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Clinicopathological spectrum of granulomatous dermatitis in a tertiary care hospital

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Abstract
Granulomatous dermatitis frequently presents a diagnostic challenge to dermatopathologists as an identical histologic picture is produced by several causes. This study aims at classifying granulomatous dermatitis based on etiology and morphology of granulomas, and to highlight significance of clinical correlation in making a specific diagnosis. A prospective analysis of 100 skin biopsies for granulomatous dermatitis was done. The salient clinicopathological parameters were assessed to bring out statistical significance. 84% of cases were diagnosed as infectious granulomatous dermatitis and 16% cases were of non – infectious granulomatous dermatitis, according to the etiological classification. The predominant cause of infectious granulomatous dermatitis was leprosy in 70.2% of cases followed by cutaneous tuberculosis in 23.8% of cases. All cases of cutaneous tuberculosis were composed of well-formed epithelioid cell granulomas with high sensitivity but low specificity. Presence of caseation necrosis and Langhans and foreign body giant cells were seen in 68.4% and 78.9% of cases respectively. The other less common causes were fungal infections in 4.7% of cases and cutaneous leishmaniasis in 1.2% of cases. Majority of cases of non- infectious granulomatous dermatitis were a result of sarcoidosis (37.5%) followed by erythema nodosum (18.7%). The other less common causes were foreign body granulomas, granulomatous cheilitis (12.5%) and necrobiosis lipoidica, granulomatous rosacea and granuloma annulare (6.25%). According to the morphological classification majority of cases were of epithelioid cell granulomas (81%), followed by histiocytic granulomas (11%). Other salient morphological pointers, such as perineural destruction and periadnexal location were also assessed. Special stains were also used to support the diagnosis. 90% of cases achieved clinicopathological correlation with combination of clinical impression and morphology being useful for making definite diagnosis in most of the cases.

Keywords: granulomatous, tuberculous, lepromatous

Introduction
Granulomatous skin lesions often presents a diagnostic challenge to derma to pathologists due to various modes of presentation and identical histological picture. Granulomas in skin may be produced by several causes and conversely a single cause may produce several histologic patterns. There is considerable variation in the microscopic appearance of granulomas producing different morphologic pictures within the same biopsy or from one lesion to another. Thus reaching a diagnosis involves combining information from clinical and pathological sources [1, 2].

Granulomatous inflammation defines a pattern of reaction to a wide range of etiologic agents, organic and inorganic, with certain morphologic correlates. According to Dorland, the term "granulomatous" was expressed initially by Virchow to describe a tumor-like mass or nodule of granulation tissue! Current definition of granulomas is "a focal chronic inflammatory response to tissue injury evoked by a poorly soluble substance characterized by the accumulation and proliferation of leukocytes, principally of the mononuclear type."

It is difficult to present a completely satisfactory classification of granulomatous dermatitis. It has been previously classified on the basis of pathophysiology, etiology, immunology, and morphology. Classification schemes are most useful when they provide insight into the purpose of events and the etiologic mechanisms that govern them. Broadly, there are two etiological groups: infectious and non-infectious [2, 3]. Infectious granulomatous dermatitis has far greater incidence than non-infectious in developing countries like India.

Materials and methods
The present study was conducted between February 2013 to August 2014 in the department of pathology in collaboration with department of dermatology. One hundred patients of all age groups and both sexes of either clinically suspected granulomatous diseases, or those showing granulomas on skin biopsy but clinically not suspected were selected. A detailed clinical history, examination findings indicating signs and symptoms of the skin lesions and provisional clinical diagnoses were collected. Associated signs and symptoms, pointing to a specific cause were also evaluated. Skin biopsy samples were received as punch biopsies for histopathological examination by the dermatologist from region of the lesion. Special stains such as Groote's, Giemsa, periodic-acid Schiff (PAS), were used for identifying fungi or any other microorganism. Alcian blue, reticulin, phosphotungstic acid hematoxylin (PTAH) etc. were employed to support a

diagnoses of non-infectious granulomatous dermatitis.

Results

Age of the patients varied from 8 to 65 years, with mean age of 33.34±14.4 years. Majority of patients were in the age group of 21-30 years (30%). Out of 100 patients, 48 (48%) were males and 52 (52%) were females. Most common site for infectious granulomatous dermatitis was upper and lower limb (54 cases, 62.79%) with majority of cases were of leprosy. The next most common site was face in tuberculosis. The most common sites for non-infectious granulomatous dermatitis was face (6 cases, 31.57%) (Table 1). Majority of patients presented with chronic skin lesions with a mean duration of 11.7 ± 12.4 months. The range of duration was from 3-4 days to about 6 years. The other significant clinical parameters are tabulated in table 1. There was no significant statistical association of any of these clinical parameters with the final diagnoses.

Table 1: Clinical characteristics of granulomatous dermatitis

S.NO	Age range (years)	Sex ratio (M:F)	Site of lesion	Clinical signs	Etiological classification
	Infectious granulomatous dermatitis				
1	8-50	30:29	Upper limb 20	Erythematous 22	Leprosy (N=59)
			Lower limb 14	Hypopigmented 27	
			Face 14	Hyperaesthetic 37	
			Neck 02	Annular 01	
			Chest 06	Ulcerated 03	
			Back 06		
			Abdomen 04		
			All over body 05		
2	17-56	12:08	Upper limb 07	Erythematous 16	Tuberculosis (N=20)
			Lower limb 05	Discharging sinuses 03	
			Face 12	Hyperpigmentation 01	
			Neck 06	Ulceration 01	
			Chest 11		
			Back 02		
			Abdomen 00		
			All over body 00		
3	34-65	1:3	Upper limb 01	Erythematous 03	Fungus (N=4)
			Lower limb 02	Ulceration 01	
			Chest 01		
4	32	1:0	Face 01	Nodular 01	Leishmania (N=1)
	Non-Infectious granulomatous dermatitis				
5	28-51	1:5	Face 03	Hyperpigmentation 01	Sarcoidosis (N=6)
			Neck 02		
			Upper limb 01		
6	40-50	1:2	Chest 01	Annular plaque 04	Erythema nodosum (N=3)
			Abdomen 01		
			Face 01		
7	38-45	0:2	Abdomen 02	Erythematous 01	Foreign body granulomas (N=2)
				Pustule formation 01	
8	50-65	2:0	Face 02		Granulomatous Cheilitis (N=2)
9	41	0:1	Back 01	Erythematous 01	Necrobiotic lipoidica (N=1)
10	36	0:1	Face 01	Erythematous 01	Granulomatous Rosacea (N=2)
11	40	0:1	Chest 01	Annular plaque 01	Granuloma Annulare (N=1)

Majority of cases were of infectious granulomatous dermatitis (84 cases, 84%) and rest were of non – infectious granulomatous dermatitis (16 cases, 16%). According to morphology, majority of cases were of epithelioid cell granulomas (81 cases, 81%), followed by histiocytic granulomas (11 cases, 11%). There were few cases of mixed inflammatory granulomas (4 cases, 4%), foreign body granulomas (2 cases, 2%) and Necrobiotic/palisading granulomas (2 cases, 2%).

