Original Research Article

Clinicopathological correlation in the diagnosis of granulomatous cutaneous disorders: a retrospective study

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ABSTRACT

Background: To ascertain the various cutaneous granulomatous disorders and clinicopathological concordance in skin biopsies.
Methods: The study included the patients with skin biopsy showing granulomatous infiltrate in a tertiary care center. The cases were categorized according to level of concordance into consistent, corroborative and inconsistent based on the concurrence between clinical and histological diagnosis.
Results: Of the total 155 granulomatous disorder, 75.48% showed clinicopathological concordance, 19.35% showed corroborative diagnosis while 5.16% were inconsistent. The maximum number of biopsies performed were in the group of young adult (19-49 years, 57.41%). The most common type of granuloma found was of tuberculoid type and disorders were Hansen's disease, fungal infection and cutaneous tuberculosis.
Conclusions: Our study showed that the coordination of dermatologist and pathologist plays a pivotal role in making accurate diagnosis of granulomatous cutaneous dermatoses.

Keywords: Biopsy, Clinicopathological correlation, Granuloma

INTRODUCTION

'Granuloma' is defined as a focal chronic inflammatory response to tissue injury characterized by a collection of activated histiocytes, epithelioid cells with variable numbers of admixed multinucleated giant cells and inflammatory cells that may or may not be rimmed by lymphocytes and or show central necrosis. Virchow described the term "granulomatous" as a tumor-like mass or nodule of granulation tissue.[1,2]

Granulomatous disorders are a diagnostic challenge to dermatologists due to similar histological features and varied clinical presentations.

Therefore, clinic-histopathological correlation of granulomatous disease plays a pivotal role in diagnosis.

In Dermatology skin biopsy is often considered as confirmatory in case of diagnostic dilemma and is the most common investigation sought by a dermatologist. Dermascopy is also used as diagnostic tool but skin biopsy is considered as gold standard investigation. The aim of this study was to determine the relative indications of skin biopsies in granulomatous groups of skin disorders and to evaluate the clinicopathological consistency in diagnosis of granulomatous skin disorders.

The objective of the study is to correlate clinical and histopathological features of granulomatous skin disorder to arrive at a conclusive diagnosis.

METHODS

This was a retrospective study over a period of three years at a tertiary care centre in Jaipur. Total number of

biopsy samples taken in the dermatology department in the specified period were recorded. Patient particulars, brief history and clinical findings, provisional diagnosis and differential diagnosis (if any) and infectious or traumatic cause (if any) were clearly mentioned in the biopsy requisition form. Special stains used were noted. The slides were reviewed by a dermatopathologist. The cases were studied for histopathological features of granuloma, predominant cell, location of granuloma in dermis and epidermal changes if any. All these data were tabulated and a clinico -histopathological correlation was attempted.

We interpreted the histopathogical reports as follows: consistent (definite)- when provisional diagnosis and histopathological diagnosis was the same, corroborative- when histopathological diagnosis was consistent with one of the differential diagnoses, inconsistent- when histopathological diagnosis was not consistent with either provisional or differential diagnoses.

RESULTS

This study includes 155 patients diagnosed clinically or histopathologically as granulomatous skin disease. Sociodemographic pattern of the patients included in our study is described in Table 1.

Table 1: Sociodemographic pattern.

Sex		Patient age (year)	
Male	99	Children (≤18)	15
Female	56	Younger adult (19-49)	89
		Older adults (≥50)	51

The age ranged between 8 to 78 years, with a mean of 30.5 years. Most (89cases,57.41%) biopsies were obtained from adults between 19 to 49 years, followed by older adults (51 cases,32.90%) and children (15cases,9.67%). Most (99, 63.87%) biopsies were from male patients, with M:F ratio of 1.7:1.

Table 2: Clinicopathological correlation.

