Journal of Research in Medical and Dental Science
2021, Volume 9, Issue 6, Page No: 62-71

Available Online at: www.jrmds.in
eISSN No.2347-2367: pISSN No.2347-2545

Clinicopathological Study on Granulomatous Lesions of Skin

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ABSTRACT

Infectious disease forms an important cause of granulomatous skin lesions with Hansen's disease as the leading etiology. Granulomatous lesions of skin are a common and intriguing problem, and the proper diagnosis is mandatory so that appropriate treatment can be meted out. Histopathology remains the time-tested tool for establishing a correct diagnosis like in many other diseases pertaining to various organ systems of the body. Clinical lesions often reveal surprising underlying pathology. Hence carrying out skin biopsies and microscopic study with routine haematoxylin and eosin (H&E) as well as special stain are must in these disorders so that the type and etiological agent of the granuloma are properly identified. Hence the present study was designed to study the various granulomatous lesions of skin and to compare the clinical features with the pathological diagnosis and analyse the predominant clinical presentation of each lesion. It can be concluded that histopathology plays an important role in arriving at a diagnosis and management of the disease. Special stains are mandatory in these diseases so that the type and etiological agent of the granuloma are accurately diagnosed.

Key words: Hansen's disease, Microscopy, Granulomatous lesions, Skin, H&E, Diagnosis

HOW TO CITE THIS ARTICLE: Subhashini P, Parijatham BO,Clinicopathological Study on Granulomatous Lesions of Skin, J Res Med Dent Sci, 2021, 9(6): 62-71

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Received: 8/05/2021
Accepted: 09/06/2021

INTRODUCTION

Skin forms the entire external covering of the body, and it is the main interface between the body and its environment. The skin is uniquely adapted to protect the body, within limits, from all sorts of external stimuli. It helps 1n regulation of body temperature and synthesizes keratin, lipids, pigments, pro vitamin D and several enzymes. It has sensory functions of touch, pain and temperature and excretes salt and metabolites through sweat.

Granuloma

A granuloma is a focus of chronic inflammation consisting of collection of a microscopic aggregation of macrophages that are transformed into epithelium like cells, surrounded by a color of mononuclear leukocytes, principally lymphocytes and occasionally plasma cells [1].

Macrophages are the cells that define a granuloma. They often, but not invariably, fuse to form multinucleated giant cells (Langhan' s giant cell) [2]. The macrophages in granulomas are often referred to as "epithelioid". This term refers to the vague resemblance of these macrophages to epithelial cells. Epithelioid macrophages differ from ordinary macrophages in that they have elongated nuclei that often resemble the sole of a slipper or shoe. They also have larger nuclei than ordinary macrophages and their cytoplasm is typically pinker when stained with eosin. These changes are thought to be a consequence of "activation" of the macrophage by the offending antigen.

The macrophages in these formations are typically so tightly clustered that the borders of individual cells are difficult to appreciate. Loosely dispersed macrophages are not considered to be granulomas. All granulomas, regardless of cause, may contain additional cells and matrix. These include lymphocytes, neutrophils, eosinophils, multinucleated giant cells, fibroblasts, and collagen (fibrosis).

The additional cells are sometimes a clue to the cause of the granuloma. For example, granulomas with numerous eosinophils may be a clue to coccidioidomycosis or allergic bronchopulmonary fungal disease, and granulomas with numerous neutrophils suggest blastomycosis, Wegener's granulomatosis, aspiration pneumonia or cat-scratch disease [3].

In terms of the underlying cause, the difference between granulomas and other types of inflammation is that granulomas form in response to antigens that are resistant to "first-responder" inflammatory cells such as neutrophils and eosinophils.

The antigen causing the formation of a granuloma is most often an infectious pathogen or a substance foreign to the body [4] (Figure 1).

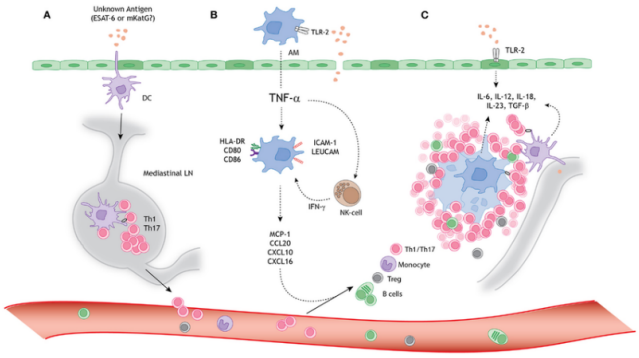

Figure 1: Schematic representation of granuloma formation.

