

Leprosy: A Persistent Culprit Behind Granulomatous Dermatitis In Northern India

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Abstract:

Background: Granulomatous skin lesions represent a distinct type of chronic inflammation characterized by the formation of granulomas. These lesions often pose diagnostic challenges due to their varied presentations and histological similarities. Accurate histopathological identification is crucial for appropriate treatment and prognosis.

Aim and Objectives: The study aimed to evaluate frequency of various granulomatous skin lesions histopathologically, especially the infectious one and correlate them with clinical findings.

Materials and Methods: A total of 103 skin biopsies from patients with suspected granulomatous skin lesions were studied prospectively over 12 months at the Department of Pathology, Muzaffarnagar Medical College and Hospital. Biopsies were processed, sectioned at 4-5 microns, and stained with Hematoxylin and Eosin (H&E). Special stains like Ziehl-Neelsen (ZN) and Fite-Faraco (FF) were utilized as needed. Histopathological diagnoses were made following microscopic examination.

Results: Among the 103 cases, there was a male predominance with 67 cases (65%). Majority of the patients were in the age group of 21-30 years (35.9%). Infectious granulomatous lesions were predominant, accounting for 84.5% of cases, with leprosy being the most common cause (73 cases, 70.9%). A clinicopathologic concordance rate of 91.3% was observed.

Conclusion: Infectious granulomatous dermatoses, particularly leprosy, remain the leading cause of granulomatous skin lesions in developing countries. Histopathology plays a pivotal role in the diagnosis and classification of these conditions, guiding effective clinical management.

Keywords: Granulomatous skin lesion, histopathology, leprosy, clinical correlation, skin biopsy.

Date of Submission: 15-12-2024

Date of Acceptance: 25-12-2024

I. Introduction

Granulomatous inflammation was first recognized as a distinct entity in the early 19th century and has since remained a topic of continual interest due to its frequent occurrence and complex clinical and pathological characteristics.¹ Granulomatous skin lesions can arise from a wide spectrum of diseases, both infectious and non-infectious, which have specific therapies and can be completely cured. Therefore, accurate classification of granulomatous pathology is crucial for appropriate clinical management.²

Granulomatous skin lesions are identified in histopathological examinations of skin biopsy samples by the detection of granulomas. These granulomas contain epithelioid cells and may also exhibit additional features such as acute inflammation, presence of lymphocytes, giant cells, necrosis, and collagen alteration.³

Six types of granulomatous skin lesions have been identified based on cellular constituents and associated changes: 1) tuberculoid, 2) sarcoidal, 3) necrobiotic, 4) suppurative, 5) foreign body and 6) miscellaneous.⁴

This study holds significant importance as infectious granulomatous diseases, such as leprosy and tuberculosis, are still prevalent in India, presenting major public health challenges. These diseases are curable with appropriate therapy, that's why combining histopathological analysis with clinical findings, the study contributes to better diagnostic accuracy, enabling earlier diagnosis and improved management of patients. This study was done to address the burden of treatable granulomatous diseases, ensuring that appropriate measures,

such as health education and national programs are implemented to raise awareness and reduce the burden of leprosy and tuberculosis.

The primary aim of this research was to evaluate the frequency of various granulomatous skin conditions histopathologically, particularly those of infectious etiology, in a tertiary care hospital and correlate them with clinical findings.

II. Materials And Methods

Present hospital-based prospective descriptive study was carried out in the Pathology Department at Muzaffarnagar Medical College & Hospital, Muzaffarnagar, Uttar Pradesh, India. The study population included 103 skin biopsy samples of granulomatous lesions during the study period of one year. The inclusion criteria for the study were all clinically and/or histopathologically diagnosed cases of granulomatous skin lesions within the specified period of time. Inadequate biopsy specimens were excluded from the study.