Types	Consistent		Corroborative		Inconsistent		Total
	Number	%	Number	%	Number	%	
Tuberculoid							115
Leprosy	78	50.32	19	12.26	1	0.65	98
Cutaneous tuberculosis	5	3.23	3	1.94	1	0.65	9
Fungal granuloma	4	2.58	1	0.65	1	0.65	6
Cutaneous Leishmaniasis	1	0.65					1
LMDF	1	0.65					1
Suppurative							28
Non-infective	6	3.87			1	0.65	7
Infective	16	10.32	4	2.58	1	0.65	21
Necrobiotic	6	3.87	1	0.65	1	0.65	8
Foreign body			1	0.65			1
Sarcoidal			1	0.65			1
Other					2	1.30	2
Total	117	75.48	30	19.35	8	5.16	155

Table 3: Inconsistent cases.

Clinical diagnosis	Histological findings	Final diagnosis
Tumid DLE/ perforating folliculitis	Granulomatous dermatitis	Granulomatous Rosacea
Pyoderma gangrenosum	Mixed inflammatory granulation, Extravasated RBCs	Stasis dermatitis
Non healing ulcer/ tuberculoid ulcer	Large aseptate fungal hyphae, PAS positive. Tuberculoid granuloma	Subcutaneous Zygomycosis
Lymphangioma circumscriptum	Tuberculoid granuloma psoriasiform dermatitis	Cutaneous tuberculosis
Palmoplantar warts Puncktate keratoderma	Granuloma at neurovascular bundle. AFB positive	BL-Hansen's disease
DLE/ Lupus panniculitis	Leucocytoclastic vasculitis, fibrin deposits, nuclear dust	Necrotising vasculitis (d/d Wegener'sgranulomatosis)
Pyoderma gangrenosum/ tuberculas gumma	Perivascular dermatitis Lymphocytic infiltrate	Hidradenitis suppurativa
ALHE/ Psuedolymphoma	Non-necrotizing granulomatous inflammation	sarcoidosis

Table 4: Comparison of the types of granuloma in different studies.

Studies	Tuberculoid	Suppurative	Necrobiotic	Sarcoidal	Foreign body	Others
Dhar et al	77.3%	9%	-	13.7%	-	-
Bal et al	87.7%	2.9%	2.7%	2.6%	1.7%	2.4%
Gautam et al	68.9%	2.8%	3.7%	1.9%	18.9%	3.7%
Present study	74.67%	18.18%	5.19%	0.64%	-	1.29%

The most frequent site of skin biopsies were lower extremities (28.1%), followed by trunk (26.5%), upper extremities (25.2%) and other (20.2%).

According to Weedon's skin pathology, we divided granuloma in five different categories. Of all the cases 74.21% granulomas were found to be tuberculoid, followed by 18.07% suppurative, 5.16% necrobiotic granuloma.

Table 5: Distribution of subtype of leprosy.

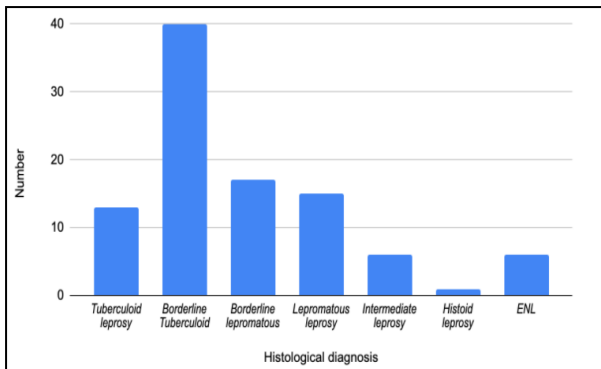| Histological diagnosis	Number	%
Tuberculoid leprosy	13	13.26
Borderline Tuberculoid	40	40.81
Borderline lepromatous	17	17.34
Lepromatous leprosy	15	15.30
Intermediate leprosy	6	6.12
Histoid leprosy	1	1.02
ENL	6	6.12
Total	98	

Figure 1: Distribution of subtype of leprosy.