The predominant cause of granulomatous dermatitis was leprosy (59 cases, 70.2%). The second major cause was cutaneous tuberculosis (20 cases, 23.8%). The other less common causes were fungal infections (4 cases, 4.76%) and cutaneous leishmaniasis (1 case, 1.2%). The cases of leprosy were further categorized according to Ridley – Jopling classification. The salient histopathological features are documented in table 2. All cases of paucibacillary leprosy (100%) and 4 cases of multibacillary leprosy (30.8%) showed epithelioid cell granulomas. Whereas, histiocytic granulomas were seen in 9 cases of multibacillary leprosy (69.2%). The p value calculated using Fisher's Exact Test was 0.001 and hence, was highly significant (< 0.05).

Table 2: Comparison of histopathological features of leprosy

HPE findings	TT (n=6)	BT (n =40)	BL (n=4)	LL (n=6)	ENL (n=3)
Type of granuloma					
Epithelioid cell granuloma	6	40	2	0	1
Histiocytic granuloma	0	0	2	6	2
Location of granuloma					
Papillary dermis	2	4	1	0	0
Reticular dermis	0	4	1	1	0
Whole dermis	4	28	1	4	2
Also involving subcutis	0	4	1	1	1
Periadnexal location	5	30	4	2	1
Perineural destruction	2	24	0	0	1
Epidermal findings					
Hyperkeratosis	0	8	0	2	1
Ulceration	0	0	0	0	0
Acanthosis	0	2	0	0	1
Atrophy	0	36	4	3	1
Basal layer degeneration	1	3	0	1	1
Presence of encroachment	5	0	0	0	0
Unremarkable	0	2	2	0	0
Inflammatory response					
Mild chronic inflammation	3	14	2	2	0
Moderate chronic inflammation	2	26	2	2	0
Dense chronic inflammation	1	0	0	0	0
Moderate mixed inflammation	0	0	0	0	0
Acute abscess	0	0	0	2	3
Langhan's and foreign body GC	5	18	3	0	0
Caseation necrosis	0	5	0	0	0
Other findings					
Subepidermal clear zone	0	2	1	2	0
Upper dermis shows edema	0	1	1	0	1
Special stains					
Lepra - negative	6	38	1	0	1
Lepra - positive	0	2	3	6	2

In this study there was no statistically significant correlation between various locations of granulomas in granulomatous dermatitis. Perineural destruction by granulomas was seen in 46% cases of paucibacillary leprosy and 15.4% cases of multibacillary leprosy. This parameter was statistically significant with a p value of 0.044. Periadnexal location was seen in 83.3% of paucibacillary leprosy and 16.7% cases of multibacillary leprosy. This parameter was not statistically significant.

In epidermal changes all parameters evaluated except atrophy showed no significant statistical association. Epidermal atrophy was found in 72% of paucibacillary leprosy and 69.2% of multibacillary leprosy, with significant statistical association (p – 0.039). Epidermal encroachment was seen in 100% cases of tuberculoid leprosy, but was not statistically significant due to less number of cases.

The cases of cutaneous tuberculosis were further categorized into clinical subtypes as described in table 3. However, majority of cases were diagnosed as cutaneous tuberculosis, not otherwise classified (6 cases, 30%) The most common location of granulomas in tuberculosis was in whole dermis (52.6%) followed by also involving subcutis (31.6%).

Table 3: Histopathological features of cutaneous tuberculosis

HPE findings	Tuberculosis Not otherwise specified (n=6)	Scrofuloderma (n =7)	Tuberculosis verrucosa cutis (n=2)	Lupus vulgaris (n=4)	Lichen scrofulosorum (n=1)
Type of granuloma					
Epithelioid cell granuloma	6	7	2	4	1
Histiocytic granuloma	0	0	0	0	0
Location of granuloma					
Papillary dermis	0	0	1	0	1
Reticular dermis	0	0	0	1	0
Whole dermis	3	4	1	2	0
Also involving subcutis	3	3	0	1	0
Periadnexal location	0	2	0	0	0
Perineural destruction	0	0	0	0	0
Epidermal findings					

Hyperkeratosis	2	1	2	1	1
Ulceration	0	6	0	0	0
Acanthosis	5	1	2	3	1
Atrophy	2	0	0	0	0
Basal layer degeneration	1	0	0	0	0
Presence of encroachment	0	0	0	0	0
Unremarkable	1	0	0	1	0
Inflammatory response					
Mild chronic inflammation	0	0	2	1	0
Moderate chronic inflammation	3	0	0	2	1
Dense chronic inflammation	1	0	0	1	0
Moderate mixed inflammation	1	5	0	0	0
Acute abscess	1	2	0	0	0
Langhan's and foreign body GC	5	4	2	1	0
Caseation necrosis	4	4	1	3	1
Special stains					
AFB - negative	5	7	2	4	1
AFB - positive	1	0	0	0	0

Furthermore, the various histopathological parameters in leprosy and cutaneous tuberculosis were compared to identify statistically significant parameters (table 4). There was no significant statistical association with type of granulomas and location of granulomas. Langhans and foreign body giant cells were present in 60% cases of cutaneous tuberculosis and 44% cases of leprosy, showing significant statistical association (p – 0.006). Presence of caseation necrosis was seen in 65% cases of cutaneous tuberculosis and 8.4% cases of leprosy, showing significant statistical association (p – 0.001). 71.2% cases of leprosy exhibited perivascular and periadnexal granulomas which were seen in only 10% cases of cutaneous tuberculosis, thus showing significant statistical association (p – 0.001). Perineural destruction by granulomas was seen in 45.7% cases of leprosy and in no case of cutaneous tuberculosis, showing significant statistical association (p – 0.001). In epidermal changes various parameters such as hyperkeratosis, ulceration, acanthosis showed slightly significant statistical association in cases of cutaneous tuberculosis.