A detailed clinical history was obtained, and thorough physical examination of the lesions was conducted. Biopsies were performed after obtaining proper consent. Detailed histopathological examination was performed on H&E stained slides. Special stains such as Ziehl-Neelsen (ZN), Fite-Faraco (FF), Alcian Blue, Reticulin, and Periodic Acid-Schiff (PAS) were also used wherever required for diagnosis. Lesions were classified according to the available literature. The clinical findings were then correlated with the histopathological results.

This study was presented and approved by the Muzaffarnagar Medical College Institutional Ethical Committee (IEC No.- MMC/IEC/2022/127), where the study was conducted.

For data collection, patient clinical data, including clinical features, were recorded. The relevant data from cases meeting the inclusion criteria were analysed in Microsoft Excel 2013. The statistical analysis was performed with SPSS version 20 software.

III. Results

The most common age group in patients with granulomatous skin lesions was the third decade (21-30 years), accounting for 37 cases (35.9%). Mean age was 34.45 ± 14.06 years. Male predominance (67 cases, 65.0%) was noted with M:F ratio of 1.86:1. (**Table 1**)

Table 1: Distribution of granulomatous skin lesions according to age and sex

Age Groups	No. of cases		Sex	
	n	%	F	M
0 - 10 yrs	2	1.9	0	2
11 - 20 yrs	9	8.7	2	7
21 - 30yrs	37	35.9	10	27
31 - 40 yrs	29	28.2	13	16
41 - 50 yrs	14	13.6	8	6
51 - 60 yrs	7	6.8	1	6
>60 yrs	5	4.9	2	3
Total	103	100.0	36	67
Mean \pm SD	34.45 ± 14.06		37.25 ± 12.07	32.94 ± 14.88

Upper extremity was the most common site of lesions accounting for 34 cases (33.0%), followed by the lower limb (26 cases, 25.2%), and the head and neck (21 cases, 20.4%).

Different etiologies of granulomatous skin lesions were found on histopathology. Infectious lesions were significantly more prevalent, accounting for 87 cases (84.5%). Among the infectious etiologies, leprosy was the most common cause, seen in 73 cases (70.9%), followed by tuberculosis in 10 cases (9.7%). Non-infectious granulomatous lesions were less common with 16 cases (15.5%), the most frequent being Granuloma Annulare (8 cases, 7.8%). (**Table 2**)

Table 2: Histopathological spectrum of Granulomatous Skin Lesions

Histopathological Diagnosis	Number (n)	Percentage (%)
A. Infectious causes	87	84.5
Leprosy	73	70.9
Tuberculosis	10	9.7
Inflamed Epidermal Cyst with Granulomatous Reaction	2	1.9
Blastomycosis	1	1.0
Suppurative Granulomatous Inflammation	1	1.0
B. Non-Infectious causes	16	15.5
Granuloma Annulare	8	7.8
Foreign Body Granuloma	5	4.8
Xanthogranuloma	2	1.9

Sarcoidosis	1	1.0
Total	103	100.0

Commonest type of granuloma observed was the tuberculoid granuloma (49 cases, 47.6%). Hansen's disease (leprosy) came out as the most common cause of tuberculoid granuloma (39 cases out of 49 cases). Second most common type of granuloma was histiocytic granuloma (34 cases, 33.0%), all cases were of Hansen's disease. This was followed by necrobiotic granuloma, seen in 8 cases (7.8%), all 8 cases were of Granuloma Annulare. Rest of the granulomas were classified as foreign body (5 cases, 4.8%), suppurative (4 cases, 3.9%), xanthogranulomatous (2 cases, 1.9%) and lastly sarcoidal granuloma with only 1 case (1.0%). (Table 3)

Table 3: Distribution of cases according to the Type of Granuloma

Morphological type of Granuloma	Etiology	No. of cases (n)	Percentage (%)
Tuberculoid		49	47.6
	Hansen's Disease	39	
	Lupus Vulgaris	9	
	Scrofuloderma	1	
Histiocytic	Hansen's Disease	34	33.0
Necrobiotic	Granuloma Annulare	8	7.8
Foreign body		5	4.8
	Suture	3	
	Tattoo	1	
	Keratin	1	
Suppurative		4	3.9
	Inflamed Epidermal Cyst with Granulomatous Reaction	2	
	Suppurative Granulomatous Inflammation	1	
	Blastomycosis	1	
Xanthogranulomatous	Xanthogranuloma	2	1.9
Sarcoidal	Sarcoidosis	1	1.0
Total		103	100.0