After assessing the clinicopathological correlation in the diagnoses of cutaneous granulomatous disorders, among all 155 cases, 117 (75.48%) were fully consistent with the clinical diagnoses, 30 (19.35%) were corroborative and 8 (5.16%) were inconsistent.

Within the group of patients with consistent diagnoses, 78 (50.32%) were diagnosed leprosy, 16 (10.32%) as of non-infective suppurative granuloma, 10 (6.4%) of fungal infection of both tuberculoid and suppurative type granuloma and 5 cases of cutaneous tuberculosis. (Table 2)
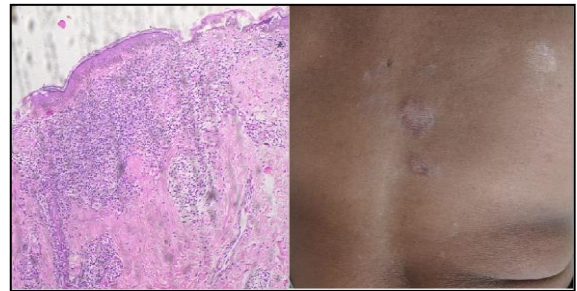

Figure 2: Hansen's disease- BT pole. Biopsy shows nodular granulomatous infiltrate centered around neurovascular bundles of dermis as well as appendages at some places.

Figure 3: Eumycetoma. Multiple discharging sinuses over right lower leg.

The patient group that have histological impressions inconsistent with clinical diagnosis are summarized in Table 3.
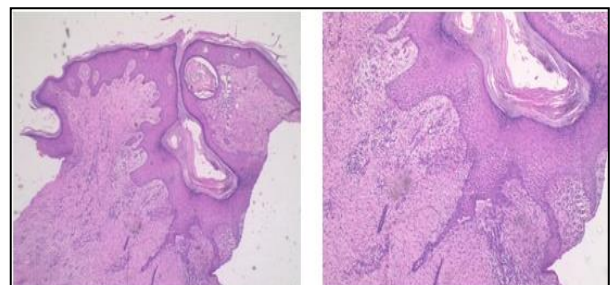

Figure 4: Eumycetoma. Biopsy shows a nodular dense suppurative granulomatous infiltrate on a background of fibrosing granulation tissue. The dermis shows edema, mucin, numerous thick walled capillaries and fibroplasia.
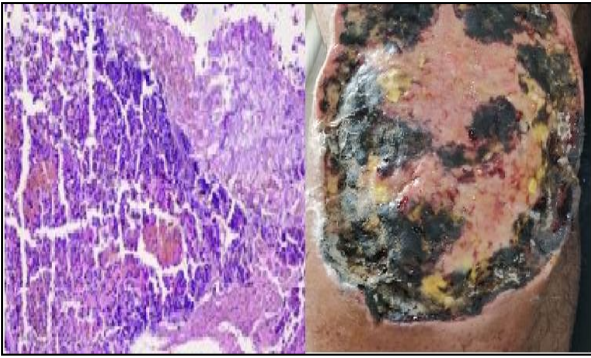
Figure 5: Mucormycosis. Biopsy shows non-pigmented non-septate broad-based hyphae.

DISCUSSION

The granulomatous reaction pattern is defined as a distinctive inflammatory pattern characterized by the presence of granulomas. Granulomas are collection of histiocytes or epithelioid cells with variable numbers of admixed multinucleate giant cells of varying types and other inflammatory cells. Different types of granuloma are sarcoidal, tuberculoid, necrobiotic, suppurative and foreign body.[1] Tuberculoid granulomas have specific central caseation with an outer rim of lymphocytes and plasma cell while sarcoidal granuloma are "naked". Necrobiotic granuloma show collagenolysis, with admixed inflammatory component or in palisading form around it. Foreign body granuloma shows identifiable foreign material along multinucleate ginat cell and other infiltrate.[1]

