoma showing brown coloured fungal bodies with granulomatous reaction. (H&E-400X)
Fig I – Actinomycosis showing Splendore-Hoeppli Phenomena. (H&E-400X)

DISCUSSION:

Present study was a retrospective study conducted at a Tertiary Care Hospital over 2 years. Histopathology is the gold standard to diagnose granulomatous dermatoses. It is the microscopic acumen of the Pathologist which decides the type of lesion after clinical correlation with Dermatologist. All granulomatous lesions are type IV hypersensitivity reactions to infectious or non-infectious antigens. Granulomatous dermatoses are very common in this part of Western Vidarbha.

We observed wide spectrum of morphological features in all cases. Results tabulated were compared with the studies in literature.

In this study, we found male preponderance (191 cases among 300) with a sex ratio of 1.75. Our findings agreed with previous studies.[2,3,7,10,11] The age distribution pattern indicated that maximum (74%) leprosy cases were found between age group of 7-82 years with the highest percentage in the 21-30 year age group (21%). The second most commonly affected age group was 31-40 years (total 59 cases – 19.6%). Mamandhar U et al[12], Moorthy BN et al[13], Sumit G et al[7] and Khatib et al[10] had similar observations with majority of their cases lying in 21-30 year age group.

The commonest etiology of granulomatous dermatoses in our study was leprosy (222 cases - 74%) followed by cutaneous TB (34 cases – 11.3%). This was comparable with the studies in the literature.[2, 7, 10, 11] Out of the typified 222 cases of leprosy, Borderline tuberculoid leprosy (BTH) constituted the most common diagnosis (37.6%) followed by lepromatous leprosy (LL – 12.6%). All the tuberculoid leprosy (TT) and most of the BTH cases were similar to non-caseating granulomas of tuberculosis and sarcoidosis.[14,15] We can conclude that the leprosy subtypes BTH is found to be more prevalent in Western Vidarbha. Incidence of cutaneous TB in the present study is higher than the worldwide incidence (0.1-1% of all cutaneous lesions).[2,3,16] This could be possibly due to overcrowding, poor nutrition, poverty and poor personnel hygiene in the tribal population of the district. 3rd common lesion in our study was foreign body granulomas (27 cases – 9%) which included calcinosis cutis, fat necrosis, epidermal cyst formation and xanthoma. These showed tuoton giant cells, cholesterol clefts and foamy histiocytes. This was comparable to the study performed by Srabani and Pawel.[2,3] In our study, back (29%) was the most common site followed by arms (11.6%) and face (8.6%). While neck (1.3%) was the least common site to be involved. While Jha and Karki[17] from Pakistan in their study found neck to be the commonest site.

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

CONCLUSION:

Histopathology is the gold standard to diagnose and categorize granulomatous dermatoses. Clinical correlation with Dermatologist is important along with proper site of biopsy. Special stains should be performed. Early diagnosis and proper treatment would certainly help WHO's mission to eliminate TB by 2025 and Accelerating Towards Leprosy Free World.

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Conflict of interest – None declared.
Ethical approval – Done.

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