Table 4

HPE findings	Leprosy (n=59)	Tuberculosis (n =20)	Other infections (n=5)	Sarcoidosis (n=6)
Type of granuloma				
Epithelioid cell granuloma	49 (84%)	20 (100%)	0	6(100%)
Histiocytic granuloma	10 (16%)	0	1(20%)	0
Mixed inflammatory	0	0	4	0
Location of granuloma				
Papillary dermis	7 (11.8%)	2 (10%)	0	0
Reticular dermis	6 (10.1%)	1 (5%)	0	0
Whole dermis	39 (66.1%)	10 (50%)	3(60%)	1(11.1%)
Also involving subcutis	7 (11.8%)	7 (35%)	2(40%)	5(83.3%)
Periadnexal location	42 (71.2%)	2 (10%)	0	0
Perineural destruction	27 (45.7%)	0	0	0
Epidermal findings				
Hyperkeratosis	11 (18.6%)	7 (35%)	3(60%)	0
Ulceration	0	6 (30%)	1(20%)	0
Acanthosis	3 (5.8%)	12 (60%)	3(60%)	0
Atrophy	48 (81.3%)	2 (10%)	0	2(33.3%)
Basal layer degeneration	6 (10.1%)	1 (5%)	1(20%)	0
Presence of encroachment	5 (8.4%)	0	0	0
Unremarkable	4 (6.8%)	2 (10%)	0	4(66.6%)
Inflammatory response				
Mild chronic inflammation	23 (38.9%)	3 (15%)	0	2(33.3%)
Moderate chronic inflammation	34 (57.6%)	6 (30%)	1(20%)	0
Dense chronic inflammation	1 (1.6%)	2 (10%)	0	0
Moderate mixed inflammation	0	6 (30%)	4(80%)	0
Acute abscess	5 (8.4%)	3 (15%)	0	0
Langhan's and foreign body GC	26 (44%)	12 (60%)	3 (show ingested fungal spores and hyphae)	3(50%)
Necrosis	Caseation 5 (8.4%)	Caseation 13 (65%)	0	Fibrinoid 2(33.3%)
Special stains positive	Lepra 13 (22%)	AFB 1 (5%)	PAS, Mucicarmine, Grocott 3 (60%)	Reticulin, PTAH 4 (66.6%)

Other causes of granulomatous dermatitis in this study were fungal infections. There were cases of Cryptococcus (2 cases, 2.3%) and Mucormycosis (1 case, 1.2%) and chromomycosis (1 case, 1.2%). Fungal infections showed presence of mixed inflammatory granulomas and histiocytic granulomas was seen in a single case of cutaneous leishmaniasis.

Majority of cases of non- infectious granulomatous dermatitis were a result of sarcoidosis (6 cases, 37.5%) followed by erythema nodosum (3 cases, 18.7%). The type of granulomas differed according to the various subtypes of non infectious granulomatous dermatitis. Majority of granulomas (78.57%) were involving subcutis location. The epidermis was unremarkable in 48.5% of cases. The most common inflammatory response was naked granulomas seen in 20.9% of cases. Giant cells in cases of sarcoidosis showed presence of asteroid bodies. Reticul in rich granulomas were seen in 66.6% cases of sarcoidosis. Ingested foreign material was seen in foreign body granulomas. A history of previous surgical procedure was present in one case of foreign body granuloma whereas the other was clinically nonconcordant.

Discussion

Granulomatous dermatitis forms approximately 7% of all skin biopsies.[4] Reaching a diagnoses or formulating a differential diagnoses in derma to pathology involves combining information from clinical data and pathological findings. This process must be completed as a chronological progression from patient's complaints, through evaluation of clinical findings and eventually terminating in the microscopic examination of the biopsy specimen. The derma to pathologists should be aware of the provisional clinical impression and they must supplement the final diagnoses with clinical information.

Granulomas usually form as a result of the persistence of a non-degradable product or as the result of hypersensitivity responses. The provocative agents of granulomatous inflammation appear to be non-degradable by both neutrophils and nonactivated macrophages. The actions of polymorph nuclear leukocytes nonactivated macrophages, and chemical mediators associated with tissue injury are insufficiently complete to digest and eradicate the offending agent. Required for such degradation are the actions of transformed macrophages with augmented enzymatic capabilities and sometimes, perhaps, of epithelioid cells. Hence it is the end result of a complex interplay between invading organism or antigen, chemical, drug or other irritant, prolonged antigenaemia, macrophage activity, a Th1 cell response, B cell over activity, circulating immune complexes and a vast array of biological mediators. Areas of inflammation or immunologic reactivity attract monocyte-macrophages, which fuse to form multinucleated giant cells [1].

In the present study 84% of cases were diagnosed as infectious granulomatous dermatitis and 16% cases were of non – infectious granulomatous dermatitis, according to the etiological classification. This was similar to a study where 87.8% of cases were of infectious granulomatous dermatitis and 12.11% cases were of non – infectious granulomatous dermatitis [4]. This is because infections such as leprosy and tuberculosis are leading etiologies of granulomatous dermatitis in developing nations such as India.

According to the morphological classification of granulomatous dermatitis 82% of cases were labelled as epithelioid cell granulomas followed by histiocytic granulomas in 11% of cases. Occasional cases of mixed inflammatory granulomas, foreign body granulomas and Necrobiotic/palisading granulomas were also seen in this present study. These figures parallel another study where most common type of granulomas were epithelioid cell granulomas in 64% of cases [5]. The versatility of morphology in granulomatous dermatitis is a result of different pathology of evolution of different granulomas.

Epithelioid granuloma describes a reaction pattern characterized by the presence of epithelioid cells within clusters and groups variably associated with histiocytes, lymphocytes, and multinucleated giant cells. Prototypical examples are forms of cutaneous and subcutaneous tuberculosis (tuberculoid granulomas), tuberculoid leprosy and sarcoidosis (sarcoidal granulomas). Tertiary syphilis, allergic reactions to metallic salts, e.g. zirconium granuloma, and lichen nitidus are also associated with a tissue morphology of epithelioid granulomas [6].