The granuloma is the result of a complex interplay between invading organism or antigen, chemical, drug, or other irritant, prolonged antigenaemia, macrophage activity, a Thl cell response, B cell overactivity, circulating immune complexes, and a vast array of biological mediators. Areas of inflammation or immunological reactivity attract monocyte/macrophages which may fuse to form multinucleated giant cells and a transformation of macrophages to epithelioid cells. The granuloma is an active site of numerous enzymes and cytokines, fibronectin, and numerous progression factors. There is a close relationship between activated macrophages bearing increased expression of major histocompatibility complex (MHC) class II molecules and CD4+ Th 1 lymphocytes. These T helper cells recognize protein peptides presented to them by antigen presenting cells bearing MHC class II molecules. The T cell induces interleukin-I on the macrophage and thereafter a cascade of chemotactic factors promotes granulomagenesis. Interferon gamma (IFN-y) increases the expression of MHC class II molecules on macrophages and activated macrophage receptors carry an Fe fraction of lgG to potentiate their ability to phagocytose. The result is the epithelioid granuloma which progresses under the impact of transforming growth factor and platelet derived growth factor towards fibrosis [5-7]

T cell activation also requues the B7:CD28/CTL: Costimulatory pathway. With CD28 mediated costimulator, there is active T cell proliferation; without it, there is ignorance, anergy, and apoptosis. Overstimulation of Th1 relative to Th2 cells leads to pronounced cell mediated hyperactivity, tissue destruction, and granuloma formation with necrosis. This is slowed down by B7-1 or B7-2 antagonists. The opposite occurs when Th2 seems to override Th 1 influences. There is anergy and apoptosis which may be reversed by CD28 agonists [8].

An important feature of granulomas is whether they contain necrosis. Necrosis refers to dead cells that, under the microscope, appear as a mass of formless debris without a nucleus. A related term, "caseation" (literally: turning to cheese) refers to a form of necrosis that, to the unaided eye (i.e., without a microscope), appears cheese like ("caseous"), and is typically (but not uniquely) a feature of the granulomas of tuberculosis. The identification of necrosis in granulomas is important because granulomas with necrosis tend to have infectious causes [9].

The granulomatous reaction pattern is defined as a distinctive inflammatory pattern characterized by the presence of granulomas. According to Dorland, the term "granulomatous" was expressed initially by Virchow to describe a tumor-like mass or nodule of granulation tissue [10]. The granulomata can show peculiar arrangements, accessory features such as necrosis, suppuration or necrobiosis and the presence of organisms or foreign material [10].

Granulomatous lesions of skin are a common and intriguing problem, and the proper diagnosis is mandatory so that appropriate treatment can be meted out. Histopathology remains the time-tested tool for establishing a correct diagnosis like in many other diseases pertaining to various organ systems of the body. Clinical lesions often reveal surprising underlying pathology. Hence carrying out skin biopsies and microscopic study with routine haematoxylin and eosin (H&E) as well as special stain are must in these disorders so that the type and etiological agent of the granuloma are properly identified [11].

Hence the present study was designed to study the various granulomatous lesions of skin and to compare the clinical features with the pathological diagnosis and analyse the predominant clinical presentation of each lesion.

MATERIALS AND METHODS

This is an analysis of 50 skin biopsies of granuloma to us lesions received from the Department of Dermatology to the Department of Pathology, Balaji Medical College, Chennai, over a period of 2 years from AUGUST 2011 to JULY 2013. Clinical information was noted. Biopsy was done for all the cases using punch biopsy technique which was formalin preserved later paraffin embedded and 5–6-micron sections were made, then Haematoxylin and Eosin staining were performed, and the provisional diagnosis was made. Special staining for Mycobacterium tuberculosis was done using Ziehl neelsen technique, for Mycobacterium leprae using FITE FARACO staining and for Fungus using Periodic acid schiffsta in were done based on the provisional diagnosis. All the slides were examined using light microscope under Scanner view (4x), low power view (10x) and high-power view (40x). Various histological findings were recorded and final diagnosis was made.

Histopathological techniques

Haematoxylin and eosin stain [12]

- Sections deparaffinised in 2 changes of xylene and then hydrated by passing through 2 changes of absolute alcohol and 2 changes of 95% alcohol before bringing sections to running water.
- Rinsed in running tap water for 1 minute and then briefly with distilled water.