Hansen's Disease was the most frequent etiology observed in the study (73 cases, 70.9%), which was further classified according to Ridley–Jopling classification. Borderline tuberculoid (BT) was the most common subtype (19 cases, 26.0%), followed by Borderline Lepromatous (BL) (15 cases, 20.5%) and Lepromatous leprosy (LL) (14 cases, 19.2%). (Table 4) (Images A, B and C)

Table 4: Distribution of cases according to type of Leprosy showing granuloma

Histopathological Diagnosis	No. of cases (n)	Percentage (%)
HD-TT	8	11.0
HD-BT	19	26.0
HD-BB	9	12.3
HD-BL	15	20.5
HD-LL	14	19.2
HD with Type 1 LR	2	2.7
HD-BT with Type 1 LR	1	1.4
HD-LL with Type 1 LR	3	4.2
HD-LL with Type 2 LR	2	2.7
Total	73	100

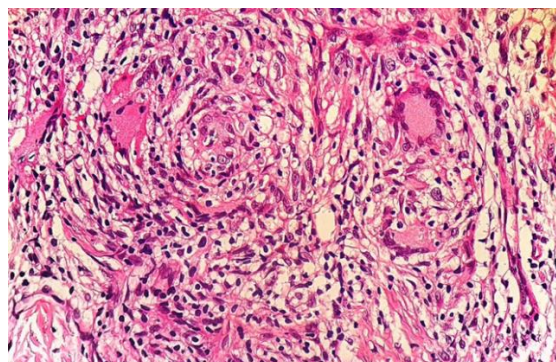


Image A: High power view of a borderline tuberculoid case, showing well formed tuberculoid granuloma with epithelioid cells, lymphocytes and Langhans giant cells. (H&E)

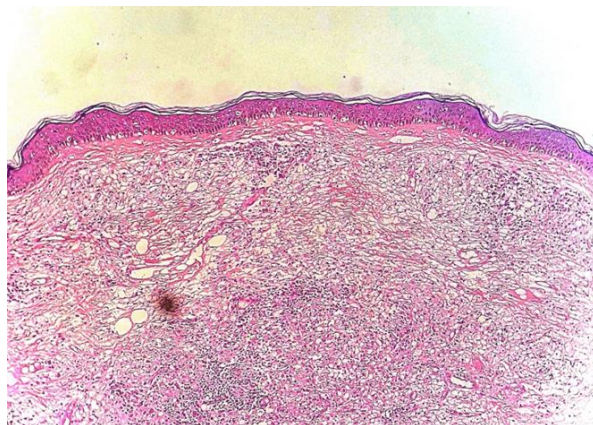


Image B: Scanner view of a Lepromatous Leprosy case, showing infiltrative foam cells and clear subepidermal grenz zone. (H&E)

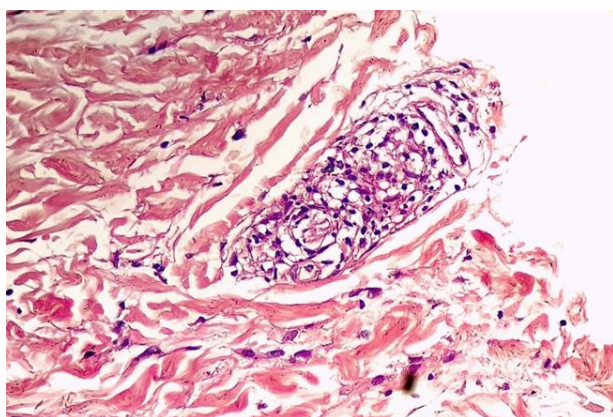


Image C: High power view of a Lepromatous Leprosy case, showing epithelioid histiocytes and lymphocytes infiltrating the nerve. (H&E)

The most common affected age group in patients with leprosy was the fourth decade (24 cases, 32.9%) with mean age of 35.86 ± 14.10 . Male preponderance was seen with sex ratio of 2.3:1.