Mycobacterial infections are a large group that include *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Mycobacterium avium complex*, *Mycobacterium ulcerans*, *Mycobacterium marinum* and several opportunistic mycobacteria [7]. *Mycobacterium leprae* is the infectious organism in leprosy. It has varied clinical presentation depending on the immunopathology. Tuberculoid leprosy (TT) and Borderline-Tuberculoid Leprosy (BT) are relatively stable form and the most common type in India and Africa. The number of lesions ranges from one to five. The lesions are scanty, dry, erythematous, hypopigmented papules or plaques with well defined edges and are distributed asymmetrically on trunks or limbs. Localized nerves along with other superficial nerves like ulnar and popliteal nerves may be enlarged leading to nerve palsy. Nerve damage occurs early. Hypoaesthesia and impairment of hair growth within the lesion is present. Clinically BT lesions resemble TT lesions, but they are more numerous, less sharply defined at margins, and may exhibit smaller adjacent satellite lesions [8].

TT shows a tuberculoid reaction throughout the dermis, with non-caseating granulomas composed of epithelioid cells and lymphocytes. The predominant lymphocyte present is the T-helper cell, which is found throughout the granuloma, whereas cytotoxic T cells predominate in the lymphocyte mantle that surrounds the granulomas. Langhans giant cells are typically absent. Nerve erosion and obliteration are typical. In BT granulomas along the superficial vascular plexus are frequent, but they do not infiltrate up into the epidermis. Rare acid-fast bacilli may be seen in nerves or in superficial papillary dermis. BI is 0 to 1+ [8, 9].

On histology, tuberculoid (granulomatous) leprosy needs to be distinguished from the other granulomatous dermatitides. Histopathological diagnosis of tuberculoid leprosy is difficult because leprosy granulomas cannot be otherwise distinguished from other granulomas that are seen in such conditions as sarcoidosis and tuberculosis. The general vertical perineurovascular distribution of granulomatous inflammation and involvement of sweat glands in tuberculoid leprosy are helpful. Unlike other mycobacterial skin infections such as

tuberculosis, and unlike granulomatous leishmaniasis, the epidermis in tuberculoid leprosy is usually flat and non-hyperplastic.

In Lepromatous Leprosy the cutaneous lesions are multiple small macules, infiltrated plaques, and nodules with poorly defined borders. Histologically in LL, beneath a clear subepidermal grenz zone lie small collections of macrophages surrounding cutaneous appendages and sheets of heavily parasitized macrophages with a sparse sprinkling of lymphocytes, the majority of which are of suppressor type. In older lesions, the macrophages have a foamy appearance (lepra cells, virchow cells). Numerous acid-fast bacilli are present in macrophages, sweat glands, nerves, Schwann cells and vascular endothelium. The organisms in the macrophages may be arranged in parallel arrays, forming clusters, or in large masses known as globi. BI is 5+ to 6+ [7, 9].

In the present study 77.9% of cases of leprosy were of paucibacillary type. Borderline tuberculoid was seen in 67.8% of cases. The second most common category was tuberculoid leprosy and lepromatous leprosy with both seen in 10.2% of cases. 6.7% of cases were of borderline lepromatous leprosy. Erythema nodosum leprosum was seen in 5.1% of cases. This was in concordance with a study where borderline tuberculoid and tuberculoid leprosy was seen in 55.2 % and 7.2% of cases respectively [4]. The study reported borderline lepromatous and lepromatous leprosy was seen in 15 % and 17.9% of cases respectively. Erythema nodosum leprosum in 2.1% of cases. In another study borderline tuberculoid was seen in 47.6% of cases, followed by 12.7% cases of indeterminate leprosy and 1.6% of cases of histoid leprosy [10].

In the present study 100% cases of paucibacillary leprosy and 30.8% cases of multibacillary leprosy showed epithelioid cell granulomas with sensitivity of 79.4% whereas, histiocytic granulomas were seen in 69.2% cases of multibacillary leprosy. Kappa statistics in this study revealed a very good agreement between morphological type of granuloma and type of leprosy. This result was comparable with other studies [4, 10, 11].

In this study perineural destruction by granulomas was seen in 46% cases of paucibacillary leprosy and 15.4% cases of multibacillary leprosy yielding a diagnostic sensitivity of 85.7%. Whereas periadnexal location was seen in 83.3% of paucibacillary leprosy and 16.7% cases of multibacillary leprosy yielding a diagnostic sensitivity of 39.7%. The result was in concordance with other studies [4, 10].

Hence, it can be highlighted that presence of perineural destruction by granuloma, periadnexal location of granulomas and epidermal atrophy are the various histopathological features for accurately diagnosing leprosy on morphological parameters.

The etiologic agent of tuberculosis, *M. tuberculosis*, is one of the most common microbial causes of skin granulomas in India. It is characterized by the presence of central caseous necrosis and is referred to as a tubercle which is encircled by epithelioid cells, lymphocytes, histiocytes, fibroblasts, and Langhans' giant cells [9]. Infection of skin and subcutis by *M. Tuberculosis* occurs by three routes:

a. By direct inoculation into the skin (causing a primary chancre, tuberculosis verrucous cutis or tuberculosis cutis orifcialis)
b. By hematogenous spread from an internal lesion (causing lupus vulgaris, miliary tuberculosis, and tuberculous gumma lesions)
c. From an underlying tuberculous lymph node by direct extension (causing scrofuloderma)

Involvement of the skin in cases of tuberculosis may have a varied clinical and histological presentation. In clinical practice, many cases do not readily fit into these clinical and histologic categories. Cutaneous tuberculosis should either be conceived as reinfection (lupus vulgaris and tuberculosis verrucosa cutis) or reactivation (scrofuloderma and tuberculosis cutis orificialis) tuberculosis. Accordingly, the diagnosis has to be made on the basis of relevant positive history [12].

In the present study cutaneous tuberculosis was further differentiated into 35% cases of scrofuloderma, 20% cases of lupus vulgaris and 10% cases of tuberculosis verrucosa cutis. 5% of cases were identified as tuberculid or lichen scrofulosorum. Rest cases were diagnosed as cutaneous tuberculosis, not otherwise classified as was suggested in the provisional clinical diagnoses. This was similar to the result obtained in a study where scrofuloderma was seen in 47.1% of cases, lupus vulgaris in 42.9% of cases and tuberculosis verrucosa cutis in 10% of cases.