- Immersed in Harris hematoxylin for 5 minutes and rins ed in tap water.
- Dedifferentiated by dipping 3-4 times 1n 1% acid alcohol and then washed briefly in tap water.
- Blueing done with lithium carbonate water until section turned blue.
- Rinsed in distilled water for 10-15 minutes.
- Stained with 1% acqueous eosin for 15 second to 2 minutes.
- Dehydrate by passing through 2 baths of 95% alcohol and 2 baths of absolute alcohol for 1 minute each and then cleared in 2 changes of xylene.
- Mounted in Dibutyl Phathalate Xylene (DPX).

Ziehl-N eelsen (ZN) stain for Mycobacterium bacilli [12]

- Deparafffinize the sections and rehydrate through graded alcohols to distilled water.
- Stain with carbol fuchin solution for 30 minutes.
- Wash well in tap water.
- Differentiate in acid alcohol until solutions are pale pink which takes around 4-5dips.
- Wash in tap water for 8 minutes and dip 1n distilled water.
- Counterstain in working methylene blue solution until sections are pale blue.
- Rinse in tap water then dip in distilled water.
- Dehydrate, clear and mount.

Fite faraco method for mycobacterium leprae [12]

- Deparaffinize the sections in two changes of xylene peanut oil for 6 minutes each
- Drain slides vertically on paper towel and wash running tap water for 3 minutes.
- Stain in carbolfuchsin at room temperature for 25 minutes.
- Wash in running tap water for 3 minutes.
- Drain excess water from slides vertically on paper towel.
- Decolourise with 5% sulphuric acid in 25% alcohol, two changes of 90 seconds each.
- Wash in running tap water for 5 minutes.
- Counterstain in working methylene blue with one quick dip.
- Wash in running tap water for 5 minutes.
- Blot sections and dry in 50-55 degrees Celsius for 5 minutes
- Once dry, one quick dip in xylene
- Mount with Dibutyl Phathalate Xylene (DPX).

RESULTS

50 cases were granulomatous skin lesion, of the 790 skin biopsies received from the Department of Dermatology, Sree Balaji Medical College and Hospital which were analyzed in the Department of Pathology. So, the incidence of granulomatous skin lesion appeared to be 6.3%.

Out of 50 cases of granulomatous lesion of skin, 29 cases were Hansen's disease in which tuberculoid leprosy was the predominant lesion. Among 29 cases of Hansens disease, 17 cases (34%) - tuberculoid leprosy, 2 cases (4%) - histoid leprosy, 6 cases (12%) - borderline tuberculoid leprosy and 4 cases of (8%) - borderline lepromatous leprosy were reported. FITE FARACO for Mycobacterium leprae was carried out in all the 29 cases, in which 2 cases of histoid leprosy and 4 cases of boderline lepromatous leprosy showed 100% positivity. Among 6 cases of borderline tuberculoid leprosy and 17 cases of tuberculoid leprosy FITE FARACO was positive only in 2 cases (33.3%) and 3 cases (17.6%) respectively.

Next predominant lesion was found to be cutaneous tuberculosis which was 14 cases (28%), of which 8 cases (16%) were 1upus vulgaris and 6 cases (12%) was tuberculosis verruca cutis. For all the 14 cases zeihl nelson staining for Mycobacterium tuberculosis was done. Out of which 2 cases (33.3%) of tuberculosis verruca cutis and 6 cases (75%) of lupus vulgaris showed positivity for zeihl neelson stain.

2 cases of sarcoidosis with non-caseating granuloma showed negative results for mycobacterium tuberculosis mycobacterium leprae and fungus. Three cases of granuloma annulare, one case of rheumatoid nodule and one case of necrobiosis lipoidica were reported.

Among 50 cases, 33(66%) were male and 17(34%) were female, with M:F=2: 1. Age ranged from 6-75yrs with the mean age of 37.7yrs. Maximum number of patients were between 21-30yrs which was in 16 cases (32%) followed by 41-50yrs in 10 cases(20%) Majority of cases were categorized as infectious granulomas that was in 43 cases (86%) and non-infectious granuloma in 7 cases(l4%). Predominantly the patient presented with the lesion in the upper extremity which was in 16 patients (32%). Most of the lesion had morphological appearance as patch and plaque in 21 cases (42%) and 16 cases (32%) respectively.

Most of the Hansen's patients were between 2 l -30yrs which was 10 cases (34.4%) and there was male preponderance with 22 patients (75.9%). Majority of the Hansen's patients presented with the lesion in the upper extremity that was in 14 cases (48.2%) and predominant morphological appearance of the lesion was hypopigmentation in 25 cases (86.2%), patches in 17 patients (58.6%), with loss of sensation in 20 cases (59%).