Despite of many advances in diagnostic technology, it is not always easy to make a conclusive diagnoses in many cutaneous granulomatous diseases. Cutaneous dermatoses undergo different stages and histological features changes with progression of disease, thus, synchronization of experienced dermatologists and pathologists is crucial for definitive diagnoses.[3] In a study performed by Rajaratnam et al, it was found that the rate of correct diagnosis without clinical information was 53%, however, the same rate was 78% with clinical information in hand.[4]

Granulomatous inflammation is a type-4 hypersensitivity reaction in response to any antigen. Histopathology is a gold standard tool for definitive diagnosis of various granulomatous cutaneous disorders. The clinical studies on various granulomatous lesions of the skin were conducted by various authors (Table 4).[5-7]

Our study showed similarity to Dhar's study with respect to the male predominance of the various granulomatous lesions of the skin.[6] Tuberculoid granuloma was the most common in all four studies (Table 4).

In our study 98 (63.23%) cases were of leprosy followed by 12 (7.74%) fungal infection and 9 (5.81%) cases of cutaneous tuberculosis. Similar result was found in a study by Bal et al, a total of 515 cases of infectious granuloma were recorded, out of which 373(72.4%) were of leprosy cases and 119 (23.1%) cases of cutaneous tuberculosis.[7] In Dutta et al commonest cutaneous granuloma encountered was leprosy (69.33%) followed by fungal (11.33%) and tubercular (8%) granuloma.[8]

We classified the leprosy cases according to Ridley and Jopling classification into indeterminate leprosy (I), TT, BT, BB, BL, and LL. (Table 5) (Figure 1). Cases of histoid leprosy and ENL were also included in the study. The largest subgroup of leprosy in our study is borderline tuberculoid (40 cases, 40.8%) similar to the finding of Gautam et al (47.6%).[5]

In this study highest number of cases of fungal granuloma comprised of mycetoma (41.6%), followed by chromoblastomycosis, pheohyphomycosis, histoplasmosis, phycomycosis, zygomycosis and candida granuloma. This pattern is similar with Permi et al while different from Dutta et al where sporotricosis was common among fungal granuloma.[8,9] This difference in clinical pattern of fungal granuloma is probably due to different geographical location, temperature and humidity.[9] Our study showed higher incidence of subcutaneous mycosis which may be due changing fungal pathogenecity similar to superficial dermatophytoses.

Few studies have been conducted in past to evaluate the advantage of histopathological correlation. Aslan et al found the concordance of 76.8% in 3949 skin biopsies while Malik et al found the same to be 61.01%.[10,11] In a study conducted by Gupta et al in 282 cases concordance was 85.8% and in Balasubramanian et al it was 59.8%.[12,13] In a study conducted by Dutta et al a total of 300 cases of cutaneous granulomatous disorder were recorded, 83.39% showed clinicopathological concordance.[8]

In a study by Malik et al out of total 2216 biopsies 555 were of granulomatous disease, which were divided into Hansen' disease, tubercular and non-infectious granulomas, showed a concordance of 51.3%, 70.77% and 40% respectively.[11] In our study, clinicopathological correlation in hansen's disease is 79.59%, which is higher than that in Malik et al and Balasubramanian et al (58.8%).[11,13]

In present study, the subtype of leprosy with maximum concordance was BT-hansen's followed by LL-hansen's , similar findings were recorded by Malik et al and Manandhar et al while Balasubramaniam et al and Bhatia et al found maximum concordance in LL-hansen's followed by BT-hansen's.[11,13,14,15]

Clinicohistopathological concordance for the fungal granulomas was (83.33%) which was higher in comparison to 76.46% of Dutta et al, direct microscopy was positive in 2 cases of chromoblastomycosis, and one

case of candida and eumycetoma while in our study one case of zygomycosis and one case of mucormycosis showed nonseptate broad based hyphae.[8] One case of chromoblastomycosis showed pigmented sclerotic bodies also called Medlar bodies. In two cases of mycetoma discharged granules were crushed on a slide and stained with lactophenol blue showing thick hyphae.