Sarcoidosis, a multisystem disease, has cutaneous lesions in 20–35% cases and is the prototype of sarcoidal granulomas. The most common cutaneous lesion of sarcoidosis are brown red or purple papules and plaques. Quite often, central clearing, annular or circinate lesions may result. Morphologically, sarcoidosis is characterized by compact non-caseating, lymphocyte poor, naked epithelioid cell granulomas with a foreign body and Langhans' type of giant cells. Clinical investigations like X-ray chest and serum calcium levels are required for confirmation [13, 14].

In the present study 50% of cases of sarcoidosis showed presence of giant cells containing star-shaped eosinophilic structures (asteroid body) and laminated calcified bodies (conchoid/ Schaumann bodies). This result was comparable with earlier study in which asteroid and/or Schaumann bodies were found in 54% of the biopsies and were a less sensitive marker of sarcoidosis [2]. Special stains like PTAH and reticulin were used to elucidate the final histomorphological diagnoses.

The term "histiocytic granuloma" defines a tissue reaction pattern characterized by an infiltrate composed predominantly of histiocytes. The various causes of histiocytic granulomas are Lepromatous / Borderline Lepromatous leprosy, Histoplasmosis, Leishmaniasis, Rhinoscleroma infection [3, 5]. Other rare differential diagnosis could be Farber's disease, xanthomas and some lipid storage disorders. Special histochemical staining techniques reveal the presence of organisms within histiocytes like giemsa stain for LD bodies (leishmania donovani) and lepra stain for *Mycobacterium leprae*.

Foreign-body granuloma encompasses a large number of tissue reactions in which the giant cell is the most conspicuous member of the granulomatous infiltrate. It could be a result of various endogenous products such as keratin, hair, fat, urate crystals (gout) or exogenous products such as metal salts, tattoos, silica, talc, suture, plant and animal products.

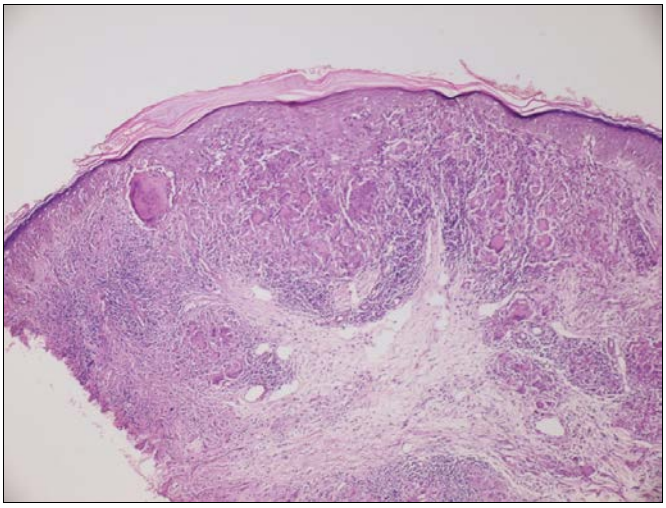

Fig 1: Tuberculoid leprosy showing granulomas destroying epidermis (10x)

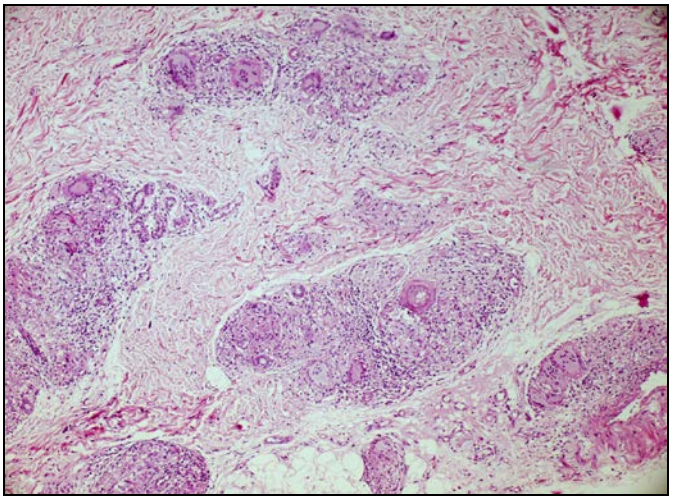

Fig 2: Borderline tuberculoid leprosy numerous granulomas in whole dermis along with foreign body and Langhans giant cells (10x)

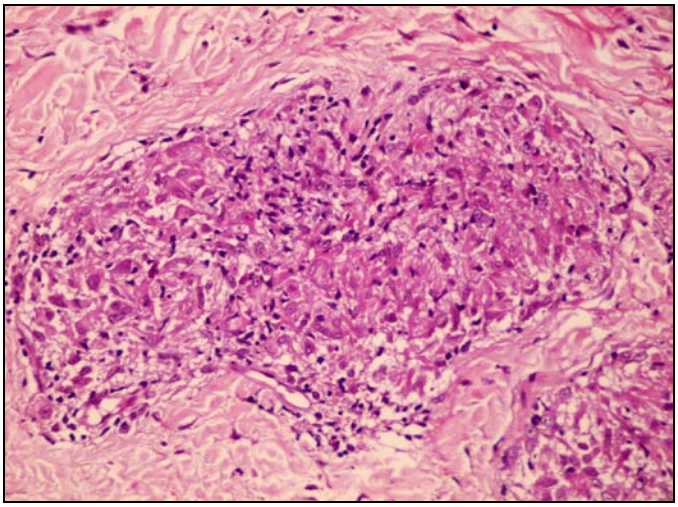

Fig 3: Histiocytic granulomas in borderline lepromatous leprosy (40x)