Most of the patients who were diagnosed as cutaneous tuberculosis were between 21-30 years which was 5 cases (35.7%). The lesion presented predominantly in the lower extremity in 8 patients (57.1%). Morphologically the lesion was plaque in 6 patients (42.9%) and verrucous in 3 patients (21.4%) and hyper pigmentation in 8 cases (64.2%).

Two (4%) cases of sarcoidosis were recorded in this study. One was a 22yr old female who presented with an erythematous lesion on the face with itching and hyper pigmentation. Other patient was a 45yr old female who

presented with hypopigmented plaques with surrounding hyperpigmented area in the upper extremity. (Fig-23). Initial diagnosis was made on biopsy and further sustained using negativity for Ziehl-Neelsen, FITE FARACO and periodic acid Schiff stain which are specific for Mycobacterium tuberculosis, Mycobacterium leprae and fungus respectively.

Histopathological features of the lesions in this study

Tuberculoid leprosy

17 patients had tuberculoid leprosy. It was the largest group comprising 34% of the total number of biopsies. The diagnostic skin lesion was the presence of epitheloid granulomas with numerous lymphocytes and a few Langhans-type giant cells in all the 17 cases. Granulomas were observed both in reticular and papillary dermis. They were found predominantly around dermal appendages and around nerve bundles. Perivascular infilteration by lymphocytes was present in all cases. Foci of caseation necrosis was present. FITE FARACO staining for Mycobacterium leprae was done in all 17 cases and positivity was present in 3 cases (l 7.6 %). Bacterial index was 1+ in all the 3 cases.

Borderline tuberculoid

The epithelioid cell granuloma with moderate number of lymphocytes and Langerhans giant were present. There was clear subepidermal zone in all 6 cases. Perineural lymphocytic and mononuclear infiltration was present. Perivascular lymphocytic infiltration was seen in all 6 cases. The granuloma was seen around sweat glands and hair follicles. FITE FARACO staining for Mycobacterium leprae was done in all 6 cases and positivity was present in 2cases (33.3%)The bacilli index was 1+ in both the cases.

Boderline leproma tous leprosy

There were 4 cases of borderline lepromatous leprosy. The granulomas in this group consisted of foamy macrophages with numerous lymphocytes densely packed over the whole granuloma in with occasional clump of epitheloid cells. The granuloma was massive in papillary and reticular dermis. The subepidermal zone was clear in all the 4 cases. Perineural invasion was present in all 4 cases. FITE FARACO staining for Mycobacterium leprae was done in all 4 cases and positivity was present in all the 4 cases (100%). The bacterial index was 4+ in two case and 5+ in 2 cases.

Histoid leprosy

There were 2 cases of histoid leprosy. The epidermis showed grenz zone and the dermis was packed with macrophages and spindle shaped histiocytes. Granuloma was present near the mid dermis composed predominantly of histiocytes. FITE FARACO stain was done for Mycobacterium leprae in both the cases which was packed with lepra bacilli along with characteristic interlacing bundles on spindle shaped histiocytes. The bacterial index was 6+ in both the case.

Tuberculosis verruca cutis

There were 6 cases of tuberculosis verrucae cutis. Among 6 cases of Tuberculosis verrucosa cutis hyperkeratosis, acanthosis and pseudoepitheliomatous hyperplasia was seen in 6 cases (100%) Dermal changes were observed in all the 6 cases (100%). Epithelioid granulomas with lymphohistiocytic infiltrate with Langhans' type of giant cells seen in mid-dermis in all the 6 cases (100 %). Ziehl-Neelsen staining for Mycobacterium tuberculosis was done in all the 6 cases to demonstrate the bacilli and it was positive only in 2 cases (33.3%).

Lupus vulgaris

There were 8 cases of lupus vulgaris, epidermal changes were seen in all 8 cases. Dermal changes were observed in all the 8 cases (100%). Epithelioid granulomas with Lymphohistiocytic infiltrate with Langhans' type of giant cells was seen in upper and mid dermis. Ziehl-Neelsen staining was done in all the 8 cases to demonstrate the Mycobacterium tuberculosis bacilli and it was positive only in 6 cases (75%).

Sarcoidosis

There were 2 cases of sarcoidosis in this study. Non caseating granuloma was present in both cases. Granuloma was present in upper dermis in 1 case and entire dermis in another case. Giant cells with asteroid bodies and schaumann body was present Ill both the cases. The cases showed negative results for Mycobacterium tuberculosis, Mycobacterium leprae and fungus.

Necrobiosis lipoidica

Epidermis shows hyperkeratosis. Entire thickness of dermis was involved with extension into subcutis. Nec robio tic granuloma was composed of inflammatory infiltrate, degeneration of collagen & sclerosis.The Inflammatory cells were histiocytes, lymphoc ytes , plasma cells and occasinal eosinophils.