We utilized the Fite-Faraco stain technique to assess bacillary load in leprosy cases. Among the cases examined, 40 (out of 73 cases) were found to be Fite-Faraco positive (54.8%), indicating the presence of acid-fast bacilli. (**Image D**)

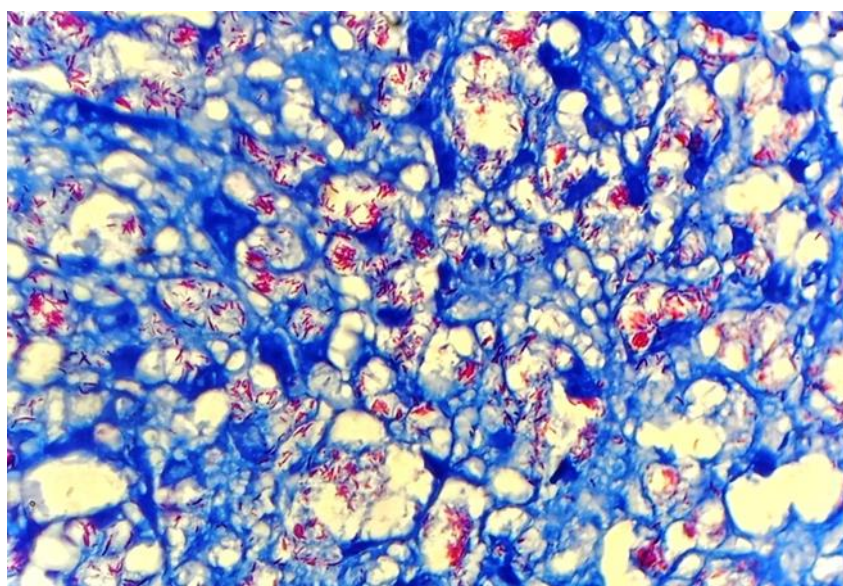


Image D: Oil immersion view of a Lepromatous Leprosy case showing numerous lepra bacilli, BI=6. (FF)

Second commonest cause of granulomatous skin lesion was cutaneous tuberculosis (10 cases, 9.7%). Age group affected most was 21-30 years (6 cases, 60%), with mean age of 24.50 ± 11.48 . Male predominance was seen (sex ratio 2.3:1). Lupus Vulgaris was the commonest subtype with 9 out of 10 cases and only 1 case of Scrofuloderma was found in our study. (**Image E**)

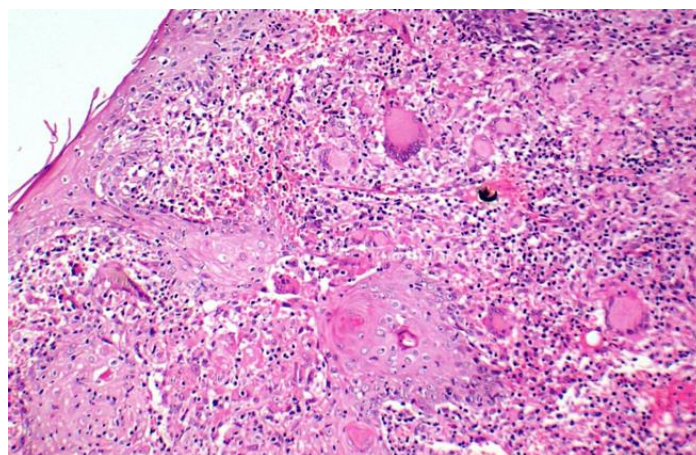


Image E: Low power view of a Lupus Vulgaris case, showing flattened epidermis and tuberculoid granulomas with Langhans giant cells and dense lymphocytic infiltrate in dermis. (H&E)

Ziehl-Neelsen stain was utilized to detect the acid-fast bacilli in these cases. Only 2 cases (20%) demonstrated ZN positivity, indicating the presence of AFB.