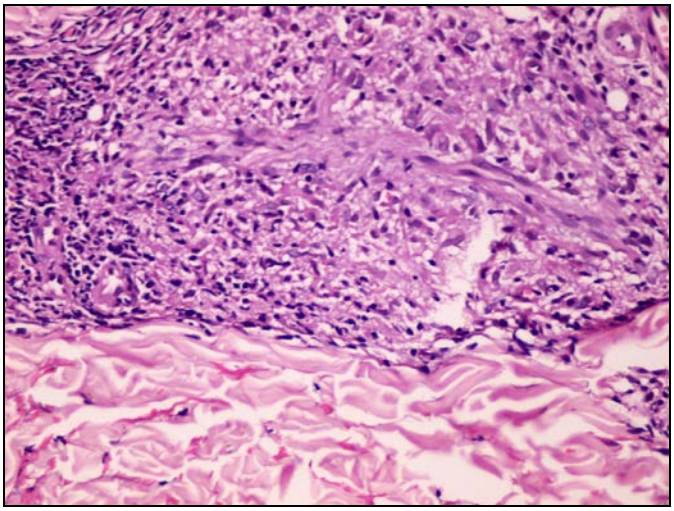

Fig 4: Perineural location and destruction by granulomas (40x)

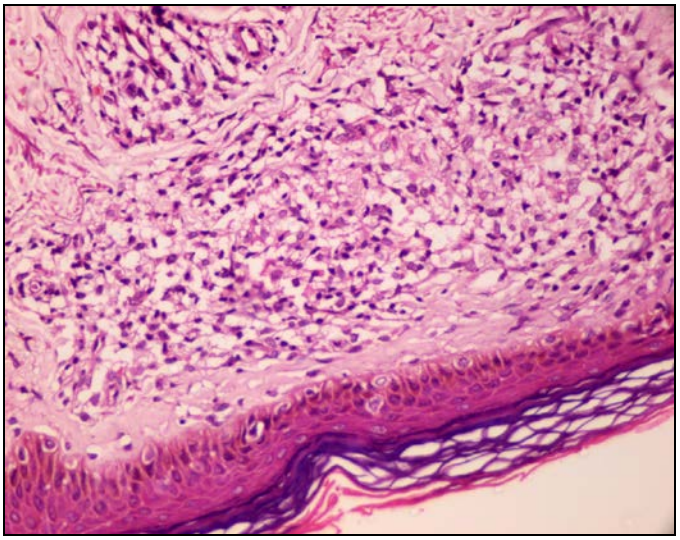

Fig 5: Atrophy of epidermis and loss of rete pegs (10x)

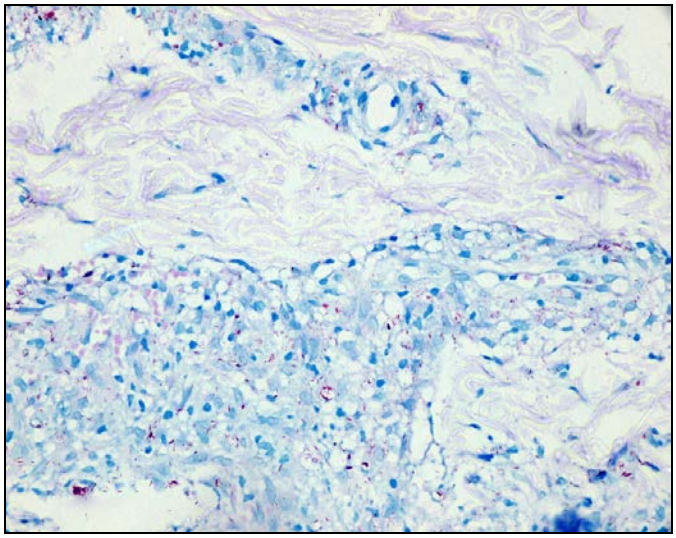

Fig 6: Lepra stain 5+ Bacterial Index (100 x)

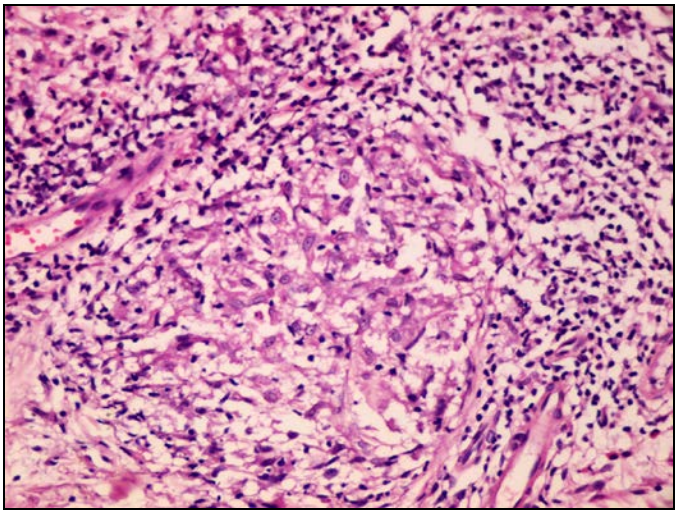

Fig 7: Epithelioid cell granulomas in tuberculosis (40x)