Necrobiotic areas were rimmed by histiocytes, multinucleated giant cells and thickened collagen bundles. Adipocytes were present in the granuloma with necrosis.

Granuloma annulare

Out of 3 cases, 2 cases showed granulomatous inflammatory pattern in upper and mid dermis and in 1 patient granuloma was present in mid and lower dermis. Palisading histiocytes were found around focus of mucin in all the 3 cases.
Multinucleated giant cells were seen in all the 3 cases. Mild perivascular and interstitial lymphocytic infiltrate was seen in the surrounding dermis with scattered neutrophils in all the 3 cases.

Rheumatoid nodule

One case of rheumatoid nodule was reported. On histology granulomatous tissue reaction patterns were identified. In the lower dermis well developed necrotizing granulomas were present.

The granulomas were rimmed by histiocytes and mixed infiltrate of lymphocytes, plasma cells, multinucleated giant cells, and few eosinophils.

Incidence of granulomatous lesions of skin

In my study there were totally 17(34%) cases of tuberculoid leprosy, 2(4%) cases of histoid leprosy,6(12%) cases of borderline tuberculoid leprosy, 4(8%) cases of borderline lepromatous leprosy, 6(12%) cases of tuberculosis verruca cutis, 8(1 6%) cases of lupus vulgaris, 3 cases (6%) of granuloma annul are, 2(4%) cases of sarcoidosis, 1(2%)case of necrobiosis lipoidica and 1(2%) case of rheumatoid nodule (Table 1).

Table 1: Incidence of granulomatous lesions of skin.

Histopathological diagnosis	No. of Cases	Percentage
Histoid leprosy	2	4
Boderline tuberculoid leprosy	6	12
Boderline lepromatous leprosy	4	8
Tuberculosis verruca cutis	6	12
Lupus vulgaris	8	16
Sarcoidosis	2	4
Granuloma annulare	3	6
Necrobiosis lipoidica	1	2
Rheumatoid nodule	1	2
Total	50	100

Incidence of age in granulomatous lesions

In this study there were totally 5(10%) cases less than 20 yrs., 16(32%) were between 21-30yrs, 8(1 6%) were between 3-40 yrs., 10 (20 %) were between 4 l-50yrs, 3(6%) were between 5l-60 yrs., 8(16%) were >60 yr.

Age distribution in each lesion

In this study there were totally 17 cases of tuberculoid leprosy among them 5(29.4%) patients were between 21- 30yrs, 3(17.4%) were between 31-40yrs, 3(17.4%) patients were between 41-50yrs,1(5.9%) patient was between 51- 60yrs,5(29.4%) patients >60yrs.

There were totally 2 cases of histoid leprosy among them 1(50%) patient was below 20yrs, 1(50%) was between 21-30yrs. Among the 6 cases of borderline tuberculoid leprosy 3(50%) were 21-30yrs, 1(16.7%) patient was between 31- 40yrs and 2(33.3%) were between 41-50yrs.

Among the 4 patients of borderline lepromatous leprosy 1(25%) patient was between 21-30yrs, 1(25%) patient was between 31-40yrs, 1(25%) patient was between 41-50yrs, 1(25%) case was between 51-60yrs. Among 6 cases of tuberculosis verruca cu tis 1(16.6%) was below 20yrs, 2(33.3%) were between 21-30yrs, 1(16.6%) patient was between 31-40yrs, 2(33.3%) patient was between 41-S0yrs. Among 8 patients of lupus vulgaris 2(25%) were below 20yrs, 3(37.5%) patient was between 21-30yrs, 2(25%) patients were between 31-40yrs, and 1(12.5%) patient was between 51-60yrs. Among 2 sarcoidosis patients 1(50%) patient was between 21-30yrs, 1(50%) patient was between 41-50yrs. Among 3 patients of granuloma annulare 1(25%) patient was below 20yrs, 2(75%) patient was >60yrs. There was 1 case of necrobiosis lipoidica and 1case of rheumatoid nodule who were >60yrs and 41-50 yrs respectively.

Gender incidence in granulomatous lesions of skin

Out of 50 cases 34(66%) were male and 17(34%) were female.

Gender distribution in each lesion

In this study there were totally 17 cases of tuberculoid leprosy among them 15(88.2%) patients were male and 2(11.8%) were female. There were totally 2 cases of histoid leprosy, and both were male. Among the 6 cases of borderline tuberculoid le pro sy 3(50%) were female, 3(50%) was male. Among the 4 patients of borderline lepromatous leprosy 2(50%) were male 2(50%) were female. Among 6 cases of tuberculosis verruca cutis 4(50%) were male and 2(50%) were female.