A provisional clinical diagnosis was provided for all 103 cases of granulomatous skin lesions. Histopathological findings were consistent with clinical diagnosis in 94 cases, accounting for a concurrence rate of 91.3%. Diagnosis of remaining 9 discordant cases show another type of granulomatous lesion which was different from provisional clinical diagnosis. (**Table 5**)

Table 5: Clinico-histopathological discordant granulomatous lesions

S. No.	Provisional Clinical Diagnosis	Histopathological Diagnosis
1	Contact Dermatitis	HD-LL
2	Lupus Vulgaris	Blastomycosis
3	Lupus Vulgaris	Sarcoidosis
4	Lupus Vulgaris	Scrofuloderma
5	Lupus Vulgaris	Suppurative Granulomatous Inflammation
6	Infected preauricular LN	Lupus Vulgaris
7	Infected cervical LN	Lupus Vulgaris
8	Dorsal Neutrophilic Dermatitis	Granuloma Annulare
9	Xanthoma	Xanthogranuloma

IV. Discussion

Granulomatous skin lesions encompass a wide range of pathological conditions, including both infectious and non-infectious causes.²

Different types of granulomas are formed based on their underlying etiologies.⁵ Many lesions are linked to an identifiable causative agent. Identifying specific types of granulomas in conjunction with clinical findings is crucial for arriving at a definitive diagnosis or, at the very least, excluding various morphological mimics.⁶ The differentiation between these conditions requires a thorough clinicopathological correlation, as well as the use of special stains and molecular techniques when necessary.

In our study, the commonest affected age group was the third decade, comprising 35.9% of cases, followed by the fourth decade with 28.2% of cases. This finding aligns with previous studies by Kumar et al.¹ and Sharma et al.,⁷ where the large number of cases also fell within the age range of 21-40 years. The predominance of this age group could be attributed to the higher exposure to environmental pathogens and increased immune system activity during this period of life. However, our findings contrast with the studies by Kumari et al.⁸ and Chakrabarti et al.,⁵ where the most age group of 11-20 years was most common, suggesting that regional and environmental factors have a role in the variability of age distribution in granulomatous lesions.

Our study demonstrated a male predilection, with a male-to-female ratio of 1.86:1. This is consistent with other studies, including those by Sharma et al.,⁷ Anand et al.³ and Bharti et al.⁹ The higher prevalence in males may be due to high exposure to pathogens through outdoor activities and occupational hazards.

Additionally, societal norms that favour male healthcare access, along with socio-economic and cultural barriers that limit healthcare visits for women, may also contribute to this trend. Although, Kumbar et al.¹⁰ and Zafar et al.¹¹ found a female preponderance.

The most common site of granulomatous skin lesions in our study was the upper extremities (33.0%), which is comparable to the findings of Anand et al.,³ Bharti et al.,⁹ and Rajbhandari et al.¹² This predominance could be due to the upper extremities' frequent exposure to environmental factors and trauma, which can trigger granulomatous reactions.

Infectious granulomatous skin lesions were significantly more prevalent in our study, accounting for 84.5% of cases, with **leprosy** being the most common cause (70.9%). Similar results were reported by Anand et al.,³ Kumar et al.¹ and Jayawardhana et al.,¹³ where infectious etiologies comprised 95.5%, 81.4%, and 86.7% of granulomatous skin lesions, respectively. The high prevalence of infectious granulomas, particularly leprosy, in our study reflects the endemic nature of the diseases. Leprosy remains a significant public health concern in developing countries, despite global efforts to control or eradicate the disease. The histological identification of leprosy is crucial for accurate diagnosis, especially in cases where clinical manifestations are ambiguous. The predominance of leprosy in our study is consistent with other research, including studies by Sharma et al.⁷ and Chakrabarti et al.,⁵ where leprosy was identified as commonest cause of granulomatous dermatitis. In contrast, studies by Zafar et al.¹¹ and Qureshi et al.⁴ reported cutaneous tuberculosis and cutaneous leishmaniasis as the frequent infectious granulomatous lesions in their respective regions. These differences highlight the influence of geographical location and environmental factors on the etiology of granulomatous skin lesions.