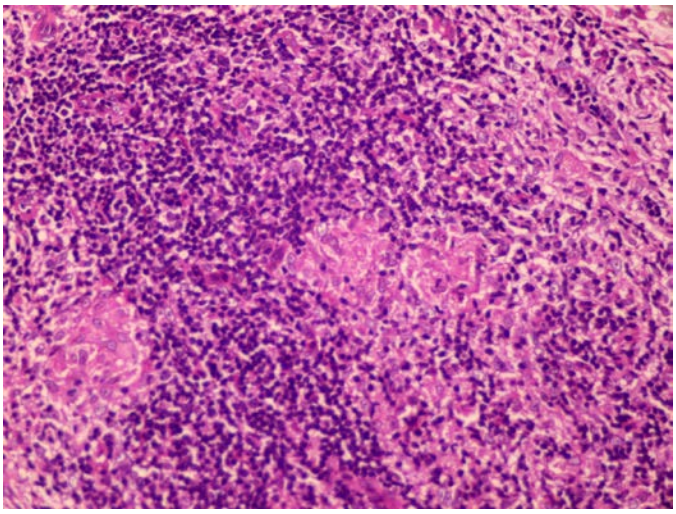

Fig 8: Dense chronic inflammation surrounding epithelioid cell granulomas

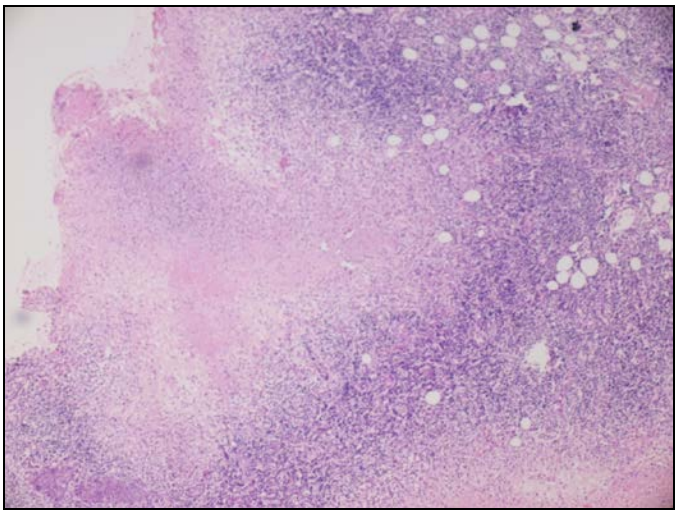

Fig 9: Large areas of caseation necrosis and dense chronic inflammation (10x)

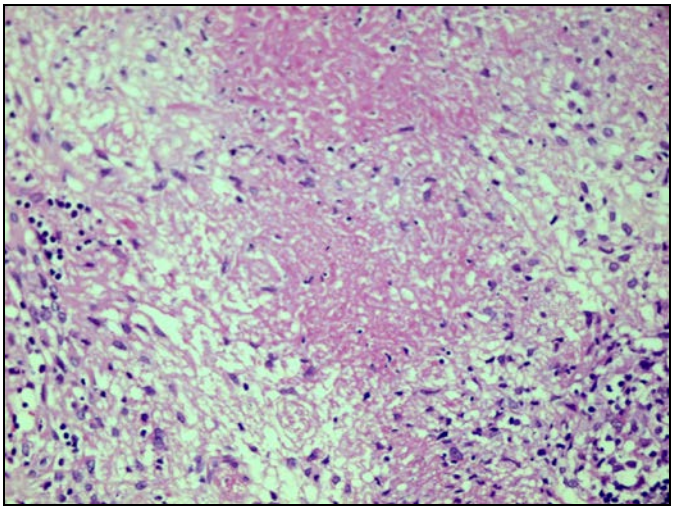

Fig 10: Minute areas of caseation necrosis and moderate chronic inflammation (40x)

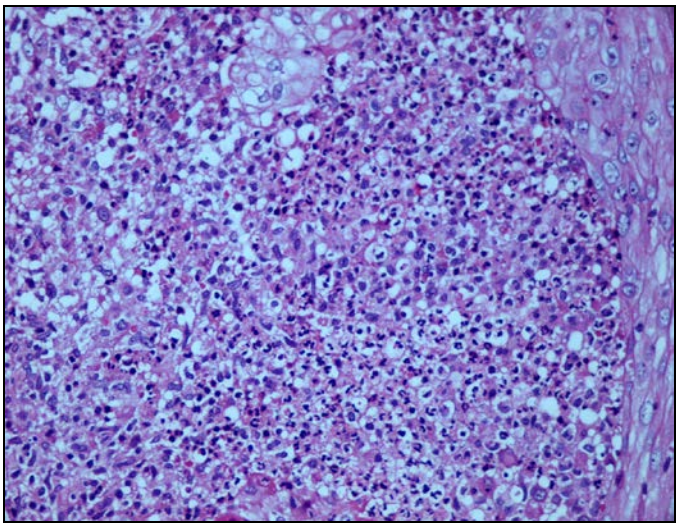

Fig 11: Mixed inflammatory granulomas in fungal infections (40x)

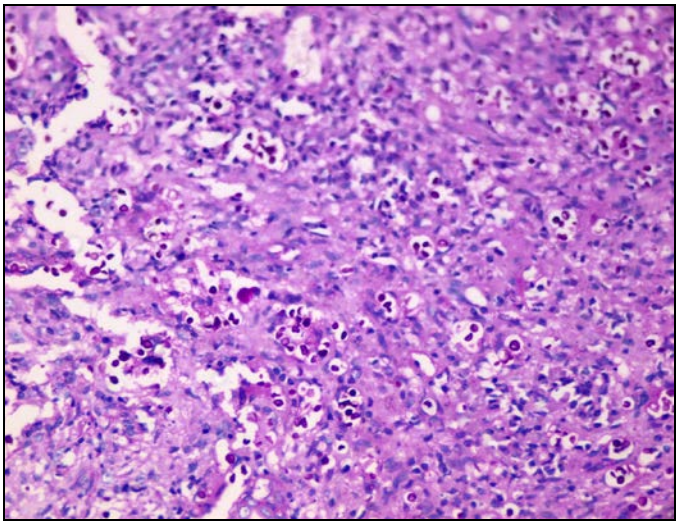

Fig 12: PAS stain showing fungal spores of Cryptococcus (40x)

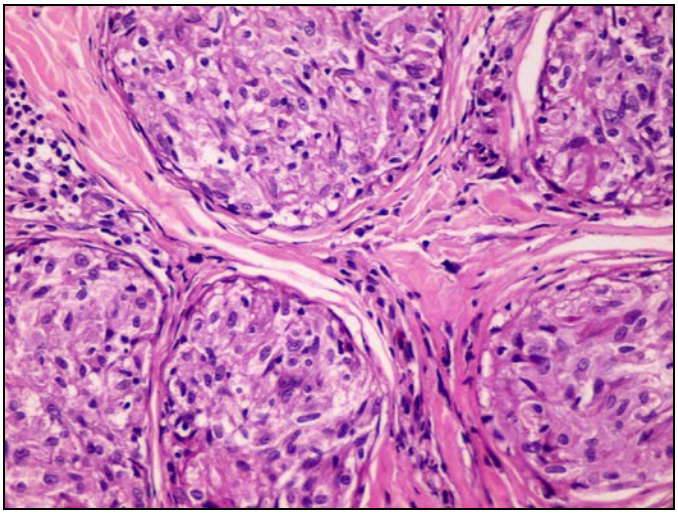

Fig 13: Naked noncaseating epithelioid cell granulomas in sarcoidosis (40x)