Among 8 patients of lupus vulgaris 4(66.7%) were male, 4(33.3%) were female. Among 2 sarcoidosis patients 2(50%) were female. Among 3 patients of granuloma annul are 2(66.7%) were female and 1(33.3%) was male. There was 1 case of necrobiosis lipoidica and 1 case of rheumatoid nodule who were male and female, respectively.

Incidence of site of lesion in granulomatous lesions

In my study there were totally 50 cases among them16 (32%) presented in the upper extremity,15(30%) presented in the lower extremity, 8(16%) at the back, 11(22%) presented in the face. In my study there were totally 17 cases of tuberculoid leprosy among them 6(35.2%) presented in upper extremity, 4(23.5%) presented in lower extremity, 2(11.8%) presented in back, 5(29.4%) presented in face. There were totally 2 cases of histoid leprosy among them, 1(50%) presented in back, 1(50%) presented in f ace. Out of 6 cases of borderline tuberculoid leprosy 4(66.7%) presented 1n the upper extremity,2 (33.3%) presented in face. Among 4 patients of borderline lepromatous leprosy 2(50%) presented in upper extremity, 2(50%) at back. Among 6 cases of tuberculosis verruca cutis 2(33.3%) presented inupper extremity, 3(50%) presented in lower extremity, 1(16.7%) presented at the back. Among 8 patients of lupus vulgaris 2(25%) each presented in face ,1(12.5%) patient presented near back, and 5(62.5%) presented the lesion in the lower extremity. Among 2 sarcoidosis patients 1(50%) patient presented in upper extremity, 1(50%) presented the lesion in the face. Among 3 patients of granuloma annulare 2(66.7%) patients presented in lower extremity, 1(33.3%) at back. There was 1 case of necrobiosislipoidica who presented in lower extremity.

There was 1 case of rheumatoid nodule who presented the lesion in the upper extremity as in table 2.

Table 2: Incidence of site of lesion in granulomatous lesions.

HPD	Back	Upper extremity	Face	Lower extremity
Tuberculoid leprosy	2	6	5	4
	-11.80%	-35.20%	-29.40%	-23.50%
Histoid	1	0	1	0
Leprosy	-50%	0%	-50%	0%
Boderline	0	4	2	0
Tuberculoid	0%	-66.70%	-33.30%	0%
Boderline	2	2	0	0
lepromatous	-50%	-50%	0%	0%
Tuberculosis	1	2	0	3
verruca cutits	-16.70%	-33.30%	0%	-50%
Lupus	1	0	2	5
Vulgaris	-12.50%	0%	-25%	-62.50%
Sarcoidosis	0	1	1	0
	0%	-50%	-50%	0%
Granuloma	1	0	0	2
Annulare	-33.30%	0%	0%	(66 .7%)
Necrobiosis	0	0	0	1
lipoidica	0%	0%	0%	-100%
Rheumatoid	0	1	0	0
Nodule	0%	-100%	0%	0%
TOTAL	8	16	11	15
	-16%	-32%	-22%	-30%

Incidence of appearance of lesion in granulomatous disease

There were totally 50(100%) cases in my study among them 21(42%) cases presented as patch like lesion 16(32 %) presented as plaque like lesion 5(10%) presented as nodular lesion 2(4%) presented as erythematous lesion 2(4%) with scaling and 4(8%) as verrucous lesions.

There were totally 17 cases of tuberculoid leprosy among them 11(64.7%) presented as patchy lesion, 3(17.6%) as plaque type of lesion, 1(5.9%) as nodule, 1(5.9%) with scaling. Among 2 cases of histoid leprosy 1(50%) presented as plaque and 1(50%) as plaque. Among 6 cases of borderline tuberculoid leprosy 4(75%) presents as patch type of lesion, 1(25%) patient presented as plaque and 1(25%) as erythema. Among 4 cases of borderline lepromatous leprosy 1(25%) patient presented as patch and 3(75%) presented as plaque. Among 6 cases of tuberculosis verruca cutis 1(16.7%) presented as patch, 2(33.3%) presented as plaque,

2(50%) as verrucous lesions. Among 8 cases of lupus vulgaris 2(25%) presented as patch, 4(50%) as plaque, 1(12.5%) as nodule,1(12.5%) as erythema and 1(12.5%) with scaling. Both the cases of sarcoidosis presented the lesion with plaques. Necrobiosis lipoidica presented with verrucous lesion. Among 3 cases of granuloma annulare 2(75%) presented with nodule and 1(25%) with patch. 1 patient with rheumatoid nodule presented with nodular lesion as in table 3.