Leprosy was the commonest granulomatous skin lesion in our study, accounting for 73 cases (70.9%). Male predominance was observed in leprosy patients (M:F= 2.3:1), which is consistent with similar studies conducted by Anand et al.,³ Rajbhandari et al.¹³ and Prajapati et al.¹⁵ The most affected age group was the fourth decade of life, closely followed by the third decade, mirroring trends observed in previous studies.^{13,16,17} The male predominance could be due to occupational exposures or social factors influencing healthcare-seeking behaviour.

The most common subtype of Leprosy in our study was BT (26%), which is in concordance with the studies done by Prajapati et al.¹⁵, Anand et al.³ and Chakrabarti et al.⁶ However in the studies done by Sharma et al.⁹ and Patel et al.¹⁸ LL was the most frequent subtype followed by BT Leprosy. A substantial number of leprosy patients fall within a dynamic immunological spectrum, classified as borderline tuberculoid (BT), borderline borderline (BB), and borderline lepromatous (BL). With treatment, borderline cases tend to shift towards the tuberculoid pole, characterized by a stronger immune response. Conversely, untreated cases drift towards the lepromatous pole, with a weaker immune response. Notably, features of both tuberculoid and lepromatous leprosy can be observed within the same tissue section, serial sections, or even in different lesions from the same borderline patient. The increased detection of borderline cases in this study, and likely in most others, can be attributed to national programs that raise public awareness about leprosy, encouraging earlier presentation at clinics.¹⁸

Cutaneous tuberculosis was the second most frequent cause of infectious granulomatous skin lesions after leprosy in our study, representing 9.7% of cases (10 cases). Male predominance was observed, consistent with studies done by Anand et al.³ and Patil et al.¹⁹ Lupus vulgaris was the commonest subtype, accounting for 90% of cutaneous tuberculosis cases (9 cases). This finding is in concordance with studies by Sharma et al.,⁹ Rajbhandari et al.¹² and Patil et al.¹⁴

In our study, we utilized Fite-Faraco stain to identify *Mycobacterium leprae* in leprosy cases, with a positivity rate of 54.8%, a result consistent with Sharma et al.⁷ (53.3%) and Roy et al.¹⁵ (50.0%). Similarly, the Ziehl-Neelsen (ZN) stain was applied to detect acid-fast bacilli in cases of suspected cutaneous tuberculosis. The ZN positivity rate in our study was 20.0%, which is lower than the rates reported by Kumar et al.¹ (54.4%) and Sharma et al.⁷ (44.4%). This discrepancy could be due to the varying bacterial load in different stages of the disease. The variability in staining results emphasizes the need for a comprehensive diagnostic approach that includes clinical assessment, histopathological examination, and the use of appropriate staining techniques.

Granuloma annulare was the commonest non-infectious cause in our study, with 7.8% of cases, followed by foreign body granuloma with 4.9% cases. Similar findings were seen in the studies by Chakrabarti et al.⁵ and Jayawardhana et al.¹³ However, in studies by Kumar et al.,¹ Kumari et al.⁸ and Rajbhandari et al.,¹² foreign body granuloma was the frequent type of non-infectious granulomatous dermatosis.