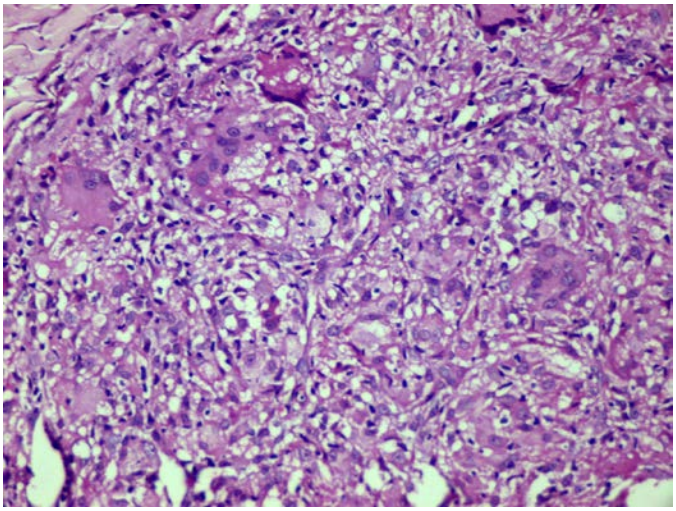

Fig 14: Giant cells show presence of asteroid bodies (40x)

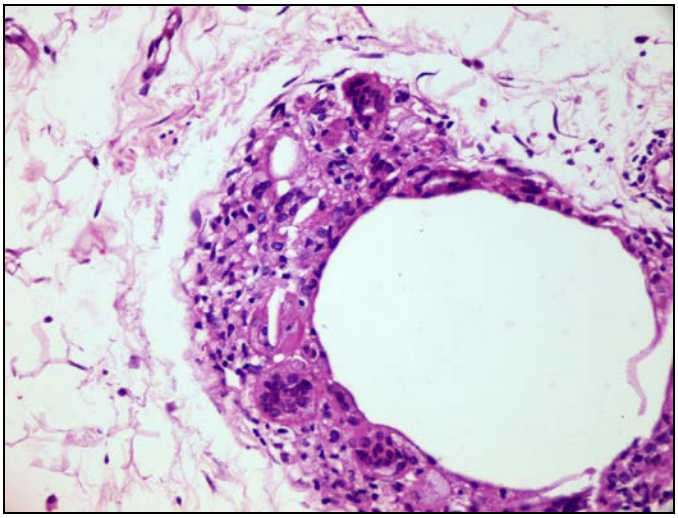

Fig 15: Giant cell showing ingested foreign body (40x)

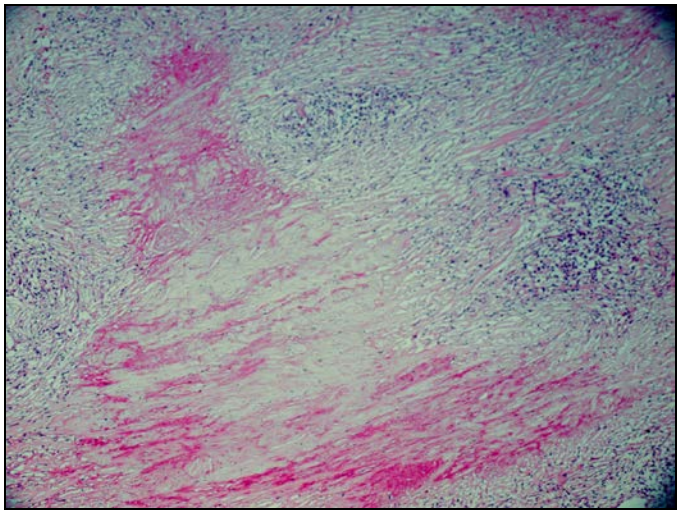

Fig 16: Granuloma annulare (40x)

Necrobiosis refers to focal alteration or degeneration of collagen and is surrounded by palisading histiocytes forming necrobiotic granulomas. These are of further two types. There are blue collegenolytic granulomas' which have central basophilic area either due to deposition of mucin or nuclear dust. These are Granuloma annulare (GA), Rheumatoid vasculitis and Wegener's granulomatosis. 'Red collegenolytic granulomas' which have central eosinophilic area due to hyalinised collagen, fibrin, or degranulated eosinophils. These are Necrobiosis lipoidica, Necrobiotic xanthogranuloma, Rheumatoid nodule, Churg – Strauss syndrome and Eosinophilic cellulitis [13, 15].

The term "mixed inflammatory granuloma" defines a histologic pattern that may have elements of an acute, chronic, and granulomatous process. The epidermis may show pseudoepitheliomatous hyperplasia as well as areas of thinning or atrophy. The dermis and subcutaneous tissue generally show an infiltrate composed of neutrophils, eosinophils, lymphocytes, histiocytes, and multinucleated giant cells against a background of fibrocapillary proliferation and occasional necrosis. The vast majority are caused by infectious agents: fungal organisms, mycobacteria, atypical mycobacteria, bacteria, or chlamydial organisms. Histochemical stains for fungal organisms, mycobacteria, and bacterial organisms are frequently rewarding [16].

There is often a granulomatous component in malignant disease. Sarcoidal granulomas may be found in various tumours, cutaneous presentation and in their draining lymph nodes, particularly in carcinoma of solid tumors and Hodgkin's lymphoma. They may also be found in tumours that have been treated by radiotherapy or chemotherapy [15].

So, clinicopathological concordance was achieved in 90% of cases which was comparable to other studies in which a concordance of 76% and 88.7% was achieved [3, 10].

Conclusion

The results of the present study indicate that granulomatous dermatitis includes a vast spectrum of diseases, both infectious

and non infectious. However, infections are clearly the most common causes of granulomatous dermatitis. The diagnosis of granulomatous dermatitis should, therefore, be based primarily on history, evolution of the disease and cardinal clinical features which should be supported by histo pathologic characteristics. The histopathological diagnoses are assisted by categorizing the granulomatous inflammatory reaction into distinct morphological types. Also additional parameters such as epidermal changes, presence of necrosis, periadnexal location of granulomas and presence of perineural destruction help in clinching the final histopathological diagnoses. Special stains also play a supporting role.

To conclude, there is significant overlap in histo pathologic picture of different granulomatous reactions; thus morphology alone is seldom specific and cannot be used as a diagnostic tool for identification of specific diseases. Thus, adequate clinical data and work up in combination of pathological resources can help in elucidation of specific etiology and good clinico pathologic correlation.

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