Table 3: Incidence of appearance of lesion in granulomatous disease.

Appearance of lesion	No. of cases	%
Patches	21	42
Plaques	16	32
Nodule	5	10
Erythema	2	4
Scaling	2	4
Verrucous	4	8
Total	50	100

Incidence of pigmentation

In my study there were totally 50 cases among them 31(62%) presented with hypopigmentation, 9(18%) presented with hyperpigmentation and 10(20%) presented with no change.

In my study there were totally 17 cases of tuberculoid leprosy among them 15(88.3%) presented with hypopigmentation, 2(11.7%) with no change. Among 2 cases of histoid leprosy, all 2(100%) presented with hypopigmentation. There were totally 6 cases of borderline tuberculoid leprosy and 2(25%) presented with no change and 4(75%) presented with hypopigmentation. There were totally 4 cases of borderline lepromatous leprosy and all.4(100%) patients had hypo pigmentation. Among 6 cases of tuberculosis verruca cutis 4(66.7%) had hyperpigmentation, and 2(33.3%) no change. Among 8 patients of lupus vulgaris all 6(75%) had hyperpigmentation and 2(25%) had no change. There were totally 2 sarcoidosis patients both had hypo pigmentation.

There were 3 patients of granuloma annulare all 3(100%) presented with hypopigmentation. There was 1 case of Necrobiosis lipoidica and it presented with hyper pigmentation. There was 1 case of rheumatoid nodule who presented with hypo pigmentation as in Table 4.

Table 4: Distribution of pigmentation in each lesion.

Histological Diagnosis	No change	Hypo pigmentation	Hyperpigmentation
Tuberculoid Leprosy	2 (11.7%)	15 (88.3%)	0 (23.5%)
Histoid Leprosy	0 0%	2 (100%)	0 0%
Boderline tuberculoid leprosy	2 (25%)	4 (75%)	0 0%
Boderline lepromatous leprosy	0 0%	4 (100%)	0 0%
Tuberculosis verruca cutis	4 (66.7%)	0 0%	2 (33.3)%
Lupus vulgaris	2 (75%)	0 0%	6 (25%)
Sarcoidosis	0 0%	2 (100%)	0 0%
Granuloma Annulare	0 0%	3 (100%)	0 0%
Necrobiosis Lipoidica	0 0%	0 0%	1 (100%)
Rheumatoid Nodule	0 0%	1 (100%)	0 0%

Total	10 (18%)	31 (62%)	9 (18%)

Distribution of loss of sensation in Hansen's disease

Among 17 cases of tuberculoid leprosy 5(29.4%) had no loss of sensation, 12(70.6%) had loss of sensation. Among 2 cases of histoid leprosy both had loss of sensation.

Among 6 cases of borderline tuberculoid leprosy, 3(50%) had loss of sensation, 3(50%) did not have loss of sensation. Among 4 patients of borderline lepromatous leprosy 3(7 5%) had loss of sensation and 1(25%) had no loss of sensation.

Distribution of ziehl-neelsen staining for mycobacterium tuberculosis in cutaneous tuberculosis

In the present study there were 6 cases of tuberculosis verruca cutis among them 2 (33.3%) were positive forZiehl-Neelsen staining and among 8 cases of lupus vugaris 6(75%) were positive for Ziehl-Neelsen staining (Table 5).

Table 5: Distribution of ziehl-neelsen staining for mycobacterium tuberculosis in cutaneous tuberculosis.

Lesion	Positive	Negative
Lupus vulgaris	6(75%)	2(25%)
Tuberculosis verruca cutis	2(33.3%)	4(66.7%)

Incidence of fite faraco staining for mycobacterium leprae in hansen's patients

Out of 29 patients with Hansen's disease 11(38%) were positive for Fite feraco staining for Mycobacterium Leprae. Histoid and borderline lepromatous leprosy patients showed 100% positivity. Out of 17 cases of tuberculoid leprosy only 3 cases (17.64%) were positive and out of 6 cases of borderline tuberculoid leprosy only 2 cases (33.3%) were positive.

DISCUSSION

Granulomatous skin lesions often present as a diagnostic challenge to dermatopathologists due to various modes of presentation and simulating histological picture produced by several causes. Hence, the microscopic appearance of the lesions using Eosin and Haematoxylin stains and certain special stains is essential to arrive with the correct diagnosis [13-15]. The studies focusing on the different kinds of granulomatous lesions of the skin were conducted by various authors. The present study showed agreement to Bal' s and Gautham et al' s studies with respect to commonest disease in granulomatous lesions of skin, which was Hansen's disease. The present study showed agreement to Dhar's and Gautham et al' s studies with respect to the male predominance in granulomatous lesions of the skin [16].