Cases of cutaneous tuberculosis showed concordance of 55.5% compared to 70.77% in Malik et al and 91.6% in Dutta et al.[11,8] Tuberculoid granuloma was found in 9 (5.81%) cases and clinical pattern matched with studies from across the country where lupus vulgaris was the commonest type followed by scrofuloderma and tuberculosis verrucosa cutis.[8]

In our study, one patient diagnosed histologically as foreign body granuloma, presenting with asymptomatic erythemaous plaque over the left breast since 2 month. In Dutta et al 4 patients were diagnosed with 100% concordance.[8]

Histopathology is a very important diagnostic modality in establishing a correct diagnosis. Development of newer ancillary tools like immunohistochemistry, slit skin smear, mantoux tuberculin skin test, in situ hybridization, polymerase chain reaction (PCR) etc. act as adjunct to histopathology for diagnosis.

CONCLUSION

Our study is one of the few studies conducted to bring out the significance of clinicopathological concordance in the cutaneous granulomatous disorders. It highlights the importance of histopathological features for diagnosing granulomatous skin disease accurately.

REFERENCES

1. Weedon D. The granulomatous reaction pattern. In: Weedon D (ed). Skin pathology, 2nd ed. Philadelphia: Churchill Livingstone. 2002;193-220.
2. Hirsh BC, Johnson WC. Concepts of granulomatous inflammation. Int J Dermatol. 1984;23:90-9.
3. Mehregan DR, Dooley VN. How to get the most out of your skin biopsies. Int J Dermatol. 2007;46:727-33.
4. Rajaratnam R, Smith AG, Biswas A. The value of skin biopsy in inflammmatory dermatoses. Am J Dermatopathol. 2009;31:350-3.
5. Gautam K. Granulomatous lesions of the skin. J path Nepal. 2011;1:81-6.
6. Dhar S, Dhar S. Histopathological features of granulomatous skin disease: an analysis of 22 skin biopsies. Indian J Dermatol. 2002;47:88-90.
7. Bal A, Mohan H, Dhami GP. Infectious granulomatous dermatitis: a clinicopathological study. Indian J Dermatol. 2006;51:217-20.
8. Dutta B, Baruah RR, Huda MM. A clinicopathological study of cutaneous granuloma. J Evolution Med Dent Sci. 2016;5(22):1184-9.
9. Permi HS, Shetty JK, Shetty PK. A histopathological study of granulomatous inflammation. NUJHS. 2012;2:15-9.
10. Aslan C, Göktay F, Mansur AT, Aydıngöz İE, Güneş P, Ekmekçi TR. Clinicopathological consistency in skin disorders: a retrospective study of 3949 pathological reports. J Am Acad Dermatol. 2012;66:393-400.
11. Malik A, Siraj F, Shruti S. Clinicopathological Concordance in 2216 Cases of Skin Biopsy over One Year: An Indian Experience. Cureus. 2020;12(4):e7752.
12. Gupta P, Karuna V, Grover K, Rathi M, Verma N. The histopathological spectrum of skin diseases with emphasis on clinicopathological correlation: a prospective study. J Diagn Pathol Oncol. 2018;3:91-5.
13. Balasubramanian P, Chandrashekar L, Thappa DM, Jaisankar TJ, Malathi M, Ganesh RN et al. A retrospective audit of skin biopsies done in a tertiary care center in India. Int J Dermatol. 2015;54:939-43.
14. Manandhar U, Adhikari RC, Sayami G. Clinico-histopathological correlation of skin biopsies in leprosy. Journal of Pathology of Nepal. 2013;3:452-8.
15. Bhatia AS, Katoch K, Narayanan RB, Ramu G, Mukherjee A, Lavania RK. Clinical and histopathological correlation in the classification of leprosy. Int J Lepr Other Mycobact Dis.1993;61:433-8.928-9.