In the present study, tuberculoid granulomas emerged as the most prevalent type, accounting for 47.6% of cases, followed by histiocytic granulomas at 33.0%. This is consistent with findings from Kumar et al.,¹ who reported a higher prevalence of tuberculoid granulomas (61.3%) and a lower prevalence of histiocytic granulomas (19.3%). Similarly, Kumari et al.⁸ found tuberculoid granulomas to be the most common (50.0%), with histiocytic granulomas as the third most common (15.3%). However, in Kumari's study, foreign body granulomas were the second most common type (19.2%),⁸ whereas in our study, they accounted for only 4.9%

of cases. This discrepancy may be attributed to differences in the geographic location and sample population, which could influence the prevalence of certain granulomatous conditions.

Our study identified suppurative granulomas in 3.9% of cases, which is consistent with findings by Sharma et al.⁷ (5.8%) and Chakrabarti et al.⁵ (4.8%). However, Kumari et al.⁸ and Rajbhandari et al.¹² reported a higher prevalence of suppurative granulomas at 10.2% and 23%, respectively. The lower prevalence in our study may be due to differences in the types of cases included, as well as variations in the criteria used for diagnosing suppurative granulomas.

The sarcoidal granuloma was the least common in our study, with only 1 case (1%). **(Image F)** This is consistent with findings from Kumar et al.¹ (3.2%), Rajbhandari et al.¹² (3.0%), and Chakrabarti et al.⁵ (1.6%). The rarity of sarcoidal granulomas in these studies may reflect the low incidence of sarcoidosis in the populations studied.

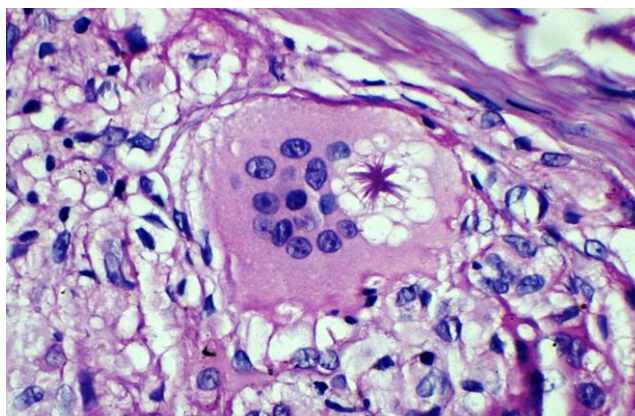


Image F: High power view of a Sarcoidosis case, showing Asteroid body within a multinucleated giant cell. (H&E)

In our study, 91.7% of the 103 clinically diagnosed cases of granulomatous skin lesions showed histopathological concurrence. This high rate aligns with the findings of Singh et al.¹⁶ (87.5%) and Gautam et al.¹⁷ (88.7%). However, it contrasts with the lower concurrence rate of 63.0% reported by Rajbhandari et al.,¹² underscoring differences in diagnostic accuracy and methodologies across studies.

The high prevalence of infectious granulomatous skin lesions in our study emphasizes the importance of public health interventions to control and prevent these diseases. Leprosy, in particular, continues to be a major public health challenge in developing countries. Early diagnosis and treatment are necessary to prevent complications and reduce transmission. The integration of dermatological services into primary healthcare systems, along with public health campaigns to raise awareness about the signs and symptoms of leprosy and tuberculosis, could significantly improve the detection and management of these conditions.

This study's limitations include a lack of diversity in the cases, with 80% of the granulomatous skin lesions caused by leprosy and cutaneous tuberculosis. This predominance limits the scope for understanding other types of granulomas, thereby restricting the comprehensiveness of the findings on the broader spectrum of granulomatous skin diseases. Further studies with larger and more diverse populations are required to explore full range of granulomatous skin lesions and their etiologies.

V. Conclusion

Granulomatous skin lesions present a diagnostic challenge due to their diverse etiologies and overlapping histopathological features. Our study highlights the importance of thorough histopathological examination and clinicopathological correlation in diagnosing these lesions. The predominance of infectious granulomas, particularly leprosy, in our study reflects the endemic nature of these diseases in the region. Continued research and public health efforts are needed to address the burden of granulomatous skin diseases and improve diagnostic and therapeutic strategies.

Conflict of interest: None

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