Infectious granulomatous lesions were predominant in the present study in accordance with the studies done by Bal et al and Gautham et al. In our study majority occurred in the upper extremity (20 %) which was compatible with that of study done by Gautham et al (22.43%). Out of the total 515 cases of infectious granuloma in Bal's study, 373 (72.4%) were Hansen's disease followed by 119 cases (23.1%) of cutaneous tuberculosis. Out of a total of 79 cases (74.5%) of infectious granuloma in Gautham' s study, 63(79.7%) were Hansen's disease followed by 6 cases (7.6%) of cutaneous tuberculosis. In our study out of 43 cases of infectious granulomas, Hansen's was 29 cases (58%) followed by cutaneous tuberculosis which was 14 cases (28%) [17].

A major bulk of the cases comprised of Hansen's disease, which were typed and analysed for clinical and histopathological correlation. Skin lesions in Hansen's were more common in males. There were 34 (68%) males and 16 (32%) females with a male to female ratio of 2:1. These results were comparable with study done by Jayalakshmi et al. [18] who also found male preponderance with a male to female ratio of 2.8: 1. Nadkarani et al. [19] Moorthy et al [20] and Gautham et al. [17] also found males to be involved more by leprosy of the skin. Tuberculoid leprosy was the most common lesion encountered in our study in accordance to various other studies [19-22].

Two out of 50 cases were diagnosed as cutaneous sarcoidosis in the present study. Sarcoidosis was rare in the series by Gautham et al [17]. Both patients were female and non-caseating granulomas were seen in the dermis in both the cases with similarity to other studies with dermal predominance.

In the present study 14 out of 50 cases of skin biopsies were diagnosed as tuberculosis (28%). A male preponderance was observed (9/14) in our series which was similar to studies done by Gautham etal and Bal' s study. Among the 14 cases in the present study the lesions were typified as Lupus vulgaris in 6 cases and

tuberculosis verruca cutis in 9 cases. Lupus Vulgaris was the commonest form in studies done by Gautham et al [17] and James et al [23] which correlated 'with the present study.

Ziehl Neelsen stain for Mycobacterium tuberculosis was indicated in all suspected cases of cutaneous tuberculosis and the results were compared with other studies. Granuloma annulare comprised 3 (6%) of the 50 cases studied which was similar in incidence with other case series of Mohan et al and Zafar et al. Majority of the patients were of female predominance like the study done by Kothari et al. [3] and Gautham et al. [17]. Clinically all the cases were of localized granuloma annulare. On histopathological examination interstitial pattern of presentation was seen in 25% of the total cases, like other case series done by Harish et al. [24].

We had only 1 case of necrobiosis lipoidica who was a 69yr old female presented verrucous, hyperpigmented lesion with history of diabetes mellitus in lower extremity. Histopathological picture showed involvement of the entire thickness of dermis with extension into subcutis. Necrobiotic granuloma was composed of inflammatory infiltrate, degeneration of collagen & sclerosis. The Inflammatory cells were histiocytes, lymphocytes, plasma cells and occasional eosinophils. Necrobiotic areas were rimmed by histiocytes, multinucleated giant cells and thickened collagen bundles. Adipocytes were present in the granuloma with necrosis which correlate with work done by Peishanyen [2] et al., Fernandez [26] et al. and Boulton et al. [27].

We found only one case of rheumatoid nodule who was a 43yr old male presented with nodular, non-tender lesion in lower extremity. Histologically granulomatous tissue reaction patterns were identified. In the lower dermis well devoleped necrotizing granulomas were present. The granulomas were rimmed by histiocytes and mixed infilterate of lymphocytes, plasma cells, multinucleated giant cells were present which correlated with study done by Betloch [28] et al., Mayo et al., [29], Sayah et al. [30].

CONCLUSION

Infectious disease forms an important cause of granulomatous skin lesions with Hansen's disease as the leading etiology. Granulomatous skin lesions have various modes of presentation hence a classical clinical picture may not always be present. It can be concluded that histopathology plays an important role 1n arnv1ng at a diagnosis and management of the disease. Special stains are mandatory in these diseases so that the type and etiological agent of the granuloma are accurately diagnosed.

FUNDING

No funding sources.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

The encouragement and support from Bharath University, Chennai is gratefully acknowledged. For provided the laboratory facilities to carry out the research work.

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